

**“It’s a bit of an oxymoron”:**

A multimethod investigation into professionals’  
views of children’s involvement in medicines  
research and development

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## **Abstract**

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Children are not being provided with the same opportunities as adults to participate in the medicines research and development (R&D) process. Reticence to accepting children as active participants in research beyond that of clinical trial participants might be due to how researchers view children.

**AIM:** To examine how professionals associated with medicines R&D construct *children* and *involvement* and understand how this affects the uptake of children's involvement.

**METHODS:** This multimethod study comprises a systematic analysis of political speeches focusing on children's medicines regulation, a scoping review of pharmaceutical medicines research presenting children's views and a discourse analysis of key informant interviews. Bakhtinian discourse analysis is used to examine the explicit and implicit attitudes and ideas surrounding children's involvement in the context of role theory. Suggested barriers, facilitators and potential opportunities to improve its uptake are presented.

**FINDINGS:** Children have clear views on medicines that have been reported in peer-reviewed journals, which some researchers find informative and valuable. Children are mainly constructed as passive actors, rarely considered beyond the role of clinical trial participants, and involvement as problematic and resource intensive. However, participants suggest that children's insight could prove valuable for generating new ideas, improving research designs, and understanding the medicine taking experience. Findings from the interviews suggest that children can be constructed differently by the same speaker, depending on the speaker's assumed role from a cast of identified salient roles - the *dramatis intrapersonæ*. This has implications for how children's involvement is perceived and adopted. A conceptual framework of factors affecting children's involvement is presented.

**CONCLUSIONS:** Children's involvement in early-stage medicines R&D can only be successful if there are fundamental changes in the mind-set of researchers regarding children's ability to actively contribute. This requires improved resources and education for researchers, and encouragement for those who develop medicines to talk directly with sick children.

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## **Declaration and Word Count**

I, Gillian Stokes, confirm that the work presented in this thesis is my own.  
Where information has been derived from other sources, I confirm that this  
has been indicated in the thesis.

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## List of abbreviations

<b>AED</b>	Anti-epileptic drug
<b>GABA</b>	Gamma-Aminobutyric acid ( $\gamma$ -Aminobutyric acid) the main inhibitory neurotransmitter in the central nervous system; reduces neuronal excitability regulates muscle tone
<b>HTA</b>	Health Technology Assessment
<b>NHS</b>	National Health Service
<b>PIP</b>	Paediatric Investigation Plan
<b>PPI</b>	Patient and public involvement
<b>PREA</b>	Paediatric Research Equity Act
<b>R&amp;D</b>	Research and development
<b>UNCRC</b>	United Nations Convention on the Rights of the Child
<b>YPAGS</b>	Young Persons Advisory Groups

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# Chapter One: Introduction to the Research

## Introduction

Is there potential to involve children and include children's views in the early stages of children's medicines research and development? This is the question that sparked my enquiry. Personal experience as a researcher and mother, whose own child's views were not recognised throughout her illness, served as the initial catalyst for my interest in issues surrounding the rights and opportunities for children to share their views. During the period of her treatment, my daughter had tried to express her views about a prescribed medicine that had long-term impacts on her health. Neither I, nor the clinicians treating her, had considered her distaste for this medicine. This combined with other encounters with children who had strong views about their medicine regimens, prompted me to consider whether adults' views of children were negatively impacting on children's opportunity to contribute their knowledge and experiences to those involved in medicines research and development. Particularly, questioning whether excluding children's views at the early stages of medicines research, might reduce the potential for improving children's medicine taking experience and result in medicines that do not address the explicit needs of children (Hodes *et al.*, 2018).

Furthermore, this exclusion could perpetuate inequalities in health service provision, an issue that has been at the forefront of global public health policy creation for decades (Condon, 2018; European Commission, 2014; Marmot, 2005; Snow, 2018). In this opening chapter, I introduce my research within the context of children, involvement and policy. I detail how I investigated my

research question, the reasons for conducting this research, why it is important and what to expect from this thesis.

### **1.1 Background to the study: children and medicines research**

In a publication by the European Commission entitled Public Health: Improving health for all EU citizens (European Commission, 2014, pp. 56-67) health equality is cited as one of the 'key challenges' (ibid, 2014, pp. 3-43-4). One such significant inequality with global implications is that of the provision of safe, efficacious, high quality medicines for children (Cram et al., 2009; Liu et al., 2014; Standing, Khaki and Wong, 2005; Vitiello, 2008b). Participation of patients within the creation of policies within healthcare is also a global issue (Thompson, 2007, p. 1297). This issue was cited by the World Health Organisation (WHO) as a prime goal of health policy four decades ago (World Health Organization, 1978). The UK Government also recognised patient involvement in healthcare decisions that directly affect them with its creation of the Patient Partnership Strategy in 1996 (NHS Executive 1996 as cited in Thompson, 2007, p. 1298). The Department of Health and Social Care (DHSC), formerly the Department of Health (DH) aimed to put "patients at the centre" of their work, to improve mutual understanding of the broader societal issues that define the success of health research. They recognised that patient and public involvement (PPI) engenders more relevant and reliable research that addresses patients' needs and is more likely to be implemented; stressing that patients and the public "must be involved in all stages of the research process" (Department of Health, 2006, p. 34). Studies that aim to elicit the views of children and young people about matters that affect them in fields such as: education, healthcare, wellbeing and social care, have increased significantly over the last decade (Coynne and Carter, 2018). However, the extent to which professionals are receptive to children's 'involvement' or indeed provide opportunities for children to be involved in 'all stages' of the

medicines research process and indeed anywhere within the health policy, remains unclear.

I chose to focus my study on professionals' views about children's involvement in early stage pharmaceutical medicines research and development (**R&D**), an area that is very much under-researched. I felt it necessary to understand how professionals viewed children, as this might impact positively or negatively, on the potential for children to have a say in the medicines that they use. The rhetoric of public involvement in services that directly affect the public is increasingly visible in healthcare discourse (Brady *et al.*, 2018; Department of Health, 1999; Gallego *et al.*, 2007; NHS Executive, 1996; Staniszewska *et al.*, 2018; Thompson *et al.*, 2009).; however, how public involvement in medicines R&D is implemented is often ambiguous and confusing. The extent to which public involvement extends to include children has also proven to be unclear (Brady *et al.*, 2018; Carter and Coyne, 2018; Coyne and Carter, 2018). Indeed it has been recognised that, until recently, children have been "invisible" within the **NHS** (Lachman and Vickers, 2004, p. 693) and omitted from medical and pharmaceutical discourse (Sawyer *et al.*, 2007, p. 1481). This situation has prevailed despite the emergence of data identifying the increased incidence of chronic conditions in children (Lachman and Vickers, 2004, p. 693), perpetuating long-term medicine use in growing numbers of children.

This can be demonstrated by the lack of effort that has been made to undertake studies that address issues such as drug metabolism or safety for children (Standing, Khaki and Wong, 2005, pp. 560-562). In part, this is attributable to the significant risk of adverse events (Conroy *et al.*, 2000, p. 1123) and unique methodological and ethical challenges associated with conducting clinical trials that involve children. In the absence of evidence, paediatricians prescribe untested 'off-label' or 'unlicensed' drugs for their

child patients (see section 2.1.2) (Auby, 2008; Schachter and Ramoni, 2007, p. 429), an approach closer to “guesswork” than evidence-based practice. Ethically this practice is flawed, yet it is a common and accepted practice in paediatric medicine. Exposure to drugs that have been untested in children can expose children to significant harm (see section 2.1.2). Further, children are not provided with the same privileges as adults to be involved in and shape medicines development. My investigation is situated within contemporary pharmaceutical medicines R&D (hereafter referred to as medicines R&D), where I have strived to generate new insights about the industry’s relationship with children and the ways that children are ‘viewed’ by professionals aligned with medicines R&D in terms of children’s ‘ability’ and capacity and the impact of this on the potential for children to contribute to the early stages of medicines R&D.

### **1.1.1 Defining early stage medicines research and development**

Drug development is the process of producing a new pharmaceutical medicine after a lead chemical substance has been identified through the process of drug discovery (Strovel *et al.*, 2016). Early research and development involves scientific specialists (i.e. chemists, biologists and pharmacologists) who develop and test new active entities from laboratory testing through to translation of the new medicine to early clinical trials in humans (ABPI, 2019). Early R&D encompasses preclinical research on microorganisms, animal testing, filing for regulatory status to enable clinical trials in humans, and procuring regulatory approval through new drug applications (Strovel *et al.*, 2016; Taylor, 2016). Early R&D involves research into disease mechanisms, preclinical safety, translational medicine, and early stage clinical trials (ABPI, 2017).

Collaboration with industry, universities and independent research institutes is commonplace via mechanisms such as TRPs (ABPI, 2019).

Translational medicine is a two-way process: i) transferring ideas, insights, and discoveries created through basic science through to early clinical research in humans for the treatment or prevention of disease (Rubio *et al.*, 2010) and ii) applying learning from clinical practice to refer to clinical model (ABPI, 2019). Early stage clinical trials are the final step in early drug development. In the UK, before any new drug can reach a human subject, a clinical trial application (CTA) must be approved. Approval is given the Medicines and Healthcare products Regulatory Agency (MHRA) an agency of the Department of Health and Social Care (CTA) Only after review and recommendation by independent medical and scientific experts can human trials commence (ABPI, 2019). The Cooksey review UK health research funding (Cooksey, 2006; Ogilvie *et al.*, 2009) identified two major gaps in translation. T1, the first gap in translation, is in “...translating ideas from basic and clinical research into the development of new products and approaches to treatment for disease and illness”. This gap covers the scope of preclinical development and early clinical trials. T2, the second gap, is in “...implementing those new products and approaches into clinical practice” and spans health technology assessment, health services research and knowledge management (Cooksey, 2006).

### **1.1.2 Defining children**

*“For the purposes of the present Convention, a child means every human being below the age of eighteen years unless under the law applicable to the child, majority is attained earlier.” Article 1 (United Nations, 1989)*

The above quotation highlights an important issue for this study, how children are categorised by adults. Childhood implies what is not adult suggesting a generational order to existence (Alanen, 2012). Defining the spectrum of humans who are not classed as adults due to: age, rights, physiology or assumed development, i.e. new-borns, babies, toddlers,

children, adolescents and young people, is challenging. In the medical genre, clinical definitions follow this physiological development, however, there is variation between disciplines and thus a call for standardisation (Williams *et al.*, 2012).

The UNCRC definition of children is one of eight legal definitions that refer to human non-adults<sup>1</sup>, spanning human rights, social care, criminal law and criminal justice (NSPCC, 2013). The UNCRC definition is adopted by many services that support and protect children (e.g. NSPCC, 2013; Save the Children, 2013; unicef, 2005). This definition includes the concept of human 'development' from new-born baby through to politically active adult a time of human 'becomings' where children are viewed as deficit (Qvortrup, 2009).

Those espousing childhood studies suggest that the way that particular humans are constructed as 'children' raises methodological questions that should not be, but regularly are, presumed in research (Sayer, 1999). The definitions 'children' and childhood are often imperfect. Social studies of childhood differ from developmental psychology perspectives of childhood, in that childhood cannot be presented simply as physiological and cognitive states of immaturity. Archard (2004) suggests that children should be viewed as human beings who live in particular place and moments whereas 'childhood' is a more general concept. Social studies on childhood differ from other approaches to studying children in assuming that childhood is viewed as socially constructed (Carter and Coyne, 2018; Honig, 2009; James, Jenks and Prout, 1998; Mayall, 2002)(Honig, 2011; James, Jenks and Prout, 1998; Mayall, 2004). The concept of children can be considered in many domains: corporeal,

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<sup>1</sup> The eight legal definitions are: Article 1 of the Convention on the Rights of the Child; Children (Leaving Care) Act 2000; Children (Leaving Care) Act (Northern Ireland) 2002; Sexual Offences Act 2003; Sexual Offences (Northern Ireland) Order 2008; Protection of Children and Prevention of Sexual Offences (Scotland) Act 2005; section 53 of the Children Act 2004 section 3(3) of the Children (Northern Ireland) Order 1995

biological and genetic on the one hand (Prout, 2005; Prout and James, 1997) and in terms of advancements in technology, society, economics and organization (Qvortrup, 1994; Qvortrup, 2009) on the other. The cultural historian Burke (2017) suggests that a good starting-point when considering defining the parameters of childhood, is between 1500 and 1800, a period of major social political and economic change that impacted on culture and resulted in the creation of shared meanings, attitudes and values. These shared meanings have evolved over time. Industrialisation and the requirement for an economically viable workforce (Qvortrup, 1994; Qvortrup, 2009) precipitated child labour, with campaigners calling for an end to such practices (Hendrick, 2000). Only when economic needs had altered, were children in industrialised countries removed from the workforce and repositioned into compulsory schooling.

‘Adult-centric’ conceptualisations of childhood evolved over time through the social constructions of children with roots in developmental psychology, which position children as characteristically ‘lacking’. Childhood has been increasingly sentimentalised, positioned as a protected and precious time of life (Prout and James, 1997). Childhood is often associated with biological susceptibility and institutionally imposed perceptions of emotional, physical and cognitive immaturity (Mayall, 1996; Mayall, 2002).

Within western society children are often subjected to generational oppression and paternalistic practices as a social consequence of their age. Archard (2004) suggests three dimensions that differentiate childhood over time and place: when it is considered to begin and end, differentiation between childhood from adulthood. The term ‘generationing’ has been used to describe the process of creating and enacting fixed meanings about childhood (Mayall, 2002, p. 27) . Archard (2004) suggested that perceptions

of childhood and adulthood evolve over time and place, and these perceptions are socially constructed (Alanen, 2012).

Whilst offering an important way to orient the landscape of childhood in social studies, conceptualising children in the context of medicines R&D is more difficult. Mayall's (2002) generationality gains significance in this context, in that children's lived experiences suffer from generation inequalities constrained by the dominance of adults in this discipline, where 'the power to define it [childhood] lies with adults' (Mayall, 2002, p. 40). Childhood is not only affected by generationality but many other factors such as politics, economics, law, geography (Alanen, 2012; James, Jenks and Prout, 1998; Norozi, Moen and Research, 2016). The attempt to maintain the social norms and protect children in the light of cultural obligations and institutional disciplines exposes children to power struggles (e.g. Alderson, 2003; Alderson, 2007; Aspinall, 2006; James, Jenks and Prout, 1998; Mayall, 1990; Mayall, 2002). Paternalistic practices are generated, positioned and maintained through ongoing social processes (Alderson, 2003; Alderson, 2007; Alderson, Sutcliffe and Curtis, 2006a). Age of childhood is reinforced by social actions and processes that are deeply entrenched in the established beliefs of: an individual's capability; various institutions; and governing bodies and processes that subdue and subtly oppress (Foucault's disciplines) (Power, 2011; Rabinow, 1984; Sawicki, 1991). This dominant influence of social and cultural institutions can be argued to contribute to the parameters that define acceptable roles for children, as suggested in the quotation below.

*"The social situation of a child is dependent on the society and cultural context in which the child is embedded. Different cultural contexts foreground particular social situations, which in turn position children to actively engage and take up particular participation structures." (Fleer and Hedegaard, 2010, p. 151)*

The consequence of defining the child, as with other social categories, is that the idea of the child becomes a site for negotiating and wielding power (Gillett-Swan and Sargeant, 2018). The result of a construction of the sick child/medicated child is that they experience greater degrees of oppression, marginalisation, paternalism and disempowerment than do well children (James and Curtis, 2012).

Contemporary theories of childhood and ways of seeing children within the field of sociology do not conceptualise children as 'passive' receivers of socialisation and the outcomes of adulthood (Prout, 2005, p. 60). Nor are they viewed as unreliable witnesses of their own realities and lived experiences (Prout, 2006; Qvortrup, 1994). Novel approaches of conceptualising children and childhood emphasize inequalities in the social status of children and their vulnerability at the hands of adults, when adults are expected to act as experts in matters affecting a child (Lee, 2001; Qvortrup, 1994). In the context of this research, the adults acting as experts would include: policymakers, research funders and medical researchers. In fact, it is suggested that a desire to maintain the social order may underpin adults' desire to protect children (Qvortrup, 1994). The resultant paradox is that children have moved so far 'under the wing' in the medical sphere that current approaches to children's medicines research is paternalistic and, I would argue, over-protective.

Researchers operating within the 'new' consciousness of childhood studies view children's competencies as different from adults (James, Jenks and Prout, 1998) and value children's experiences and perceptions of the world (Punch, 2002). The social scientist Qvortrup (1994) suggests that it is critical to ensure that children are at the centre of the research and not their parents or carers. Yet despite this change in perspective, traditional theories of childhood and the mythical "supposed chasm between foolish child and

wise adult” (Alderson and Montgomery, 1996, p. 5) still persist within the contemporary medical paradigm. In addressing why prejudices still persist, Alderson and Montgomery (1996, pp. 10-12) cite “custom or convenience” and lack of time or interest in keeping abreast in changes in thinking regarding children. As suggested above, there is a need by many to believe in adult superiority and adult competence, and if this order is questioned there is possibility of loss of “adult control and professional prestige” (Ibid 1996, p. 11; Qvortrup, 1994).

This thesis positions children as valuable citizens who are of equal importance to adults, particularly within the context of the medical research and pharmaceutical paradigms being studied. As discussed, children understand their own lives and processes and can provide important and reliable information based on their own lived experiences. Children can therefore give unique insight into the issues that affect them. Yet inequalities in the social status of children compared to that of adults remain within the medical paradigm, which have resulted in inequalities in medicines provision by restricting children’s inclusion in medical trials irrespective of the benefits.

### **1.1.3 Conceptualising childhood and children as actors within medical research**

This study is founded on a particular way of seeing children, which is predominantly influenced by contemporary sociological theorists who recognise children as social actors with an ability to make decisions and act upon them (e.g. Alderson, 2007; Alderson, Sutcliffe and Curtis, 2006a; Alderson, Sutcliffe and Curtis, 2006b; James, Jenks and Prout, 1998; Lee, 2001; Mayall, 2002; Mayall, 2006; Qvortrup *et al.*, 1994).

The conceptualisation of children spans many disciplines and discourses; historical, political, rights, sociological, economic, biological, pedagogical, philosophical and psychological (Archard, 2004; Norozi, Moen

and Research, 2016; Savahl, 2010). The focus is on Western concepts of childhood, as international and cross-cultural conceptualisations are vast and, though important, do not bear relevance to this study. Within the UK, legal age limits are set for various personal circumstances: leaving care (16); the age of sexual consent; and the age of criminal responsibility (HM Government, 2000; HM Government, 2003; HM Government, 2017; NSPCC, 2013). I initially resorted to defining children as humans who have not yet reached the questionable status of the western concept of maturation, and confined them into an age-related definition, that of the under eighteen-year-old, however the issue of conceptualising children in terms of age is flawed. Age related definitions are generally the most familiar ascriptions for determining childhood. In the UK a 'child' is a human that has not had their 18th birthday and upon turning 18, makes the legal transition to 'adult' (NSPCC, 2013), yet the legal age of consent (the age to have sex) in the UK is 16 years old (HM Government, 2003). Even this is confusing, in that to protect younger children, legally anyone under 13 years of age cannot legally give consent on any matters that affect them. However, UK legal definitions are not straightforward, for example in Scotland people under 16 years old are children (Scottish Government, 2014) and when leaving care at 18, young people are entitled to support until they reach 21 (HM Government, 2000). However in terms of child protection, over-16s who live independently, or are in further education, a member of the armed forces; in a custodial setting; or hospitalized, still legal qualify as children and afforded the same protections and entitlements as any other child (HM Government, 2017). Conversely, criminal responsibility in the UK is between 8 (Scotland) and 10 years old (England, Wales and Northern Ireland) (HM Government, 1998). This issue of giving legal consent is an issue in medicines R&D in that children under 18 can only provide assent, and consent is assigned to parents/guardians (GMC, 2013; Lepola *et al.*, 2016). However, there are calls to reassess assent capacity suggesting that the threshold age should be 14 (Wendler, 2006).

Indeed it is a recognised paradox in that children of the same age, can be recognised as criminals but not provide assent for a clinical trial (Lepola *et al.*, 2016). The extent of variation of 'age' categorisations imposed by adult law makers over time, suggests that children are constructed almost conveniently, dependent upon context and the extent of freedom and personal control under adults' control in that context. Age-based categorisation is commonplace in the medical setting and indeed globally (i.e. the United Nations Convention on the Rights of the Child), therefore is normative and relatively stable (Carter and Coyne, 2018).

As mentioned earlier, theories have moved away from the concepts of children as 'passive' receivers of socialisation and the characteristics of adulthood (Prout, 2005, p. 60), to commanding the respect of children's views. Modern theorists recognise children's ability to make decisions and act upon them (e.g. Alderson and Montgomery, 1996; Mayall, 2002). The tenet generated from this perspective is that children have a contribution to make to society in their own right and not just a partial view embedded within the context of the family, as highlighted by Ann Oakley (1994) and Berry Mayall (1996). Literature examining children's medicines and pharmaceutical R&D focuses mainly on adults' views on children's medicines (see Chapter Six), suggesting that theories of children and childhood have not transcended commonly held views of children. This suggests that an inequality in the social status of children compared to that of adults is still manifest, particularly in the medicines R&D arena. Here children's views remain hidden within the context of involved adults: the family, the parent, the carer, the healthcare practitioner or even the institution (i.e. hospitals, schools, etc.). For this study, I am positioning children as valuable citizens of equal importance to adults, who understand their own lives and processes and can provide important and reliable information based on their lived experiences. In other words, children are also experts.

I do not contest the categorisation of 'children' as a social construction commonly defined by age but embrace the spectrum of capabilities, experiences and knowledge of the person constructed as a child, as I would any human.

#### **1.1.4 Children as the expert 'public' in public involvement**

If we acknowledge that the 'child' is a socially constructed category of human, who is capable of living, breathing and interacting with the world (Prout, 2002; Qvortrup, 2005), then their experiences, by definition, make them 'expert'. Etymologically, 'experience', 'experiment' and 'expertise' stem from the common Latin root '*experiri*', to test or to try (Tromans, 2017). It is naïve to consider the 'public' as an undifferentiated whole (Stokes, 2018). The public not one homogenous group of people, rather it is complex and diverse (Martin, 2008). Publics are diverse and their sense of self and agency is influenced by many factors such as: location, socio-economic status, personal interest, gender, physical ability, sexuality and age, which influence peoples' sense of self and agency (Martin, 2008; Oliver *et al.*, 2015; Stokes, 2018). Indeed, the term 'public' creates almost as many problems as it might address, therefore it is suggested that the term 'public' should be replaced with 'publics' to convey this complexity (NCCPE, 2017). The 'public' encompasses every living person, who are individuals (micro level), or belong to organisations (meso-level) and are the drivers of research (Oliver *et al.*, 2015). In the UK, children are recognised as experts by a number of organisations aligned with medicines R&D: National Institute for Health Research (NIHR) INVOLVE, Medicines for Children Research Network (MCRN), International Children's Advisory Network (iCAN) and GenerationR (iCAN, 2019; INVOLVE, 2018).

These not for profit organisations encourage children's involvement through advisory groups; including Kids Impacting Disease Through Science

(KIDS) and Young Persons Advisory Groups (YPAGS). Working to provide a voice for children and families on healthcare related issues including medicines research and innovation (iCAN, 2019). iCAN is an international organisation consisting of 20 chapters. Members, aged 8-19 (predominantly 10-15 year olds), support the design and delivery of paediatric research by sharing ideas, best practices, advocate for health and collaborate with various stakeholders in research innovation and advocacy (iCAN, 2019). GenerationR is the UK chapter of the iCAN network, funded by the NIHR and other NHS organisations. This National Young Persons' Advisory Group consists of five regional groups based in Liverpool, Birmingham, London, Bristol and Nottingham, plus one topic-focused group looking at Mental Health based in London, that meet six weekly and come together for a national meeting once a year.

GenerationR Alliance YPAGs are predominantly made up of 10-15 members who are aged between 8-19 years. Most YPAGs meet every six weeks either at weekends, in the evenings, or during school holidays and come together for a national meeting once a year. Their views feed into the design and delivery of health research in children and young people (iCAN, 2019).

## **1.2 Rationale**

### **1.2.1 Involving children in medicines R&D**

Patient involvement in medicines (PPI) R&D is acknowledged as important and its merits are commonly recognised due to the benefits for all involved (Haerry *et al.*, 2018). Working collaboratively with patients can enhance drug discovery, development, and evaluation of new effective medicines, as new insight surrounding unmet needs, research priorities, clinical study design, appropriate outcome measures, and endpoint development is provided (Haerry *et al.*, 2018; Klingmann *et al.*, 2018). Further,

this builds trust and improves transparency between all parties (Unni, Van Wagoner and Shiyanbola, 2019). PPI is recommended at all stages of medicines R&D pathway: industry-led research, regulation and licensing, and appraisal by health technology assessment (**HTA**) bodies (Warner *et al.*, 2018) but requires structure and clear rules to be effective. Current codes of practice for PPI do not comprehensively cover the full scope of R&D (Haerry *et al.*, 2018; Klingmann *et al.*, 2018). The European Patients' Academy on Therapeutic Innovation (EUPATI) aimed to address this gap with its development of four separate guidance documents for selected stakeholders, covering PPI in: pharmaceutical industry-led medicines R&D; ethics committees; regulatory authorities; and HTA (Warner *et al.*, 2018).

Some researchers feel that preclinical research is too far removed from public understanding and therefore PPI in complex settings such as laboratories, is impossible (Dobbs, 2016). However, there are examples where researchers are thinking creatively and finding ways to involve patients in laboratory settings (Cowan, 2018; Dobbs, 2016). If we recognise that children can be both patients and publics, then it holds that children could be actively involved in early medicines R&D.

### **1.2.2 Gaining new perspectives**

The value of acknowledging other people's perspectives on an issue of shared interest is apparent from the Johari window. I first encountered the Johari window when training as a healthcare practitioner back in 2002, in a module focused on practitioner-patient relationships. The Johari window (from their given names, Jo-seph and Harri-ngton) was presented to us in a workshop for clinical practice. We were encouraged to role play that of practitioner and patient, in an attempt to diagnose a mental health condition.

The Johari window seeks to define the extent of open communication between people and was originally applied in clinician-patient interaction in a psychology setting (Luft and Ingham, 1961).

I first applied the Johari window to a research setting when, with colleagues, we involved patient groups in a large systematic review (Brunton *et al.*, 2017b). A prior task was to produce a map of the relevant research literature (evidence map) (Stokes *et al.*, 2017b). The research team had not planned PPI for the map; indeed, including stakeholders in the conduction of systematic mapping is atypical. The benefits of involvement were not obvious to all parties at the time and it was not until a year later that the some of the benefits emerged and the relevance of the Johari Window came to mind (Stokes and Sutcliffe, 2018). The Johari window is still most commonly used in healthcare settings (e.g. clinical consultations) but its application has spread to other disciplines interested in shedding light on unknown-knowledge (Walker, 2018). It is an imaginary window that consists of four panes, where each pane represents knowledge held by different parties, seeking to develop awareness about what is known and what is not known by either party (Luft and Ingham, 1961) and encourage communication about behaviour (Oliver and Duncan, 2019) (see Figure 1.2). Oliver and Duncan (2019) suggest that “we can consider what is ‘known to us’ and ‘known to others’ when thinking about research as a collective activity”.

**Figure 1.2 A Joharian rationale for PPI in research**

	<b>Known by researchers</b>	<b>Not known by researchers</b>
<b>Known by patients</b>	<b>Open area</b> What is known about the research and is known by the research team and the patient groups	<b>Blind area</b> What the research team does not know but the patient groups did know
<b>Not known by patients</b>	<b>Hidden area</b> What the research team knows about the research, but the patient groups do not know	<b>Unknown area</b> What is not known by the research team and is not known by the patient groups

Source: Adapted from a Joharian rationale for PPI in evidence mapping (Stokes and Sutcliffe, 2018)

Oliver and Duncan (2019) suggest that different standpoints in a research setting may offer different views that are nevertheless equally important. In the evidence map example, what was known by each party was different in terms of experience, skill set and data access among many things. Researchers know more about the research literature, while patient groups know more about symptoms of importance.

Within research there are potential knowns and unknowns that are neither predictable nor obvious, for both the researchers and participants. All parties bring to the table a bank of different types of knowledge and expertise (Crowe *et al.*, 2015). Through collaboration these knowledge gaps, issues of importance among other things, can be identified, explored and addressed. PPI proved to be highly valuable, having significant benefits for both researchers and patient groups, helping to contextualise findings,

understanding research relevance and application in a way that researchers alone cannot do, resulting in a significantly improved product from which all users of the evidence map benefitted (Stokes and Sutcliffe, 2018). Oliver and Duncan (2019) suggest that only: “some knowledge is widely held (common knowledge); that although we may hold some specific knowledge not held by others, they also hold specific knowledge not held by us; and that some aspects of the world around us are unknown to all of us”. If researchers could recognise the complexities of knowledge and appreciate that by collaboration different knowledge can be revealed, as suggested by the Johari Window, then this might go some way to reducing reticence to involving children.

### **1.2.3 Anecdotal experience**

I was awarded a Bloomsbury Scholarship to conduct research into medicines for children. This was a broad and non-specific brief, which I welcomed but focusing on a single topic in such a diverse area proved challenging. Two conditions were of personal importance: cystic fibrosis, as a close friend’s daughter had just been diagnosed, and epilepsy, as my eldest daughter had suffered seizures and was under investigation for the condition. I also knew three families with children under ten years old with pharmaceutically managed epilepsy. Talking with these children on several occasions revealed how knowledgeable they were about their condition. They also had strong views about their dislike of their medicines. When I asked one boy (8 years old) what he disliked about his medicine, he told me that all he wanted to do was play football and stay awake in class, but his medicine made him sleepy and fall over so could not take place in sports. He told me that he just wanted a medicine that made his legs work properly. Another child I knew (girl aged 11), revealed that she did not mind the seizures, but the medicines made her sleepy and it was affecting her learning in the classroom. Anecdotally, children had demonstrated their ability to contribute their experiences with medicines to medicines discourse.

However, during this process of deciding which child population to talk to and which medicine, I had a chance encounter with a translational researcher at a party. Making polite conversation, the researcher enquired about my PhD topic and, upon hearing, responded defensively with words to the effect of: *I don't really care what the children have to say – I make medicines. I like finding new entities and making use of them. Children don't understand what I do, so why should I listen. Anyway, they don't have views and that's that!*" accompanied by several expletives. This was a pivotal event in the evolution of my thesis and made me radically reconsider the direction of my research and focus instead on professionals' views on children's involvement. I questioned whether there was a fundamental area that had been overlooked; a void in the literature? My preconceptions had blinkered me somewhat and consequently falsely guided me down an overly biased path to my research. I was so pro children's rights and human rights; I had naively presumed that those working for the benefit of children's health would be too. I searched the literature for professionals' views on children's involvement and found no research at that time, back in 2010. I needed to understand whether the negative view of children's abilities that I had encountered at that party was a commonly held view of those working in the development of children's medicines and whether professionals' views of children might be impeding the uptake of children's involvement (*potential barriers*) and what might help children be involved in the process in the future (*potential facilitators*). Are children viewed as experts whose opinions not only matter, but could shape research and future pharmacotherapies? Or are they viewed as ignorant, incapable and vulnerable, to be protected from the intricacies of medicines R&D?

#### **1.2.4 Why do we need this research?**

The literature surrounding attitudes towards PPI in health research has focused on talking to researchers who are advocates of its practice (e.g.

Staniszewska *et al.*, 2007; Thompson, 2007; Thompson *et al.*, 2009). Fewer studies have been conducted that focus on children's views of medicines (e.g. Mukattash *et al.*, 2012b). Further, there is limited research on resistance, cynicism, or hostility towards the practice of PPI in medicines research. A recent study by Parsons *et al.* (2016) has investigated the views of pharmaceutical industry professionals about PPI in general. However, no research has investigated professionals' views of children's involvement in medicines R&D. This suggests that much is to be learned from a study that explores professionals' views of children's involvement in medicines research and the factors that affect its potential. The time is opportune, both socially and politically, with increased demand for proof of patient involvement in research ventures (Boote *et al.*, 2012; Boote *et al.*, 2013; Molloy *et al.*, 2019; Walker and Pandya-Wood, 2013) and patient-centred pharmaceutical design (Liu *et al.*, 2014). To adequately serve child patients and observe children's rights, policymakers, funders and researchers must look beyond children's assumed physiognomic characteristics and seek to understand children's social worlds and lived experiences from the children's own perspective.

I argue then that children's medicines R&D can benefit from children's involvement and, by involving children earlier in the process, fulfil children's basic rights to freely express their views, seek, impart and receive knowledge, and receive the highest standards of health.

### **1.3 Research aims, objectives and questions**

Given the constructed nature of children and childhood within the Western orthodoxy (Mayall, 1998; Norozi, Moen and Research, 2016) and the absence of children's voices within medical discourse, I initially set out to investigate the potential to involve children and include children's views in the early stages of children's medicines R&D. However, this question comprises many elements and upon consideration identified a need to understand the

influence that those conducting research had on the opportunities for children to become active participants in research. For children's views to be included, they first need to be involved and it is the responsibility of those conducting research to involve them. My interest focused more after reading a paper on dissemination of innovation (Berwick, 2003), how new ideas are adopted and progress towards the normative – in this case the innovation being children's involvement in medicines R&D. Eventually, cementing the focus of my study on researching the views of professionals aligned to children's medicines research. The aim of this study therefore is: *to investigate how professionals associated with medicines R&D construct children and involvement and understand how these constructions might affect the uptake of children's involvement in research and policy.*

The objectives are to:

- Investigate the status of children's involvement in the children's medicines process from policy-making to clinical trial execution
- Understand how children are viewed within the children's pharmaceutical R&D paradigm
- Create a framework of factors affecting children's involvement within the context of early-stage children's pharmaceutical R&D

To address the above aim and objectives, the research questions that I examine in this thesis are:

- Can children express views that could usefully inform children's medicines R&D?
- Have children been involved or have their views been recognised in the policies that govern children's medicines R&D?

- Are children involved in medicines R&D? If so, how are they currently involved?
- How are children viewed by those involved in medicines R&D?
- Is there potential to apply involvement methods to the children's medicines R&D process?

#### **1.4 Format and outline of this thesis**

Sandelowski and Barroso (2002) acknowledge the challenging nature of research that has a “transdisciplinary nature” but highlight the importance of accurately reporting the participants’ views whilst providing “clearly delineated findings”. Although there are recognised conventions to presenting a quantitative study, in qualitative research there are various ideas about what constitutes a ‘finding’ and how findings should be communicated within a report or thesis. This is very applicable to multimethod research (McKenzie, 2017). Regardless of the researcher’s approach or methods, the findings must be clear and easy for the reader to locate. I, like other researchers, appreciate innovatively presented research but I have also experienced frustration at not locating the findings and being left confused and unsure about what to take from the work.

*“If the aim of inquiry in the practice disciplines is to generate knowledge for practice,... ..., any report of a study in which the findings cannot be discerned might just as well not have been written. Indeed, the study might just as well not have been conducted.” (Sandelowski and Barroso, 2002)*

Considering the above criticisms, to clearly delineate the findings, each research component is presented in a separate chapter that details the specific methods followed by the findings for that component.

I occasionally employ diagrams to visualise complex processes and concepts. An idea born from the frequent interruptions of my children who, being naturally inquisitive, asked me to explain what I was doing and what my research was about. Diagrams are suggested to enable communication and understanding of complex ideas (Hou and Fetters, 2018). Engaging with my children not only helped me produce understandable explanation, but supported my thinking that children are capable of understanding complex issues and contributing to research. The diagrams therefore should facilitate understanding to all that read this thesis, be they qualified researchers, scientists, academics, children or other non-specialists interested in this field. To aid the reader, commonly used abbreviations are shown in **bold** on its first use to alert the reader of its inclusion in the list of abbreviations (see page 19). Further, certain text within included quotes and transcripts is underlined to emphasise key utterances.

**Chapter Two** reviews the broad spectrum of literature relating to children's medicines R&D, children's rights, and public and patient involvement. Historical perspectives on children's involvement in medicines R&D are presented and illustrate the path to modern practices and, possibly, attitudes. A contextual background is given in a description of current policies and practices that govern and/or impact on the creation of children's medicines.

**Chapter Three** focuses on the theoretical and epistemological foundations of this research, social constructionism and constructions of childhood, and how this impacted on my methodological and analytical approach.

In **Chapter Four** I present the methodological foundations employed in this thesis: systematic analysis, thematic synthesis, and Bakhtinian discourse analysis. This is followed by an interpretation and application of

selected aspects of Bakhtinian theory: dialogism, monoglossia, heteroglossia and utterance. A discussion of the research design process, research components and ethics are provided.

**Chapter Five** presents the methods and findings from the first research component, an analysis of political speeches leading up to the creation of children's medicines legislation and regulation in the UK/EU. It presents the emergent discourse on children's medicines research and the politically embedded institutional constructs within which professionals operate.

In **Chapter Six**, the methods and findings of a systematic scoping review of children's views in medicines research is provided. A map of included studies is presented, evidence of professionals' views on children's input and evidence of children's views on research and development.

**Chapter Seven**, the methods and findings of the semi-structured interviews of key professionals are presented. A step-by-step account of my approach to conducting Bakhtinian discourse analysis is provided along with a summary of constructions of children and involvement elicited from the interviews.

**Chapter Eight** presents analysis of data generated from key informant interviews. Findings, in the form of exemplars, are presented thematically on constructions of children and involvement. Findings are discussed in the context of the wider discourse of children's involvement and rights and suggest a conceptual framework for children's involvement in medicines R&D.

In **Chapter Nine** participants' constructions of the discursive objects (*children* and *involvement*) is examined in the context of Bakhtinian discourse analysis. An investigation into the dominant voices that guided participants'

constructs and discussion about the potential impact of and how this might impact on participants' constructions of children's involvement, practice and approaches to children's medicines research. I introduce the concept of the *dramatis intrapersonæ*.

The final chapter, **Chapter Ten**, summarises my findings in relation to the research questions, pulling together the key arguments emerging from the three component studies in the context of diffusion of innovation theory. I summarise the implications for practice; discussing the issues for improving children's involvement, implications for the future, study limitations and final conclusions.

## Chapter Two: Review of the Literature

### 2.0 Overview

“Reading well is also essential to appraise the varied styles for reporting qualitative studies and to discern the importance of style in reflecting and reproducing norms and values concerning inquiry.” (Sandelowski and Barroso, 2002, p. 219)

This chapter focuses on how children have been conceptualised as a problematic population within the pharmaceutical R&D paradigm. Historically children have been subjected to exploitation within medical research (Lederer, 2003), I posit that because of this history children are now a paternalistically suppressed population enshrined in political correctness. I will examine how medical research involving children has been influenced by evolving concepts of childhood. To achieve this, I provide a brief historical overview of clinical trials in the child population. This overview also serves to frame the problem of children’s pharmaceutical research being viewed as high risk and ‘unattractive’ and thus underfunded and underserved. I also discuss how, despite the current trend for patient-stakeholder involvement in healthcare research, there has been little involvement of children challenged by chronic conditions whose lives require daily interaction with pharmaceutical interventions. Later, I focus on how the introduction of US legislation and later the EU regulation has changed the focus of current and future children’s medicines provision moving it to a topic of high priority in the medical research agenda. Issues regarding paediatric drug-development and innovation are also addressed.

Although I highlight the key problems of continued use of children as ‘lab-rats’, the unrecognised stakeholder status of children and the exclusion of children’s perspectives from medical discourse, I do not portray all contemporary medical research and healthcare services as inadequate and badly designed. Instead, I close this chapter by reflecting on a story of contradiction and exclusion within the medical research paradigm and the need for a fundamental change in attitudes towards children’s capability in this discipline. A change that could spark a new progression in the children’s medicines story and propel children’s medicines into a new era of pharmaceutical innovation inspired by the children themselves. What follows is a short but comprehensive review of the issues that underpin this research: children, epilepsy, participation, rights, ethics, practice and policy.

## **2.1 A history of experimentation and exclusion**

Children have had a complex and uncomfortable association within the medical research and clinical trials paradigms. The historical foundations of the relationship between children and medical researchers are entrenched within theories of childhood and this has created a paradox for contemporary paediatric medicines research.

### **2.1.1 “Little medical heroes”**

The history of medical experiments on children is an old phenomenon. Children, alongside other vulnerable groups, have served as unsuspecting and unwilling subjects of medical experimentation (Lederer, 2003, p. 1). One of the most famous examples of a child being used for medical experimentation occurred in the 18<sup>th</sup> Century. In 1721, the practice

of variolation<sup>2</sup> was introduced into England from Turkey, by the writer and feminist Lady Mary Wortley Montagu. Variolation was used to protect humans against smallpox (*Variola virus*), an airborne disease that had a profound effect globally, proving fatal for 10-20% of the population and 1 in 3 children in 18<sup>th</sup> Century England (Jenner Museum, 2009). Edward Jenner was seeking to find a way of protecting people against “The Speckled Monster” as he called it. Jenner was consulted by Sarah Nelmes, a dairymaid, about a rash presenting on her hand. He diagnosed that she had contracted cowpox and seized the opportunity to investigate the protective properties of cowpox by infecting a human subject unexposed to smallpox. The subject he selected was an eight-year-old boy named James Phipps, the son of his gardener. On the 14<sup>th</sup> May 1796, Jenner rubbed exudates from one of the pocks on Sarah’s hand into scratches he had made on one of James’ arms. James displayed mild symptoms of cowpox but recovered within a week, thus confirming person-to-person infection of cowpox was also possible. Next, to investigate whether exposure to cowpox could protect James from smallpox, Jenner variolated him on the 1<sup>st</sup> July 1796 with smallpox and, as Jenner had anticipated, James did not develop smallpox. Jenner subjected James to several subsequent trials with the same result. Thus, vaccination was born, thanks to the unwitting involvement of an eight-year-old boy. After a worldwide vaccination programme, on the 8<sup>th</sup> May 1980 smallpox was certified by the World Health Assembly to have been eradicated, with no evidence that it will return as an endemic disease (WHO, 1980, p. 12). Jenner’s experimentation on James Phipps secured them both a place in medical history: Jenner, for creating a means of disease eradication (Levine, 1996) and thus changing the nature of medical interventions forever, and

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<sup>2</sup> Variolation was an early form of inoculation performed by the excoriation of scab material from a mildly infected human subject and rubbing these dried exudates into the skin of a healthy human subject. This promoted an immune response and, with variability, protected the human subject.

James Phipps, for being one of the earliest documented children unethically involved in a clinical trial.

The science writer John Lentz champions James Phipps, along with James Greenlees, an 11-year-old boy first used by Joseph Lister to test antiseptics and Joseph Meister, a 10-year-old French boy used to test the rabies vaccine, as “little medical heroes” (Lentz, 1940). Although Lentz acknowledged these children’s contribution to medical science in his article, he did not address the risks that these children were exposed to by participating in such trials (Lederer, 2003, p. 2). These boys were essentially utilised as ‘lab-rats’ without their consent. There is no evidence to suggest that they had any control or understanding of the possible consequences of taking part in these experiments. As Susan Lederer (2003, pp. 4-5) highlights, the practice of using children as the subjects of medical experimentation was already being criticised when Lentz was celebrating their heroism.

Medical experiments were often conducted on institutionalised populations, and orphaned children were an easily accessible sub-group with few rights or protection. In 1908, a trial was conducted on orphaned children at the St. Vincent’s Home in Philadelphia, USA (New York Times, 1910). Children were injected with tuberculin into their eyes, which resulted in temporary blindness in some cases. This atrocity, unsurprisingly, caused public outrage, as the University of Pennsylvania investigators (Dr. Samuel McClintock Hamill, Dr. Howard Childs Carpenter and Dr Thomas A. Cope) were aware of the pain and distress that the administration of injections into the eye would cause. They were also aware of the risk of permanent visual disturbance and stated that:

*“we are strongly of the opinion that any diagnostic procedure which will so frequently result in serious lesion of the eye, irrespective of the way in which it produces them, has no justification in medicine”* (New York Times, 1910, p. 2).

Yet these scientists from Pennsylvania University continued with such experiments. The practice of experimentation on vulnerable children continued. In 1921 children housed at the Hebrew Orphan Asylum were withheld orange juice from their diets in an experiment designed to initiate the haemorrhages and inflammation associated with scurvy. Attempts to reverse the scorbutic symptoms failed but, rather than terminate their experiments, the physicians then proceeded to subject the children to further physiological harm and psychological distress by devising a diet that induced rickets (Bercovici, 1921, p. 912). Later in the chequered history of clinical experimentation, between 1958-1960 severely mentally challenged residents at Willowbrook State School, Staten Island were exposed to hepatitis to enable researchers to document its pathogenesis (Barfield and Church, 2005). The school’s history was tainted with controversy and closed in 1987.

Further experimentation continued for many years with little legislative input to curb such atrocities but after one horrific tragedy in 1926, headway was made into protecting children from clinical experimentation. In Lübeck, Germany 246 children were administered a virulent form of *Mycobacterium tuberculosis* instead of the intended vaccine, resulting in the death of 76 infants (Brimnes, 2008, p. 864). Following this, in 1931 the German Ministry of Health created guidelines for conducting clinical trials in novel drugs involving children under 18-years of age (Lederer, 2003, p. 9). This regulation was continually breached by Nazi scientists who conducted particularly gruesome experiments on children during the Second World War. After the conclusion of the War, 23 Nazi scientists were put on trial for

atrocities and war crimes. During this time the *Nuremberg Code*, a 10-point code of Permissible Human Experiments was issued. This code restricted experimentation on children due to their 'reduced capacity' in terms of giving consent. However, as children are believed to hold the biological answers to many conditions, medical researchers and physicians searched for a way to include children in experiments whilst protecting them as 'subjects' (Lederer, 2003, p. 9). These efforts culminated in the World Health Association's 1964 Declaration of Helsinki (WMA, 1964).

As illustrated, children have been exposed to horrific risks at the hands of biomedical researchers for more than two centuries. Now children are protected due to the intervention of reformers and critics of medical experimentation practices. However, this protection was resisted in the name of science by many physicians who viewed children as "essential participants in the advance of medical knowledge and the development of new drugs and vaccines intended to benefit all children" (Lederer, 2003, p. 14). Despite the initial resistance, practices have changed. The changes in attitude over time towards experimentation on children, appears to be intrinsically linked with the changes in the perception and conceptualisation of childhood within Western society.

The current Westernised concept of childhood is a very recent one. Prior to the 19<sup>th</sup> Century, children were not exposed to the salient contemporary features of modern childhood such as play, learning and innocence. Life-expectancy was short due to factors including poor sanitation and limited medical knowledge of now common and easily manageable conditions (Hendrick, 1992). Ironically, as outlined previously, many medical advances enabling treatment of these conditions have been attributable to the unwitting participation of children.

### 2.1.2 “Therapeutic orphans”

There are an estimated 75 million children under the age of 16 residing in the European Union (EU), equating to 20% of its total population (Oosterwijk, 2002). Many diseases specifically, or principally, affect children including cystic fibrosis and many rare cancers. Over 50 per cent of medicines (up to 90% for new-born babies) “have not been tested for safe use” in children (Bouzom and Walther, 2008, p. 579). This means that existing pharmaceutical interventions may be inefficacious and may also expose treated children to significant risks such as unwanted adverse side-effects or, in the worst case, death. It also means that children are denied new innovative pharmaceutical interventions being developed by the pharmaceutical industry – interventions that could, in some instances, prolong life or improve the quality of life for children living with chronic or debilitating conditions (Europa, 2004).

Reluctance to include children in clinical trials has led to them being described as “therapeutic orphans”, a term coined by Dr Harry Shirkey in 1963 to describe the plight of children who were prescribed medications that had not been subjected to adequate investigation (Baum and Ahrens, 2004, pp. 2-3). As I discussed earlier, children are invisible in medical discourse and their services viewed as an addendum to adult ones within the NHS (Lachman and Vickers, 2004, p. 693). To address the undesirable situation of insufficiently evaluated children’s medicines and to improve the future development of novel medicines, it has been acknowledged that a large-scale coordinated and multidisciplinary approach is required (EGAN, 2002). The MRC Ethics Guide for medical research involving children (2004) has a chapter on the contributing factors limiting research in this area. They cite four main challenges underpinning the reticence in conducting clinical trials: difficulty in reaching a consensus about research involving children; methodological challenges; cost and inefficient licensing; and legislation (2004, p. 9).

Children represent a small population from the perspective of pharmaceutical companies and the risk of adverse events is significantly higher (Schachter and Ramoni, 2007, p. 429), estimated to be three times more likely to occur in children compared with the adult population. Further, despite the creation of interventions to reduce dosing errors in children, child mortalities were occurring, even with the introduction of safeguards such as computerised physician order entry (CPOE) (Conroy et al., 2000, p. 1123). Indeed, a recent systematic review investigating the nature and extent of paediatric medication errors in the UK, highlighted that dosage errors still appear to be commonly problematic in both primary care and acute care. However, as error reporting is often not compulsory and significant inconsistency in the recording and categorising of errors exists, obtaining a precise and complete picture of the rates and types of medication errors is not currently possible (Sutcliffe *et al.*, 2014).

This illustrates the importance of getting dosing protocols correct with children and why pharmaceutical companies might still be reticent to develop paediatric formulations, especially for chemical entities with a low therapeutic dose and low risk-benefit ratio. The increased risk of error threatens potential termination of an otherwise successful drug (Rose, 2019), and thus reduces the incentive to conduct the clinical trials necessary to provide accurate dosage information for paediatric labelling. As a result, pharmaceutical companies regularly delay conducting paediatric clinical trials (Joseph, Craig and Caldwell, 2015; Sutcliffe *et al.*, 2014) for several years after a drug's first New Drug Application (NDA) approval.

Children are suggested to have similarities to older adults with regard to accepting oral medications and difficulties in swallowing conventional tablets and capsules (Liu *et al.*, 2014). However it is generally accepted that children should not be regarded as 'small adults' as they differ

developmentally, metabolically, physiologically and psychologically (Caldwell *et al.*, 2004, p. 803; Johnson, 2003; Klassen *et al.*, 2008, p. 37). This culminates in major pharmacokinetic (Smyth and Weindling, 1999 s.21), pharmacodynamic and toxicological differences and impacts on patient safety, therapeutic outcomes and adherence (Liu *et al.*, 2014). Children therefore, present unique challenges in paediatric drug development, as these fundamental differences require tailored clinical trials to establish drug safety and efficacy in this population (Chatelut, 2008; Schachter and Ramoni, 2007, pp. 575-576).

Many of the published drug trials that have included children have not addressed these unique challenges and have been of doubtful reliability and validity because drug absorption was neither tested nor reported (Standing, Khaki and Wong, 2005, p. e562). Paediatric drug formulation has been reported inadequately in peer-reviewed journals for trials in children under 12 years, with only 37% of publications providing adequate information for the study to be reproducible and of these only 49% used a paediatric formulation (liquid, chewable tablets, granules) (*ibid*, 2005, p. e560). When studies such as these are published in highly cited journals, it perpetuates the myth that children come to no harm when inappropriate formulations are used, further reinforcing the lack of drive in the industry to produce child-friendly medicines (Standing, Khaki and Wong, 2005, p. 562).

The absence of paediatric clinical trials has resulted in a paradoxical increase in the number of instances when paediatricians are forced to prescribe 'off-label' or 'unlicensed' drugs in order to provide state-of-the-art medicines for their child patients (Auby, 2008; Schachter and Ramoni, 2007, p. 429). Off-label use is when treating or prescribing doctors, paediatricians or clinicians prescribe medicines outside of the parameters for indications, dosages, or populations that are detailed on the label (Balan, Hassali and Mak,

2018). Unlicensed medicine use occurs when medicines are prescribed that have not received an approved licence to be used (Aronson and Ferner, 2017; Gray and McGuire, 2019). Occasionally it is necessary to change the formulation or dosage strength of a medicine for children, which requires the prescribing practitioner to request the manufacture of a special medicine or 'specials'. Specials are unlicensed medicines manufactured, supplied and prescribed to meet the individual clinical need of patients in the absence of suitable licensed medicine (Ernest *et al.*, 2012; Ernest *et al.*, 2007). They account for approximately 1% of all UK prescriptions (Pharmacy Magazine, 2018). However, this does not reflect their use in children's medicines and this number, although suspected to be dramatically higher, is unknown. More than 75,000 different formulations are prescribed per annum, including suspensions, liquids, injectables, and intravenous drugs. Off-label, unlicensed and 'specials' prescribing can be viewed as a form of experimentation that according to Schachter and Ramoni (2007, p. 429) has "no consistent eligibility criteria, no consistent dosing regimens, no pre-defined response criteria or stopping boundaries, no data safety monitoring, and inadequate sample sizes to power informative analyses, which means that nothing is learned". For example, in a study to determine licensed versus "off-label" use of newly marketed medicines in children by general practitioners in England, it was revealed that although only a small proportion (10%) of newly marketed drugs were licensed for use in children, most children (78%) were treated with these licensed products. However, 22% of children in the study received drugs 'off-label' during the first few years that the drug was marketed and a small number were prescribed drugs that were in fact contraindicated for use in children (Wilton, Pearce and Mann, 1999, s.37). This compounds the risk of medication error, which was found to be a common problem in both primary and acute care due to lack of adequate reporting (Sutcliffe *et al.*, 2014).

Lack of adequate research and 'off-label' use can result in children being exposed to drugs that are untested in the paediatric population. This can result in serious, albeit unintentional, harm for example: use of thalidomide causing phocomelia in unborn children; staining of the teeth with use of tetracycline; Reyes' syndrome arising from use of aspirin in children compromised by viral infection; grey baby syndrome in neonates from the use of chloramphenicol; supraventricular tachycardia resulting in refractory hypotension and death in infants prescribed verapamil; and use of domperidone causing severe extrapyramidal dysfunction, bladder retention and hospitalisation (Caldwell *et al.*, 2004, p. 803; Garson, 1987, p. 84; Johnson, 2003, p. 42).

Children remain therapeutic orphans to this day and although policy and practice are progressing in the right direction, there are still major gaps that need to be addressed in order to secure for children, medicines of equal quality, safety and innovation as those for adults.

### **2.1.3 Children with chronic conditions: a marginalised subgroup**

Children with chronic conditions, as a population, have historically been omitted from the related discourse (Sawyer *et al.*, 2007, p. 1481). There is a growing body of literature focussing on the perceptions and experiences of parents or caregivers of these children (Case-Smith, 2004; Chernoff *et al.*, 2001; Fawcett *et al.*, 2005; George *et al.*, 2006; Hummelinck and Pollock, 2006; Johnston and Marder, 1994; Lowes and Lyne, 2000; McNeill, 2004; McNeill, 2007; Olson *et al.*, 2004; Pianta *et al.*, 1996; Swallow and Jacoby, 2001) and an acknowledgement of the growing number of children presenting with chronic conditions. Despite this there is a deficit of literature available on the experiences, perspectives or perceptions of the children themselves, with only one study systematically reviewing studies of 'young people' with health conditions (Taylor, Gibson and Franck, 2008) and that highlights the

limited amount of research available. This review by Taylor, Gibson and Franck (2008, pp. 3084-3085) did not focus on children *per se* but reviewed studies investigating the perceptions of adolescents living with a chronic condition. Their findings form a significant contribution to the argument that young people's views are not being considered. The authors identified 46 studies, 20 of which they evaluated and identified seven "overarching themes" which were: developing and maintaining friendships; being normal/getting on with life; the importance of family; attitude to treatment; experiences of school; relationship with the healthcare professionals; and the future. With regards to attitudes to treatment, only seven studies of young people were identified (Admi, 1996; Woodgate, 1998; Snethen et al., 2001; Arkin and Ahmad, 2001; Eklund and Sivberg, 2003; Damiao and Pinto, 2007 Rhee et al., 2007 as cited in Taylor, Gibson and Franck, 2008). These studies identified that attitudes to treatment varied depending upon the stage of adolescence and thus can be suggested to be age dependent. Those in early adolescence experienced less difficulty because they were under the protection of parents, who were perceived as supportive. Studies in this review suggested that as young people got older, they started to understand their treatment and take control of their routine. Younger children are generally acknowledged to have their medicines administered to them by parents or carers, but how this impacts on the children themselves is not understood and cannot be understood if studies are not conducted that address this issue. The literature suggests that to effect control of a chronic condition it is crucial to understand young people's perspectives and seek to comprehend their world by gaining an understanding of that individual's complete circumstances (Karlsson, Arman and Wikblad, 2008, p. 563). I suggest that medicines cannot improve in formulation or address the specific needs of the children without addressing perceptions regarding the impact of taking medicines. Indeed patient centric medication is suggested to be essential not only to improve safety and efficacy but children's acceptance of

medicine, and ‘adds additional biopharmaceutical considerations to an already complex problem’ (Salunke and Tuleu, 2014) including practical and technical challenges such as defining ‘acceptable taste’ in children, research design and reliability of paediatric responses (Cram *et al.*, 2009; Davies and Tuleu, 2008).

Although children with chronic conditions generally view themselves and their lives as similar to their healthy peers, negative attitudes of peers to those with chronic conditions can be profound and may even precipitate bullying (Smith *et al.*, 2008, p. 3084; Taylor, Gibson and Franck, 2008). Prescribers should always consider the number of required daily administrations children are expected to undergo, wherever possible (Smith *et al.*, 2008, p. 543), and take into account the effect of a particular drug administration regime and formulation in order to minimise the impact of perceived difference between chronically challenged children and their healthy peers. This could also be being considered in the design of the pharmaceutical interventions themselves.

The literature available on chronic illnesses and young people paints a picture of difficulty and challenges, with individuals struggling to “gain autonomy” and being “forced to consider the limitation caused by their illness” (Karlsson, Arman and Wikblad, 2008, p. 563). Karlsson *et al.*’s (2008) phenomenological study of adolescents with type 1 diabetes found that there was “growth through individual self-reliance” (including self-determination, psychological maturity and increased motivation) and “growth through confirmation of others” (i.e. parental encouragement, peer acceptance, support from healthcare team) (Karlsson, Arman and Wikblad, 2008, pp. 567-568).

Paediatric medicine is essentially a “neglected” area of medicine, which has left children in a state of liminality regarding pharmaceutical R&D.

The paradox that has emerged from the complexity of developing children's medicines, is that to ensure the safety of children in research, historically, children have not been encouraged to participate in clinical trials. However, to ensure children's safety and to supply high quality and effective medicines for children, children need medicines that have been rigorously tested in clinical trials conducted in children.

## **2.2 Engagement, involvement and participation – semantics and hyperbole**

Engagement, involvement or participation are terms used all too loosely within the sphere of public health policy to generate notions of interaction, control, comprehension, and active influence upon research. Despite the apparent semantic similarity of these commonly interchanged terms, I argue that these terms should not be conflated. Conflation of these terms, it appears, is endemic within English medical and social sciences literature. Terminology varies geographically, inter-disciplinarily and periodically (Stokes and Oliver, 2017). Regularly authors seamlessly flit between the terms participation and involvement within a single paper and rarely do they define the meaning or provide their own definitions. This is understandable as the discourse surrounding the concepts and definitions of participation, involvement and engagement is at best contentious, convoluted and ambiguous, not to mention beset by rhetoric and hampered by hyperbole, making universally accepted definitions problematic and ambiguous. The growth in the use of these "buzz words" in policy creation and especially within the public service sector, is apparent. There are even jobs created on the basis of addressing public participation in policy creation or service provision within organisations

In the Concise Oxford English dictionary (Oxford, 2002) the definition of the word engage is: 1. to attract or *involve* (someone's interest or

attention), 2. to employ or hire and finally, 3. (engage in/with) *participate* or become *involved in* (Oxford, 2002: 472); noticeably beset with semantic crossover. This is also manifest in the definition of *involve*, which is defined as: 1. to be included “as a necessary part or result” cause to experience or *participate* in an activity or situation; 2. connected, typically on an emotional or personal level; and 3. complicated (Oxford 2002:746). However, the word ‘participate’ is given a very basic definition - take part (Oxford, 2002: 1039). Thompson (2007, p. 1298) suggests two ‘distinct approaches’ to patient involvement; one advocating ‘individual freedom’, consumerist, and the other a more ‘collective’ democratic approach. He argues that both approaches stress empowerment, but the collective approach of giving ‘voice’ would affect change more directly. Thompson suggests that the distinction between *patient involvement* and *patient participation* is the degree of input into the decision-making process, the “transfer of power from the professional to the patient in the form of increased knowledge, control and responsibility” (Thompson, 2007, pp. 1307-1308). From my perspective, to participate is to be an active player or have a valid role within an organisation, system, or process.

For the purpose of this thesis when I refer to the term *participation*, I adopt Oliver et al.’s (2015, p. 45) definition of “people’s participation in a shared research task”. More specifically, in the context of medicines R&D, I view *involvement* as active researcher-laypeople exchanges and contributions that are recognised within an environment aimed to create, design, or modify pharmaceutical interventions for children.

### **2.3 Considering children’s rights in medicines R&D**

It is recognised that children have the same right as adults to benefit from high-quality, efficacious and safe medicines in order to achieve “the highest attainable standard of health” (United Nations, 1989: Article 24.1)

(see Appendix 1). This, in part, is dependent on pharmaceutical interventions. In the context of children's medicines, there has been little attempt to provide properly trialled safe, efficacious and high-quality children's medicines, which means that this right is, in effect, not being fulfilled. Children also have the right to freely express their views on matters that concern or affect them (Article 12.1), and to freedom of expression and to "seek, receive and impart information and ideas of all kinds, regardless of frontiers..." (Article 13.1) (United Nations, 1989). By reference to these rights, children are entitled to exercise control over their healthcare provision, including the pharmaceutical interventions they are prescribed.

### **2.3.1 Involving children in research – a basic human right**

Involving laypeople in research has been suggested as essential to: identify patient-important outcomes for medical research to assess treatments; design patient information leaflets; aid recruitment for clinical trials; create more relevant research and improve the uptake of research evidence (Ahern, 2007, p. 69; Hope, 1998, p. 292; Undercover Project, 2004; Whitstock, 2003, p. 222). It is further suggested that lay-people could be involved in various stages of the research process to: decide research priorities; identify problems and formulate research questions: identify research funding priorities; research design; interpretation of findings and systematic reviews (e.g., Entwistle *et al.*, 1998; Oliver, 1995). Because of the potential benefits, service user involvement in healthcare service provision is becoming more commonplace (see: Department of Health, 1999; NHS Executive, 1996). Within the medicines R&D paradigm, children's involvement in research is predominantly restricted to that of being passive research subjects in clinical trials. There are several reports that demonstrate that children who participate in clinical trials experience health benefits (Schmidt *et al.*, 1999; Smyth and Weindling, 1999, p. 22; Vist *et al.*, 2007, p. 6). However, shifting children's role beyond that of clinical trial subjects (*passive*

*involvement*) to active participation would have further benefits for both the children and professionals conducting medicines research. Children challenged by chronic illness who are frequent and long-term users of pharmaceutical interventions have much to contribute to inform service development (Lightfoot and Sloper, 2003). In a study involving children with chronic illness or physical disability in local health services development, Lightfoot and Sloper (2003, p. 283) identified the benefits of involvement. They concluded that involving young people “has the potential to result in positive outcomes for the personal development of young patients and professional development of staff” (Lightfoot and Sloper, 2003, p. 289). Yet despite the potential benefits, within pharmaceutical R&D the uptake of children’s participation is slow, suggesting that children are not being readily consulted as experts, stakeholders or even users.

Children have a right to air their views and to have those views acted upon in an attempt to facilitate change (Van Blerk and Ansell, 2007). Listening to children can improve understanding of children’s priorities, interests and anxieties, and helps to contextualise medicine in children’s lives and feelings of Self (Pascal and Bertram, 2009, p. 254). However, priority setting for children’s medicines research is being assessed by policymakers nationally and internationally (i.e. the Food and Drug Administration (FDA) and the European Medicines Agency (EMA formally the EMEA)) without including the perspectives of children for whom the medicines are intended. To fulfil a basic human right, those involved in creating children’s medicines must consider children’s requirements and values for their health, healthcare and medicines and be made aware of, understand and address those children’s views. Currently, no evidence exists that clarifies whether the policy-led ideals that direct children's medicines R&D and the researchers operating within this discipline, have at any point involved or recognised the views of the children for whom the medicines are intended.

### 2.3.2 Rights of children to have a say in healthcare, including medicines

“Good law does not necessarily lead to good health. Research must also address whether human-rights initiatives and law reform are effective tools of public-health advocacy” (Loff, Burris and Lazzarini, 2001, p. 1901).

Children’s right to receive safe, efficacious and high-quality pharmaceutical interventions was addressed in 1989 in the United Nations Convention of the Rights of the Child (**UNCRC**). The UNCRC was the final stage of a process which had commenced ten years earlier with a draft convention (subsequently amended and expanded extensively), which was submitted by the Polish Government during 1979, the International Year of the Child (UNHROHC, 1993). This convention was born out of the requirement, by some member States of the United Nations, for an official document of children’s rights that would be binding under international law (ibid, 1993). The General Assembly of the United Nations (UN) adopted the convention on 20<sup>th</sup> November 1989 and the convention was ratified by the UK government in 1991 (Sinclair, 1998, p. 137). With more than 190 countries ratifying this treaty, the UNCRC is the most extensively ratified human rights agreement ever (Coyne, 2008, p. 1683). Countries that ratify a human rights document make a powerful symbolic gesture, however whether countries honour treaty obligations, is another matter and the “world is replete with examples of countries that... ..have not honoured them” (Loff, Burris and Lazzarini, 2001, p. 1901; Palmer *et al.*, 2009, p. 1987). Human rights ratification and improved health outcomes have not been demonstrated to be associated. Nevertheless, all children are entitled to receive good healthcare provision as outlined in Article 24 of the UNCRC (United Nations, 1989). This right should be applicable irrespective of age, social status, mental capacity and physiological capability. Several articles are particularly relevant to children

rights in healthcare (Article 5, 12, 13 and 24) and should therefore be considered as a matter of course when creating policies relating to medicines.

**Article 5** states that parties shall respect the responsibilities, rights and duties of parents or, where applicable, carers to provide appropriate direction or guidance in a manner consistent with the evolving capacities of the child. **Article 12.1** refers to the right for a child, who is capable of formulating opinions, to freely express their views on matters that concern or affect them. Furthermore, **Article 13.1** details the right to freedom of expression; to “seek, receive and impart information and ideas of all kinds, regardless of frontiers, either orally, in writing or in print, in the form of art or through any other media of the child’s choice” (United Nations, 1989). Therefore, children are entitled by reference to these rights, to exercise control over their healthcare provision, including treatment that they are to be engaged in and pharmaceutical interventions that are prescribed, but these rights are dependent on the age and capability of the children concerned. Children’s development is idiosyncratic, and I would argue that within the children’s medicines context this might relinquish children’s agency, as judgement of capacity would lie with those conducting the research, who might, for example, view all children as incapable of expressing their views.

**Article 24.1** is of particular relevance; specific reference is made to the recognition of the right to the highest standard of health by the State Parties (United Nations, 1989). To have the “highest attainable standard of health” then, the resources (i.e. pharmaceutical interventions) used to ensure this, also need to be of the highest attainable standard, which is questionable in the context of children’s medicines. As I have previously discussed, despite the introduction of the UNCRC, the provision of safe, efficacious medicines

designed specifically for children and ones that are of a high quality and equal to those developed for adults, has not been fulfilled.

Children are often constructed as a vulnerable and marginalised group, particularly when children are in a state of ill health or relying on medication to control various chronic or acute conditions. Younger children in some ways are similar to non-English speaking citizens, as they are not able to access written information without such information being interpreted and one could argue edited/censored for them by family members, carers or healthcare professionals. Within the social and medical sciences despite consulting with sick children, their views are seldom elicited, acknowledged or acted upon (Cavet and Sloper, 2004; Lightfoot and Sloper, 2003). Social scientists such as Priscilla Alderson, Virginia Morrow, Patricia Sloper and Jane Lightfoot have written extensively on the rights of the child in the healthcare setting (Alderson, 2003; Alderson, 2007; Alderson, 2008; Alderson, 2012; Alderson and Montgomery, 1996; Alderson, Sutcliffe and Curtis, 2006a; Alderson, Sutcliffe and Curtis, 2006b; Aspinall, 2006; Morrow, 2008). Coyne (2008, p. 1683) conducted a literature review in an attempt to understand the principle of children's involvement in the healthcare setting by focussing on children's experiences in consultations and decision-making. She concluded that the literature reviewed suggests that children want to be involved in decision-making processes, however the degree to which this is the case is not clear and it may in fact be that children would prefer less involvement. She suggested that more research into decision-making and participation preferences is needed to inform healthcare practitioners (ibid, 2008:1687). This review provided insight into studies that addressed participation within one section of the healthcare environment but does not help to address the issue of children participation in policy creation.

## **2.4 Policy and practice: The challenges of children's medicines research**

Children have different treatment requirements from those of adults, requirements that vary significantly depending on their age and stature. However, the lack of reliable and valid published paediatric drug trials (Standing, Khaki and Wong, 2005, pp. 560, 562) has led to an unsubstantiated belief that adult drug formulations are not harmful to children and therefore has reduced the impetus for the pharmaceutical industry to produce child-friendly medicines. Not only do many medicines fail to suit children physiologically, they also fail to suit their social lives. The stigma associated with medicine use is an important factor that may lead to poor control of common chronic conditions such as epilepsy, with potentially harmful long-term consequences.

In response to the obvious inadequacies of medicine provision for children and concern regarding the lack of public confidence in the safety of paediatric trials, policies designed to encourage paediatric research have recently been introduced.

### **2.4.1 US legislation: The Best Pharmaceuticals for Children Act**

In 1906 the Food and Drug Administration (FDA) was formed to control "long-standing, serious abuses in the consumer product marketplace" (FDA, 2015). Its first commissioner was the noted chemist Harvey Washington Wiley (FDA, 2009b). Pharmaceutical regulation in the USA commenced with the introduction of the Food, Drug and Cosmetic Act of 1938 (Allen and Michelson, 2002, p. 45) then in 1962 the Kefauver-Harris amendments introduced the requirement that "drugs must be demonstrated by well-controlled studies to be effective for their intended uses as well as safe". The origins of the Best Pharmaceuticals for Children Act started back in 1996 when the American Academy of Pediatrics testified to Congress that, since 1962,

80% or more of pharmaceuticals produced had the disclaimer that they were not approved for use in children (Allen and Michelson, 2002, pp. 45-46). Congress responded with the introduction of Section 111 of the 1997 Food and Drug Administration Modernization Act entitled Pediatric Studies of Drugs, which focused on many issues including: conducting trials, patents, and market exclusivity. In January 2002, President Bush signed the Best Pharmaceuticals for Children Act introduced by the US Food and Drug Administration Agency (United States, 2002; US, 2002). This Act was expanded in 2007 (Auby, 2008; US Congress, 2007). Further, the Pediatric Research Equity Act (**PREA**) was introduced to Congress on 18<sup>th</sup> March 2003 by Senator Mike Devine, which was enacted on 3<sup>rd</sup> December 2003 (govtrack, 2016). This Act enabled the US government to require selected medicines were tested in children. The introduction of the BPCA and PREA has led to the execution of over 400 studies and changes to 652 medicines<sup>3</sup> reflecting improved information on specific use of medicines (FDA, 2009b; Poortman, 2007; FDA, 2016 #2029). Conversely, Young et al. (2008) evaluated the Physicians' Desk Reference for changes in the listing of medicines licensed for children in the USA between 1998–2007 and discovered that of the prescription entities listed, 55.9% (538) were licensed in children in 1998, 54.3% (488) in 2002 and 51.3% (394) in 2007. The formulations that were deemed suitable for children were 611 (63.4%), 550 (61.2%) and 430 (60.6%), in 1998, 2002 and 2007 respectively. They concluded that overall access to prescribing information about paediatric drugs has not increased over the past decade. In fact, there were concerns being aired in the literature that response by the pharmaceutical companies to the Paediatric Rule was discouraging (The Lancet, 2004, p. 732).

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<sup>3</sup> Data correct as of 31 October 2016

Sustaining and expanding the medical research infrastructure is viewed as important, as is the need to create more “rapid and efficient” methods of conducting paediatric clinical trials (Hoppu *et al.*, 2011; Vitiello, 2008a). The expansion in paediatric pharmacological research has been significant in the United States; in part due to legislative enforcement but also because of financial incentives. One of the more potent incentives that triggered an increase in size and variety of funding, was the introduction of the six-month extension to drug patent exclusivity upon conducting specific studies in the paediatric population (US Congress, 2002), an incentive that has been criticised.

#### **2.4.2 European legislation: The Paediatric regulation**

Following the US FDA BPCA there were landmark movements to address inequalities in provision of medicines for children within the EU. On the 18<sup>th</sup> December 1997 it was agreed that EU legislation needed to be reinforced to surmount existing obstacles that prevent the use of novel medicines in children (EMA, 1997). European Health Ministers called on the European Commission to make legislative proposals to ensure that new and existing medicinal products for children would be tailored to the specific needs of children, in a Council resolution of December 2000 (European Union, 2000). It was not until October 2004 that a proposal for a “Regulation on medicines for paediatric use” was issued by the Commission. Following in the footsteps of the US, the EU paediatric regulation was created to increase Europe-wide availability of high-quality child-specific medicines. To address this substantial inequality within the EU, on 29<sup>th</sup> September 2004 the European Commission took on a proposal for a regulation of the Council and the European Parliament on paediatric medicinal products to improve the health of European children by increasing research, development and the authorisation of medicines designed for use in the child population. The Regulation was agreed by the European Commission, the European Council

and the European Parliament in June 2006 and on 26<sup>th</sup> January 2007 the new legislation was introduced – Regulation (EC) No. 1901/2006 – the Paediatric Regulation.

Like the Best Pharmaceuticals for Children Act, the EU Paediatric Regulation<sup>4</sup> was created to address the paucity of children’s medicines research and is based on the unacceptability of prescribing drugs unproven for safety and efficacy for children and young people (Westra *et al.*, 2009). **Article 1** describes how the Regulation is structured to “lay down rules” that concern the development of medicinal interventions “in order to meet the specific therapeutic needs of the paediatric population, without subjecting the paediatric population to unnecessary clinical or other trials” (European Union, 2006a: Title 1, Chapter 1, Article 1).

The Paediatric Regulation consolidated previous EU Regulations and introduced new obligations and compliances. These include: obligations to include results of clinical studies regarding any new indications, pharmaceutical forms or administration routes that must comply with a paediatric investigation plan (**PIP**). A PIP is defined as a “development plan aimed at ensuring that the necessary data are obtained through studies in children, when it is safe to do so, to support the authorisation of a medicine for children” (EMA, 2015). The European Commission (EC) is responsible for creating the comprehensive arrangements for PIP applications, waivers or

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<sup>4</sup> The full and correct title of the Paediatric Regulation is Regulation (EC) No 1901/2006 of the European Parliament and of the Council of 12 December 2006 on medicinal products for paediatric use and amending Regulation (EEC) No 1768/92, Directive 2001/20/EC, Directive 2001/83/EC and Regulation (EC) No 726/2004

deferral requests. This comprises the layout and content of applications for agreement or modification, “operation of the compliance check” and proposed assessment criteria for ‘significant’ studies (EMA, 2008a) (See Article 7 and Article 8 of Paediatric Regulation No 1901/2006: European Union, 2006a). Pharmaceutical companies submit proposals to the Paediatric Committee of the European Medicines Agency for approval and must include a description of the trial/study, measures to adapt the medicine’s formulation, cover the requirements of all children from birth to adolescence and define the timing of the study in relation to adult trials. The Paediatric Regulation was amended on 20<sup>th</sup> December 2006 (European Union, 2006b).

As with the Best Pharmaceuticals for Children Act, the Paediatric Regulation contains a provision for obtaining incentives or rewards, including financial incentives that were viewed as controversial (Dunne, 2007, p. 178). The Commission proposed a 6-month extension to the duration of Supplementary Protection Certificate for medicines that met the criteria of including an agreed PIP (along with a number of other criteria being filled) and an additional 2-year extension to market exclusivity for orphan medicines (Dunne, 2007, p. 178).

Although the FDA and EU regulations go a long way to improve medicines research for children, critics have raised doubts with regard to the regulations’ ability to address issues such as those of pharmacogenetics (Krekels *et al.*, 2007, p. 1796). The consequence of this is slow uptake of pharmacogenetic research into the regulatory framework. Some critics argued that paediatric labelling needed to be advanced in order to integrate the developmental changes that occur throughout childhood (Krekels *et al.*, 2007, p. 1796). Others questioned whether the EU paediatric legislation addressed children’s real needs (Auby, 2008; Permanand, Mossialos and McKee, 2007; Vassal, 2009). Indeed there is still an absence of commercially

available age-appropriate formulations for children (Salunke and Tuleu, 2013). Issues emerging in the discourse highlighted problems in transparency, industry cooperation and access to extramural expertise, need for unity between the FDA and European Medicines Agency (EMA) (Milne, 2006, pp. 13-14), methodologically weak trial plans (Kölch, Schnoor and Fegert, 2007), and ambiguity of 'children's needs'. Further, there was concern that legislation would promote a proliferation in available children's medicines, as opposed to medicines designed to fulfil children's needs (Permanand, Mossialos and McKee, 2007).

### **2.4.3 Two heads are better than one: EU and US collaboration**

Within the literature there was also a call for global initiatives to improve the safety and efficacy of clinical trials. Vitiello (2008a) called for greater global collaborations and coordination to achieve better methodological standardisation of research and data sharing. In recognition of the need for global standardisation the EMA and FDA launched a joint Good Clinical Practice (GCP) initiative in 2009. The three main objectives of the Initiative were to: conduct periodic information exchanges on GCP-related data; conduct collaborative GCP inspections and share data on interpretation of GCP (EMA, 2011; EMEA, 2009a; FDA, 2009a). This joint initiative was judged by both parties to be extremely successful and productive.

The initiative:

“lays the foundation for a more efficient use of limited resources, improved inspectional coverage and better understanding of each agency's inspection procedures. It demonstrates how the agencies can work together to improve human subject protection and better ensure the integrity of data submitted as the basis for drug approvals.” (EMA, 2011)

More than 250 documents were exchanged, and processes of information exchange were developed and refined, which facilitated improvements in the agencies' inspection coverage and decision-making processes. Information generated from regular communications proved useful to identify potential inspection reports for exchange and applications submitted to both agencies in parallel, with the aim of identifying candidates. Each agency benefited from knowledge of each other's inspection procedures; and by attending each other's training meetings. In total, the agencies exchanged information involving 54 different products. Both parties wished to continue the initiative and expand the initiative outside of the US and the EU (EMA, 2011).

Much discourse has evolved around the determinants influencing paediatric pharmaceutical progression and the policy reforms designed to improve them (see: Auby, 2008; Auby and Simonnot, 2008; Kölch, Schnoor and Fegert, 2007; Permanand, Mossialos and McKee, 2007; Westra *et al.*, 2009). However, the importance of understanding children's perspectives with regards to taking medicines has not been raised and research into the benefits of involving children in medicines R&D is absent.

## **2.5 Public involvement and policy-making: whose priorities?**

"...engagement helps empower people, broadens attitudes and ensures that the work of universities and research institutes is relevant to society and wider social concerns" (Research Councils UK, 2013)

The RCUK Concordat outlines the public engagement responsibilities and expectations of research funders, providing four key principles with the aim of strengthening good PPI practice to ensure that it is "valued, recognised and supported" (Research Councils UK, 2013). Both the UNCRC (Article 5) and

the UK Human Rights Act 1998 (Article 10) (UK Government, 1998) advocate the right for individuals to “have their say” in matters that affect them irrespective of age or status. The social implications of medicine taking are complex and focus on safeguarding individuals with respect to medicine use, risk and abuse. Safeguarding is usually associated with protection of individuals from healthcare professionals who prescribe medicines but also includes safeguarding from personal abuse that could result in grave consequences such as addiction or suicide. The right for an individual to have “their say” spans all aspects of life and therefore includes being afforded adequate information to make informed decisions about the pharmaceutical interventions they receive. This arguably suggests that people should be involved in how pharmaceutical interventions are developed. Children are often uninformed of their rights regarding healthcare provision and the policies that are in existence to safeguard their interests. Priority setting for paediatric medicine research is continually being assessed by policy makers nationally and internationally (i.e. the FDA and EMEA). Investment in and focus on children’s medicines has increased in recent years, but those guiding regulation and medicines R&D (i.e. the investors, the patient organisations, the governmental organisations and non-governmental organisations), leave little room for the voices of children to be heard. As these policy-led priorities have omitted to include the perspectives of children, it is unclear whether the medicines research priorities being set, match the priorities of the children.

Paragraph 32 of the Paediatric Regulation calls for the Paediatric Committee to establish an “inventory of the needs of the paediatric population... after consultation with the Commission, the Member States and interested parties” (European Union, 2006a: paragraph 32.). Upon reaching a final agreement for the Regulation of children’s medicines, the European Parliament Vice-President and Rapporteur, Françoise Grossetête, was quoted as saying; “Europe’s citizens do not want big words, they want action. This

regulation for children's medicines is a concrete answer to their expectations<sup>5</sup>. This text shows what Europe can do for its citizens. A member state on its own cannot deliver such a policy which will benefit all children" (Europa, 2006). Ambiguity surrounds the meaning of "their expectations" in this context. Is it the expectations of Europe's citizens in general, or the children themselves? If Françoise Grossetête is referring to the children of Europe, the expectations of these children are unknown as children were not and have not been invited to detail 'their expectations'.

There has been a specialist committee evaluating paediatric needs in place in the EMEA for several years. The Paediatric Working Party (PEG) (EMEA, 2005) was superseded by the Paediatric Committee (PDCO), which was established alongside the Paediatric Regulation in January 2007. The role of the PDCO includes evaluating PIPs, formulating opinions on the safety, efficacy and quality of paediatric medicines, issuing advice on paediatric medicine related queries, creating and revising a PIP inventory and advising and supporting the EMA and the EC on "the communication of arrangements available for conducting research into paediatric medicines" (EMA, 2010b). The PDCO consists of 24 members: representatives of the Committee for Medicinal Products for Human Use (CHMP) (five members plus alternates), EU appointed member for areas not represented by the CHMP, healthcare professionals (three members plus alternates) and patient associations (three members plus alternates) (EMA, 2010b). The inclusion of the patient associations indicates a respect for including the voice of the patient-consumer, however, it would seem logical to have a mechanism to hear from children themselves.

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<sup>5</sup> Italics and underlining have been added by the author to stress key points within the quote

There are rules outlined with regard to how the EMA involves patients or consumers in terms of consultations on an “advisory basis” on products, diseases or treatment specific issues (EMA, 2009b). With regard to section 3), Consultation, the EMA state that no deliberations or formal opinions or decisions will be conducted in the presence of a patient/consumer organisation representative and that “the relevant section of the minutes will be circulated to them for comments, excluding the section on the deliberations or any formal opinions or decisions reached by Committee/Working Party/Scientific Advisory Group” (EMA, 2009b). Participation of patient-consumer organisations centres on creation of information leaflets (EMA, 2010a) but does not extend beyond or above this i.e. in terms of influencing policy, at this stage representatives from these organisations are excluded due to the Rules of Involvement protocols discussed above. Despite this limited participation, in a press release about the first survey of representatives of European patient and consumer organisations in June 2008, the EMA stated that over 92% of representatives were “either satisfied or very satisfied with their overall interaction with the EMA” (EMA, 2008b). Interaction is clearly not the same as participation. Yet again semantics appear to be massaging the reality of the relationship between the policy makers and the adult patient-consumers. In the same press release the EMA “confirm” that patient and consumer participation is “progressing well” and that the survey has assisted in identifying areas where patient and consumer participation can be “further developed” (EMA, 2008b). It would be good to know to where the participation extends and whether children will be involved in the process.

Other organisations involved in priority setting include the Task-force in Europe for Drug Development for the Young (TEDDY) and ERA-NET PRIOMEDCHILD (Priority Medicines for Children). TEDDY was established in June 2005 and was expected to run until 2010 but continues to operate in a

revised format. Its role was to add to the promotion of safe and efficacious medicines for children in the context of the European Paediatric Regulation. TEDDY's seven objectives and 12 Work-Packages cover the main aspects of paediatric drug development and utilization. As TEDDY acts as a network for developing research or trials and as a consultative regulatory body, it stands as a novel entity in the paediatric pharmaceutical field. TEDDY has focused on three aspects of paediatric pharmaceutical research: increasing awareness about the Paediatric Regulation; reaching agreement on the terms and instruments to be used for common research; and favouring close relationships among different stakeholders and partners from different EU Member States. It emphasises the importance of reaching consensus on best practices among stakeholders across Member States (19 partners from 11 countries), stating that this is the main challenge to be surmounted (Ceci *et al.*, 2009). In 2007 TEDDY was involved in addressing how to prioritise research from a clinical perspective in conjunction with the UK Paediatric Infectious Disease Research Network (Faust and Klein, 2007).

TEDDY recognises the importance of incorporating pharmacogenetics applications and the time-dependencies associated with the developmental issues of the child from prenatal period to adolescence (TEDDY, 2009). The 6<sup>th</sup> objective was to unite industries and *other relevant stakeholders* to promote the new drug development, optimise paediatric formulations and supply labelling recommendations for existing drugs. This is a heartening objective in the light of children's absence in the process to date. Today TEDDY consists of 41 partners from 14 countries with the aim of "facilitating the performance of good quality paediatric studies and research" (TEDDY, 2014).

ERA-NET PRIOMEDCHILD is a partnership between research funding organizations from across Europe to generate "coherence and cooperation to

national research programmes and policies on research” for priority paediatric medicines. They aim to achieve this by initiating a network for national programmes and programme managers in order to facilitate the exchange of expertise in the field of paediatric pharmaceutical research. They were also involved in setting the European research agenda for medicines for children and like TEDDY aim to involve stakeholders in the process of fostering research priorities (ERA-Net, 2009).

The work of both of these organisations and the EMA has focused on improving the safety, efficacy, quality and innovation of paediatric pharmaceuticals. All of these organisations are involved in setting priorities and state their desire to include stakeholders in generating priorities. However, ambiguity surrounds the identity of the “stakeholders” and to what level they will be involved. None of the organisations has a proviso ensuring that the priorities of children themselves are being addressed. It can be argued then, that children are not regarded as valid stakeholders from the perspective of these organisations.

## **2.6 Drug research and design: medicines for children**

“Medical research involving children is important for the benefit of all children. It leads to innovations in healthcare that can substantially improve their health and quality of life. Furthermore, the scientific opportunities for developing better methods of preventing and treating disease that affect children, or begin in childhood, have never been greater” (MRC, 2004, p. 1).

The rapidity of children’s physiological development can prove problematic for R&D due to the protracted time taken to progress a drug from synthesis to approval taking on average 14.2 years (PHARMA, 2002 as cited in Allen and Michelson, 2002, p. 44; Hawkins and Law, 2005), so a child joining a

trial at aged 12 would be 26 by the time the drug secured approval and for eight of these years would be an adult. Continuity and attrition of study participants over such protracted times might also be argued to be an issue for researchers. As the R&D process can be extensive, with many years elapsing between the commissioning of research and its results being integrated into the evidence base, development of a new chemical entity is also expensive. As stated above, synthesis to approval it is estimated to take 14.2 years (1990s), this has increased dramatically from 8.1 years in the 1960s (PHARMA, 2002 as cited in Allen and Michelson, 2002, p. 44; Hawkins and Law, 2005). The additional risks of conducting clinical trials on children exacerbates the reluctance of pharmaceutical companies to direct research funding into paediatric formulations, as the additional risk factors could prove extremely costly in terms of time and money if a drug had to be terminated (see also section 2.1.2). The “rapid and frequent pace” of discoveries by basic science and the creation of biotechnology companies to generate products based on these discoveries, has forced the pharmaceutical industry to reevaluate their efforts from research to portfolio management. For example, areas such as pharmacogenetics are evolving rapidly. Pharmacogenetic data can make an important contribution to paediatric drug development and prescription practices in clinical practice. Difficulties are manifest in terms of the harmonisation of regulatory guidelines to ensure pharmacogenetic information is included in the drug approval process and also in integrating the findings into label statements or statistical process control (SPC). The SPC is a method of quality control based on the findings from statistical data. The shortage of pharmacogenetics information included in SPCs or drug labels is explained in part by the exploratory nature of pharmacogenetic research, which significantly restricts its use for regulatory purposes in paediatric indications. Advancement in clinical and scientific understanding relating to paediatric pharmacotherapy for children of all ages reside within gaining an enhanced understanding of the effects of growth and developmental biology

on drug metabolism (Bartelink *et al.*, 2006; Kearns *et al.*, 2003; Rakhmanina and van den Anker, 2006). The genetic foundations of age-specific diseases and age-related differences in drug response will initiate enhanced drug interventions in the paediatric population. To fulfil the remit of improving drug safety and efficacy in paediatric medications, it is suggested that it will be crucial to “convince the public, their legislative representatives and the pharmaceutical industry that research in the area of paediatric pharmacogenetics has long-term benefits and is justified”. This is dependent upon recognition of the ethical challenges presented by the paediatric population (Krekels *et al.*, 2007, p. 1797).

An evaluation of global R&D was recently published by the Centre for Medicine Research (CMR) in London, which assessed expenditures, development times, medicines reaching market and sales. It was found that between 1996-2005, new medicines output had declined by 20%, with 2004 being the lowest output for 20-years (CMR, 2006; as cited in Delamarter, 2006). Simultaneously, reports had emerged that drug development was on a positive trend. Tufts Center for the Study of Drug Development found that the number of new clinical trials executed by the top 10 pharmaceutical companies had grown by 50% since 2002. The annual rate that drugs were entering clinical testing increased by 31% from 1991/2001 compared to 2002/2007 for the top 50 global companies and nearly 75% of the drugs in the top pharmaceutical companies’ portfolios reached clinical testing between 1993 and 2007 and were developed by the companies. The trend was for oncologic/immunologic and central nervous system (CNS) drug candidates entering clinical testing over the same period (Tufts, 2009). Delamarter (2006, p. 623) discussed a climate of poor returns on investment by the pharmaceutical industry talking about the influence of push-pull forces to improve its performance. The ‘push’ being factors such as poor return on investment in R&D and patients’ demand for new treatments to address

unmet needs. The extent of this is obvious in the funding of research for academic or small company pharmaceutical development by patient associations (Delamarter, 2006, p. 624). Delamarter suggests that pharmaceutical development is also being 'push'ed by apprehension regarding limited innovative medicines reaching the market with increasing pressure from the general public, patients and patient organisations. This culminates in a strong 'pull' of new opportunities such as the dramatic increase in scientific discoveries and an "exploding scientific knowledge of disease mechanisms" to translate novel entities and develop innovative medicines (ibid, 2006, p. 623 and 625). However, as noted, clinical development of medicines now takes longer. The average drug development timeline for drugs approved between 2005 and 2009 was 6.4 years (Kaitin and DiMasi, 2011). However, data from the CMR indicates that the average duration for ongoing development projects (2008–2012) was 9.1 years, which indicated a trend towards increased interval durations in 2004-2012 in both preclinical development (+17 %) and phase I clinical trials (+58 %) (CMR, 2014) and now stands at 14.2 years (PHARMA, 2002 as cited in Allen and Michelson, 2002, p. 44; Hawkins and Law, 2005). This reduction in R&D efficiency is suggested to necessitate pharmaceutical companies to realign their R&D notions. It is argued that top pharmaceutical innovators should aim to follow knowledge creator or knowledge integrator models where innovation is created internally or by integrating external assets (Schuhmacher, Gassmann and Hinder, 2016). What is meant by external assets is unclear but could be argued to include involving patients and the public in helping to identify areas in need of innovation. However, companies need to accept the high costs required for product innovation using this method and ensure "a sustainable investment in R&D to generate a steady flow of new innovative drugs" (ibid, 2016).

### **2.6.1 Drug development and involvement of stakeholders**

Historically the pharmaceutical industry has guided the direction of innovative drug development but funding for medicines research is increasingly generated by patient organisations pushing for research in their area of interest. In the UK, INVOLVE was established in an attempt to counteract the “disproportionate influence of the pharmaceutical industry and academics working alone by involving patients and practitioners in developing health services research” (Oliver, 2006, p. 936). The move to involve a variety of stakeholders in guiding research in the field of pharmaceuticals is also being promoted. In a presentation to the EMA, Klaus Lindpaintner (2006) championed collaboration with all stakeholders in the quest for innovative medicines, suggesting that it will stimulate creativity and enhance learning, ultimately leading to more innovative solutions. As suggested above, the influence of the stakeholders, in the USA, is also exerting pressure on the pharmaceutical companies to be innovative.

Although clinical trials in children have undergone a “renaissance”, progress has been slow (Joseph, Craig and Caldwell, 2015). The future of children’s medicines rests on the success of clinical trials in children and greater advocacy and collaboration but deficiencies remain due to inadequate funding and “conflicts of interest with trials still being driven by financial and political incentives” (Joseph, Craig and Caldwell, 2015). Many conflicts exist in research funding with no perfect solutions. Two opposing forces are “top down” research and “bottom up” research that responds to requests from those seeking funding who are already in the field. Top down funding is not guaranteed to resolve the problems that have been determined in government strategy and there are calls for a “diversity of funding strategies” to promote innovative ideas and give them a receptive platform (Patton, 2005, p. 1101). New sources of priorities such as those that might be generated by children could be investigated to improve innovation. Children’s

health research has for some time been locked in a vicious cycle. New research in child health needs to be funded if the clinical evidence base for policymaking is to improve, but the level of government funding allocated to child and family health does not reflect the importance of children. Furthermore, clinical evidence is necessary so that the funding allocated for children's health is the "best possible value" (Patton, 2005, p. 1101).

Funding for child and family health comes from many organisations and involves many disciplines and methods, with different sectors of the research community conducting research; through 'blue skies research' (basic science), and health promotion to economic analysis. Historically, funding has been inadequate and it has generally been criticised by child and family health researchers that their area of research has been viewed by funding organisations as low priority (Hawkins and Law, 2005, p. 1107). Hawkins and Law (2005, p. 1109) conducted a review of research activity across the financial year of 2002/2003 on child and family health research. They surveyed 31 organisations and found that 567 research projects were funded during this period with an estimated expenditure of £32,140,000, however only 3% was allocated to child and family health research. It can be conjectured that to improve the outlook for children's medicines, funding has to be allocated right across the broad spectrum of disciplines. To optimise investment in paediatric research funding, it is imperative that research is pursuing the right direction and to do this, it is imperative to understand what is required by children.

## **2.7 Chapter summary: the next progression**

In comparison to the superfluity of adult literature, discourse surrounding children in medical research is limited, generally sporadic and broadcast over many disciplines including pharmaceutical, medical, sociological, psychological, R&D, nursing, legal, human rights and more.

I have presented a picture of historically abusive experimentation on children, and their more recent exclusion due to over-protection stemming from restrictive ethical codes creating a generation of 'therapeutic orphans'. Children's status within contemporary Western society is in state of constant flux. New policies and interventions designed to improve pharmaceutical development in favour of children are frequently being developed and adjusted, therefore highlighting the importance of resolving participatory issues as a matter of urgency. Isolating children from the policy creation and R&D processes and treating them as incapable "lessers" could result in badly constructed policies and failure of applications. Indeed, considering children as one of the "external assets" in the knowledge creator or knowledge integrator models of drug development suggested by Schuhmacher, Gassmann and Hinder (2016) could prove beneficial when applying for research funding.

Forging close relationships between children and researchers could help to increase the impact of children's agency in medicines R&D. This was proven to be effective in the Young Lives initiative, which introduced discussions between government and children and young people. This gave children a voice and expanded the "concepts of participation and grassroots democracy" (Jones and Villar, 2008, p. 14). The issue in children's medicines R&D is whether children's ability to help problem solve is acknowledged and whether the concepts of children's participation can be shifted in order to operate a "grassroots democracy" within this paradigm.

Children's participation in medicines R&D and policy creation at a basic level, creating an open, dynamic, valid and interactive platform, is in my opinion, the vital next step in the medicines for children story, but a dialectical relationship between children, researchers, funders and policy makers can only transpire with a radical alteration in attitude and practice globally. The

aim of involvement then is arguably empowerment. I recognise that this is a grossly simplified summative sentence, but one which forms the foundation of my research ethic; to involve children and more specifically children challenged by chronic conditions in the research process.

## Chapter Three: Theoretical perspectives

### 3.0 Overview

In this chapter I discuss the theoretical perspectives that governed my approach to conducting research. I provide a brief overview of the epistemological foundations of this research, that of social constructionism, addressing the current debates within this theoretical paradigm both advocating and critiquing its application. I indicate concepts and issues that are important to this study, in particular with regard to the concepts of my *a priori* (initially influential) theories and *a posteriori* (retrospectively applied) theories, which I also introduce and discuss in this chapter.

### 3.1 Researcher development – epistemology and openness

Throughout the research process I considered my personal history and experience and how this might impact on my contribution to children's medicines R&D discourse (McKenzie, 2017). This practice is known as *reflection, reflexivity or reflective practice* (Finlay, 2003; McNair, Taft and Hegarty, 2008). There are nuances between these terms, as they have been interpreted and utilised differently over recent years within qualitative research. In general, this practice refers to the way that researchers think about (*reflect*) on their own personal contribution to the research process and act on (*reflexivity*) aspects of their personal learning (McNair, Taft and Hegarty, 2008).

Who I am and my position in this research is inexorably influenced by my previous experiences; personal and professional, physical and mental,

tangible and abstract. My position has developed and changed during the time that I have been conducting this research. By being a player in the social contexts in which I have been present in the perpetual process of my own life, and by the process of immersing myself in this research, 'I' have changed. The PhD has been described by many as an academic apprenticeship, an induction period into the practices and values of the academic community (Finn, 2005). It is also metaphorically likened to a journey (Finlay, 2003) or, at the extreme, an adventure (Willig, 2013). Willig (2013) asks us to think about what 'adventure' means and how it incites responses such as 'new' and 'as yet unknown' or 'something we have not experienced before'. Yet at the same time there are negative connotations such as 'risk' (2013, p. 4).

*"Talk of an 'adventure' captures the imagination. We want to know what it was like, how it felt, what happened next. We look upon the adventurer as someone who has been changed by the experience, someone who will never be quite the same again."*  
(Willig, 2013, p. 3)

I concur that once the research 'adventure' commences researchers take a moderate risk, investing a huge amount of time, energy, emotion, and thought into answering questions. However, I feel that the risk is never too great, as questions are usually generated from a personal or professional motivation and so are of great importance both to the researcher and society.

As a researcher it is vital to be explicit about prior knowledge (Potgieter and Smit, 2009), experiences, motivations and choices that I have made during this PhD apprenticeship (Hillman and Ethics, 1995). Taking a critical stance on my epistemological position, allows for a clearer understanding of me as a researcher and the research presented in this thesis.

### 3.2 Epistemological perspectives and ‘objectivity’

The theoretical stance that I applied to this study involved a lengthy process of reflective questioning. One cannot, and indeed should not, work under the pretence of viewing the world in a particular way just to suit a piece of research. A researcher cannot produce valuable and honest work, if they are attempting to write from a perspective that is completely alien to them. I was compelled to stop and think honestly and thoroughly about the optic through which I view the world.

Stronach (2005) in a chapter discussing the key concepts of philosophy, argues that “[m]ost new researchers tend to start from philosophical positions that match their already existing political inclinations ...”. Epistemological reflexivity’ as suggested by Carla Willig (2013) involves a self-analysis of the researchers assumptions about what it is possible to be known and studied. She suggests that researchers engage in ‘epistemological reflexivity’ as a means to uncover ‘facts’ represented by the data and is a valuable resource that can enhance research. In the spirit of epistemological honesty, I now present my ‘epistemological reflexivity’. I want to make explicit that where I started from in the processes of commencing this PhD research, is *not* where I started from when writing up this research. To clarify, I am a healthcare practitioner, scientist, anthropologist, and philosopher. Initially my approach was governed heavily by positivist ideology. Positivism has historically shaped much of Western scientific thought and concepts, and is founded on the essentialist principle that reproducible and controlled scientific enquiry can define ‘truths’ (Burr, 1995; Burr, 2003; Etherington, 2004; Willig, 2013). These traditional analytical methods assume that the world is predictable and that these ‘truths’ and outcomes can only be scientifically confirmed by observation. Therefore, when I embarked upon

reading the literature about theoretical perspectives, I expected to confirm that my views were formed by reductionism. My natural science background encouraged me to view the world as having one scientific 'truth'; provable or disprovable, right or wrong. This reductionist approach meant that I did not allow for nuances and this filtered through to my academic writing.

It is not unusual that I held these views, as whilst studying medicine, pathology and pharmacology, this was the taught scientific approach. Several studies suggest that medicine continues to be a positivist science. Walsh and Gillett (2011) in their paper examining whether evidence-based medicine is positivist conclude that it is positivist, as it emphasises observation, verification and method over theory, so differentiating itself from complementary and alternative medicine by following scientific theory. Tavakol and Zeinaloo (2004), in a paper discussing the positivistic tendencies of medicine, suggest that the method of medical inquiry employed by epidemiologists and biostatisticians is positivist (quantitative) due to the types of studies undertaken: case-control studies (retrospective), Cohort studies (prospective), randomised clinical trials and survival analysis. They conclude that quantitative and qualitative research are neither better nor worse than each other but are complementary. They also conclude that:

*“While qualitative researchers have made a great effort to find the position of qualitative inquiry approach in health services research, clinical staff cannot easily accept the research methodologies of social sciences, in which the generation of hypotheses replaces the testing of hypotheses, explanation replaces measurement, and understanding replaces generalisability.” (Tavakol and Zeinaloo, 2004, p. 79).*

Conversely, due to much reading and a modicum of research experience, my 'view' has changed and shifted away from positivism. When I deliberated my approach to life and people, I concluded that my lens is

shaped by the acceptance of difference and a desire for fairness and equality. Positivistic approaches have great importance in scientific enquiry, for example in the case of clinical trials. However, when conducting this research about people's perspectives, my view is that the world is perceived differently by each and every living Being; perceptions that are constantly changing with each moment a Being interacts with their environment. This is in line with a number of qualitative research traditions that challenge the positivist approach; traditions that theorise that knowledge is founded upon supposition and examination of phenomena from a subjective position. This legitimises the influence of a researcher's own views and personal experience in the interpretation of the data and allows and accepts that there are many ways of understanding phenomena and gaining knowledge.

*"... even the most objective observers or interpreters bring themselves and their prior knowledge and personal and cultural histories into the equation."* (Etherington, 2004, p. 46)

I translated these characteristics into academically recognisable and acceptable terms and concluded that I am, by definition, a social constructionist. This is the approach I have chosen, and I am therefore an advocate of conducting my interdisciplinary research from a social constructionist perspective; a perspective that considers the social, cultural and historical influences on knowledge formation. This position has undoubtedly influenced my choices and directed the theoretical and methodological path I have trodden throughout this research evolution.

Despite advocating epistemological honesty, I find it easier to announce what I am *not*, rather than what I *am*, because the *not* elements of who I am have proven problematic during the course of this research and are therefore more tangible to me. Firstly, I am *not* a trained psychologist, yet

most of my influences and preferred reading has come from this academic discipline, more specifically, social psychology. Nor am I a lawyer, linguist, or teacher and as such I have felt overwhelmed by the often-complex theories emerging from these disciplines on children and participation. Despite being learned in academic medical terminology, I was *not* familiar with the exclusive and often technical languages employed by many writers in these fields; language that excludes all but those well versed in the respective disciplines. I have had to grasp these new languages and philosophical theories, dissect my own knowledge and existence in this research and interpret information in a way that, as a medical scientist, I have not previously had to do. The process of which, although challenging, has helped me to analyse and understand the data that I generated, and produce a valid, robust and, I hope, engaging thesis.

My desire for objectivity and candid research caused me to think about and identify my motivations, previous experiences, strengths, weaknesses, and biases. These processes, known as reflection and reflexive practice, have helped me to understand my changing position in this research.

Reflexivity aims to reduce bias by permitting the process of subjectivity to flow throughout the research. Apart from being a means of scrutinising likely causes of subjective bias, Etherington (2004) also views this as essential to qualitative research methodology and can be used as a “primary methodological vehicle for an inquiry” or a way of bridging the gap between research and practice. Furthermore, its use is also considered a sign of high-quality research by its advocates. For example, Sandelowski and Barroso (2002) in their study into the problems surrounding locating the findings in qualitative research state that:

*“Reflexivity is a hallmark of excellent qualitative research and it entails the ability and willingness of researchers to acknowledge*

*and take account of the many ways they themselves influence research findings and thus what comes to be accepted as knowledge. Reflexivity implies the ability to reflect inward toward oneself as an inquirer; outward to the cultural, historical, linguistic, political, and other forces that shape everything about inquiry; and, in between researcher and participant to the social interaction they share.” (Sandelowski, 1994, p. 222)*

Reflexivity has helped me to understand who I am and helped me to identify how what I have experienced has impacted on the design and content of this thesis. Additionally, it has helped me to understand how the process of conducting research and engaging with the relevant discourse and participants had impacted on me as a healthcare practitioner and researcher.

Engaging in this process of reflection and reflexive practice has helped me develop my theories and analytical approach. The terms ‘reflection’, ‘reflective practice’, ‘reflexivity’ and ‘reflexive practice’ are known to carry multiple meanings (Finlay, 2008) and the processes are often conflated and oversimplified (Lambert, Jomeen and McSherry, 2010). At this point, I must stress that from my experience I see reflection and reflexive practice as two distinct processes, with reflection being more theoretical (passive) and reflexivity being more methodological (active). Reflection focuses on thinking about an event or experience and its positives and negatives, remaining connected to the past, to events that are finalised. Reflection influences future action, in other words changing what one might do or be in the future, this is the process of reflexive practice, the point where researchers’ experiences are processed and applied. I view reflexive practice as pro-active, a tool to stimulate improvement in practice and impact on research, participants and the researcher. Whereas reflection promotes introspection of self after an experience, reflexivity takes that introspection and applies its findings to provide a route for change. Practices such as

education, nursing and psychotherapy endorse reflection as means of self-development (e.g. Finlay, 2008; Ryan, 2006; Sandelowski and Barroso, 2002).

The Harvard lecturer John Dewey is generally credited with the origin of the necessity to reflect on practice and have awareness of our actions, in his lectures on aesthetics. He argued that: *“all direct experience is qualitative, and qualities are what make life-experience itself directly precious. Yet reflection goes behind immediate qualities, for it is interested in relations and neglects qualitative setting”* (Dewey, 1934).

If we do something and lack awareness of how the composite elements of this action are related, this can inhibit personal understanding and development. It hides how one constructs one’s ideas, beliefs and approaches to understanding phenomena and denies insight into how we interact within our society and the world in general. The lens through which I initially viewed my inductive/deductive study consisted of a combination of theories; social constructionism and contemporary theories of childhood. Now, I will discuss these *a priori* theories that have informed this research and the issues of combining disciplines and theories.

### **3.3 Social constructionism - definitions, characteristics and debates**

*“Relativism is a way of being nowhere while claiming to be everywhere equally”* (Haraway, 1991, p 191)

The 'equality' of positioning is a denial of responsibility and critical enquiry. Relativism is the perfect mirror twin of totalization in the ideologies of objectivity; both deny the stakes in location, embodiment, and partial perspective; both make it impossible to see well. Relativism and totalization

are both 'god-tricks' promising vision from everywhere and nowhere equally and fully, common myths in rhetoric surrounding Science. But it is precisely in the politics and epistemology of partial perspectives that the possibility of sustained, rational, objective inquiry rests" (Haraway, 1991, p. 191).

The principal question underpinning this research is how 'children' and 'involvement' are constructed, or talked into being by professionals, practitioners and policymakers who make medicines and shape the course of children's medicines R&D. The participants in my research are involved in the social construction of 'children' and 'participation' in the medicines R&D paradigm. I address the issues surrounding a social constructionist approach to conducting research and why it is relevant to this study in terms of how it focuses the use of language in generating social phenomena or 'social constructs' relative to social context. For this study I look at how institutionalised constructs of children and children's ability to contribute to scientific research is affecting participation in paediatric medicines R&D (facilitating or hindering).

Social constructionism is associated with the emergence of postmodern and post-structuralist worldviews that, some argue, is the 'source' of this movement, examining language, knowledge (Agger, 1991) and power, viewing 'truth' as pluralistic. Postmodern worldviews, such as social constructionism challenged the long-standing positivistic orthodox approach (Delamont, 2006) that aimed to generate 'truths' based on reproducibility and controlled scientific enquiry. Constructionism gained prominence in the U.S. with Peter L. Berger and Thomas Luckmann's (1966) book, *The Social Construction of Reality*. Berger and Luckmann argued that all knowledge, including basic and taken-for-granted common-sense knowledge of everyday existence, is copied from and maintained by social interactions. People

interact assuming that their respective understandings of reality are related and as they put these understandings into play, their 'common knowledge' of reality are reinforced. Since common-sense knowledge is traversed by people, human typifications, significations and institutions come to be positioned as an integral aspect of objective realities, particularly for future generations of people who inherit the outcomes of the original processes.

Social constructionism starts with the concept that there is no single location from which to view the world. Therefore, social construction is founded on the principle that individuals perceive the same phenomena idiosyncratically and thus construct them differently (Crotty, 2003, p. 79). Therefore, social constructionism is a theory of knowledge based on how social phenomena or “objects of consciousness” evolve within social contexts. It recognises all forms of knowledge and knowing as determined and formed by cultural and historical “preoccupations”. A ‘social construct’ or ‘social artefact’ is defined as a concept or practice constructed by a particular group (Bourdieu, 1996; Cojocaru, Bragaru and Ciuchi, 2012; Shotter and Lannamann, 2002). These artefacts such as ‘children’ and ‘involvement’ are ‘realised’ through the use of language.

Social construction is reliant on contingent variables of our social selves as opposed to the inborn qualities that an object or process possesses. The focus of this research then is the notion of ‘the child’ and ‘involvement’, what these idioms include and/or exclude and their meanings to an individual can be argued to be non-existent in the ‘real’ world, but only within and via the social institutions that assign meaning to the term. Postmodern social constructionism contextualises the understanding of ‘reality’ and the use of terms to represent this ‘reality’ within patterns of relationships and the history underpinning specific cultures or institutions (Burr, 1995; Willig, 2013). Social

constructs are generally understood to be the derivatives of innumerable subjective and inter-subjective human interactions, choices and experiences, as opposed to laws based on “divine will” (Berger and Luckmann, 1966) created in a vacuum. These constructs are generally internalised and incorporated into our being and its cognitive processes, unconsciously serving as the lenses that shape our worldview; helping people make sense of not only themselves but the myriad of ‘chaotic and meaningless experiences’ that one is exposed to throughout their lives (Burr, 1995; Burr, 2003; Parker, 1998). For example, a medical researcher’s subjective experience of children’s involvement in R&D is influenced by the discourses, institutional disciplines and wider cultural constructs that define the idioms ‘children’ and ‘involvement’, which in turn affects how children’s involvement is viewed and received within this discipline. I argue that terms ‘children’ and ‘involvement’ do not sit happily together in the medicines R&D paradigm. Indeed, children’s participation has not been constructed and is therefore viewed as a violation of the norm in this context, resulting in children being alienated from both the discourse and the normative practices of paediatric medicines R&D.

*“The alternative to relativism is partial, locatable, critical knowledges sustaining the possibility of webs of connections called solidarity in politics and shared conversations in epistemology.” (Haraway, 1991, p. 191)*

I am aware that there are issues surrounding data generated from the social constructionist epistemological foundation and arguments exist for and against its application. Due to the relativistic stance of social constructionism it attracts many criticisms (Stam *et al.*, 2001) and presents the researcher with numerous limitations. The lack of a single standpoint and which standpoints can be identified as or labelled as social constructionism is confusing (Stam *et al.*, 2001, p. 294). It is also argued that social constructionism is fragmented,

utilising many sources and defines itself in various ways; being different things to different people. Further critics view the theory as being flawed by internal contradictions (John Maze as cited in Stam *et al.*, 2001), failing to distinguish content from process, i.e. 'Self' is dramatically different by culture but processes to generate the 'Self' are the same (Adelbert Jenkins as cited in Stam *et al.*, 2001). Jenkins argues that dialectically, the ideas of 'Self' and 'other' are mutually created and sustained and that this humanistic conception prevents the individual and the sociocultural processes that are vital for our understanding of people.

In the case of this research, I considered that I would encounter individuals with polarised views of medicines R&D. Medical researchers are generally viewed as *the people who do construct children's medicines R&D*. Medical researchers might construct medicines research as: the discovery of new chemical entities, pharmacokinetics, pharmacodynamics, designing and executing clinical trials and publishing papers. These constructs are formulated from the perspective of the medical researcher, someone who has trained in medicines, pharmacy, chemistry or pharmacognosy and operates within the context of pharmaceutical R&D processes. The medical researchers are creating medicines to be used by children but the constructs of medicines research from the perspectives of researchers and children might be very different. Currently children's medicines research does not consider the views of children, so for this research I moot that children are *the people who could construct children's medicines R&D*. Children might construct medicines research very differently for example, as: ways of finding better tasting medicines, improving ways of taking medicines, making them feel better or finding cures to diseases. People who consider themselves to be constructionists, often view constructionism as being a liberating theoretical approach. Advocates of this theoretical perspective view constructionism as a

conduit for the voice of oppressed populations, by recognising their views of the world rather than forcing the views of the dominant/powerful groups in their societies upon them. Constructionism also gives voice and credence to the views of the unheard populations, as there is no benchmark for judging inferiority; all views count. Furthermore, it is suggested that advocates of this perspective are able to transcend and elucidate the concepts of a society and the balance of power (Acharya, 2000, p. 184; Tan, 2006, p. 244). However, social constructionism does not always perpetuate fairness. There are instances where constructionism can work malevolently, by harbouring negative social constructs that can suppress, rather than liberate, members of society and perpetuate bad ideas (Hacking, 1997). Although I can classify my characteristics as similar to those of social constructionists, my characteristics are not set and have shifted in the past and may again in the future. I find myself conducting internal arguments (reflecting) about whether this theoretical perspective over-simplifies my thought processes. My inherent qualities determine my personal theoretical perspective but each piece of research that I conduct will be shaped by idiosyncratic theoretical perspectives; perspectives formed by the topic being researched, the discourse that surrounds it, and new experiences that might influence the way I view the world. Reading different literature and therefore being exposed to different theories will create unique combinations of theoretical perspectives. For this research, my idiosyncratic *a priori* views are influenced by theories of childhood and my *a posteriori* views shaped by theories of internal role conflict.

### **3.4 Chapter summary**

Social constructionism and contemporary theories of childhood provided a framework for understanding how current processes and practices have arisen in children's medicines R&D. The relevance of social

constructionism to this study is its focus on uncovering the ways in which individuals and groups of people contribute to the construction of their perceived social realities; how phenomena are created, institutionalised, known, understood, and traditionalised by humans. Social construction is chronologically fluid, as components of reality and objects of knowledge, both tangible and intangible, are not set by nature, and must be continually reaffirmed and sustained in order to endure.

If all knowledge is derived from and maintained by social interactions as was suggested by Berger and Luckmann (1966), then excluding children from discourse or social interaction can be argued to be distorting the social construction of children. People interact and do so with the understanding that their respective perceptions of 'reality' are related and when they act upon this understanding, common knowledge becomes reinforced. People negotiate common knowledge and therefore signification and institutions come to be presented as part of objective reality, or "givens", for future generations. Is it to be a "given" that children are not capable of contributing to scientific advancement of paediatric medicines due to institutionalised objective realities of childhood? This was one of the initial conundrums that inspired this research.

## Chapter Four: Methodological foundations, research design and ethics

### 4.0 Overview

My intention in this chapter is to discuss the methodological approaches involved in this study, commencing with the multimethod approach. I then discuss the methodological underpinnings of the components of the research: systematic reviewing, thematic analysis and Bakhtinian discourse analysis. The central concepts and practices relevant to this study are discussed, my rationale for elucidating data by analysing the spoken word and Bakhtin's principles used in this research and their application.

### 4.1 Methodological foundations

I adopted a multimethod, or multiple-method, research design (Gubrium *et al.*, 2012) to investigate the research question, an approach first recognised in the late 1980s (Brewer and Hunter, 1989) which has gained popularity in many disciplines, including the social and health sciences. Multimethod research includes the use of more than one method of data collection (Creswell, 2009; Creswell and Plano Clark, 2011). 'Mixed methods' research has a more specific definition of mixing of qualitative and quantitative data, and my analytical focus is qualitative (Barbour and Schostak, 2006). Following a multimethod approach as opposed to monomethod, facilitates data triangulation which provides a more comprehensive view of the research phenomenon (Johnson, Onwuegbuzie and Turner, 2007; Sargeant, 2012). In multimethod research designs each both core and supplementary components

are considered complete research outputs (Morse, 2016). , as opposed to mixed-methods research where supplementary components are not considered complete but only to be interpreted in the context of the whole study i.e. the data is too 'thin' to stand alone (ibid, 2016). Therefore, for multimethod research, issues of inappropriate sampling and analysis do not arise, and components can be published as standalone research, as well as integrated in the results narrative that combines all the complementary components (ibid, 2016).

This study consists of three components. The core component being key informant interviews. To better understand interviewees operational context within and the evidence that exists on children's involvement, two supplementary components were executed. Although the methods selected were different: systematic reviewing (speeches and research evidence) and key informant interviews, the main analytical approach was qualitative in nature.

Qualitative research is commonly used to understand stakeholder perspectives and their attitudes towards health service delivery (Hodges *et al.*, 2007, p. 361; Marshall *et al.*, 2009). It is a relevant approach for this study due to its application for contextualising complex processes and giving insight into new or relatively unexplored areas (Clarke and Jack, 1998, p. 845). The data that are generated from qualitative studies are multi-dimensional, allowing the researcher to witness reactions to the questions or situations being experienced, so the feelings, attitudes, tone, body language and facial expressions can all be recorded. Further, qualitative data is increasingly suggested to have clinical application, including understanding and enhancing patient involvement (Kearney, 2001b, p. 145), the focus of this study.

An essential tenet of qualitative methodology is that "researchers cannot be truly neutral or detached from data generation and analysis" (Clarke and Jack, 1998, p. 845). The process of self-examination and personal appraisal

aids to reduce potential problems, such as bias, during the process of conducting a study (Finlay and Gough, 2003; McNair, Taft and Hegarty, 2008). To retain the critical freedom and maintain flexibility within the research process (Strauss and Corbin, 1990b), my methodological approach matched the characteristics of grounded theory.

Grounded theory is a methodological 'framework' that can be utilised to construct or create novel theories via analysing research generated data (Strauss and Corbin, 1990a); suited to the study of "processes of contextualized understanding and action" (Kearney, 2001a). In the case of this study, two components involve examining oral discourse to generate theory on how children and involvement. As theory is extrapolated from the data, it is "likely to offer insight, enhance understanding and provide a meaningful guide to action" (Strauss and Corbin, 1990a, p. 12). Grounded theory facilitated the freedom to be critical, think abstractly, be flexible, and open to criticism, whilst acknowledging my role in the research, my motivations, fatigue, sensitivity and research credibility. Within the context of grounded theory, I employed three studies using two research techniques: a speech analysis, systematic review and key informant interviews. Methods for each study are presented in Chapters Five to Seven. These methods were vehicles to generate theory regarding professionals' views of children's involvement. Systematic reviews using inductive analytical methods share much with grounded theory in that reviewing facilitates synthesising data from multiple sources allowing space to generate theory (Thomas and Harden, 2008b). Interviewing is now synonymous with qualitative research and may be the "accepted method of data collection irrespective of methodology" and viewed as "generic and lack a clear connection to the methodological framework" (Wimpenny, 2000). Interviews served to generate theory surrounding attitudes, constructs, opportunities, facilitators and barriers to children's participation in medicines R&D, thus are particularly suited to the methodological approach of grounded

theory. Finally, using grounded theory as an approach to data analysis strives to ensure that the theories evolving from the data analysis both ‘fit’ and ‘work’ (Glaser and Strauss, 1967, p. 3) and an interconnectedness between data and theory is maintained to ensure credibility and relevance. Reflection on the data facilitates interconnectedness, thus encouraging theory to emerge (Hibbert *et al.*, 2014). Grounded theory links with the philosophical positioning of **pragmatism**, attributed to the Anselm Strauss’ sociological foundation in the Chicago School tradition (Bryant, 2009). Pragmatists aim to solve problems by focusing on real-world practices and the consequences of action, to bridge the gap between theory and practice (Creswell, 2009; Morris, 1934) and grounded theory positions the act of theorising as practice (Charmaz, 2006).

*“A social constructionist approach to grounded theory allows us to address why questions while preserving the complexity of social life. Grounded theory not only is a method for understanding research participants’ social constructions but also is a method that researchers construct throughout inquiry. Grounded theorists adopt a few strategies to focus their data gathering and analysing, but what they do, how they do it, and why they do it emerge through interacting in the research setting, with their data, colleagues, and themselves.”* (Charmaz, 2008, pp. 397-398)

There are many schools or methodologies within grounded theory. I will not attempt in this thesis to go into all of these but I would guide the reader to Udo Kelle’s chapter in *The SAGE handbook of grounded theory* (Kelle, 2007). I was guided by Kathy Charmaz’s (2008) constructionist grounded theory, the pragmatist roots of the methodology and the ability to address the *what, how* and *why* questions matched with my research. Holton (2007) suggests that grounded theory can fit any research paradigm saying:

*“Grounded theory methodology in the classic sense, does not fit within established research paradigms whether positivist, interpretivist, postmodern, or otherwise; rather, as a general methodology, classic grounded theory transcends the specific*

*boundaries of established paradigms to accommodate any type of data sources and expressed through any epistemological lens. Yet, the varying perspectives on what constitutes grounded theory and how it should be conducted presents the researcher with a baffling array of methodological options that have more the shape of a maze than a roadmap for guidance and clarification.” (Holton, 2007, p. 268)*

Grounded theory is nested within my qualitative inquiry to help investigate both the implicit and explicit meanings and responses of the participants with respect to children and involvement. This approach also encourages the use of reflective-reflexive responses acknowledging the researcher’s view and bias.

In summary, grounded theory combined with Bakhtinian discourse analysis (see section 4.4) is fitting for my research for three key reasons. Firstly, my research question is one of investigating processes (i.e. how involvement is realised and implicated in professionals’ operational R&D endeavours) to which grounded theory is particularly suited (Charmaz, 2008; Glaser and Strauss, 1967; Kelle, 2007). Secondly, pragmatically speaking, Bakhtinian discourse analysis addresses the interview interaction and institutional voice but does not allow the freedom to generate new theories. Thirdly, my research question has not been addressed with these professionals before and grounded theory is particularly useful in novel areas of study (Bryant, 2009; Kelle, 2007). In combining these methodological approaches I have openly aligned my epistemological, philosophical, theoretical and methodological perspectives as suggested by Michael Crotty (2003).

## **4.2 Systematic reviewing as a method**

Systematic reviewing is a means of gathering together existing primary research in order to understand what is known or indeed not known about particular topics (Gough, Oliver and Thomas, 2017b; Higgins and Green, 2011).

This process can help to guide new 'primary' research undertakings and also ensure that researchers do not unnecessarily repeat research (ibid, 2017b). Systematically reviewing qualitative research stemmed from the understanding that evidence based healthcare and health policy needed a breadth of evidence that extended beyond the "rationalist' model of systematic reviewing of quantitative research (Tong *et al.*, 2012). The benefit of conducting systematic reviews of qualitative research is the insight provided into: human behaviour, emotion, attitudes, motives and experiences (Tong *et al.*, 2012) affording researchers to draw together evidence based on the need to understand particular populations views on matters that affect them. Noblit and Hare (1988a) suggest two types of qualitative synthesis integrated reviews that aggregate and summarise the data often thematically and interpretative reviews that interpret the data. However, over time many ways have been described: meta-ethnography, grounded theory, textual narrative synthesis, meta-study, meta-narrative, critical interpretive synthesis, ecological triangulation, framework synthesis, content analysis, meta-interpretation and qualitative meta-summary (Barnett-Page and Thomas, 2009; Noblit and Hare, 1988b; Oliver *et al.*, 2008a). One of the newest products of systematic reviews is mapping of research evidence. Systematic mapping provides insight into both the nature and extent of evidence, but also is able to reveal what is unknown the 'gaps' in research. The process of mapping research evidence in the form of systematic maps to understand what is known *and* unknown has grown in frequency in recent years (Miake-Lye *et al.*, 2016). A recent study into the use of systematic mapping found that, back in 2002 no evidence maps were published and in 2010 only ten evidence maps could be identified (ibid, 2016). Evidence gap maps, or evidence and gap maps, have proven popular particularly with the field of policy development (Gough and Thomas, 2017) and are a particularly useful tool to help researchers navigate through diverse and complex landscapes (Stokes *et al.*, 2017a), especially in the light of the rapidly increasing numbers of published research (Bornmann, Mutz and

Technology, 2015). The qualities of systematic reviews were suited to address a key element of this thesis in terms of understanding: the extent to which children views had been elicited for medicines research; what children were contributing to the knowledge base for medical researchers; the nature of research in which they had been involved

### **4.3 Discourse analysis as a method**

Discourse analysis is a generic term for multiple practices used in the examination of spoken, textual, visual (semiotic) and aural communication. Simplistically, discourse analysis is the “study of language in use” (Wetherell, Taylor and Yates, 2009, p. 3). The discourse generated is perceived as a social action, being both 'productive and constitutive', therefore 'language both creates social phenomena and is representative of social phenomena' (Morgan, 2010, p. 1). Discourse analysis can be used to analyse power struggles and the impact of institutions, making it an ideal method for understanding and critically analysing practices in the health related and medical sciences (Gotti and Salager-Meyer, 2006)<sup>6</sup>. Further it can be used to analyse the whys and hows surrounding issues, provide insight into attitudes (Antaki *et al.*, 2003; Burman and Parker, 1993; Parker, 2014; van Dijk, 2006), therefore is suited to provide insight into social constructions of children and participation from those working in the field of medicines research. Investigating the potential for children's involvement on in children's medicine R&D can be argued to be dependent on the social constructions of these artefacts. Children's involvement can only evolve with the willingness and receptiveness of those conducting the research (Berwick, 2003; Staley, 2017). It is important to understand how professionals involved in medicines R&D view children and

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<sup>6</sup> A useful collection of works edited by Gotti and Salager-Meyer (2006) entitled *Advances in medical discourse. Oral and written contexts*, which looks at sociolinguists in the medical world.

their involvement before strategies are implemented to ensure a process that benefits for both children and researchers.

#### **4.3.1 Issues with discourse analysis**

The use of discourse analysis is a relatively recent occurrence in research terms. Discourse analysis as a methodology comprises of a complex terrain with disparate approaches in terms of method, theory and the nature of discourse (Antaki, Billig, Edwards and Potter, 2003). There is conflict between the aims of discourse analysis and the associated styles of work produced (Billig, 1999; Stokoe and Smithson, 2001; Wetherell, 1998). Quantitative researchers often feel that discursive practices lack credence and thus dismiss the work as non-methodological or systematic and just that 'anything goes' (Antaki et al., 2003); and whether the textual structure of discourses are autonomous from and external to the subjects that generate them (Ruiz Ruiz, 2009) thus questioning whether discourse analysis is analytical method at all.<sup>7</sup>

Potter and Wetherall (1987, p. 159) warn that “developing an adequate theoretical understanding or interpretation is at least as important as perfecting a cast iron methodology”. In the first article of his then newly founded journal *Discourse and Society*, Teun van Dijk emphasises the requirement for 'explicit and systematic analysis' to be founded on 'serious methods and theories' (van Dijk, 1990, p.14). Yet even now I do not feel that this has been addressed. With caution still being expressed regarding formulaic approaches to analysis and methodological stages, this leaves researchers in a difficult position. Indeed, how can this change unless there is consensus.

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<sup>7</sup> For a comprehensive discussion on the problems associated with discourse analysis see Parker and Burman (1993, pp. 155-172) who identify a rather specific thirty-two problems with discourse analysis including methodological, epistemological and political issues.

### 4.3.2 Identifying the right approach to discourse analysis

Discourse analysis has been utilised extensively in various disciplines with some writers suggesting that there are fifty-seven types of discourse analysis (Gill, 2000, p. 173). I found the boundaries separating these ambiguous and looked for a more clearly defined descriptions of the types of discourse analysis approach. Wetherall *et al.* (2003; 2009) describe the types of discourse analysis within psychology, as 'traditions' and outline six different traditions of discourse analysis: conversation analysis; critical discourse analysis; discursive psychology; interactional social linguistics; Bakhtinian discourse analysis; and Foucauldian discourse analysis. These 'traditions' are often competing and are situated at different points along the realist-relativist epistemological continuum, therefore they can be applied in accordance with the epistemological position of the researcher and also the research questions being addressed.

I had considered analysing institutionally based social constructions of children and childhood, as pharmaceuticals is an institution within which the key informants in this research operate that generally excludes non-scientists/medics from its world by use of technical language. I focused on examining individual constructions of phenomena and how these constructions manifested and were presented in talk. I chose a 'tradition' that allowed a less biased approach to discourse data; one with which I identified and felt could methodologically support my inquiry and allow me to concentrate on the viewpoint of participants and to take notice of the underlying discourses that have impacted on the participants' responses, namely **Bakhtinian discourse analysis**.

#### **4.4 Bakhtinian discourse analysis as a framework for investigation**

Mikhail Bakhtin's philosophical and interpretive theories, along with his ideologies, sit within the realm of social constructionism, and therefore fit with my epistemological and ontological approach to conducting research. Bakhtin's work recognises the importance of language to social interactions, relationships, power dynamics and ideologies, and is seen to be "profoundly interdisciplinary", drawing on theories, philosophies and concepts that span boundaries (Grace, 2002, pp. 25-26). His chief principle was that humans utilise voice and dialogue to convey thoughts, feelings and identities, giving an insight into an individual's personality. He suggested that the individual voices that transpire within discursive interactions are influenced by 'other' voices that are constructed within genres of discourse, and are influenced by cultural history, space and time. Bakhtin suggested that discourse is in a constant state of flux, being pulled and pushed by external and internal factors (Morgan, 2010) that are conveyed within people's words, or utterances (Grace, 2002). Therefore, social conflicts and ideologies can be proven in appraising dialogue, voice, or judgements that are conveyed by spoken or written language. The selection of Bakhtinian discourse analysis as a methodological basis for this study is based on the hypothesis that dialogue is possible for most humans through use of voice from an early age. Within dialogue, social constructs are created, realised and maintained. Simply put Bakhtin viewed language exchange as an experience; two people talking to each other in a specific dialogue, at a particular time, in a particular place (Bakhtin, 1981, p. xx). In the following sections I describe the main currencies that feature in my application of Bakhtinian discourse analysis and its application as a key methodological informant. For the purposes of this study, I have drawn on key concepts from

theories emanating from the Bakhtinian School of thought that I feel best represent the breadth and depth of Bakhtin's ideas.<sup>8</sup>

#### 4.4.1 Monoglossia and heteroglossia [*Raznorečie*]

Bakhtin (1981) uses the concepts of monoglossia and heteroglossia to describe language forms. '*Monoglossia*' refers to dominant forms of language that represent the world-view of socially dominant groups, which are positioned or imposed as unitary and total. At the macro-linguistic level, language appears to be stable (monoglossia), serving to "guarantee" mutual understanding within speech by imposing limits and rules to its use. It is "*the unity of reigning conversational [everyday] and literary language, "correct language"*" (Bakhtin, 1981).

At the micro-linguistic level there is flexibility, contradiction and resistance, this is 'heteroglossia' (Francis, 2012). Heteroglossia, meaning literally 'different-speech-ness' (Morris, 1994), is the idea that there are multifarious voices, genres and social languages that guide and influence social interactions; diversity of speech different strata present in the same language, (e.g. professional terminology, dialects, technical language or jargons), or different groups (e.g. genres, profession or culture). Thus, heteroglossia is opposed to unitary language, its diversity making it unique, and is both historical and normative.

Bakhtin generated a *heteroglossic scene* for examining the dynamics of language; such as voice, role and politics. This heteroglossic scene can be

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<sup>8</sup> Due to the nature of the Bakhtinian circle(s) and ambiguity over the source of some of the writings, it is not always possible to attribute unquestionably the source of the ideas, but I hope that I have remained true to Bakhtin in this study. For a complete historical account of Bakhtin's life or a critical account of his or the associated Bakhtinian Circle's work, theories and philosophies, I direct the reader to the writings from the Bakhtin Centre (Brandist and Branham, 2004), Caryl Emerson, Michael Holquist and Bakhtin's published work (Bakhtin, 1965; Bakhtin, 1981; 1984; 1986; 1993; Emerson, 1997; 2000; 1990; Holquist and Liapunov, 1990).

described as the playing field where the opposing forces collide. Within this scene, ubiquitous (heteroglossia or centrifugal) and unifying (monoglossia or centripetal) forces interplay in various ways in the construction, and destruction of meaning by individuals using language strategically in social settings to create new meaning. Language emerges from the heteroglot differently depending on the nature of the forces affecting it at that time. Centripetal forces (monoglossia) are seen as the pushing (authoritative, fixed, inflexible discourse) that keep language contained and controlled moving in a circular path. The centrifugal forces (heteroglossia) are more powerful, acting to pull the language apart and these forces are subjected to a complex interplay resulting in change via the heteroglot with language being merged, dispersed, silenced, amplified, diluted, and much more.

Here the concepts of *dialogicality* and the *chronotope* are introduced. Dialogicality refers to the idea that within vocal interactions there is always one other voice implicit in the *utterance*. The *chronotope* infers the spacio-temporal nature of language – how situation and time influence an interaction. Bakhtin's epistemological foundations of narrative space and time originate from Emmanuel Kant's philosophy and Albert Einstein's relativity theory (Bemong and Borghart, 2010).

#### 4.4.2 Dialogism

Whereas heteroglossia describes the different languages being used, **dialogism** (double-voicedness) is the way languages interact. Not to be confused with dialogue, dialogism, is a vehicle that facilitates exploration of 'voice' and its authorship – how it is realised, constructed, enacted, and interpreted by others. Rather than 'voice' being viewed as a singular phenomenon, Bakhtin holds that there is always more than one voice talking at any one time and that there are no neutral words as, once words are used, they are loaded. He viewed *voice* as a collaboration of a multiplicity of internal and

external dialogues that are employed by an individual to facilitate communication with an 'other' (even when no 'other' is evident). In this approach, attention is focused on the extent to which voices are strategically employed and how these voices change or create meaning in social encounters. A simple example regarding the variation of meaning of simple utterances depending on the socio-historic and local context of articulation/hearing in the context of children's participation could be a participant forming an utterance such as 'Children are really helpful'. This utterance on reading suggests that the participant values children's input. However, if this utterance is spoken in a resentful or sarcastic tone its meaning shifts to a construction of children as a hindrance. Therefore, context is essential.

Language carries with it history, where meaning is born and dies, ventriloquating man (Bakhtin, 1981). "Ventriloquation" is how Bakhtin described the concept of internal dialogue of voices, an action where experience is linguistically formulated within the available "speech genres" in a particular space and time. He suggested that all words are only partially our own, they belong to others who have used them before and only become our own when the speaker inhabits it with their own intentions. Therefore, we all speak, position, and actualise ourselves through the voice of others, i.e. "ventriloquate".

I suggest that capturing 'voice' and its ventriloquistic properties is vital to understanding openness to children's involvement. Bakhtinian theory is an eclectic approach to discourse analysis and multidisciplinary like my own. This is suggested to be due to the influence of several academics and writers from a variety of disciplines that are associated with producing a cumulative body of work, the Bakhtinian circles (Brandist, 2002; Brandist and Branham, 2004). Bakhtin positioned himself as a philosopher as opposed to a literary critic and theorist, but Bakhtin scholars suggest the necessity to read Bakhtin

from an ideological perspective as well as a philosophical one. I read Bakhtin purely to understand voice as a social and ideological act, and to help me to identify what influences the voice of the adult professional in children's medicines discourse<sup>9</sup>. See Figure 4.4.1 for a diagramatised portrayal of my interpretation of Bakhtin's dialogic interaction.

#### 4.4.3 Authors and heroes

For Bakhtin there are two protagonists in the voice; the hero and the author. The Bakhtinian **hero** is the person who attempts to communicate; and the **author** is the interpreter, the one who attempts to understand what is being communicated; this can be one in the same person. My role as a researcher employing dialogic approach is to focus on the dialogue between **hero** and **author**. The participants in this instance are both **heroes** (message givers) and **authors (internal)** of what was being generated in the interview setting. I was the evaluator or the **external author**, interpreting what was being said and producing meaning in the form of a thesis (see Figure 4.5.2). Medical studies that have employed Bakhtin's idea of heroes and authors centre on medical discourse, therapy and patient-practitioner interactions (Bowers and Moore, 1997; MacIntosh, Beech and Martin, 2012; Puustinen, 1999; Rober, 2005; Washburn, 2001), not, as in this study, on professionals' attitudes towards children.

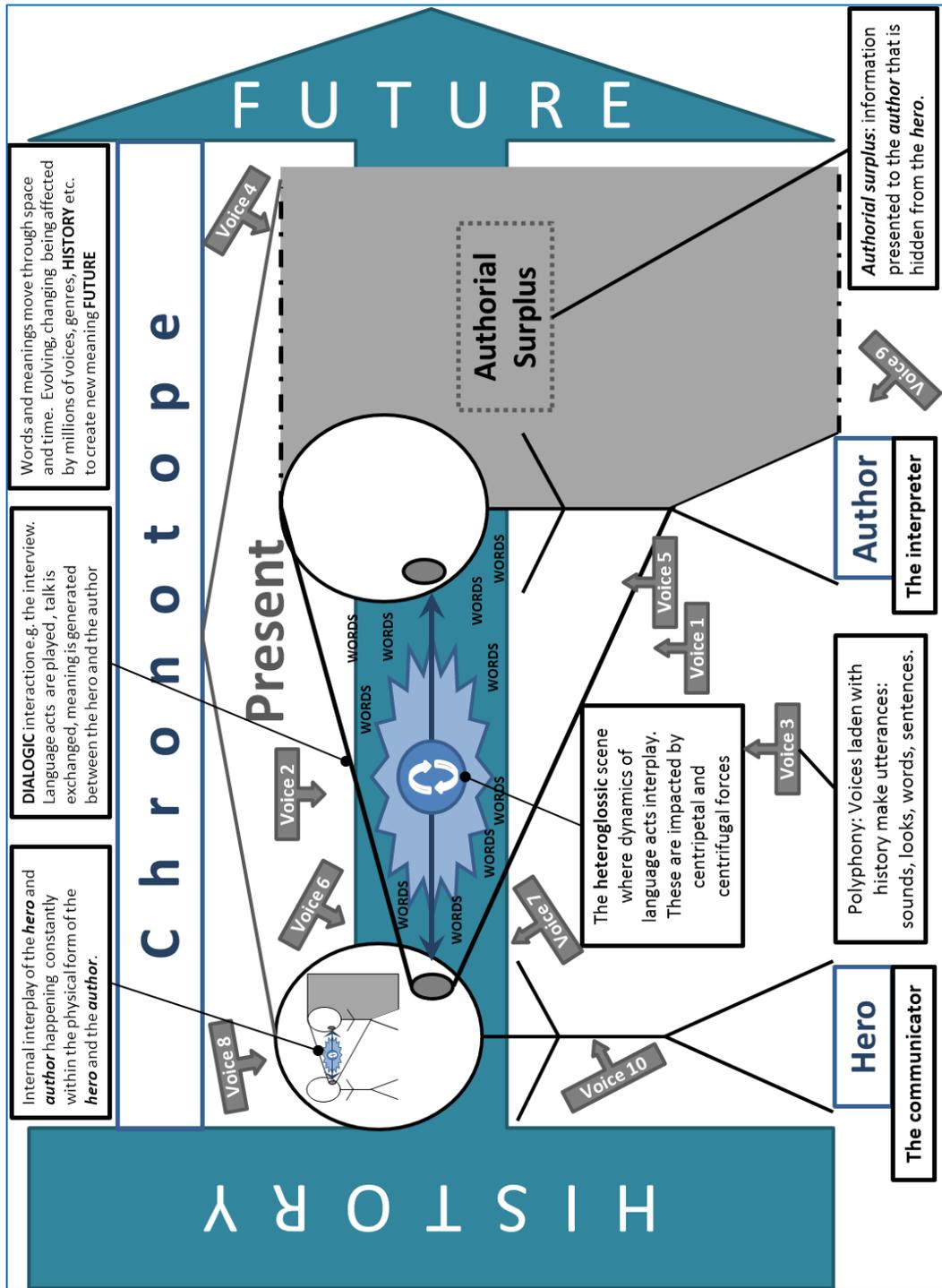
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<sup>9</sup> I avoid a political stance throughout this research. I am of a mind that political motivations for ideas and theories are personal. I do not wish to present a politically motivated study; I endeavour to avoid imposing my political views on people I encounter. This may be viewed as passive; I see this as reducing bias. Therefore, I do not incorporate the politics of the theorists whose ideas I have chosen to use. It could be argued that I am ignoring the influence on these histories on my research; however, I want to let the history of the data from the participants paint the picture, not my own views.

#### 4.4.4 Authorial surplus

Bakhtin refers to internal authorship as the **authorial surplus**, the idea that there is much more presented in dialogism or vocal social interactions than the hero (participant) can see themselves. This surplus is used to interpret what has been presented to the author (see Figure 4.5.1). As the *external* evaluator, I had the opportunity to witness the emergence of the multiplicity of voices impacting on the participant and the dynamic of the pulling and pushing (conflict) being enacted when the participants were presented with my questions. I could also explore how institution, environment, space and time had impacted on the respondents' responses.

Figure 4.4.1 Dynamics of the Bakhtinian dialogic interaction



N.B. Here I show 10 voices to represent the impact of voice. Millions of voices or just one can shape utterances: e.g. words, looks, sentences.

#### 4.4.5 Genres

*Speech genres* for Bakhtin are the disciplines from which utterances emerge and are contained within the word. The genre can be seen as the mechanism fuelling the heteroglossia; its “inner dynamics” (Grace, 2002). These genres are positioned as pliable and diverse. In a later essay entitled *The Problem of Speech Genres* (1986, pp. 60-102), Bakhtin goes to great lengths to expound issues surrounding the idea of speech genres in relation to language use and sentence formation. His motivation was that although written work has been categorised over time, with clear genres, e.g. novels, plays, commentaries, speech had never been categorised. He claims that because of the nature of the complexity of communication encompassing the diversity and the heterogeneity of genres, speech genre is therefore complex and movable, so difficult to categorise. Bakhtin posits that the disparity between perceived and true communication must be dissected and communication must not be viewed as a passive interaction between speaker and listener. He claims that listeners are reactive to speech and that the roles of the speaker and listener shift during verbal or written discourse. He argues that an individual sentence is only a fraction of an **utterance**. The creation of sentences is argued to be founded on an entire context, rather than just the sentence itself. What I extrapolated from this, was that to analyse a speech genre properly in discourse analysis, one must view the utterances as being complete and an insight into the context of what is being said. For this study, pharmaceutical R&D, policy, clinical practice and patient advocacy are the genres within which the participants operate.

#### 4.4.6 Polyphony

Polyphony, or multivoicedness, is the concept that allows all voices to stay in the act rather than giving priority to one voice. Polyphony is used to represent participant ideology as opposed to narrative events. Importance is

given to the voices and characters that remain in play during a social interaction; voices that speak for themselves and the variety of genres that have impacted on them. This was an approach employed by the 19<sup>th</sup> century Russian author, Fyodor Mikhailovich Dostoevsky, to which Bakhtin was drawn<sup>10</sup>. Bakhtin admits that his definition of polyphony is deliberately vague, stating that it is merely “a graphic analogy, nothing more” (Bakhtin, 1984, p. 22). Indeed contemporary scholars support this ambiguity of the term borrowed from music, suggesting that Bakhtin was conscious of the peculiarity of the concept and that Bakhtin’s “method of presentation may have been an ill-considered strategy to preclude the misunderstanding that he correctly anticipated” (Morson and Emerson, 1990, pp. 231-232; Steinby, 2013). Scholars remain divided as to whether Bakhtin’s understanding of the concept is extremely clear (Steinby, 2013), or “deeply counterintuitive”, as he discusses the concept of polyphony within dialogue but is not clear as to which type of dialogue (Morson and Emerson, 1990, p. 232). Based on my understanding, I have taken polyphony that I applied as an *a posteriori* method, as a way to explore internal conflict by examining the dynamics of the persuasive and authorial discourses that arose in and through the interview dialogue.

#### 4.4.7 Utterance

Utilising Bakhtin’s dialogic approach I argue to position children and participation as the social creation of symbolic construction and meaning reinforced by discourses. Bakhtin’s **utterance** is one way of addressing the data generated from the social interactions, i.e. children and involvement are constructed within social interactions that take place due to the utterances that are made within the genre of medicines R&D. These language acts are

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<sup>10</sup> I must confess here to not having read Dostoevsky’s complete works but due to time constraints only having read three novels where *polyphonism* is employed: *Poor People*, *The Idiot* and *Crime and Punishment* (Dostoevsky, 1845; Dostoevsky, 1866; Dostoevsky, 1868).

interpreted by some but not by others. To Bakhtin utterance is anything from silence to complex exchanges taking place in isolation, or within the context of genres. Utterances are language acts that are rooted within the context of genres, space and time. Utterances exist to be answered. I embraced the concept of utterances because I wanted to use it as a unit of analysis (Brandist, 2002; Brandist and Branham, 2004; Edwards, 2001; Mkhize, 2004) for the speech that was generated in my interviews. However, as the author of this thesis, there are difficulties in presenting what was said by a participant, as including one sentence from a paragraph does not present the whole meaning. The reader cannot experience the tone of voice used, the looks on the participants' faces or their body language. One would not give one letter of a word and expect a reader to understand it. If what is written or said can be understood, then the utterance is whole.



professionals, as I felt that professionals' views of children was a fundamental factor in the potential for children's involvement in medicines research and development. This chapter describes my approach to conducting this research, the rationale for my research design and how each of the elements of the research combined to create a substantive study. When conducting mixed methods research the design process is often bespoke. Each stage of my research design was borne out of consideration of the literature, the problem and my personal preference.

#### **4.5.1 Design Process**

My research focuses on attitudes of professionals involved in children's medicines R&D towards children and children's involvement. Research into this area is sparse and over-assumed. To gain insight into the challenges of and potential for children to be involved in the medicines R&D process, I had to understand children's R&D policy, what research existed had tried to elicit children's views of medicines and how the adult professionals perceived children's involvement and their attitudes towards involving children in the early stages of medicines R&D. To investigate the potential to bridge the currently large gap between researchers and the children who utilise the medicines they design, I thought it necessary to understand professional stakeholders' perceptions at varying points along the R&D chain.

This thesis comprises three pieces of primary research that are combined to provide a comprehensive understanding of the problem (see Table 4.5.1). The studies are: i) a preliminary systematic speech analysis/synthesis of political speeches that shaped the creation of children's pharmaceutical policy, ii) a systematic review of studies that have elicited children's views and iii) in-depth interviews with adult professionals involved in the development of children's medicines. The findings of each of these studies are combined to provide insight into the issues surrounding children's agency in medicines R&D,

from policy to practice in the context of a Bakhtinian discourse analysis and role theory (see Figure 4.5.1).

**Table 4.5.1 Matrix detailing the function of each of three elements of the research**

<b>Component</b>	<b>Study Component</b>	<b>Function</b>
1	Systematic speech analysis	To reveal how children are constructed within the political and policy genres of children's medicines R&D and to help inform questions for interviews with professionals
2	Scoping review	To explore the extent and nature of research that seeks to understand children's views and potential contribution to medicines research and development discourse.
3	Interviews with researchers, funders and involvement specialists	To explore the perceptions and views of paediatric pharmaceutical researcher with regard to the children's participation in early stage R&D
4	Integrating findings	To provide a clearer understanding of how children could participate in the children's medicines R&D process and to help to generate a theoretical framework for involvement.



#### **4.5.2 Component 1: A systematic analysis of political speeches: why it is important to understand what the politicians said**

After reading the EU Paediatric Regulation (European Union, 2006a; European Union, 2006b) and the Best Medicines for Children Act (United States, 2002) and finding no obvious evidence of children's input, I was inspired to find evidence of children's participation in policy governing children's R&D. If children are to be involved in medicines R&D, then it is necessary to understand how they were and still are viewed, whether they had been involved before and to what extent, and the current attitudes towards children and towards children's knowledge about medicines. A study of political speeches focusing on children's medicines has never been conducted to the best of my knowledge. This study then served to provide insight into the discourse surrounding children's medicines by generating an understanding of the attitudes and influences within the genre of children's medicines R&D. Exploring professionals' implicit/explicit attitudes towards children and childhood can facilitate understanding into existing barriers and facilitators (Moore *et al.*, 2017) to practices; in this instance resistance or acceptance of children's inclusion in the medicines R&D process. Further, it might indicate whether children's participation in the early stages of drug development is viewed as a viable venture.

#### **4.5.3 Component 2: A systematic map and scoping review**

The focus of my research is on the views of professionals towards children's involvement, but I felt a necessary to investigate whether children did indeed have views on pharmaceutical medicines which was accessible via published research and to understand the nature of their perspectives that had been researched. As previously stated, one of the catalysts that drove me to conduct this research was my encounters with children with epilepsy, who had expressed clear opinions about what they 'wished' the medicines would do for them.

#### 4.5.4 Component 3: Interviews with professionals – case of epilepsy

Having completed both a general reading around the literature on children's involvement and children's medicines (Chapter Two) and a systematic map and scoping review (Chapter Six), I found no research about professionals' attitudes towards children's involvement in medicines R&D, thus I embarked on interviewing professionals to provide insight.

Interviews are an established and recognised qualitative research tool that sit in the realms of exploratory research methods. Several qualitative studies have attempted to understand the perspectives of children by interviewing their parents or carers (Case-Smith, 2004; Fawcett *et al.*, 2005; George *et al.*, 2006; Hummelinck and Pollock, 2006; Lowes and Lyne, 2000; McNeill, 2004; McNeill, 2007; Olson *et al.*, 2004). Though I located one study that examined the views of professionals towards PPI in general (Parsons *et al.*, 2016), I found no evidence directly addressing the attitudes of adult professionals towards children's involvement in medicines R&D. Thus, I thought it an important and original contribution to medical and sociological discourse to present and analyse the seldom reported views of key professionals who work within children's medicines R&D.

Considering the enormity of the field of children's drug development, I chose to examine the case of professionals' views of children and participation within context of epilepsy. Epilepsy was a particularly relevant area of children's medicine to examine as it is: 1) a condition that is managed primarily by an extensive number of pharmaceutical interventions; 2) an under-researched condition; and 3) a chronic condition, often requiring children to take medicines for their entire childhood or potentially for a lifetime. Between an estimated 50-60 million people worldwide (NSE, 2018; WHO, 2019). In the UK, it affects 500,000 people, of which approximately 112,000 are young

people under 25 years old (UCL Institute of Child Health, 2003; Young Epilepsy, 2011).

Understanding how adults conceptualise children and involvement, provides insight into professionals' relationships with current practices in medicines R&D. Further, potential routes to improve and increase collaboration between adult professionals and children as experts might emerge. Thus, I conducted interviews with key informants from the fields of children's medicines R&D.

#### **4.6 Ethics and responsibility**

It is a requirement for a PhD thesis, indeed for all research, to provide evidence of the researcher's ethical considerations, understanding and approaches (ESRC, 2019; UKRI, 2018). Ethics are necessary to ensure the confidentiality and anonymity of participants throughout the research process and a process that I feel strongly about, as one of the issues highlighted by my literature review is the ethical practice of involving children in clinical trials and how this has been executed historically. However, there is little emphasis on the responsibility of the researcher for their research. I feel that it is not just important to provide evidence on ethical considerations but to provide insight into the issue of responsibility of the researcher to themselves, their research participants and all those who the research might impact upon. This feeling of responsibility ran deep throughout my research and has caused me numerous problems regarding the direction of my research and how it is presented.

I digitally recorded interviews with adult participants and took written notes, in the event that the data became corrupted in any way, which indeed it did during the write up of the thesis. I obtained written consent prior to conducting interviews and was explicit that I was using a voice recorder. The recordings were given an interview number and date only and I do not specify

who is speaking on the recordings or the in the quoted exemplars that I use in this thesis. Indeed, I make no direct references to companies or institutions in this thesis and will not do so in any published data. All participants are given a code number to ensure that the information cannot be matched to a particular person and the coding system is kept in a separate book in such a way that only I am able to identify the participants. I only indicate a participant's field of expertise if this does not make them recognisable

I contacted the participants by letter or email (see Appendices 2 and 3) and obtained informed consent, supplying a consent form to be signed by the participant prior to interview (see Appendix 4). I conducted interviews in public/offices spaces, so neither I nor the participant were exposed to unsafe or threatening situations. No financial incentives were offered and as I travelled to meet the participants in their professional locations, I did not have to provide travel expenses.

From my research experience, ethics underpin all aspects of research and far from being another box to tick, it is a taxing and considered process.

Ethics bear particular relevance throughout the children's medicines R&D process. It is vital that ethical practices are addressed by all researchers prior to, during and after any research is undertaken. As a researcher I have not only an obligation, but a responsibility, to those involved in my research, those who my research is about and have provided me the opportunity to do the research and those who, hopefully, read and use my research. I also have a responsibility to myself and my own integrity. To be viewed as a professional and ethical researcher who produces valuable work, then one must be ethically responsible from the start.

During my time as an undergraduate and post-graduate researcher I have read several codes of ethics and/or principles and practices. As my

academic journey has crossed various linked disciplines, the ethics that I have encountered include: medical, anthropological and sociological. The ethics guidelines are varied and cover many branches of social and medical research. The guidelines relevant to this research include: the American Anthropologist Association (AAA), the Association of Social Anthropologists of the UK and Commonwealth (ASA) and, the main reference for my ethical considerations, the Economic and Social Research Council Framework for Research Ethics (FRE) (Economic and Social Research Council, 2010).

My first experience of ethics was from a medical perspective. As a qualified medical phytotherapist, understanding and adhering to ethical practices within a clinical environment was paramount. As a practitioner it is necessary to behave appropriately at all times within the clinical setting whilst interacting with patients and in terms of protecting extremely sensitive data. I had to abide by the strict codes of medical ethics set by the National Institute of Medical Herbalists; ethics that were modelled on the General Medical Council and the British Medical Association requirements and protocols. Veering from ethical protocol could have dire consequences for a patient, in terms of safety or dignity, and for me as a practitioner.

One's ethical behaviour can be tested in multifarious ways throughout a research project. What is apparent from reading ethics frameworks is that ethics are rarely straightforward and often ambiguous. However, despite the diversity of disciplines, associations or councils, the fundamental principles governing research ethics are very similar.

This study was designed so that the findings could be integrated in order to suggest a possible framework for the inclusion of children in early-stage pharmaceutical R&D process. It could be argued that conducting the systematic speech analysis prior to analysing the interview data could have influenced my findings, therefore calling into question the objectivity of this

research. Each element helped to answer the questions underpinning this thesis. By combining Bakhtinian principles with Foucauldian discourse analysis methods, and following a stepwise approach as outlined by Parker (1994), I created a novel, substantive and repeatable method for applying Bakhtinian analysis.

#### **4.7 Chapter summary**

The constructions of children and involvement are generated within social interactions, where the hero and the author battle for meaning. I have argued here for the use of Bakhtin's dialogism as one of my methodological approaches in my research; a means to generate more ideas about how the constructs of children and involvement were enabling or disabling children's opportunities to interact and contribute to medicines R&D, in short, impacting on the presence of children's voice.

This study was designed so that the findings could be integrated in order to suggest a possible framework for the inclusion of children in pharmaceutical R&D process. Each element was designed to cast further light on the research question.

## Chapter Five: Political speech analysis

### 5.0 Overview

In this chapter, I present the aims, methods and findings of the systematic speech analysis. I describe the processes that I employed in the first component of this study to analyse political speeches that focused on the creation of paediatric pharmaceutical regulations in Europe (European Union, 2006a; European Union, 2006b) and the United States of America (United States, 2002).

### 5.1 Aims of first component – why look at political speeches?

The aim of this component was to primarily inform the key informant interviews, providing a backdrop to the policy discourse governing children's medicine by appraising and synthesising political speeches on children's medicines that focused on the introduction of new legislation. Speeches made within the British Parliament, the European Union Parliament and the United States Congress were sought. The questions addressed were: i) are children considered in the speeches?; ii) how are children referred to within the debates discourse?; iii) are children's views presented within the speeches?; and iv) how are children constructed by those involved in creating policies that govern children's pharmaceutical choices?

### 5.2 Methods

In the absence of specific methods for conducting a review of political speeches, I adapted methods used in systematic reviews. The four key activities being undertaken matched with those of systematic reviews:

investigating a question; identifying and describing located data; bringing together the findings; and establishing what evidence claims can be made (Gough, Oliver and Thomas, 2017a).

### **5.2.1 Identifying speeches for the analysis: searching and eligibility criteria**

Systematic strategies were applied and adapted techniques employed in conducting a systematic review; a method of identifying all relevant research on a particular topic (Gough, Oliver and Thomas, 2017a). Only verbatim speeches accessible online from the associated political websites that focused primarily on children's medicines were included. Speeches had to have been presented on the floor of the governmental institutions and not written amendments or comments. I created explicit eligibility criteria (Oliver *et al.*, 2017), which were piloted on a sample of speeches before applying them generally, which ensured that the method was valid and repeatable. This facilitated an analysis that focused on discourse within political arenas to political peers, and discourse that was used to build a case for changes in legislation or paediatric medicine regulation. Speeches on child abuse, children's access to medicines or children's rights were excluded. All discourse available via the databases that focused on providing improved pharmaceutical interventions for children was included (see Table 5.2.1). The speeches were identified from within debates retrieved solely from publicly available electronic library sources for each of the governmental institutions being analysed: Thomas for the United States Congress (Senate and House of Representatives); Hansard for the British Parliament (House of Lords and House of Commons) and EuroParl for the European Parliament (see Table 5.2.2). The only timeframe restrictions were those that were imposed by the databases themselves (Thomas – 101<sup>st</sup> Congress – from Tuesday, 3<sup>rd</sup> January 1989; Hansard – from 22<sup>nd</sup> November 1988; EuroParl – from 1999). The final search period was 3<sup>rd</sup> January 1989 to 17<sup>th</sup> April 2010. I only included speeches conducted on the floors of the United States Senate and

the House of Representatives; the European Parliament; and the United Kingdom House of Commons or House of Lords. It was vital that the speech transcripts were verbatim and had been transcribed in the English language. Although the subsequent interview study was conducted in the UK, the introduction of international legislation such as the FDA Better Medicines for Children Act and the European Union Paediatric Regulation 1996/01 - had a direct impact on children's medicines research in the UK and therefore were considered relevant to this analysis (see Table 5.2.1).

After applying these criteria, a list of speeches was generated from each of the databases. To factor for duplication, I created separate Microsoft Excel spreadsheets for each political forum obtained from the online archive to enable recording of each of the debates within which the speeches were embedded. A duplicate search based on date, forum and title of debate was conducted and duplicates were deleted. The titles of each debate were screened for relevance. Full transcripts of the remaining debates meeting the criteria, or where titles provided insufficient information on the speech, were downloaded. Each debate was screened for key search terms for relevance. This was achieved loading speeches into Microsoft Word 2007 and entering search terms into the 'find' function. The final stage was to reapply the eligibility criteria to the full transcripts. Transcripts that did not satisfy the criteria were then excluded, leaving me with a data set of relevant speeches to analyse.

**Table 5.2.1 List of eligibility criteria summary**

<b>Criterion</b>	<b>Inclusion/exclusion summary</b>
Scope of speech	<p>Speeches must focus on the requirement, creation, development, or design of paediatric pharmaceutical policy</p> <p>Speeches that focus on paediatric medicine including surgical developments will be excluded. All speeches that explicitly name another Act or Bill in their title were excluded, e.g. Medical Devices Act.</p>
Arena of speech	<p>Speeches must have been delivered within the: Houses of Parliament, (House of Commons or the House of Lords) in the United Kingdom, United States Congress (Senate or House of Representatives) or the European Union Parliament.</p> <p>The focus of this analysis is on the main political arenas; therefore, speeches that have been delivered within other political establishments that meet the scope criterion will be excluded.</p>
Speech type	<p>Speeches must be orated and verbatim or as close to verbatim as is possible</p> <p>All written speeches and extension of debates will not be included in this analysis</p>
Language	<p>Speeches must be published in the English language</p> <p>Due to the fact that I only speak English fluently and would not have a budget to employ translators, the inclusion of anything other than speeches/debates that are published in English would be problematic. Taking this action would ensure that the analysing process would be attainable.</p>
Date inclusion	<p>There is no date inclusion/exclusion criterion</p> <p>The online databases from which the speeches will be retrieved have varying start dates from when the data is stored on-line.</p>

Table 5.2.2 Web addresses of governmental online archives

Database Source	Website Addresses*
Hansard	<a href="http://www.parliament.uk/business/publications/hansard/commons/">http://www.parliament.uk/business/publications/hansard/commons/</a>
	<a href="http://www.parliament.uk/business/publications/hansard/lords/">http://www.parliament.uk/business/publications/hansard/lords/</a>
EuroParl	<a href="http://www.europarl.europa.eu/omk/omnsapir.so/searchdeb?ORATEUR=yes&amp;LANGUE=EN">http://www.europarl.europa.eu/omk/omnsapir.so/searchdeb?ORATEUR=yes&amp;LANGUE=EN</a>
US Congress	<a href="http://thomas.loc.gov/home/r111query.html">http://thomas.loc.gov/home/r111query.html</a>

\* Website addressees correct as of March 2019

I then created a list of keyword/phrase search terms that were applied to each of the three electronic sources (see Table 5.2.3). The keyword search was very much an iterative process as, when scan reading the speeches, words were noted that I had not initially included in my *a priori* list, such as the use of the words 'kid' or 'kids'. This then required me to run the searches again to encompass any previously overlooked key terms. As I was the sole person identifying the speeches, I repeated the process twice to ensure that there was no variation in the number of the debates that were retrieved for each search term.

**Table 5.2.3 List of search terms entered into government electronic archives**

Number	Search Term
1	children [AND] medicine
2	medicine(s) for children
3	children's medicine(s)
4	p(a)ediatric medicine(s)
5	medicinal products for p(a)ediatric use
6	p(a)ediatric regulation
7	p(a)ediatric legislation
8	better pharmaceuticals for children
9	best pharmaceuticals for children
10	p(a)ediatric pharmaceuticals
11	medicinal products for use in children
12	pharmaceuticals for children
13	kid(s) [AND] medicine
14	kid(s) [AND] pharmaceuticals

The format required for conducting searches of debates and speeches was different for each archive. I will now summarise each process.

**British Parliament (Hansard):** I entered the exact phrases, for all years. Hansard online goes back as far as 22<sup>nd</sup> November 1988. The document types that I searched through were *Commons Hansard Debates* for speeches that were made in the House of Commons and *Lords Hansard Debates* for speeches given in the House of Lords.

**European Parliament (EuroParl):** Speeches on EuroParl are accessed through the debates section and I completed a search of data both in the archives and on the site for the search terms as detailed in Table 5.2.3.

**United States Congress (Thomas):** I accessed speeches embedded in the debates accessible via the Congressional Record, which is linked to Thomas website. This search included all variants of the search terms entered, for speeches by any *Representative* or *Senator* and all occurrences. I selected speeches from the floors of the Senate and the House of Representatives but did not include the Extension of Remarks or the letters from the Daily Digest from all sessions, as these are written communications.

### **5.2.2 Characterising and appraising speeches and synthesising data: in-depth critical appraisal using discourse analysis, rhetorical analysis and thematic synthesis**

Speeches that met the initial inclusion criteria outlined in section 5.2.1 were then critically appraised to provide a full understanding of their potential contribution to the analysis. To minimise any potential bias introduced in analysing and interpreting the speech analysis data I took steps to ensure that my analysis was systematic, progressive and verifiable. Following a systematic path creates a 'trail of evidence', that increases the dependability, consistency and conformability (Lincoln and Guba, 1985) of the data. These issues are viewed as important with regard to assessing the quality of qualitative data (Secker *et al.*, 1995). To add a further dimension to the synthesis and analysis of the data, I considered the motivation for the speeches.

There are numerous methods available with which to analyse qualitative data such as verbal transcriptions. However, it is generally recognised that most research uses a combination of methods (Green and Thorogood, 2014)

Speech analysis like any qualitative analysis commences from the time that data are collected, as decisions about what data to include in one's data set involves reading and understanding the data that is available in the

first instance. Conducting the speech analysis was not a linear process as I had to navigate around copious amounts of textual data and interpret it, therefore each stage of analysis often overlapped, and I found that all stages were interconnected.

The process of the speech analysis then began during the data collection itself, by having to source the speeches and ensure that the speeches were relevant. The action of looking for the speeches meant that I familiarised myself with the scope and type of data available from the offset. Once all the speeches had been selected, my next step was to further familiarise myself with the data in-depth, by reading and re-reading the transcripts in their entirety. This immersion in the data was vital to understanding the context of the speeches and as I was reading speeches that I had not witnessed first-hand, I had to understand how the arguments were building, not only within each session but over time, before I could feel confident enough to breakdown the speeches into parts (deconstruct). To facilitate this process, I characterised each of the speeches in a systematic and manageable way.

### **5.2.3 Characterising speeches**

To gain a general insight into the focus of speeches and the language used to describe children and children's involvement in medicines R&D, I conducted a basic content analysis (Hopkins and King, 2010). This was to count the frequency of the nouns to describe children: child, kid or minor, but also adjacent adjectives used to refer to a child. This process provided a means of investigating how children were being positioned within the speeches. It gave insight into how children were being constructed in the institutional context at the time of the children's medicines legislative process and how this changed over time. Further, it provided a basic insight into how often children were referred to within the legislative process and gave me a

greater understanding of what was being said and how this was framed; the character of the speeches.

To evaluate the large amount of data I characterised the speeches by creating a framework. Framework synthesis has been demonstrated to have application for the analysis of both primary and secondary research (Oliver *et al.*, 2008b). Framework analysis can be used to structure spoken data enabling data to be organised according to key themes, concepts and categories that emerge from both the research questions and the data being analysed. The framework provided a means to describe, appraise and data extract from the speeches.

Iterative coding was conducted using a combination of deductive a priori codes and inductive codes were created. Relevant quotes were uploaded onto NVivo8 software.

Next was to identify a thematic framework. I achieved this by making notes about various quotes or paragraphs in the margins of the transcripts in the form of ideas or concepts that arose from the speeches. I began to develop categories but more than this, my research questions could be addressed, and new theories were beginning to be formed. The main themes identified were entered into a matrix that I created, which was also grouped with related emergent sub-themes. This exercise facilitated identification of patterns and relationships within the data.

I then grouped the quotes together under my thematic headings by removing them from their original state as part of a speech. The data was now being managed by removing superfluous data and collating like data. Although it can be argued that reducing rich data such as speeches and taking quotes out of context could affect (even bias) the findings, data reduction is

seen as one of the most important aspects managing a qualitative study (Krueger, 1994).

The tool that was developed enabled me to extract information from the speeches such as theories of children and childhood and identified attitudes towards children's perspectives. This analysis also help me to identify whether children were ever consulted by those advocating or opposing the improvement of children's medicine provision. I recognised that speeches were solely about what was said or the context, but of how arguments were being explicitly or implicitly framed. The speeches were re-read to gain an understanding of the: context, primary focus (e.g. children's rights); study population (e.g. age); types of approach; and emergent theories underpinning the speech. The speeches were well-suited for me to identify how children were constructed and these constructions were presented or framed, because the speakers employed rhetoric. Rhetoric is associated with the art of persuasion, the "necessity to convince, persuade, and communicate efficiently in the context of shaping and implementing public policies" and is generally recognised as being an important feature of the political process (Gottweis, 2007, p. 240). I applied a further coding strategy that involved looking for use of Aristotelian rhetoric.

Aristotelian rhetoric, or rhetorical criticism, provides a means of describing speeches in terms of their ability to persuade the audience. Aristotelian rhetoric is founded on three suppositions. Firstly, that there is a speaker, secondly, that the speaker has something to say, and thirdly that they have an audience or someone to listen. Rhetorical theory from Aristotle to the present day has differentiated three concepts of argumentation: *logos*, *pathos* and *ethos*. *Logos* (logical argument) draws on the underlying logic, effectiveness or supporting evidence or reasoning behind an argument or propositions, in short, the facts (*logos*). *Pathos* (emotional argument) utilises

emotion to promote appeal of what is said, or the interpretation of the facts. Finally, *ethos* (credibility or ethical appeal) focuses on the appeal of the speaker's character and reputation or the legitimacy of the speaker (Bade, 2009, pp. 616-617). Although rhetorical criticism has been suggested to be unsystematic and non-elucidatory in its approach (van Leeuwen, 2008), used in combination with the framework synthesis tool also being applied in this analysis, it served to set the scene and highlight the extrinsic approach of the speaker.

I then created a matrix of theoretical perspectives and constructs of children within medicines R&D policy creation. I adapted a method structure adopted by Sutcliffe (2010) to investigate children's shared decision making, to draw out implicit and explicit perceptions of children and their agency.

#### **5.2.4 Analysing and synthesising speeches**

The final step was to synthesis and interpret the data: make sense of the speeches, find relationships between the quotes and ultimately construct an argument based on the located data. The process of synthesis and analysis required creativity and the development of new skills, to ensure the resultant findings had application and reliability.

The combination of content analysis, thematic synthesis, and discourse analysis enabled the development of 'descriptive' themes. The iterative process of line-by-line coding was used to generate 'analytical' themes. The analytical themes were then used to investigate the research questions and generate of interpretive constructs, explanations or hypotheses to inform the participant interviews.

### **5.2.5 Quality of data synthesis**

I entered the data independently for this study, which could be criticised in terms of the quality assurance of the findings (Higgins and Green, 2011; Oliver *et al.*, 2017). Data synthesis was an iterative process; the framework was created as new themes emerged and adapted after each iteration to incorporate emergent theories and themes (Boyatzis, 1998). Strict compliance with the eligibility criteria, and repetition of all aspects of the speech analysis, minimised error and bias, which helped to assure the quality of the analysis.

## **5.3 Findings from the speech analysis**

*“I am arguing for politics and epistemologies of location, positioning, and situating, where partiality and not universality is the condition of being heard to make rational knowledge claims.” (Haraway, 1991, p. 195)*

Like Haraway in the above quote, I wanted to gather epistemologically partial perspectives. I sought to examine the positioning and constructing of children in the professional paradigm, within the context of political governance. In this chapter I describe the findings from my analysis of political speeches for the years building up to the creation of paediatric pharmaceutical legislation in Europe and the United States of America.

### **5.3.1 Speeches identified from searching and screening**

An extensive online search was conducted between 19<sup>th</sup> March and 17<sup>th</sup> April 2010. This search identified 2,225 debates that contained in excess of 5,000 speeches by numerous politicians. Screening titles for suitable debates reduced this number to 848, which further reduced to 311 debates after full text screening. I also screened the debates for written speeches

(arguments, defenses, *in absentium* etc.), written amendments and vote lists, which I excluded from the analysis. After this stage, 216 debates were identified as potentials for inclusion. These debates were then screened to exclude duplicates that had been returned from the process of entering different search terms that may have appeared in a speech on several occasions. This reduced the number of viable debates (n=86), which were then scrutinised more closely for their content (see Table 5.3.1 and 5.3.2). This was achieved by printing off the full text of the speeches and scanning each debate; this enabled me to identify speeches that had only made a passing reference to medicines for children regulation/legislation or that focussed on completely different legislation, for example health provision for children or paediatric medicine as a medical discipline. The screening and scanning exercise identified 86 debates that met the inclusion criteria for the British Parliament (n=31); the European Parliament (n=6) and the US Congress (n=49).

After full text screening, 31 debates met the eligibility criteria, which yielded 161 individual speeches for analysis (see Table 5.3.1).

**Table 5.3.1 Number of debates returned from an electronic search of government archives by governmental institution – including and excluding duplicates**

<b>Governmental Institution</b>	<b>No. of returned hits</b>	<b>No. of inc. debates after title scan</b>	<b>No. of listed debates inc. duplicates after content screening</b>	<b>No. of listed debates exc. duplicates</b>
British Parliament	84	84	84	31
European Parliament	17	11	11	6
United States Congress	2,124	743	216	49
Total	2,225	838	311	86

Source: Hansard, EuroParl and US Congress

**Table 5.3.2 Number of debates and speeches included in the study by governmental institution – after full text screening**

<b>Governmental Institution</b>	<b>Nº. of included debates</b>	<b>Nº. of included speeches embedded in the debates</b>
British Parliament	7	31
European Parliament	4	43
United States Congress	20	87
Total	31	161

Source: Hansard, EuroParl and US Congress

### 5.3.2 Chronological mapping of included speeches

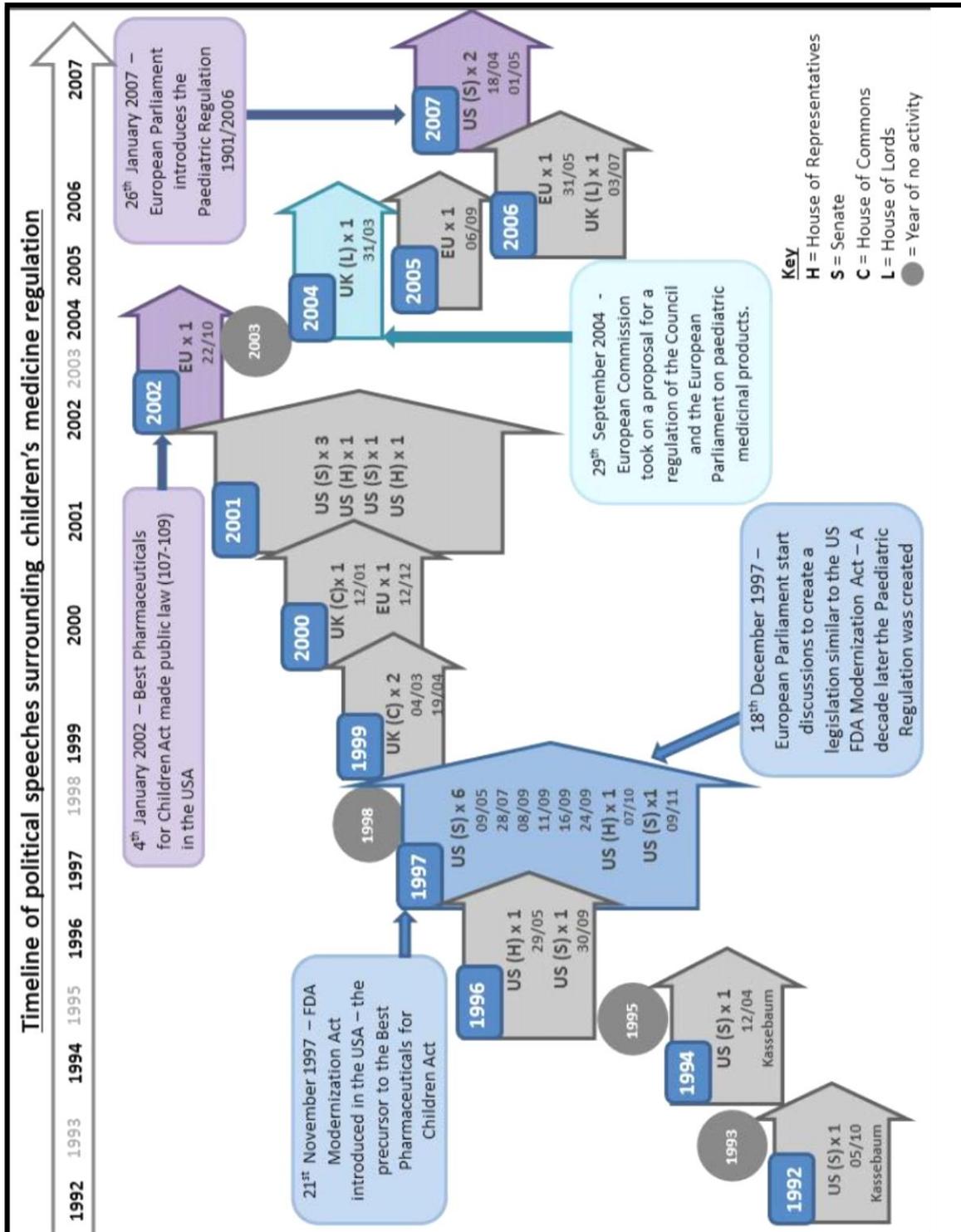
The earliest speech identified was made by Nancy Landon Kassebaum, Senator for Kansas, USA on 5<sup>th</sup> October 1992. Mrs Kassebaum introduced the Better Pharmaceuticals for Children Act to “improve the safety and effectiveness of pharmaceutical products used by children.” Her co-sponsors for the bill were Senator Orrin G. Hatch and Senator Christopher Dodd.

*“Mr. President, the use in children of pharmaceuticals developed for adults is an area which so far has not received the attention it deserves. Under current law, physicians have the discretion to use any lawfully marketed drug for any patient, according to their best judgement. Ordinarily, this discretion works well, as it allows physicians to adapt available medications to the needs of their patients. There are particular challenges, however, in wisely using children drugs which were developed with adults in mind.” ... “For these reasons, children have long been considered therapeutic orphans.” (Kassebaum, 102<sup>nd</sup> Congress 5/10/1992)*

Mrs Kassebaum’s speech highlighted the lack of incentive for drug manufacturers to conduct trials for medicines that were not intended to be marketed for children and which were expected to “return little additional revenue” from the children population. This speech focused on improving manufacturer interest in researching children’s medicines by “providing special incentives to help assure more widespread and consistent testing of drug products for use in children” and by applying the “Federal Food, Drug, and Cosmetic Act to grant 6 months’ marketing exclusivity for products for which FDA-approved pediatric studies are conducted.”

A map of included speeches showing their distribution by year, with reference to the legislation and country, gives an overview of the speeches and helps visualise the context of the paediatric pharmaceutical legislative process, the timelines involved and the concentration of political activity (see Figure 5.3).

Figure 5.3 Chronological map of political speeches about children’s medicines leading up to the Paediatric Regulation



### 5.3.3 Speech analysis findings: Framing and constructing children

In this section I present the two major findings of the speech analysis. In the following section, I reveal how children are rhetorically framed, centring on children's medicines legislation, and in section 5.3.4, I present the ways that children are constructed in those speeches. I provide examples from the speeches, retaining as much of the speech necessary to provide context.

To emphasise keywords and phrases in the speeches, I have added underlining to the text to signpost these for the reader.

#### 5.3.3.1 Use of rhetoric in political speeches

**Logical appeal:** Most of the speeches presented factual and clinical data using logical argument (*logos*): I located 296 examples of logical speech. The use of facts and numerical data to highlight an issue or express concern over the nature of children's medicines access and the dearth of research was particularly evident when the speakers wished to highlight the lack of appropriate medicines.

Two years after she first introduced the problem of pharmaceuticals for children, Mrs Kassebaum presented a logic-based argument to demonstrate the necessity of research into children's medicines and implies that children are different from adults. She said:

*"This incentive to conduct studies is sorely needed. Currently, fewer than 30 percent of the prescription medications on the U.S. market are approved for use by pediatric populations and labelled for pediatric use. Pediatricians using drugs developed with adults in mind but which may also be effective in children or be the only option for treating the same diseases or illnesses in children must estimate dosages from dosages found safe and effective in adults. Such estimates are uncertain because children, and particularly those under 2 years of age, often metabolize drugs differently than do*

*adults. Further, some drugs can be less safe in children than in adults even when appropriate doses are used.” \US002 – (Mrs Kassebaum 12 04 1994 US –Senate)*

Some two and half years later she again raised the issue of the necessity for new data but is more explicit about children’s difference.

Talking of the Food, Drug and Cosmetic Act, she said:

*“It is now clear, however, that children are not small adults. They do not necessarily react to drugs the same way. New data are necessary to ensure that America's children have the same benefit of safe and effective drugs as our adults do. As it stands now, however, 80 percent of the drugs taken by children are not labelled for pediatric use.” (Mrs Kassebaum – 30/09/1996 U S - Senate)*

The following year Mr DeWine picks up Mrs Kassebaum’s argument at the US Senate. The logical rationale for the requirement for clinical trials is that children are different and combined with a lack of market incentives for the pharmaceutical companies. He uses the same language as Mrs Kassebaum “not small adults”, to talk about children:

*“The problem this bill addresses, is a very serious one. About 80 percent of the drugs on the market today have not been approved by the FDA for use in at least one pediatric age group--80 percent. As a consequence, the drugs do not carry labelling information explaining how they should be taken by children. This is because clinical trials are expensive. It is a dollars-and-cents issue, and often there is little market incentive for pharmaceutical companies to conduct these tests. The result is that drugs are usually prescribed for children on the basis of adult trials and the pediatrician's own experience. Children are not just small adults, and therefore this is a somewhat risky business. Physicians deserve better information and children deserve, as well as their parents, better information.” (Mr DeWine 09/05/1997 US – Senate)*

A couple of months later at the US Senate, Mr Frist follows the argument made by Mrs Kassebaum and Mr DeWine. Here Mr Frist focuses on

hospitalized children using technical language and a variety of high percentages to make his point about off-label use in children's medicines:

*"In treating hospitalized children, it has been estimated that over 70 percent of the drugs are prescribed to be off-label, and that can vary anywhere from 60 to as high as 90 percent, and for diseases such as cancer the figure can be as high as 90 percent."* (Mr Frist 28 07 1997 US - Senate)

The issue reaches the UK parliament some twenty months later, when Andrew Love spoke in the House of Commons. In an open debate he raised the issue of unlicensed drugs and used supporting evidence about the risk of accidents and death reported by the Health Committee, saying

*"In a recent report of the Health Committee, the situation was described as "unacceptable". The issue is extremely important and should be discussed by the House. Will my hon. friend find time for that discussion in the near future?"* (Mr Andrew Love 04/03/1999 HOP – Commons)

He continues his argument a month later but combines logic with emotional appeal, using the noun "babes" to describe new-born children and dramatic language like "disaster" in close proximity to the word children. Percentages, meant to surprise the listener, feature commonly in the speeches – facts that can be easily absorbed and potentially stick in the minds of the listener. Here we encounter a shocking "90 per cent".

*"In addition, a more recent study showed that the figure for new-born babes admitted as patients is even higher: 65 per cent. of all treatments are either unlicensed for that purpose or prescribed off-label, and 90 per cent. of them receive such treatments. I remind the House that those drugs are either totally unlicensed for human administration or licensed solely for use on adults, yet they are still regularly given to children." ...*

*"There is an irony here, in that the Medicines Act 1967--which introduced the licensing system--came as a result of the thalidomide*

*disaster, a drug which directly affected children, yet the present system effectively excludes children from the licensing process. That cannot continue to be justified.”* (Mr Andrew Love 19/04/1999 HOP002 – Commons)

Nine months later, presenting a fact-based speech after quoting the 25% estimate for unlicensed drug use in children, Mr Love again stressed the higher percentages for younger children.

*“For babies admitted as patients, the figures are even higher: 65 per cent. of off-label or unlicensed treatments were given to nine out of every 10 infant patients, many of whom had been born prematurely.”* (Mr Andrew Love 12/01/2000 HOP002 – Commons)

Back in the US, the issue emerges in the House of Representatives. In December 2001, Ms Eshoo, who presented a short speech as co-sponsor of the Best Medicines for Children Act, talks of the use of untested medications “widely used by paediatricians” (*Ms Eshoo – 18/12/2001 - HOR*)

Logical appeals featured highly in speeches made in the European Parliament. For example, four years after Andrew Love’s speech we see a similar rhetorical framing, with use of percentages to stress the urgency of the problem. Here the percentages repeatedly presented are lower at 50%, as opposed to the 80% I frequently encountered in the US and vague but more dramatic estimates of 65-95% in the UK. We also encounter derision of the pharmaceutical industry in Hiltrud Breyer’s speech, suggesting that it is money focused and contradictory, with use of the “preaching personal responsibility” versus “making a killing”.

*“Over 50% of the medicinal products used on children in the European Union today are neither tested on children nor authorised for paediatric use. This means that we cannot always be sure that these medicines are effective or safe. As I understand it, none of us is prepared to take that risk anymore.”* (Gunther Verhaugen 06/09/2005 – EU Strasbourg)

*“The fact that over 50% of the medicinal products used in Europe to treat children are neither tested on children nor authorised for paediatric use is preposterous and no longer acceptable. Why has the pharmaceutical industry, which is, after all, always preaching personal responsibility, not seen fit in the past to conduct these very studies itself? This is an indictment of the pharmaceutical industry: it is out to make a killing, a huge profit.” (Ms Hiltrud Breyer 06/09/2005, EU –Strasbourg)*

Across in the UK in the same year, the argument is debated in the House of Lords, taken up by Baroness Howarth, who uses a similarly structured speech to Andrew Love from the House of Commons. She also reinforces the construct of children as different but also implies that children are vulnerable, using dramatic terminology and close proximity adjectives suggesting vulnerability i.e. suffer, that were commonly used in the speeches over time within the three countries. In her evidence-based speech she said:

*“We have heard several times that children are not small adults. We heard from the excellent evidence of Sir Cyril Chantler that there are two major problems with the use of unlicensed medicines: how children's metabolism deals with the drug, and the effect on the child. The European Commission stated that 50 per cent to 90 per cent of all medicinal products used in the paediatric population have never been studied or authorised for use. Consequently, among the long list of problems outlined by Sir Cyril and well known to those dealing with children is the control of pain. Were the situations where children suffer to happen to adults, they would simply not be accepted. There would be a major campaign. We hope that our report will help the Government to take forward this important issue of paediatric medicine.” (Baroness Howarth of Breckland 03/07/2006 HOP – Lords)*

During the time when the specifics of the legislation/regulations were being outlined, the structuring of the speeches were primarily logoi driven. Logical appeal featured highly when discussing plans for the 6-month product license extension, e.g.

*“With regard to the impact of this measure on the public health budgets of our countries, a study presented to the Council concludes that, with a fixed six-month period, the increase in health spending would be infinitesimal, between 0.7 and 1%.”* (Ms Françoise Grossetête – 06/09/2005, EU – Strasbourg).

In the US, EU and UK concern regarding, or to clarify issues about, the potential benefits to the pharmaceutical companies, supporting data is provided in the form of percentages and costs, which dominated speech as demonstrated in Mr Tauzin and Lord Colwyn’s speeches below. Mr Tauzin’s speech provides an excellent example of combining logical with emotional appeal, and dramatic language to reinforce the construct of children as vulnerable.

*“We are told that this extra 6 months of exclusivity may add about one-half of 1 percent to the drug costs in America during that 6 months of extra exclusivity under the patent. What do we get back for it? According to the study, we save \$7 billion a year in health care costs for our children, and so we are not crippling them and hurting them with drugs that could hurt and cripple them instead of helping them.”* (Mr Tauzin 18/12/2001, US House of Representatives)

*“The impact assessment of the proposed EU regulation estimated that to deal with the increased number of applications, the EMEA budget would have to be increased by between 67 to 150 per cent, or €130 million to €195 million, the cost to the pharmaceutical industry being about €4 million per product.”* (Lord Colwyn 03/07/2006, UK House of Lords)

**Ethical appeal:** Broadly speaking ethos is divided into two forms: extrinsic and intrinsic. Intrinsic ethos is the manner in which the speaker goes about presenting their argument, supporting their statement with reason generated by their knowledge or experience (Eberly and Serber, 2013). Portrayal of knowledge in this instance is implied, not stated. If a speaker shows a lack of understanding about the subject matter being presented, then their argument becomes less persuasive. For the subject area being examined

in this thesis, the speakers readily inferred knowledge in their speeches. It was not clear cut to identify examples of intrinsic ethos but after much analysis I identified 171 examples.

Initially, I did not feel that the use of intrinsic ethos had implications for the how children are constructed within the context of children's medicines. However, whilst analysing the speeches it became apparent that when presenting their arguments, the speakers often adopted a paternalistic style, constructing children as in need of protection and care from adult professionals. This was often reinforced by using adjectives such as 'little', 'weak' or 'vulnerable' in close proximity to the words protect or look after.

*"Let us pass it so we can protect our little ones, because the health of our children has been greatly improved as a result of this act. Let us not go away saying that we should continue to do guesswork." (Mr Towns 13/11/2001, US House of Representatives)*

*"And, passage of our bill today, is just one more example of how he has dedicated so much of his time and energy to protect our Nation's kids, our Nation's future." (Mr DeWine 12/12/2001, US Senate)*

This association of the children and protection also arose when speakers employed extrinsic ethos. Extrinsic ethos manifested in terms of how the speaker highlighted their expertise to their peers. Of particular interest to me was whether the speakers were open about their knowledge and experience of children or working with children from the perspective of a professional or as a parent. I refer to this as role announcement. I identified 149 examples of extrinsic ethos within the text, yet of these there were only four examples of role announcement in the speech. In two cases (Mr John Hutton, 1999 and Mr DeWine, 2001) the speaker announced their parental expertise, a role associated with the protection of children. In another instance, extrinsic ethos was used to support another speaker by the use of role announcement to secure professional ethical appeal and camaraderie. For both professional role announcement ('doctor') and parental role

announcement ('father' and 'parent'), children are openly constructed as being vulnerable and in need of protection. These roles and their associated 'duties' of protection and acting on behalf of the children, feature strongly in Mr Dewine's speech below.

*"... but first let me say that as a father myself, I sympathise deeply with the parents of all the children to whom he referred." (Mr John Hutton, 19/04/1999 – HOP Commons)*

*"... Let me tell you what this means for me as a parent: We now have dosage, safety and adverse event information that we did not previously have ... The more information doctors and parents have on dosing, toxicity, adverse effects, and adverse drug interactions--the more informed our decisions will be when giving medicines to children and ultimately, the more we will be protecting our kids." (Mr DeWine, 07/05/2001, US - Senate)*

*"As a doctor I am in favour of and strongly support the view that research into paediatric medicines must always be compulsory, safe, highly professional and subject to constant checks, if for nothing else, because there is still a shortage of medicines for children, and because the development of new substances must go ahead. ..." (Mr Miroslav Mikolasik, 06/09/2005 EU- Strasbourg)*

*"As a doctor, I believe that the draft's most important feature is its attempt to afford greater protection to child patients, in view of the fact that they constitute a particularly vulnerable group of patients." (Mr Jiri Mastalka, 06/09/2005 EU Strasbourg).*

**Emotional appeal:** I found 142 examples of the use of emotional appeal (*pathos*) to support the speaker's arguments. The way in which the children were constructed using pathos varied substantially. There were instances of melodramatic language and mental imagery being employed by some speakers, framing children as particularly vulnerable and in danger of being damaged by the pharmaceutical industry. Indeed, on a couple of occasions speakers appealed to the religious beliefs of the listeners to highlight the vulnerability and value of children.

*“Seven billion dollars, ten-to-one benefits for the most vulnerable, the most sacred of all the charges that **God** has ever presented us with on this Earth, the protection of our own children and their health. That is what we are talking about.”* (Mr Tauzin, 18/12/2001 US – House of Representatives).

*“Mr President, every human life is unique and valuable because it is a gift from God. Accordingly, every life deserves the best possible protection and care from the cradle to the grave.”* (Mr Johannes Blokland, 22/10/2002, EU-Strasbourg)

The predominant construction for children within the use of emotional appeal was to talk about children in terms of suffering, with use of the adjectives such as “sick” to describe children. Or the use of morose adjectives and nouns, such as “fatal” or “death”, in close proximity to promote concern. This practice was more common in the US political arenas and in the UK. Emotional appeal was employed less frequently in European Parliament, but I encountered a number of examples, best demonstrated by these excerpts from the September 2005 EU Parliament meeting in Strasbourg by Gunter Verhaugen and Kathy Sinnott.

*“This is a very important proposal, which will improve child health in Europe and spare many families the suffering which the premature death of a child brings.”* (Mr Gunter Verhaugen 06/09/2005, EU Strasbourg)

*“This truth is that an alarming number of children are sick and the number suffering from chronic, acute and fatal diseases is on the increase. As the scourge of contagious diseases among children in the West has been largely contained, all other types of illness are increasing, some to epidemic levels.”* (Ms Kathy Sinnott 06/09/2005, EU Strasbourg)

In the year leading up to the FDA Modernization Act, Mr Greenwood’s speech provides an excellent example of calling on the listener to engage with their powers of mental imagery, asking “Americans” to:

*“... imagine that their mother or father, their elderly parent, lies in a bed in a hospital, with a condition that is fatal, and the doctor takes you outside the room and says, ‘It does not look good for your mom or your dad. It does not look like he or she is going to make it,’ and why.”*

*“Or imagine your little child, boy or girl, the same situation, in a hospital, suffering, and as a parent you want to relieve that suffering. And the doctor tells you that there is a drug, there is a medicine, it is a wonderful medicine that has fixed these kids up elsewhere in the world, but we cannot get it through the FDA. It is still bogged down there. ‘If I could only get that, I could relieve your child's suffering or save his life.’” ...*

*“I think if Americans picture themselves in that situation as sons and daughters of their elderly parents, or thinking about their husband or their wife in that situation, or in the worst case of all, a small child, they would say, somebody has to take care of this.” (Mr Greenwood 29/05/1996 US House of Representatives)*

In one speech by Senator Klug in 1997, although framing his speech in pathos, he employed a different emotional technique to present his argument. He constructs children as his peers, implicitly calling on the listener to think about their “young friends”. He amplifies the impact and emotional appeal of the argument by personalising the argument, giving names of the children to the listener and making the children ‘real’, more tangible, thus making a connection.

*“I have watched a number of young friends in my district grow a head taller as we have worked on this bill for the past 3 years. And while they have outgrown last year's school clothes, unfortunately they cannot outgrow their diseases. Amber still has juvenile diabetes. Cody still has epilepsy. And Kristin still has asthma. Today's bill will go a long way toward easing their suffering by setting up special testing for new drugs aimed at children and expediting new uses for drugs also aimed at treating children's diseases”....*

*“This bill is going to go a long way towards easing the suffering of millions of Americans across this country and obviously not just children.” (Mr Klug 07/10/1997, US Senate)*

All political speeches are embedded with either logos, ethos or pathos, as they are designed to persuade. The examples I have provided, are ones where the rhetoric is clearly discernible. Logic formed the backbone of persuasion of these speeches. However, the heavy use of ethos (n=171 instances) and pathos (n=142 instances) compared to logos (n=126), suggests that when children’s health and wellbeing are the focus of the argument, emotional and paternalistic arguments prevail.

#### **5.3.4 Constructing children in medicines R&D**

My main objective for this piece of research was to investigate the social construction of children within the institutional setting of the three political arenas, to try to understand what constructions dominated the politicians talk.

I had a list of five *a priori* constructs that I was looking for in the speeches, which I adapted from Sutcliffe (2010): social actors, developing adults, minority group, crucial informants and unreliable witnesses. I also included four further *a priori* constructions that I proposed from my experience of the literature: therapeutic orphans, medical heroes, stakeholders and capable others. A further 15 constructions emerged from the analysis (total n=26). In this section, I present the list of elicited constructions with illustrative exemplars.

##### **5.3.4.1 Children as passive actors**

The most common way of constructing children was as passive actors, which is implied throughout most of the discourse. I identified 103 examples but in the majority of cases, the construction is implicit, rather than explicit. As I was reading the text, I noticed that there were numerous

references to doing research ‘on’ children, as opposed to ‘for’ or ‘with, as illustrated below:

*“In addition, we are in favour of more research into the effects of medicines on children.”* (Mr Johannes Blockland 22/10/2002, EU Strasbourg)

This alerted me to speakers constructing the children as inert elements of the research process. Often this was revealed by providing examples of speaking to the parents or carers about decisions and not the children directly. Or making decisions on the children’s behalf, without having evidenced that they have consulted with the children, or it is the children’s wishes.

*“I would ask all of those who have a fixed opinion on this whether they have spoken to patients’ representatives; I have. I have also spoken to parents with sick children. They could not understand it. ... They were just saying, ‘We want these medicines for our children’.”* (Ms Dagmar Roth-Behrendt 06/09/2005, EU Strasbourg)

*“Britain should take a lead by placing a statutory duty on the pharmaceutical industry to supply paediatric data on new products when their use on children is likely.”* (Mr Andrew Love 12/01/2000, UK House of Commons)

*“Our ultimate aim is a healthy child.”* (Ms Irena Belohorska 06/09/2005, EU Strasbourg)

**a) Children viewed as incidental:** I felt this should be highlighted as a sub-category as this construction is more extreme. I identified 11 examples where children were constructed as remote from the creation of the legislation and the medicine taking process. Here the speakers refer the importance of legislation to provide better information for the “parents”, “physicians”, “paediatricians”, “doctors”, “children’s groups”, or “children’s health advocacy groups”.

*“Too often, physicians and parents are forced to guess about dosages or possible side effects. They should not have to play this kind of Russian roulette with their sick children.” (Mr DeWine 09/05/1997, US Senate)*

*“In addition to ensuring that critical pediatric drug studies continue, the Best Pharmaceuticals for Children Act will also ensure that the new safety information from pediatric studies is promptly added to drug labels, require drug manufacturers to pay user fees to participate in the program, and require the Food and Drug Administration to quickly disseminate information gathered from pediatric studies to pediatricians and parents.” (Mr Dodd 07/05/2001, US Senate)*

*“Mr. Speaker, unfortunately, the legislation we are considering today, named the Best Pharmaceuticals for Children Act, is not about children; it is about money.” (Mr Brown of Ohio 18/12/2001, US House of Representatives)*

#### **5.3.4.2 Children as therapeutic orphans**

I located 59 examples of the use of this expression, which appeared to be very much a ‘buzz-phrase’ in medical discourse. I had identified this theoretical construct *a priori*. The over use of this term positions children as helpless and unwanted. At the time I questioned whether this term should be merged within the under-served sector of society construction but felt that it positioned children differently, i.e. as disowned or abandoned, rather than disenfranchised. This construct was sometimes implicit, for example:

*“Mr. President, the use in children of pharmaceuticals developed for adults is an area which so far has not received the attention it deserves.” (Mrs Kassebaum 05/10/1992, US Senate)*

Or explicitly used as a term in its own right, as below:

*“The problem, Mr. President, is that there is little incentive for manufacturers to perform studies for medications which they do not*

*intend to market for children and which are therefore expected to return little additional revenue from that source. For these reasons, children have long been considered therapeutic orphans.” (Mrs Kassebaum 05/10/1992, US Senate)*

#### **5.3.4.3 Children as a vulnerable or at-risk group**

I found 53 examples of children constructed as vulnerable or at-risk. There was a fairly even split between the explicit and implied construction of children in this way. This construct was associated with the use of pathos in the speeches and, when used explicitly, melodramatic language.

*“Thimerosal contains Mercury. Mercury is a toxic substance that should not be put in anybody's body, let alone children. Children get as many as 25 to 30 vaccinations by the time they go to school. Children get sometimes as much as 45 to 50 times the amount of Mercury in their systems that is tolerable in an adult and, as a result, many children suffer mental disorders because of this, according to some leading scientists. ... The number of children in America that are autistic has gone from 1 in 10,000 to 1 in 500. We have an absolute epidemic of autism in this country. ... But mercury should not be injected into any child.” (Mr Burton of Indiana 18/12/2001, US House of Representatives)*

*“Notwithstanding the importance of competition, Mr. Speaker, this legislation is about harnessing the promise of the most advanced pharmaceuticals for the most vulnerable members of our society, our children.” Ms Harman 18/12/2001, US House of Representatives)*

#### **5.3.4.4 Children as a medical discipline**

I identified 44 examples of this construct. These are utterances where medical language was used to refer to children, e.g. ‘paediatric population’, or the ‘preterm neonate’, as opposed to referring to children as children, young people or babies. For example, Mr John Hutton medicalised children throughout his speech

*“My hon. Friend might be aware--I am sure that he is--that the formulary will cover some 300 medicines commonly used in the treatment of the paediatric population. ... It is true to say that a sizeable proportion of medicines is available and formally licensed for use in the treatment of many illnesses that can occur in the paediatric population. ... There are other products for which specific clinical trials of a product have not been conducted in the paediatric population, but where the manufacturer and the licensing authority have no reason to suppose that its safety and efficacy will be such that it should not be used in the treatment of children.” (19/04/1999, UK House of Commons)*

**a) Children as guinea pigs:** I have positioned this as a sub-category as this term is widely used to refer to people involved in experimentation. I isolated 14 examples. Unlike the main category, here the use or inference of children as guinea pigs is to highlight the plight of improving medicines for children and that children should not be used as guinea pigs.

*“These medicinal products must have a therapeutic benefit. After all, it is senseless to knowingly allow children to be made guinea pigs in tests in the absence of any therapeutic benefit: this is unacceptable.” (Ms Hiltrud Breyer 06/09/2005, EU Strasbourg)*

*“We should, however, not lose sight of the ethical side of the matter, and must prevent children from being used as guinea pigs.” (Mr Jules Maaten 31/05/2006, EU Brussels)*

#### **5.3.4.5 Children as kin (attachment)**

I had originally identified this emergent construction as the speakers positioning the children as 'political tools'. However, after discussions with my supervisor Sandy Oliver, I recognised that the speakers were trying to demonstrate kinship with children by use of terms such as “our children”. In total, 41 examples were identified the two examples demonstrate the association of kinship with protection.

*“Notwithstanding the importance of competition, Mr. Speaker, this legislation is about harnessing the promise of the most advanced pharmaceuticals for the most vulnerable members of our society, our children.”* (Ms Harman 18/12/2001, US House of Representatives)

*“And, passage of our bill today, is just one more example of how he has dedicated so much of his time and energy to protect our Nation's kids, our Nation's future.”* (Mr DeWine 12/12/2001, US Senate)

**a) Children as citizens:** I have characterised this as a subset of kinship, however for the 28 examples identified in this emergent construction; children are talked about in relation to their ties to their country or Nation and therefore their entitlement to better medicines.

*“Mr President, 20% of our citizens are under 19 years of age; in other words, 100 million of our fellow European citizens are children.”* John Bowis 06/09/2005, EU Strasbourg)

*“America's kids are counting on it.”* (Mr Greenwood 18/12/2001, US House of Representatives)

*“The safety of our Nation's children is not a partisan issue.”*  
18/04/2007, US Senate)

**b) Children as equals:** This emergent category was usually explicit. I found only 12 examples of this. For these the speaker referred to children being treated in the same way as adults.

**c) Children as real human beings:** I have included this as a subset of kinship as these were examples when the speakers discuss children using their real names. This puts a personal slant on the speakers' argument and makes the emotional appeal element explicit. I found 13 examples of this construction. In both the following examples from the UK and the US the stories are associated with tragedy:

*“Finally, I draw the House's attention to the main reason for this debate--the human cost of not taking any action. Lexie McConnell*

*was nine years old when she died in November 1992. Her immune system collapsed following a steroid overdose after she had been given doses licensed only for use on adults. Lexie was being treated by a specialist at the John Radcliffe teaching hospital in Oxford for a relatively minor eye injury, yet her treatment still went tragically wrong.” (Mr Andrew Love 19/04/1999, House of Commons)*

*“I can remember standing about 6 weeks ago in a press conference in Madison with the family of a young boy, Cody Young, who lives in Baraboo about an hour from Madison, the place where the Ringling Brothers Circus was founded. And he has a severe case of epilepsy. And the tragedy of this story, as you will hear over and over tonight, is that the original medication developed for Cody Young's severe case of epilepsy was first conceived at a United States research facility. It was tested in the United States, and it now sits essentially at the FDA's desk, ready to be approved, while the drug is already available in Switzerland. And here is Cody Young's family saying, I do not get it.” (Mr Klug 29/05/1996, US House of Representatives)*

**d) Children as precious and special:** This category emerged when I noticed the use of words “gift from God” in an explicit example but this was mainly subtler. I only found only 3 examples of this construction, which have been discussed in the use of pathos to frame an argument (see 6.3.1 *ethical appeal*).

#### **5.3.4.6 Children as stakeholders**

I located 37 examples of this construction in the speeches. I searched the speeches for examples of when children were referred to as child patients or where weight of the importance of children could be identified, or when the speakers positioned children as being an integral part of the process, as demonstrated below:

*“We need with this report to safeguard the important right of child patients to protection both from the needless administration of medicinal products and from their subjection to treatment or research protocols of unknown value and efficacy.” Ms Evaneglia Tzampazi 06/09/2001, EU Strasbourg)*

*“It is this delicate balance that we need to maintain in our vote tomorrow, a balance that meets the expectations of paediatricians, families and the millions of young patients in Europe.” (Ms Frederique Ries 06/09/2005, EU Strasbourg)*

**a) Children as social actors:** I found 25 examples mainly the inference was implicit. For example, use of the wording “by children”.

*“It is now clear, however, that children are not small adults. They do not necessarily react to drugs the same way. New data are necessary to ensure that America's children have the same benefit of safe and effective drugs as our adults do. As it stands now, however, 80 percent of the drugs taken by children are not labelled for pediatric use.” (Mrs Kassebaum – 30/09/1996 U S - Senate)*

#### **5.3.4.7 Children as different from adults**

I identified 25 examples of this construction. Mainly the speakers were referring to the fact that children are not ‘small adults’. Usual use of this construct was not in reference to the children’s cognitive ability, but in terms of physiology, pharmacodynamics and pharmacokinetics.

*“It is recognised that children's bodies absorb and process drugs differently from adults. Dosages cannot be based simply on a child's size, weight, body surface area or age. That is why specific, rigorous studies are important.” (Mr Andrew Love 12/01/2000, UK House of Commons)*

*“However, children do not have the same metabolism as adults. Children therefore need specifically adapted pharmaceutical forms, not only so that they are better tolerated, but also so that they are safer and more effective.” (Ms Françoise Grossetête 06/09/2005, EU Strasbourg)*

*“Mr President, a child is not a small adult. A pill for a child is not half of that for an adult, and a child's coat is not a shrunken version of an adult's.” (Mr Lasse Lehtinen 06/09/2005, EU Strasbourg)*

**a) Children as a different species:** This sub-category was created where children were talked about in such an extreme way that the resultant construction of children was like those of aliens, with reference to them being “completely different”. Only the following two examples of this extreme form of differentiation were identified.

*“Children have their own specific characteristics, completely different metabolism, and different susceptibility to medicines, as Dr Belohorská said just before me.”* (Mr Miroslav Mikolasik 06/09/2005, EU Strasbourg)

*“That may do no harm, it may do no good or it may even harm the child, because it may not be correct for it to have the dose at all, or it should have more or less than that.”* (John Bowis 06/09/2005, EU Strasbourg)

#### **5.3.4.8 Children as a minority group**

I located six examples of this construction. In most cases the inference was implicit. I struggled with whether to consider this as a stand-alone construct or linked to marginalisation and lack of service and concluded that these three constructs sit very closely together. I concede that this is contentious, because being a group in the minority does not necessarily result in marginalisation.

*“Yet with the pediatric incentive already used for these drugs, the younger kids are out of luck. What makes it worse for these younger kids is that there is almost no commercial incentive to study drugs in these age-groups. The raw size of this young population is so small, obviously even smaller than the population of children as a whole, that there is hardly ever sufficient market incentive for a drug company to perform the studies needed to help the youngest children.”* (Mr Bond, 01/08/2001, US Senate)

*“Children are defined as “someone under 19”. It seems obvious to me that the pharmaceutical companies should ideally provide information about how drugs work in several stages of childhood. A drug will have a variable effect on a neonate, a new-born infant, a one to four-year-old, a four to 10-year-old, a 10 to 13-year-old and a 13 to 19-year-old, but they are all classified as “children”. (Lord Colwyn 03/07/2006, House of Lords)*

**a) Children as an under-serviced sector of society:** For this construct I found 17 examples were identified. Most examples are implicit ones.

**b) Children as a marginalised group:** An emergent construction that I have linked to the minority group construction. I found five examples that refer to the disfranchisement of children.

#### **5.3.4.9 Children as developing adults**

This construction is based on ‘human becomings’ (James, Jenks and Prout, 1998) but I think that, as this is about medical R&D, it is clearer to say developing adults. I found 12 examples of this within the speeches.

*“Children are not simply smaller versions of adults. Their bodies actually metabolize drugs quite differently as they grow older.” (Mr Dodd 09/05/1997, US Senate)*

*“The long-term effects on children must be studied not just to look at accumulative effect, as we do with adult medicines, but to look at the particular effect the medicine has at different stages of a child’s development and on the health of the young adult they become.” (Ms Kathy Sinnott 31/05/2006, EU Brussels)*

#### 5.3.4.10 Children as incapable others

I identified seven examples of this construction. Only four explicitly stated that children were incapable of completing a task, such as giving informed consent.

**a) Children as unreliable witnesses:** I list this as a sub-category as for children to be viewed as unreliable, they must be deemed to be incapable of acting in a reliable way. Only one example was identified.

*“Children also may not give doctors accurate information about how medicines are affecting them, making diagnoses difficult, involving a large-degree of guess work.” (Mr DeWine 12/12/2001, US Senate)*

#### 5.3.4.11 Children as capable others

On the other end of the capability spectrum, children were rarely constructed as being capable. This was an *a priori* category for which I only isolated 3 examples. I grouped reliable witnesses and crucial informants as sub-categories as to be either of these the child has to be capable.

**a) Children as reliable witnesses:** I only found 2 examples of this within the speeches.

**b) Children as crucial informants:** There is overlap here and so two of the three examples found, I have also categorised under reliable witnesses. I have not merged the two constructs however as they are different, albeit subtly. For reliable witnesses children are seen as capable of reporting information accurately to another person. With crucial informants children are positioned as important to consult, regardless of their ability to report accurately.

*“We have talked to the practitioners treating those patients and talked to patients who suffer from multiple sclerosis and Lou Gehrig's disease, kids who suffer from diabetes, and Americans who suffer*

*from coronary artery diseases and a long, long list of diseases that is extensive.” (Mr Greenwood 29/05/1996, US House of Representatives)*

*“I talked to a little girl in Madison, 7 years old, whose fingertips are covered with scars because she has to prick them several times a day to do blood testing, ...” (Mr Klug 29/05/1996, US House of Representatives)*

#### **5.3.4.12 Children as medical heroes**

I only found 2 examples where children were constructed as champions of medical research. In both examples by the same orator, children are not named but are championed for their contribution to medical advancement.

*“One example of new information is the drug propofol, the very drug I mentioned earlier that caused a serious problem for the 18-month-old boy in the ICU. What they found in extensive pediatric studies done on propofol as a result of the new incentive is that the drug is more dangerous than other alternatives that could be used to sedate pediatric ICU patients. So because of this testing, propofol would not be used in the same situation today. And that little boy wouldn't have had a life-threatening incident.” (Mr Bond 01/08/2001, US Senate)*

#### **5.3.4.13 Children as active participants**

I only identified one example of children being constructed as active participants but as this focussed on informed consent, which although not strictly the area I am researching, support the construction of children being capable.

**Table 5.3.4 Ways of constructing children in the context of medicine legislation creation (1992-2007) - Speaker's theoretical standpoint**

	Theoretical construct	N° of speeches	Speeches %	N° of References
1	Passive actors	63	39	103
2	Therapeutic orphans	39	24	59
3	A vulnerable or at-risk group	38	23	53
4	Medical discipline	27	17	44
5	Attachment/kinship	30	19	41
6	Stakeholders	27	17	37
7	As citizens	24	15	28
8	Social actors	22	14	25
9	Different from adults	22	14	25
10	Underserviced sector of society	14	9	17
11	Guinea pigs	13	8	14
12	Real human beings	9	6	13
13	Developing adults	8	5	12
14	Equals	8	5	12
15	Incidental	9	6	11
16	Incapable others	5	3	7
17	Minority group	4	2	6
18	Marginalised group	3	2	5
19	Capable others	3	2	3
20	Precious possessions	3	2	3
21	Crucial informants	2	1	3
22	Reliable witnesses	2	1	2
23	Medical heroes	1	1	2
24	Different species	2	1	2
25	Unreliable witnesses	1	1	1
26	Active participants	1	1	1
	<b>Total</b>	<b>161</b>		<b>529</b>

## 5.4 Chapter summary

The findings from this speech analysis provide valuable insight into how children were constructed in the context of medicines R&D within the political genre preceding the creation of the EU Paediatric Regulation. The findings suggest how political actors have contributed to the discourse of children's medicines, and how they have spoken about children within the context of improving medicines available to and for use by children. Adopting a systematic approach to synthesising data enabled me to produce unbiased and robust evidence of how children are constructed within the political and policy making arenas. This exercise enabled me to examine how the genre of policy making might influence (centripetally) the utterances of professionals regarding children. In other words, the language utilised in the political discourse filters down into the subsequent documentation that is produced to create new protocols and practices for, in this case, pharmaceutical regulation. I argue that language used in the political genre and the perceptions of children and childhood embedded in this policy construction can influence how children are viewed by those operating within the regulations and policies that govern medicines R&D. This study revealed an obvious lack of children's involvement and absence of children's voice in the political genre. Speakers adopted paternalistic tones, drawing on ethical and emotional appeal to persuade those present. Indeed, when children were talked about within the legislative rhetoric, they were predominantly constructed as passive actors, vulnerable and in need of protection.

## Chapter Six: Systematic scoping review and map of children's views

### **6.0 Overview**

This second component investigates whether children's views on pharmaceutical interventions have been elicited and presented within empirical evidence. I conducted a systematic review of published research to map the extent and nature of this evidence and conducted a thematic analysis of the included studies to categorise topics covered. In this chapter, I present the aims, methods and findings of this second research component.

### **6.1 Aims of second component, review questions and scope**

The aims of this systematic review were three-fold. Firstly, to systematically map research literature that aimed to elicit children's views on medicines and secondly, to extract, appraise and synthesise the research evidence on children's views presented in the studies to gain insight into how children have contributed to knowledge on medicines research and how professionals viewed children's involvement. I chose a broad category of pharmaceutical interventions as I hypothesised that children can indirectly influence R&D efforts when their priorities are inferred from what they say about medicines. For instance, the problems of taking medicines away from home might inspire R&D efforts to focus on reducing dosage frequency or producing more discrete medicines.

I located and analysed the evidence in this area, with a view to answering the following review questions:

- What empirical research has been conducted, from 1988 onwards, into children's views on pharmaceutical medicine?
- What is the focus of studies that investigate children's views on pharmaceutical medicines? (i.e. country, questions addressed, health condition, setting, study design features and demographic characteristics)?
- To what extent are children's views of pharmaceutical medicines reported within research papers pharmaceutical interventions for children?
- Do children have views about pharmaceutical medicines that are relevant to medicines research and development?

## **6.2 Methods**

Methodologically sound systematic reviews are characterised by rigour, transparency, replicability, with clear inclusion criteria, coding frameworks and synthesis (Belur *et al.*; Gough, Oliver and Thomas, 2017a). Conducting systematic reviews are lengthy and highly resource intensive process and usually require the input of a large team of people. A recent study by Borah *et al.* (2017) estimated the mean estimated time to complete and publish a review was 67.3 weeks (IQR=42) and a mean number of review team members of 5 people. Though completing this for a PhD as opposed to a funded project with the resource of a review team, I strived to ensure the quality of this review would be to a high standard by following recognised reporting guidelines. Several guidelines have been developed to improve the quality of systematic reviews and to ensure clear reporting of the findings.

The most commonly used tool is the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), which consists of a 27-item checklist and flow diagram (Moher *et al.*, 2009). The PRISMA checklist focuses primarily on improving the quality of systematic reviews of intervention studies, such as quantitatively focused randomised controlled trials. However, the study designs and narrative findings presented within the research required for this review differ significantly in terms of reporting. Consequently, the methods for evaluating elements such as risk of bias, or outcomes differ from those employed for intervention studies. Therefore, I felt that the PRISMA items were not appropriate for this systematic review and instead employed a specialised qualitative reporting guideline, the Enhancing Transparency in Reporting the synthesis of Qualitative research, known as the ENTREQ statement (Tong *et al.*, 2012). This consists of a 21-item checklist covering five domains: introduction, methods and methodology, literature search and selection, appraisal and synthesis of research findings (ibid, 2012).

### **6.2.1 Searching for studies**

The search strategy that I developed was designed to be a comprehensive search to seek all published literature from a variety of online databases. This was supplemented by a citation search of reference lists from relevant systematic reviews, to help identify further studies that may have been missed by the search (Brunton *et al.*, 2015). Individual databases were searched using a combination of predefined vocabulary and free-text terms. Free-text terms were restricted to the title or abstract fields. The search string was tailored to each database and was designed to be broad and sensitive but also manageable, as I was to conduct the majority of the screening (see Appendix 5). Though aware that there might be research located by specialist involvement websites, my aim was to search for

publications from non-involvement specialist fields to gauge research that had been conducted by non-involvement specialists, those more likely to be encountered by medicines R&D professionals. The database searches were run to capture citations for studies published from 1 January 1999 and were first run back in November 2015 to assist with my literature review, but the search string was later refined, and the dates of the search extended back to 1 January 1988 and was last run on 10 December 2018.

To capture literature from a variety of clinical and social science disciplines, I searched the following databases: ASSIA, Child development and Adolescent Studies, CINAHL, Dentistry and Oral Sciences Source, PubMed, Web of Science Core Collection (inc. BIOSIS Citation Index, SciELO Citation Index). Further I manually added citations that I had found through reading around the literature when writing my literature review. There are in excess of one hundred alternative free online searchable databases for scientific research (Scribendi, 2018), and growing every year. As the purpose of this review was to investigate the nature and extent of research that reported children's views on pharmaceutical medicines, I was aware that the returned number of studies might be unmanageable without the assistance of a review team, therefore I was selective of the databases that I searched. The databases that were selected are highly cited and cover both medical and social sciences. I also applied some limits to the research that I would include.

A date limit was applied to the search of 1 January 1988 to 21 December 2018. This provided thirty years' worth of studies, which can be argued to be an arbitrary time span but one which I felt would suffice to source studies that reported children's views in medicines research and encompass any policy, as children's involvement in research is a relatively

recent phenomenon. This timeframe allowed insight into the growth of studies in this area and encompassed the introduction of key policies relevant to the study sample, i.e. the introduction of paediatric legislations (European Union, 2006a; European Union, 2006b; US Congress, 2002) and the introduction of National Service Frameworks in the UK (Department of Health, 2004; Department of Health, 2005). I am aware that there may be a number of earlier studies that might be relevant, however I had to set limits on the number of studies in order to keep the review manageable. The search was designed to be broad and inclusive, however, to minimise the likelihood of excessive and irrelevant research, studies that were indexed as being about animals were excluded and the search was limited to articles that were written in the English language and that had abstracts and full-text available.

### **6.2.2 Screening studies for inclusion in the review**

To locate relevant studies inclusion/exclusion criteria were developed. These were piloted on a sample of studies and agreed with a co-reviewer (SO) before being applied generally. As per the recognised screening method of systematic reviewing, the screening process has two phases (Brunton *et al.*, 2017a). The first phase was to screen the titles and abstracts of the located studies against the inclusion/exclusion criteria that I developed. I then located and retrieved the full text of studies that met the inclusion criteria on their title and abstract and completed the second phase of screening by applying the inclusion/exclusion criteria against based on the full text of the studies.

To test and refine the inclusion criteria, I had the assistance of a co-reviewer (KD) who donated some of their time. An initial set of studies were double-screened by the two reviewers (GS, KD) to ensure the rigour of the

screening process. During this time, differences in interpretation of the inclusion criteria were discussed and any ambiguous criteria were refined. As is good practice in systematic reviewing, single-reviewer screening could only continue a high interrater reliability score (IRR) was achieved (Minenko *et al.*, 2006). A systematic reviewer (KD) agreed to screen 31 studies and the inter-rater agreement level was 96.7% meaning that there was complete agreement on 30 out of the 31 studies. Although we both agreed that one study should be excluded we disagreed as to which exclusion code it went out on. This led to a refining of one of the exclusion codes. The remaining studies were then single-screened by one reviewer (GS), as this review was for a PhD and therefore not funded for staff time.

To be included in this review, identified studies had to meet all of the following inclusion criteria:

- i) be published in 1988 or since (this predates the NHS &RD strategy by 3 years, which marked the first policy effort in the UK to develop a user-led agenda; AND
- ii) be reported in the English language; AND
- iii) be a study of humans; AND
- iv) be a report of empirical research collecting data (systematic reviews that met all other criteria were not included but their reference lists were screened for other includable studies); AND
- v) be a report on children's pharmaceutical interventions; AND
- vi) not be about the development, validation or evaluation of a research tool; AND

- vii) not be focused on the training, knowledge or education of healthcare professionals or students; AND
- viii) not be focused on substance abuse, misuse or risky behaviour (e.g. alcohol, illicit/recreational drugs; AND
- ix) not be a case study, case series or case report; AND
- x) not focus on new-borns, infants or elderly; AND
- xi) be focused on children's views (any reports that solely focus on the views of parents, caregivers or other adult participants were excluded); AND
- xii) not be focused on: medication adherence, medication compliance, contraception, medicines use, children's knowledge of medicines, access to medicines, control of medicines, or risk

It was decided in the full text screening phase that studies that focused on medication adherence, compliance or children's knowledge of the concept medicines would be excluded. Firstly, because the motivation for the adherence and compliance studies can be argued to stem from a desire to make particular populations take their medicines by finding out what is preventing adherence or compliance, rather than to elicit views to inform future research. However, it can also be argued that an understanding of why children do not take their prescribed medications can be used to inform future medicines research. Secondly, I found a large body of research that focused on adherence. Studies solely on children's understanding/knowledge of medicines was excluded, as these were deemed not help to inform medicines R&D but rather informs pedagogical approaches to teaching children about medicines, children's health belief model and children's cognitive development (Probstfield and Rheumatology, 1989). Furthermore, I

found a systematic review had already been executed into this area (Hämeen-Anttila and Bush, 2008).

### **6.2.3 Coding studies**

To ensure validity of a systematic review accurate and meticulous application of a standardised coding tool must be applied, a tool that is understood by the different review and one that allows for each reviewer to apply the codes to the located studies identically (Sutcliffe, Oliver and Richardson, 2017). A coding tool is a means to facilitate ways of aggregating data and examining the predefined questions for this review and should include clear and explicit definitions and coding guidance on how to apply each code. Although I had some pre-specified concepts for the coding, from being sensitised to important concepts to which I was exposed in particular from engaging with a review on children's perceptions of medicines (Hämeen-Anttila and Bush, 2008), I employed an open coding approach (Sutcliffe, Oliver and Richardson, 2017) which allowed both questions and answers to emerge from iterative reading of the studies. This was initially agreed by two reviewers (GS, SO) and tested on a set of 50 studies, during which time the coding tool was further refined. This process helped to produce a coherent coding framework, which was agreed with a second reviewer (SO) after all superfluous or ambiguous codes were removed or refined, and we were satisfied that the coding framework answered the review questions. The coding of the studies was then executed by me, as the single reviewer at this point.

### **6.2.4 Critical appraisal**

To understand the quality of the included studies, I critically appraised the literature using a recognised quality assessment tool. There are

several quality assessment tools that can be applied to qualitative research papers (CASP, 2018; Hawker *et al.*, 2002; Long and Godfrey, 2004; Long *et al.*, 2002; NICE, 2012). For example, the Long and Godfrey (2004) tool describes four elements of quality to be assessed against a 7-point checklist. The Critical Appraisal Skills Programme (CASP) suggests a 10-point checklist you help researchers to understand qualitative research. The CASP (2018) checklist is designed to cover three broad issues that need to be considered: study validity, quality of the findings and research value. As the checklist was a pedagogic tool designed to educate healthcare professionals and healthcare organisations, they do not suggest a scoring system. Although the specific questions asked within qualitative quality assessment tools vary in length and specificity, they are similar in that they focus on the appropriateness, relevance and clarity of the: phenomenon, context, method, sampling, ethics, data collection, data analysis and value of findings.

The tool applied to appraise the qualitative studies in this theses was taken from a tool outlined in Appendix D of Hawker *et al.* (2002). I had encountered this tool in a study on by Lorenc *et al.* (2014) and found it a clear and useful framework to appraise studies in that responding to the questions is less subjective due to the clear requirements for each score. The Hawker *et al.* (2002) comprises a 9-point checklist and allows for grading on each question covering: abstract and title, introduction and aims, method and data, sampling, data analysis, ethics and bias, results, transferability or generalisability, and implications and usefulness. Each of the nine questions included in the tool can be graded 'good', 'fair', 'poor' or 'very poor'. I then applied a numerical scoring system as suggested by Lorenc *et al.* (2014) by ascribing the answers from 1 point for very poor to 4 points for studies where the answer was good. Studies therefore can score a minimum of 9 points to a

maximum of 36 points. The overall quality was graded using the definitions developed by Lorenc et al. (2014) where the total score from the nine questions was ascribed as: high quality was graded A (score of 30-36 points); medium quality was graded B (score of 24-29 points); and low quality was graded as C (score of 9-24 points) (see Table 6.3.1.2).

### **6.2.5 Information management**

I utilised EPPI-Reviewer 4 (V.4.9.0.0) the EPPI-Centre's on-line tool for research synthesis (Thomas and Brunton, 2006) to monitor studies throughout the review process. This software facilitates the recording of the bibliographic details of studies included in the review, how it was identified, where it was found, rationale for inclusion or exclusion, coding data and storing text about the included studies and data that are utilised and generated during the review synthesis.

### **6.2.6 Data synthesis**

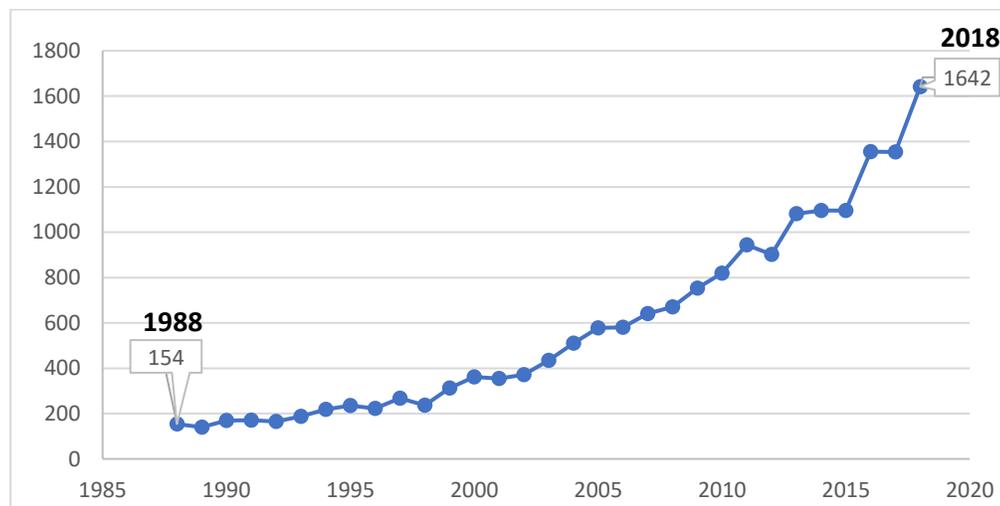
The next stage was to examine the nature of the views reported in the included studies. Two of the research questions for this review focus on the extent that are children's views of pharmaceutical medicines reported within research papers on pharmaceutical interventions for children and whether these views are relevant to medicines R&D and the researchers operating within this field. Review synthesis is the process through which a transformation of data from the included primary studies occurs, resulting in a 'connected whole' ness, that can generate new knowledge and understanding (Thomas *et al.*, 2017). As the purpose of this review was to identify evidence that reported children's views without a predefined conceptual framework and to understand the nature of what was reported, a narrative approach was applied in the form of a thematic synthesis. Thematic synthesis is a type of 'narrative' synthesis, an umbrella term that also includes: thematic

summaries, framework synthesis, and meta-ethnography (Brunton *et al.*, In press; Thomas *et al.*, 2017). Thematic synthesis configures the studies into themes via detailed assessment of the study findings helping to provide a synthesis that is “systematically grounded” in the included studies (Thomas and Harden, 2008b; Thomas *et al.*, 2017, p. 190). Themes can be defined as concepts or textual categories of ideas that emerge from data (Snilstveit, Oliver and Vojtkova, 2012). Thematic analysis therefore is a search for themes which emerge as significant to the description of the phenomenon being studied (Daly, Kellehear, & Gliksman, 1997, as cited in Fereday and Muir-Cochrane, 2006) and is a method that “preserves an explicit and transparent link” connecting the text and conclusions of primary studies, a feature that is viewed as central to the process of systematic reviewing (Thomas and Harden, 2008a). According to Boyatzis (1998, p. 31) a well-defined theme should contain five key elements: 1) a label; 2) a definition of the theme characteristic; 3) a description how to identify the theme; 4) a description of the qualifications or exclusions that should be applied to that theme; and 5) positive and negative examples of the theme to eliminate the possibility of confusion. The skill of the researcher lies in the recognition of patterns within data, which I achieved through applying an iterative reading process, reading of the study findings again whenever a new theme emerged. These patterns became the themes for analysis and were applied to and across the included studies. The first round of thematic analysis led to the development of ‘descriptive’ themes. Through iterative reading and line-by-line coding, I was able to generate ‘analytical’ themes that used to answer the review questions and facilitate the generation of interpretive constructs.

### 6.3 Findings from the systematic review

The search located 19,243 studies that related to the search string that was created on children’s views and medicine (see Figure 6.3.2). The comparative number of studies that were located increased significantly year on year with a couple of exceptions where the number of studies dipped; this was between 1997 and 1998 and between 2011 and 2012, where there were 11.2% and 4.5% fewer studies captured respectively. The number of studies in 2018 (n=1,642) in comparison to thirty-years previously has increased tenfold (1988, n=154).

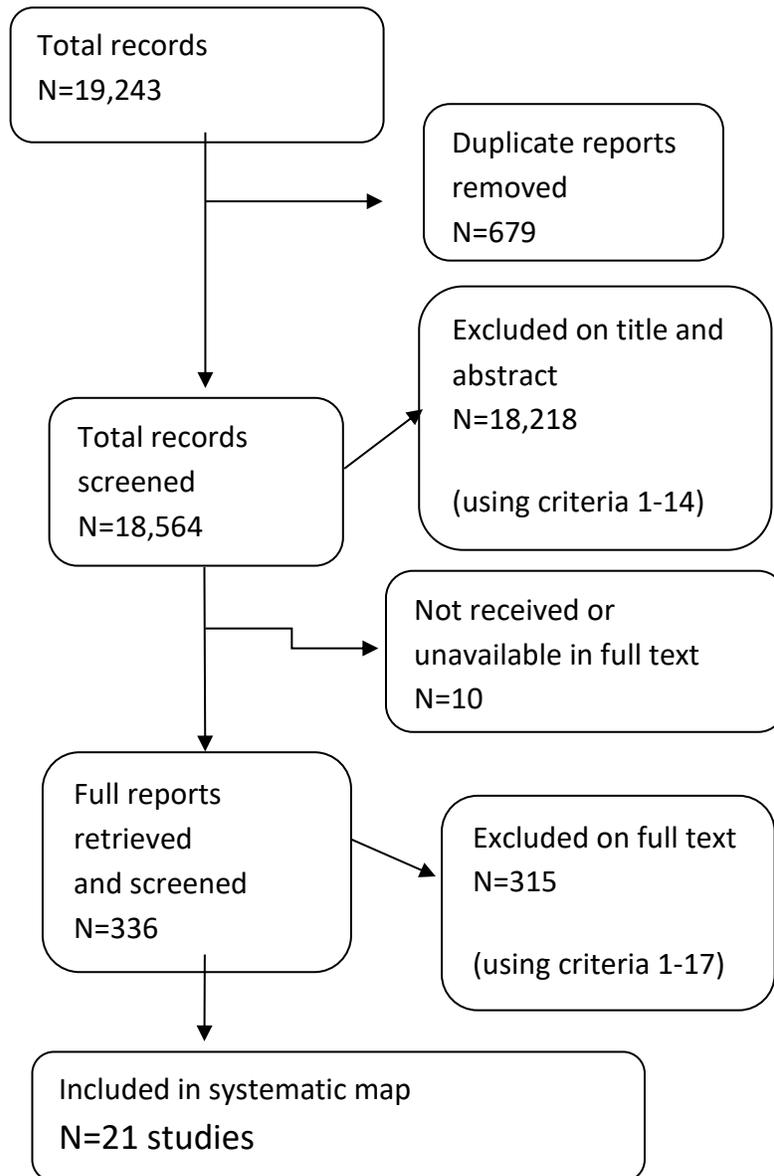
**Figure 6.3.1 Number of studies located by year**



After the two phases of screening (title and abstract and full text), 21 studies remained that were included in the review (Barnard, Speight and Skinner, 2008; Bernays *et al.*, 2017; Carpenter-Song, 2009; Cuenca *et al.*, 2015; de Graaf *et al.*, 2017; Doherty *et al.*, 2000; Gallagher *et al.*, 2011; Hodes *et al.*, 2018; Kosse *et al.*, 2018b; Lindholm Olinder, Kernell and Smide, 2007; Low *et al.*, 2005; Maroun, Thackeray and Midgley, 2018b; Mukattash *et al.*, 2012b; Murphy *et al.*, 2015; Parsons *et al.*, 2017; Pradel *et al.*, 2001; Sandler

*et al.*, 2008; Townsend, Floersch and Findling, 2009; Veinot *et al.*, 2006; Webster, 2017; Williams *et al.*, 1998). It should be noted that, though excluded from this review, I located 62 studies that focused on medication adherence or compliance. These types of studies have the potential to provide some insight into children's views on pharmaceutical interventions.

Figure 6.3.2 Summary of the flow of studies through the review\*



\*See Appendices 6.3.1 and 6.3.2

### **6.3.1 Critical appraisal**

The results of quality assessment measured against the Hawker et al (2002) tool for qualitative research, found that twelve (57%) of the studies received a high study quality rating (A), eight (38%) received a medium quality rating (B) and the remaining study received a low quality rating (C) (5%). For the purposes of this review, none of the studies were excluded on grounds of poor quality. It must be noted however that the extent to which the quality assessment tool is indicative of the usefulness or validity of the finding presented in the studies is questionable. This may be due to the fact that the focus for any “reasonably transparent” quality assessment tool is on the reporting of methods (Lorenc *et al.*, 2014, p. 81) as opposed to the reporting of findings.

**Table 6.3.1.2 Results of the quality assessment for the included studies (n = 21)**Grade key: **A** = High quality (30–36 points); **B** = Medium quality (24–29 points); **C** = Low quality (9–24 points)

Author/ Year	1. Abstract and title		2. Introduction and aims		3. Method and data		4. Sampling		5. Data analysis		6. Ethics and bias		7. Results		8. General’ability		9. Implications and usefulness		Total	Grade
	Good	4	Good	4	Fair	3	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4		
Barnard (2008)	Good	4	Good	4	Fair	3	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4	35	<b>A</b>
Bernays (2017)	Good	4	Good	4	Good	4	Fair	3	Poor	2	Very Poor	1	Good	4	Fair	3	Good	4	29	<b>B</b>
Carpenter-Song (2009)	Good	4	Fair	3	Fair	3	Poor	2	Fair	3	Very Poor	1	Fair	3	Fair	3	Poor	2	24	<b>B</b>
Cuenca (2015)	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4	Good	4	36	<b>A</b>
de Graaf (2017)	Good	4	Good	4	Good	4	Good	4	Good	4	Fair	3	Good	4	Good	4	Good	4	35	<b>A</b>
Doherty (2000)	Fair	3	Good	4	Good	4	Poor	2	Very Poor	1	Poor	2	Good	4	Good	4	Good	4	28	<b>B</b>
Gallagher (2011)	Good	4	Good	4	Good	4	Good	4	Fair	3	Poor	2	Good	4	Good	4	Good	4	33	<b>A</b>
Hodes (2018)	Fair	3	Good	4	Poor	2	Good	4	Very Poor	2	Good	4	Poor	2	Fair	3	Poor	2	26	<b>B</b>
Kosse (2018)	Fair	3	Poor	2	Fair	3	Good	4	Poor	2	Good	4	Poor	2	Good	4	Poor	2	26	<b>B</b>
Low (2005)	Fair	3	Good	4	Fair	3	Fair	4	Poor	2	Very Poor	1	Good	4	Fair	3	Fair	3	27	<b>B</b>

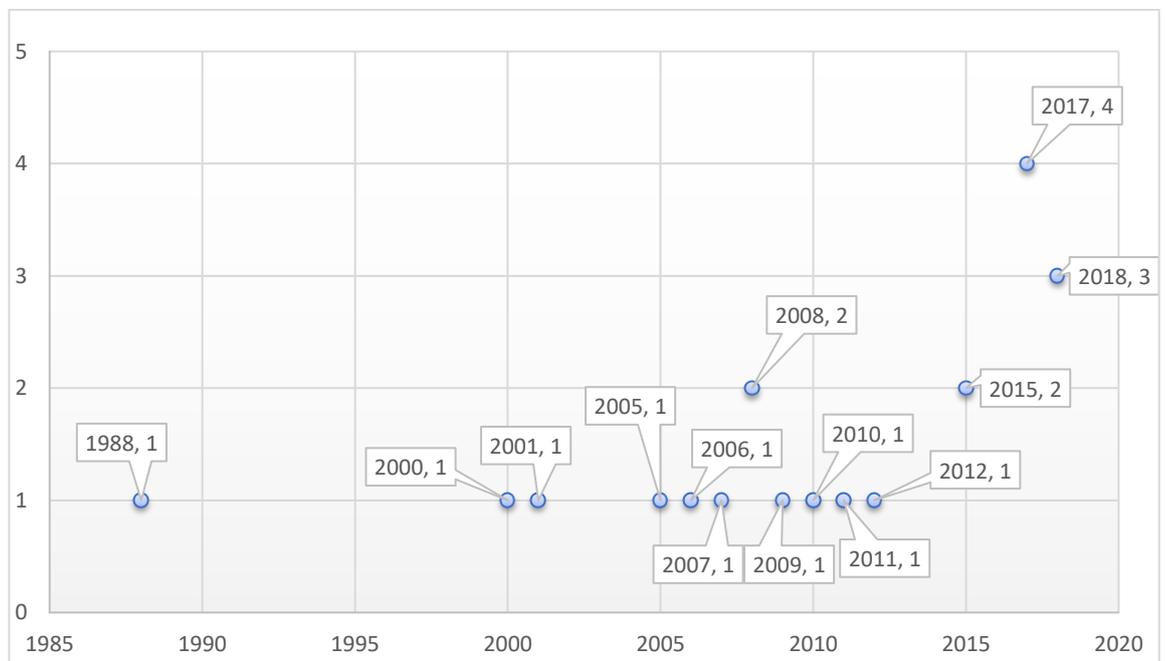
**Table 6.3.1.2 Results of the quality assessment for the included studies (n = 21) (cont’d)**

Author/ Year	1. Abstract & title		2. Introduction & aims		3. Method and data		4. Sampling		5. Data analysis		6. Ethics & bias		7. Results		8. General’ability		9. Implications & usefulness		Total	Grade
Maroun (2018)	Fair	3	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Good	4	Good	4	33	A
Mukattash (2012)	Good	4	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Fair	3	Good	4	33	A
Murphy (2015)	Fair	3	Poor	2	Poor	2	Poor	2	Poor	2	Very Poor	1	Good	4	Poor	2	Fair	3	21	C
Lindstrom Olinder (2007)	Good	4	Fair	3	Fair	3	Good	4	Fair	3	Poor	2	Good	4	Good	4	Fair	3	30	A
Parsons (2017)	Good	4	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Fair	3	Good	4	33	A
Pradel (2001)	Fair	4	Good	4	Fair	3	Fair	3	Fair	3	Poor	2	Good	4	Fair	3	Fair	3	29	B
Sandler (2008)	Fair	4	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Fair	3	Fair	3	32	A
Townsend (2010)	Poor	2	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Good	4	Good	4	32	A
Veinot (2006)	Good	4	Good	4	Good	4	Good	4	Good	4	Poor	2	Good	4	Good	4	Fair	3	33	A
Webster (2017)	Fair	3	Good	4	Good	4	Good	4	Fair	3	Poor	2	Good	4	Good	4	Fair	3	31	A
Williams (1998)	Good	4	Good	4	Good	4	Fair	3	Very Poor	1	Very Poor	1	Fair	3	Fair	3	Good	4	27	B

### 6.3.2 Dates of publication of included studies

Since 1988, studies investigating children’s views that met the inclusion criteria were sporadic. Though one study was located back in 1988, it is not until over a decade later from 2000 that studies on children’s views became more frequent but still only averaged one study per year. Only in four years did the number of studies located exceed one: 2008 (n=2), 2015 (n=2), 2017 (n=3) and 2018 (n=4) (See figure 6.3.2).

**Figure 6.3.2 Rate of publication (n=21)**

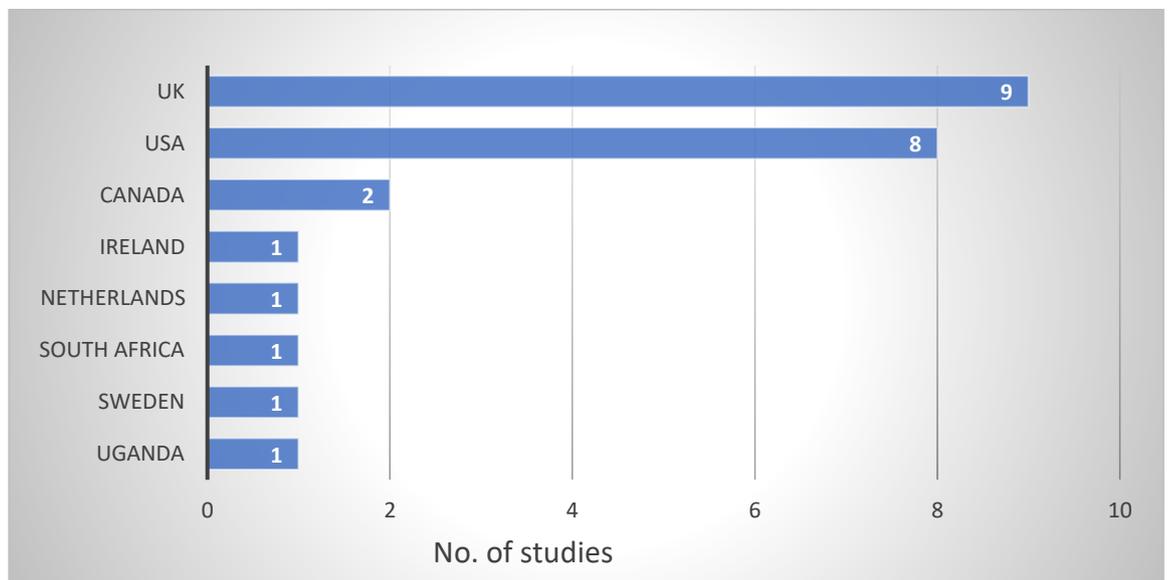


### 6.3.3 Geographical location

For the purposes of this map there were no geographical restrictions. Most of the included studies were conducted within countries under the Organisation for Economic Co-operation and Development (OECD) country umbrella (OECD, 2016) (n=20), with two studies being conducted in low and middle-income countries (LMIC).

Of the included 21 studies, nine were conducted in the UK (43%) (See Figure 6.3.3) and eight in the USA (38%). The remaining studies were conducted in Canada (n=2), with one study each in Ireland, Netherlands, South Africa, Sweden and Uganda. There was one international study (Bernays *et al.*, 2017), and the remainder were all single country/national research endeavours.

**Figure 6.3.3 Geographical location of included studies (n=21)\***



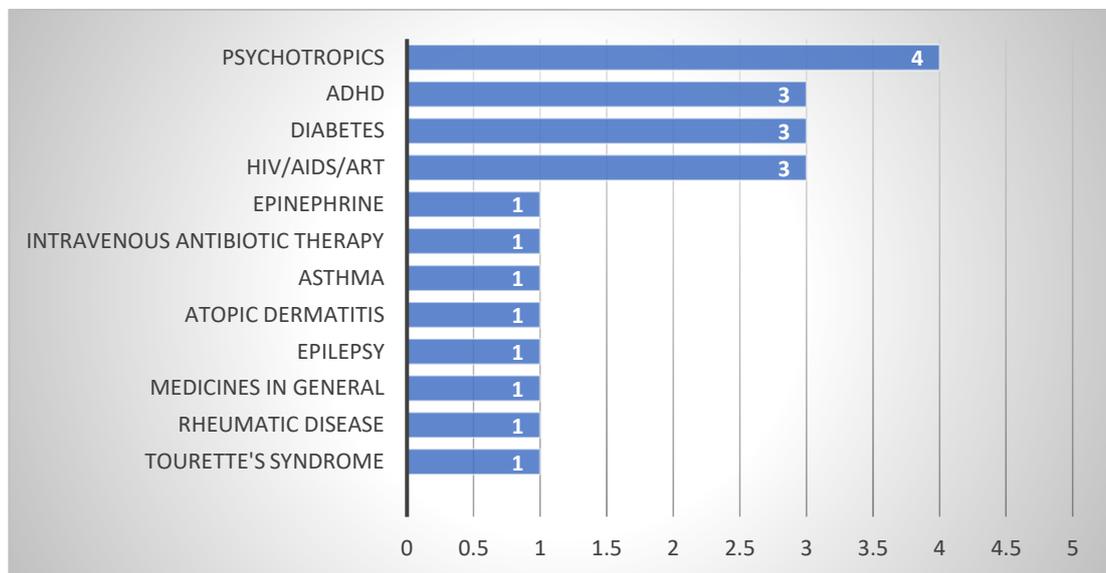
\*One study was conducted across four countries: UK, USA, Ireland and Uganda

#### **6.3.4 Condition or pharmaceutical intervention focus**

Figure 6.3.4 presents the number of studies identified by health condition or pharmaceutical intervention. The largest group of studies (n=4) focused on psychotropic medications, which included selective-serotonin

reuptake inhibitors (SSRIs), antidepressants and antipsychotic medication. This was followed by studies on attention deficit and hyperactivity disorder (ADHD) (n=3), diabetes (n=3), HIV/AIDS or anti-retroviral therapy (ART) (n=3) and specific pharmaceutical interventions (epinephrine and intravenous antibiotics) (n=2). There was one study each on atopic dermatitis, asthma, epilepsy, pharmaceutical interventions in general, rheumatic disease and Tourette's syndrome.

**Figure 6.3.4 Health condition or pharmaceutical intervention: included studies (n=21)**



**Table 6.3.4 Health condition or pharmaceutical intervention by country of research origin (n=21)\***

Condition or pharmaceutical intervention	UK	USA	Canada	Ireland	Netherlands	Sweden	South Africa	Switzerland	Uganda
Psychotropics	1	2	1						
ADHD		4							
Diabetes	1	1				1			
HIV/Aids and ART	1	1	1	1			1		1
Specific medicines									
Epinephrine	1								
Intravenous antibiotic therapy	1								
Asthma		1							
Atopic dermatitis					1				
Epilepsy	1								
Medicines in general	1								
Rheumatic disease	1								
Tourette's syndrome	1								

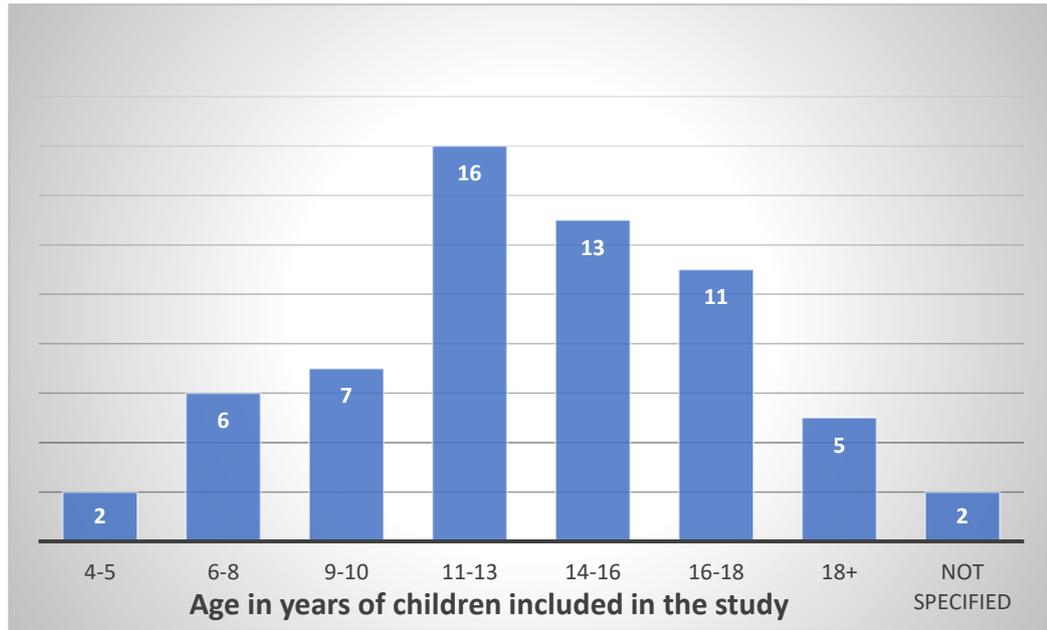
\* N.B. includes one international study

### 6.3.5 Age, gender and ethnicity of children under study

The ages of the children included in the studies varied dramatically and there as there are no agreed age categories within the child demographic the categories that are represented I based around UK school key stages and phases: reception (4-5 years), key stage 1 (6-8 years), key stage 2 (9-10 years), key stage 3 (11-13 years), GCSE (14-16 years), Advanced level (16-18 years). Most studies focused on eliciting the views children aged 11-18 years. As

every category used within a study is selected in the coding tool, the numbers do not represent the number of studies, rather a frequency of age selection.

**Figure 6.3.5 Age of the children included in the studies**



Most studies included both male and female participants in the study (n=19). One study included only female participants (Williams *et al.*, 1998) and one study did not report the gender of the participants (Barnard, Speight and Skinner, 2008).

Most studies did not report on the ethnicity of the study participants (n=14). Those that did report ethnicity, did so with varying levels of detail. One study (de Graaf *et al.*, 2017) provided a detailed breakdown of twelve different ethnicities. The other studies focused on a variety of one or two ethnicities. Studies focused on Caucasian Americans (n=5), African Americans (n=4), North/East/Mid Europeans (n=2), sub-Saharan African/Caribbeans (n=2), and Native American (n=2).

**Table 6.3.5 Reported ethnicity and study details (n=21)\***

<b>Ethnic category</b>	<b>No. of Studies</b>	<b>Study details</b>
European (north/east/mid)	2	de Graaf et al. 2017; Kosse et al. 2018
European south (Mediterranean)	1	de Graaf et al, 2017
European (Roma)	1	de Graaf et al. 2017
African/Caribbean (North African)	1	de Graaf et al. 2017
African/Caribbean (sub-Saharan)	2	de Graaf et al. 2017; Hodes et al. 2018
African/Caribbean (Afro-Caribbean)	1	de Graaf et al. 2017
American (Caucasian)	5	Carpenter-Song, 2009; Low et al. 2005; Sandler et al. 2008; Townsend et al. 2010; Veinot et al. 2006
American (African)	4	Carpenter-Song, 2009; Sandler et al. 2008; Townsend et al. 2010; Veinot et al. 2006
American (Hispanic)	4	Townsend et al. 2010
American (Native American/Aboriginal)	2	Pradel et al. 2001; Veinot et al. 2006
Asian (Indian subcontinent)	1	de Graaf et al. 2017
Asian south-east (Vietnam, Thailand, Indonesia, Malaysia, Philippines)	1	de Graaf et al. 2017
Asian east Asia (China, Japan, Korea)	1	de Graaf et al. 2017
Asian west Asia (Afghanistan, Iran)	1	de Graaf et al. 2017
Middle eastern (Arab peninsula)	1	de Graaf et al. 2017
Other mixed	1	de Graaf et al. 2017
Not reported	14	

\* N.B. includes one international study

### **6.3.6 Study design and setting**

Most of the included studies employed qualitative research designs specifically to elicit views data (n=19). Three studies employed a mixed methods design (Hodes *et al.*, 2018; Sandler *et al.*, 2008; Townsend, Floersch and Findling, 2010) The majority of studies employed one-to-one interviews to elicit the views of children (n=15). Of these, the majority were semi-structured interviews (n=11). The remaining studies consisted of unstructured interviews (n=3), ethnographic or drawing interviews (n=2), and one study that used a structured interview design. Group interviews in the form of focus groups were used for seven of the studies. One study (Hodes *et al.*, 2018) used participant observations to provide insight into adolescents' experiences of healthcare and medicines taking. Three studies used self-completion questionnaires alone to elicit insight and one study (Townsend, Floersch and Findling, 2010). Further, one study employed game play (Hodes *et al.*, 2018).

### **6.3.7 Data analysis methods**

Data analysis was mainly in the form thematic analyses, either inductive (n=11), or a combination of inductive and deductive (n=3). For six studies the type of thematic analysis used was not specified. The remaining studies used content analysis (n=4), descriptive analysis (n=1) or the analysis methods was not specified (see Appendix 6.3.7).

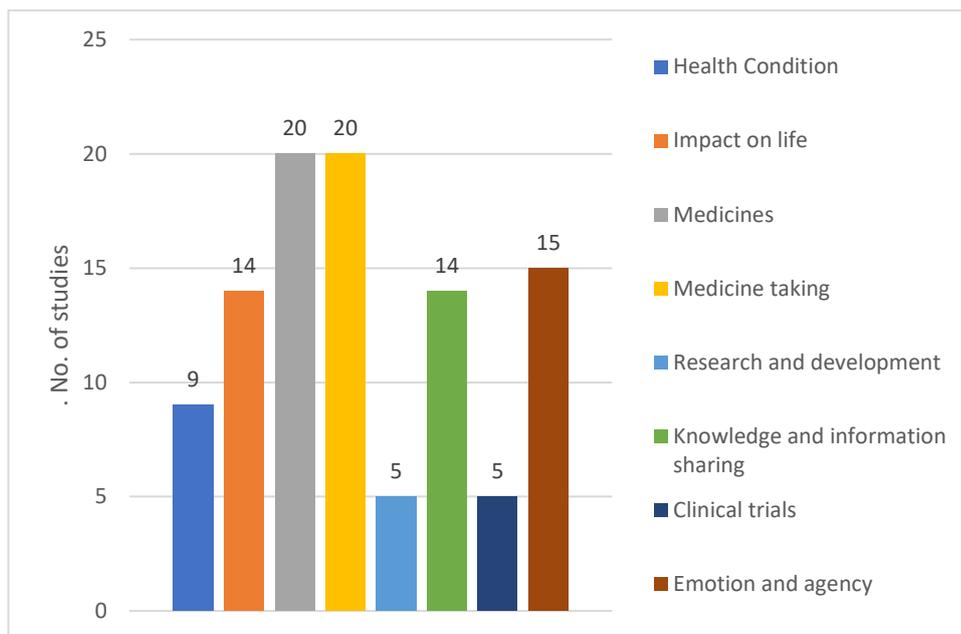
## **6.4 Children's views of medicines**

In this next section, I present a summary of topics where children's views had been elicited. The data I identified resulted in eight emergent themes: health condition, impact on life, medicines, medicine taking, research and development, knowledge and information sharing, clinical trials and emotion and agency. An overview of the views data is presented to provide

insight in to the nature of the data available from the studies. A summary of researchers’ views on children’s involvement is also provided.

Alongside issues directly about medicines (n=20), medicines taking (n=20), and medicines research and development (n=5), studies also reported the views of children on a variety of related topics: emotion and agency (n=15), impact on the lives (n=14), knowledge and information sharing (n=14), health condition (n=9), and clinical trials (n=5). The following graphs and tables map the topics covered within these themes. For details of the studies see appendices (6.4.0 to 6.4.8)

**Figure 6.4 Themes covered by study**



**6.4.1 Theme: Medicines**

The range of issues discussed around medicines was varied and comprehensive with studies presenting children’s views surrounding: adverse events and side-effects (n=11), the physical characteristics or medicines including palatability, size, texture (n=8), cost of medicines (n=5), quality (n=5), safety (n=5), acceptability of medicines (n=4), medicines as a concept

(i.e. as a support tool (n=4) or a sign of disease severity (n=2)), dosage form or elegance (n=2), caution surrounding medicines (n=2), choice of medicines (n=2), efficacy (n=1), packaging (n=1), and the use of off-licence or unlicensed (n=1) (see Appendix 6.4.1).

#### **6.4.2 Theme: Medicine taking**

Twenty studies reported children's views related aspects of medicine taking. A wide range of topics discussed were reported within this theme: the practicalities of taking medicines (n=12), negative feelings towards medicine taking (n=11), adhering to prescription guidance (n=11), positive impact of taking medicines (n=9), stigma (n=7), compliance (n=6), frequency and duration of medicine taking (n=4), the purpose and value of taking medicines (n=4), difficulties taking or using medicines (n=4), ambivalence towards taking medicines (n=3) and pain or discomfort experience when taking medicines (n=1) (see Appendix 6.4.2).

#### **6.4.3 Theme: Emotion and agency**

Children spoke about various concerns related to being a child who takes medicines from both emotional aspects and aspects of agency. From the studies views on fear (n=9), feelings of and coping with difference (n=6), risk (n=3), ability (n=2), age (n=1), altruism (n=1), assent and consent (n=1), honesty and reliability (n=1) and autonomy (n=1) (see Appendix 6.4.3).

#### **6.4.4 Theme: Impact on life**

Fourteen of the included studies contained children's views on how medicines were impacting on their lives. The themes that emerged were independence and shared decisions (n=10), impact on family and home life (n=7), impact on friends, friendships and peers (n=7), impact on their quality of life (n=5), impact on school and learning (n=5), impact on food and diet (n=3), freedom (n=2), support (n=1) and impact on sport and exercise (n=1) (see Appendix 6.4.4).

#### **6.4.5 Theme: Knowledge and information sharing**

Another emergent theme that occurred in a high number of studies (n=14) was that of children's views surrounding knowledge and the sharing of information about their condition or treatment. The knowledge in question is either children's knowledge or that of professionals and relatives. The subthemes that were identified under this theme were: children's knowledge of medicines actions (n=8), provision of information on medicines (n=6), children's understanding of their condition (n=6), truth, trust and transparency (n=4), knowledge of professionals, parents and carers surrounding their condition and treatment (n=3), training and knowledge of medicines licencing (n=1) (see Appendix 6.4.5).

#### **6.4.6 Theme: Health Condition**

In the nine studies that reported children's views related to their health condition, the issues that children discussed focused on diagnosis (n=3), accessing or receiving specialist care (n=5), seeking treatment (n=1), finding a cure for the disease (n=2), outcomes of recovery (n=4), issues about aetiology and genetics (n=1), development of predictive tests for the condition (n=1) (see Appendix 6.4.6).

#### **6.4.7 Theme: Research and development**

Five studies reported children's views related to research and development. A variety of R&D related topics were identified in the included studies: young people's ideas for medicine development (n=4), research priorities (n=2), health services research (n=1), factors influencing research priorities (n=1), suggestions to improve treatment (n=1), basic science (n=1) clinical medicine research (n=1), psychosocial research (n=1), public health research (n=1) and funding for research (n=1) (see Appendix 6.4.7).

#### **6.4.8 Theme: Clinical trials**

The final theme to emerge from the studies was that of clinical trials. I identified three sub-themes: being a trial participant (n=4), seeing clinical trials as a sign of progress (n=1) and three elements of clinical trials the nine studies that reported children's views related to their health condition, the issues that children discussed focused on diagnosis (n=3), accessing or receiving specialist care (n=5), seeking treatment (n=1), finding a cure for the disease (n=2), outcomes of recovery (n=4), issues about aetiology and genetics (n=1), development of predictive tests for the condition (n=1) (see Appendix 6.4.8).

#### **6.4.9 Authors' views about children's involvement**

Eleven of the included studies discussed issues related to children's involvement in research (Barnard, Speight and Skinner, 2008; Bernays *et al.*, 2017; de Graaf *et al.*, 2017; Hodes *et al.*, 2018; Kosse *et al.*, 2018a; Maroun, Thackeray and Midgley, 2018a; Mukattash *et al.*, 2012a; Murphy *et al.*, 2015; Parsons *et al.*, 2017; Pradel *et al.*, 2001; Sandler, Glesne and Geller, 2008; Webster, 2017).

Two studies discussed the importance of understanding young people's views regarding the impact of side-effects (Bernays *et al.*, 2017; Webster, 2017). Bernays *et al.* (Bernays *et al.*, 2017) described young people's views as "vital" and "crucial" and should be given "serious consideration" as they had enriched their understanding of short cycle antiretroviral therapy, which could contribute to the wider success of interventions. Suggesting that including young people's perspectives and experiences is crucial for interventions to be effective beyond the trial and shared their concern over the "ongoing reticence among many leading clinical journals to publish this research alongside trial findings", despite the recognition of the relevance of qualitative research to understand public health challenges. Further they suggest that their experience of young people's involvement provides evidence of the need for careful post-trial dissemination and communication.

de Graaf *et al.* (2017) in a study on the duration of intravenous antibiotic therapy for children with acute osteomyelitis or septic arthritis commented on children's ability to provide clear views in terms of recovery and treatment for acute osteomyelitis or septic arthritis, recommending that researchers reflect on children's perspectives about recovery and outcomes. This was echoed by Parsons *et al.* (2017) in a study looking at factors that influenced young people's research priorities. Found that the young people in their study had "clear opinions on what should be researched in the rheumatology arena" and that these opinions will be essential to both future involvement exercises and research strategies and should be evaluated in terms of impact.

Hodes *et al.* (2018) in a study on anti-retroviral therapy suggest that health outcomes could be improved by "practical engagement" and may expand the evidence base on adherence. Stating that the research should be on the immediate and explicit need of the HIV positive youth.

Kosse et al. (2018a) indicated contradictory views about adolescents' views on atopic dermatitis treatment. They reported ingenuity of adolescents who developed their own way of using topical treatment and recognised the practical suggestions adolescents mentioned to improve medication use. However, they suggest that health care providers should work with adolescents to make ensure proper use.

Maroun et al. (2018a) stated that their study on meaning and medication highlighted the value of bringing adolescents' voices into the debate on the use of antidepressants in their age group and their views are to be included the development of future guidelines, as it may impact on adolescents' treatment decisions, adherence, and response to medicines. They emphasise the importance of working collaboratively to enhance their treatment experience. Suggesting that a valuable body of literature could be created over time.

Mukattash et al. (2012a) investigated children's views on unlicensed/off-label paediatric prescribing and paediatric clinical trials. They found children as young as 10 years old were aware of medicines that are not fully licensed for use in children and the potential risks, expressing views around testing and licensing more medicines in children.

Murphy et al. (2015) commented on the importance of patient involvement in a study on antipsychotic medication experiences of youth. However, the focus was more on shared decision-making in psychotropics, as opposed to involvement in other aspects of research such as research design or priority setting.

Not all researchers set out to elicit children's views. The decision to have a qualitative component came after the start of a clinical trial (Sandler *et al.*, 2008) when they recognised the need to better understand elements of the study from the child and parent perspective. They commented that strong

relationships developed between study personnel and participating children parents but did not elaborate as to whether this was a positive or negative consequence.

Webster et al. (2017) suggest that it is important to explore the meanings that children attach to medications in a study on the similarities and differences in the meanings children and their parents attach to epilepsy medications, as children's are likely to views differ from adults. They also suggest that children's views may develop or change over time, which has implications for children's adherence to medicine regimes;

## **6.5 Chapter summary**

The number of located studies was extensive due to the broad and inclusive search strategy. It was my intention to be inclusive, so as to enable access to papers where children's involvement might not have been obvious.

The breadth of topics discussed by children covered a range of topics from emotion to basic science, suggesting children have much to add to the medicines R&D discourse. As the focus of this thesis is on the views of professionals, I have only included the views of professionals. It is, however, my intention to publish a systematic review on children's views in medicines R&D in the coming months, as this is a unique piece of research in its own right.

## Chapter Seven: Adult interviewees constructing children and involvement

### **7.0 Overview**

In Chapter Five I found that children are constructed in the political genre as vulnerable and passive, yet the scoping review (Chapter Six) revealed that researchers are seeking their views regarding medicines suggesting that some researchers view children as a valuable source of information. In this third component, I present the case of interviews with professionals who have worked on the development of epilepsy medicines or aligned professions. I examine how children are constructed by these professionals, using excerpts (utterances) from the interviews. Bakhtinian discourse theory is applied to examine how children are talked about, and the professionals' views on children's capability and rights. I focus predominantly on identifying different ways that the discursive object (children) is constructed and pinpoint discursive constructions within the politico-medico discourse. The data were collected between November and December 2012 and the transcription process began during this time and concluded in December 2013.

### **7.1 Aims of third component – why talk to professionals?**

The aim of the interviews was to provide first-hand/salient accounts of examples of implemented practices and insight into the attitudes, practicalities, potential facilitators and/or barriers. I wanted to ask those directly involved in the R&D process to provide candid real-world insight into the motivations and processes behind research design and priority setting.

## 7.2 Methods

The interviews were intended to gain insight into the complexities of children's participation in medicines R&D. The questions were designed to elicit: stories concerning the participants' actual experiences of working with children; their concepts and constructions of children; their openness to the abilities of children to contribute to medicines R&D; potential opportunities for involving children more in research; what interviewees thought were the real issues with working with children; explanations for their operations and practices; and their suggestions for improving children's participation. The interview questions covered five subject areas: the Paediatric Regulation; patient involvement; children's participation; children's rights and children's abilities. The kinds of questions that I posed were as follows:

- Could you talk me through how conducting children's medicines R&D has changed for you since the introduction of the EU Paediatric Regulation?
- Could you talk me through the consequences of introducing the EU Paediatric Regulation, the benefits and problems?
- What are your feelings about patient/public involvement in research?
- How do you think children are currently involved in children's medicines R&D?
- How would you describe your experience of working with children?
- How do you think that children could become more involved in future R&D projects?
- Could you tell me whether you believe these rights (articles 12.1 and 24.1/24.2 of the United Nations Convention on the Rights of the Child) are applicable, or not, to children's medicines R&D, and why?
- Can you tell me where within the R&D process you think the rights of children are or may be considered, if at all?

- In what ways do you think that children have the ability to contribute to medicines R&D?
- Can you tell me about a time where a child has talked to you about the medicines they use?
- What do you think could be done to create a good working relationship between children who take medicine and those involved in the medicines R&D?
- In what ways do you think that drug development companies could be motivated to involve children in research?

Once the interview ended, I asked whether there were any further questions about my research and asked how the participant felt about the interview.

### **7.2.1 Semi-structured interviews**

The nature of the research question favoured the use of semi-structured interviews, as I aimed to obtain general information relevant to specific issues and gain insight (Wimpenny, 2000). They allow a freedom of dialogue with the use of predetermined questions and allows for flexibility in responses and ordering (Barbour and Schostak, 2006). The interview protocol, guide, prompt sheet and interview record are provided in the appendices (see Appendices 7-10).

### **7.2.2 Sampling**

Professionals are gatekeepers to children's access to information about medicines research (Coyne, 2010; Martin-Kerry *et al.*, 2019). The key informants who were selected, I viewed as gatekeepers of research at various points on the medicine's development pathway. T1 translational researchers are gatekeepers of research at the preclinical development and early clinical trials stage, T2 translational researchers are gatekeepers at the bedside (HTA,

health services research and knowledge management), funders are gatekeepers to the resources that support research and the involvement specialists are gatekeepers to potential child participants.

Purposive sampling, also known as purposeful or judgement sampling, was used to identify informants for this study. Purposive sampling is a type of non-random sampling that requires pre-defined criteria for who will be included in the research sample (Barbour and Schostak, 2006; Bernard, 2006). As suggested for qualitative research sampling, participants were selected who could best inform the research questions and develop understanding of the phenomenon being studied (Sargeant, 2012), i.e. children's involvement in epilepsy pharmaceutical research. I understand that study populations require a representative sample to ensure generalisability (Barbour and Schostak, 2006; Kuper, Lingard and Levinson, 2008). Though the sample might not be representative across the entire range of children's medicines (Bernard, 2006), I strived for a sample, that allowed for a spread of roles and acceptable for a case example (Barbour and Schostak, 2006). I sourced key informants using two methods: direct contact and snowballing. I was conscious that it might prove difficult to find participants through contacting them by letter with no prior knowledge of me or of my research. I was aware of an international conference that attracted leading epileptologists and pharmaceutical companies, to which I enrolled with the intention of meeting and accruing potential participants.

From reading the literature, I had an idea of whom to contact in terms of the pharmaceutical companies and the epileptologists. However, finding the T1 and T2 translational researchers proved more problematic and this emerged using snowballing. I scoped the conference and introduced myself to many key speakers and exhibitors. I found many people there whom I knew would be important to talk to. I explained to each potential

participant that I was a PhD student and would like to interview them as part of my research and in most cases, people were happy to provide their contact details for me to contact them and explain more about my research. I contacted potential participants by email which consisted of a letter, a summary of my research and a reply slip (see Appendices 2-4 and 11) if they wanted to participate. I was aware that most of the people I spoke to were very senior in their fields and were very busy, so even a response to my emails was gratefully received.

Considering the nature of the questions I was addressing I wanted to preselect the nature and experience of the participants, but apart from a couple of names I was unsure whom I should interview. To help me to locate professionals who could provide insight into my research area, I employed a snowballing strategy. Snowballing is a method of participant identification by recommendation (Barbour and Schostak, 2006). I asked participants to recommend other key informants whom they felt I should talk to at the end of the interview. This method was much more efficient at helping me to identify informants. It became apparent very quickly that the same names were coming up regularly and I was being directed to individuals whom I would not have identified from my knowledge base, or indeed from the literature. I ensured that I followed up all the recommended names to contact.

Sample sizes for qualitative studies are contentious with little agreement as to the number of participants required for samples to be considered robust (Hennink, Kaiser and Marconi, 2017; Mason, 2010). This is further complicated by the variations between different disciplines. (Mason, 2010). Indeed guidelines range from five to 50 participants (Charmaz, 2006; Creswell, 2009) In a study of interview sample sizes from PhD studies Mason (Mason, 2010) found 44 discourse analyses, which had a range of 5-65 interviews (mean = 25/mode=20) (Mason, 2010).

The aim for my sample was to reach a point of theoretical saturation, a point where no new themes, properties, dimensions, or relationships emerge during data analysis (Strauss and Corbin, 1998). However, saturation is also contentious in that some authors feel that, though a laudable endeavour, it has many practical weaknesses, such as time and funding (Fusch and Ness, 2015; Green and Thorogood, 2014; Guest, Bunce and Johnson, 2006), as research generally do not have to option of open-ended research without deadlines. Concurrently, analysing at the time of data collection is suggested to alert the researcher as to when saturation has been reached.

### **7.2.3 Inclusion/Exclusion for the participants**

An important element of the study design is to ensure that the appropriate research participants have been included (Sargeant, 2012). Decisions regarding selection are based on the research questions, theoretical perspectives, and evidence informing the study. The subjects sampled must be able to inform important perspectives related to the phenomenon being studied. Inclusion criteria for qualitative studies are designed to identify the study population in a consistent, reliable, uniform and objective manner and are inclusive of exclusion criteria (Garg, 2016). Factors or characteristics that make the recruited sample ineligible for the study should therefore be made explicit. To be included in this study, the key informants had to meet the following criteria:

- i) Be working one or more of the following:
  - translational researcher (T1); OR
  - translational researcher (T2); OR
  - epileptologist; OR
  - research funder; OR
  - clinical researcher; OR
  - clinician; AND

- ii) Have been a principal investigator OR co-investigator OR funder OR facilitator of a paediatric pharmaceutical trial for seizure medication; AND
- iii) Be fluent in the English; AND
- iv) Be employed in the United Kingdom

No gender, age, or socioeconomic restrictions were applied.

#### **7.2.4 Data Analysis**

Data was analysed using thematic synthesis. I adapted Thomas and Harden (2008a) three stage approach. Although this approach was described for synthesising data in systematic reviews, I found the application uncomplicated and applicable. The first stage was to conduct free line-by-line coding using NVivo9 and NVivo10 software. I applied a combination of inductive and deductive coding techniques. Coding to be more explicit within NVivo9/10 where codes were structured as 'free' codes or 'tree' codes, allowing the codes to expand with the ideas emerging from the data.

##### **7.2.4.1 Conducting Bakhtinian discourse analysis**

In the absence of a universally accepted analytical approach, I created a step-by-step approach that was unambiguous and allowed me to explore my data extensively. To examine the data in greater depth I combined the six stages of Foucauldian discourse analysis suggested by Willig (2013, pp. 131-137) with Kurban and Tobin's (2009, pp. 27-28) four core Bakhtinian principles. This resulted in the following seven stages.

##### **Stage One: Constructing discursive objects**

The initial stage of analysis is to investigate how the discursive objects are constructed by the participants (adult professionals). I identified two discursive objects to address my research question. The first was how

participants constructed children with reference to ability and importance, and the second set of constructions was about 'participation' in the context of medicines R&D.

**Stage Two: Utterances within discourses: locating the discursive constructions in the context of monoglossia, heteroglossia and the chronotope**

For Willig the second stage of analysis would focus on locating the discursive construction of the object in the wider discourses. At this stage I incorporated this with Kurban and Tobin's (2009, p. 27) first core principle – *the meaning of an utterance is always contextual*. I examined utterances for the wider discourses at play and evidence of how monoglossia, heteroglossia and chronotope impacted on participants' constructions.

**Stage Three: Orientations: action and ideological**

In Bakhtinian analyses all talk uses words and ideas that others have used before, therefore *the word is only half ours* (Kurban and Tobin, 2009, p. 27). During this stage of analysis I looked to find what the participants did with their talk i.e. the purposes of the discourse; who would benefit from what was being said. Bakhtin (1981, pp. 354-356; Holquist, 1981, p. xx) argued that all utterances are made by the citation, plagiarism, mimicry and repetition of other's voices and because of this languages are essentially "double-voiced". Predominantly who is ventriloquating the speaker and the impact this has on choice and intention in speaking, i.e. to accomplish social actions and form constructions of children. When I asked professionals about their views on children's participation, I looked for ways that they crafted their responses by: tracing the sources of their utterances (citationality); whose voices they incorporated into their speak (hybridity); and the attitudes or inflections ascribed to their citations (i.e. endorsing, parroting or parodying the voices that they cited). This helped to understand how some ways of

speaking about children's participation might facilitate or prevent future practices.

#### Stage Four: **Positioning the subject within talk and psychic life**

I used the utterances to identify manifestations of stress, conflict and contradiction that might be present and expressed by professionals that work in a genre that is high pressured, heavily legislated, monoglossic and set in its ways. Considering how subject positions were influenced by the psychic life helped me to identify which discourses and voices were being drawn into the interview space and whether subject positions were constrained by or transcended the chronotope. For example, when talking to a person who has retired from medicine, they might draw on subject positions that are not recognised by current practitioners of medicine. Willig (2013) suggests that subject positions differ from roles, as rather than acting out a particular role, the participant is able to speak from various discursive locations. I expand on this in Chapter Nine, where I introduce the concept of the *dramatis intrapersonæ*.

#### Stage Five: **Implications for practice**

The next stage is to focus on the relationship between verbal and non-verbal discourse and practices. Here I looked for ways that constructions facilitate or prevent opportunities for participation.

My research is concerned with the possibilities for involving children in medicines R&D provided by the participants' discourse. I wanted to examine how discourses relating to children's medicine contribute to a situation where the scope and opportunity for participation seems to remain limited despite changes in legislation and public involvement rhetoric.

**Stage Six: Examine how discourse shapes subjectivity**

Willig's (2013) final stage of analysis is to examine how the experience of being a self-aware human being is created in the discourse. Subject positions have consequences (see Stage Four) which she considers the "most speculative" aspect of discourse analysis (ibid, 2013, p. 136). She attributes this to the process of making attempts to make connections between the discursive constructions and their implications for the subjective experience. This process requires the researcher to focus on our sense of self, self-awareness, intentionality and personal history in terms of experience and memories. This composition of self emerges in various and often unpredictable ways during a social interaction. Therefore, subjectivity can have marked implications for the discursive object.

**Stage Seven: Interpretation and answerability**

It is suggested that it is never possible to *know* what someone is thinking or feeling, we can only listen "empathetically" to the speaker, consider what is said and then respond instinctively and creatively.

*"To answer means to listen carefully and then reply, as best we can, even when we fear we have not fully understood what was said to us and even we know that our reply is inadequate." (Kurban and Tobin, 2009, p. 27).*

Replying is considered to be important in a Bakhtinian approach, so the researcher must not just "analyse, categorize and evaluate" but make meaning out of what is being said (Ibid, 2009, p. 27). My goal is to share my interpretations in the context of the evidence known about the participants in this study and the wider institutional discourse, not to present them as correct.

### 7.2.5 Transcribing the interviews

Written permission was obtained from the informants to digitally record the interviews. I refrained from taking notes whilst talking to the participants, due to time limitation and to ensure the flow of the interaction, maintain eye contact and rapport. However, once the interviews were concluded, I documented details about the interview experience including: the environment, atmosphere (e.g. tense or at ease), background noise, disturbances and my perception of the interview's overall success. To avoid losing data due to malfunction such as data corruption, I used two digital recorders. With the interview period being so condensed, I was not in the position to transcribe all the interviews immediately as is recommended (Mason, 2010) to identify the point of saturation but I transcribed interviews in order over the next few weeks.

Transcribing recordings proved far more challenging and time consuming than I had expected. Some qualitative researchers argue that transcription is a crucial phase of data analysis (Bird, 2005), viewing it as an interpretive act rather than a purely mechanical one of transferring spoken sounds onto paper (Lapadat and Lindsay, 1999). It is during this phase that the researcher starts to create meaning from their data, a time when early analysis occurs and ideas start to develop due to an in-depth understanding of the data (Lapadat and Lindsay, 1999).

Initially, I considered getting a professional audio typist to transcribe the data for me and work from the written texts. However, evidence suggests that this would not only have precipitated unwanted processes, such as having to check the accuracy of the transcriptions, but I would have lost vital time to really connect with the data. I, like Bird (2005), learned to “love” not “dread” transcription. I appreciate that transcribing was a necessary process to re-connect and familiarise myself with the data. Indeed, repeated

exposure to the recordings, after transcription process was complete, transported me 'cognitively' back to the actual situation and enabled me to relive the: experience, recall the nuances of the interaction, interview and to witness my own mind-set at the time of conducting the interviews.

I started by doing a straight transcription of the interviews. I used Express Scribe to play back the interviews but did not have a foot pedal to assist me, making what was already a laborious process, even more laborious. Initially, I ran the tape at 33% speed, as slow transcribing (playing a few words and stopping) enabled me to listen more carefully, absorb the words, and focus on what was being said. I then listened to the interviews again at full speed to capture the essence of the interview by detailing length of significant pauses, repetitions, overlapping speech, word emphasis, non-verbal expressions or notes of any occurrences that interrupted the interview such as people entering the room, and background noises. Recordings were stored on a separate, password protected hard drive, except for the deleted recordings of people who withdrew their consent. There are various methods available for converting spoken words into written texts.<sup>11</sup> The level of detail that is included in transcripts varies greatly among discourse analysts. My aim in the transcriptions was two-fold: to record ideas and attitudes that were made explicit, so that I could synthesise themes, and to look for implicit expressions of feelings towards children and participation.

No single set of guidelines to follow exists when producing transcripts. Furthermore, there is also much variation in the level of detail that discourse analysts include within their transcripts (Taylor, 2001). Thematic synthesis and indeed Bakhtinian discourse analysis do not require great levels of transcription detail, but I was looking for verbal utterances, so

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<sup>11</sup> See Lapadat and Lindsay (1999) for a comprehensive outline of various conventions.

needed a transcription method that afforded me the right level of understanding into what was said. At the very least, I needed to produce a verbatim transcript that retained all the vital information for me to analyse and captured the nature of the situation. I also wanted to capture the pauses and stresses of words, but not necessarily all the phonetic intonations. I decided to apply an adaptation of Gail Jefferson's notation to my transcription (see Table 5.3.7), a notation system developed for conversation analysis (see Hutchby and Wooffitt, 2008). I did not use all of Jefferson's notations, as I did not want the level of transcription data as is employed in linguistics, or for performing a conversation analysis. I wanted a method that allowed transcription at a level that afforded me the opportunity to gain insight into dialectics and voice as discussed in Bakhtin's theory. However, I realised early in the transcription process that to analyse meaning and constructions in an interaction, I needed to identify a recognised and appropriate notational method.

**Table 7.2.5 Key to transcription symbols**

<b>Symbol</b>	<b>Meaning</b>
:	Colon – extended or stretch sound, syllable or word
<u>Underlining</u>	Stressing
(.)	Short pause
(1.4)	Timed pauses – number of seconds paused before resuming talk
( )	Transcription doubt
[ ]	Speech overlap
!	Exclamation – speaker is animated
-	Abrupt cut off of a word or sound
CAPS	Capital letters denote really loud speaking voice verging on shouting
Pt	Indicates a tutting or lip-smacking sound often before an inhalation or sigh
\$ \$	The dollar sign indicates a smiling voice laughing or chuckling
I also created one further symbol to represent a change of direction of thought,	
(,)	Comma in bracket indicates a change of direction of thought – *
.	Falling pitch of voice
?	Rising pitch
↑↓	Pitch resets
=	Latching of contiguous utterance with no interval or overlap
> <	Less than/greater than signs : portions of the utterance delivered at a pace noticeably quicker than surrounding talk

Transcription symbols selected from (Jefferson, 2004, pp. 13-31)

\* N.B. I created this symbol as I wanted to identify where participants were rephrasing their responses, changing the direction of their responses or apparently editing out information.

### **7.3 Findings from the interviews**

The seniority of the participants impacted on their availability and time allotted for interviews, i.e. short interviews at short notice. Interviews took between 30 minutes and two hours and were held at the participants' place of work in all but two cases.

Conducting the interviews under time pressure proved to be challenging, due to less time to build rapport and thus facilitate free-flowing dialogue. My supervisor had highlighted my activist tendencies which made my questions seem aggressive. Being aware of this, during the interviews I adopted a less aggressive, more open-minded style, thereby ensuring participants felt.

Although I had a list of questions, my interview style was not overly structured so that I had the freedom to follow the participants' lead and for them to expand in the areas they felt were more pertinent to them. I often found it challenging to address all my questions within the allotted time (see Appendices 7-10). Throughout the interview I ensured that I did not curtail the participants' answers and allowed for interesting digressions, of which there were many. I encountered several challenges during this phase of the research process, including: having three key participants withdraw from the study; struggling with interviews being conducted in noisy environments, conducting interviews around the country, and last-minute cancellations. My previous medical and natural sciences background proved to be extremely useful for the interviews, as my understanding of medicines and medical conditions and the issues of research was appreciated by the participants. This made participants feel comfortable talking about their subject area in a way in which they were accustomed. However, the language that was utilised in the interview could prevent people from accessing and understanding this research and so except for direct quotes from participants, I have decided for

this thesis to minimise the use of the technical and exclusive language utilised in medical discourse, so as not to exclude the very people I hope will benefit from my research.

I transcribed 139,997 words of speech. The average speed of talk worked out to 155.1 words per minute (wpm), based on the number of words spoken over the duration of the interviews and the total recording time (15hrs:2mins:47secs). However, after three participants withdrew from the study the final number of included words were 121,652 and the total recording time 12hrs:58mins:40secs averaging a speech rate of 156.2. Speech rate ranged from 126.8 wpm to 202 wpm, which proved very difficult to transcribe. Sound quality was affected for two interviews. Background music significantly impeded transcription for one interview, conducted in a café, resulting in several inaudible words. Another interview, held in a public library, though quiet, suffered from sound distortion due to echoing and banging.

### **7.3.1 Characteristics of the key informants**

Informants who met the inclusion criteria for this study worked in various stages of translational research, drug development, epileptology, research funding, patient groups, or and involvement. I generated a list of 37 potential informants, intending to cease interviewing upon saturation. Contact details could not be located for four participants, the remaining 33 key informants were invited to participate via email at various points across the period of the interviewing process.

Of the 33 people contacted, five did not respond and seven did not wish to or were unable to participate in the study.

I interviewed 21 participants in 12 locations around the UK, equating a to 63.6% acceptance rate. Of those interviewed, five participants performed

multiple roles (boundary spanners) and 14 (77.8%) specifically worked in the field of epilepsy. Unfortunately, three participants withdrew from the study after failing to secure institutional permission. They were employed by pharmaceutical companies and had not requested the specified approval/clearance. They were very apologetic, and it was unfortunate to lose such rich data as their interviews were very informative. Of those who did not participate (n=12), four were epileptologists, one was an academic translational researcher, six were pharmaceutical company based translational researchers and one was an involvement specialist.

Five interviewees often had multiple roles. For example, research funders also had positions as patient group administrators (n=3), or epileptologists were also clinical researchers (n=2). Their main roles are characterised in Table 7.3.1.1

**Table 7.3.1.1 Distribution of interviewee’s specialism**

Specialism category	Description	No. of interviewees (n=18)	Percentage of interviewees
Translational Researcher – T2**	Health technology assessment Health services research Knowledge management	7	30.4%
Translational Researcher – T1**	Preclinical development Early clinical trials.	5	21.7%
Epileptologist	Hospital based research	2	8.7%
Research Funder		3	13.0%
Epilepsy Specialism	Nursing/Carer/Psychologist	4	17.4%
Involvement Specialist		2	8.7%
Total:		23*	100.0%

\* Five participants performed roles that fell into more than one category

\*\* As defined in the Cooksey Review (Cooksey, 2006)

**Table 7.3.1.2 Gender profile of key informants**

<b>Gender</b>	<b>Original contactees</b>	<b>Participants interviewed</b>	<b>Final no. of participants after withdrawals</b>	<b>Percentage of interviewees</b>
Female	17	13	13	72.2%
Male	16	8	5	27.8%
Total:	33	21	18	100.0%

I was somewhat surprised at how balanced the profiling of the participants was by using snowballing. The female bias arose due to three male informants withdrawing from the study and fewer people being interviewed. The key informants had a combined number of years of experience of 259 years. Years of experience in their specialism ranged from two to 30, with 33.3% having over twenty years of experience. Informants said that they were inspired to follow their chosen career path (45.5%), shared a personal affinity with their work (16.7%) or stressed that they were passionate about what they do (22.2%).

**Table 7.3.1.3 Key informant years of experience in profession**

<b>Years</b>	<b>Combined years of experience</b>	<b>Number of participants (n=18)</b>	<b>No. of interviewees (%)</b>
0-4	9	3	16.7%
5-9	27	4	22.2%
10-14	33	3	16.7%
15-19	32	2	11.1%
20+	158	6	33.3%
Total:	259	18	100.0%

All participants were happy to reveal their parental status, with 61.1% being parents. Of these, 54.4% had two or more children; 38.9% had

teenage children, 16.7% had children under 10 years old and one participant was the parent of a toddler.

Demographic profiling revealed that half of the informants performed a translational research role either in an academic or pharmaceutical setting and a third having more than 20 years' experience in their professions. Most participants were parents and there was a female bias.

### **7.3.2 Overview of constructions of children**

I identified 424 codes inductively, in addition to the 41 *a priori* deductive codes, making a total of 465 codes. The third stage then was to organise the free codes into descriptive themes. This was a painstaking and lengthy process, however, after completing this venture the number of codes reduce from 424 to left with 26 descriptive themes. This process introduced the potential for me to influence the data and allow my insights and understanding of the data to emerge, which can be viewed as controversial (Thomas and Harden, 2008a). Further refining resulted six key themes emerged from the interviews: 1) definitions and descriptions of children; 2) definitions and descriptions of PPI; 3) ability, capability and understanding; 4) professional dilemmas; 5) rights and control; and 6) improving children's medicines research. A surprising overarching theme emerged through examining the data, that of role transition and role conflict.

I identified 38 different ways of constructing children from the interview data, 17 were new constructions that had not emerged in the political speech analysis. Children were constructed in a variety of ways from passive to active. Predominantly children were constructed as passive. Children were rarely considered equal to adults. Constructions varied

dependent on the subjective position adopted and the questions to which participants were responding (see Table 7.3.2).

Direct insight into children's views was perceived as valuable, but the majority of interviewees were reticent to open communication pathways with children directly. It emerged that children's views were hidden behind a variety of gatekeepers, e.g. parents, clinicians and researchers. Indeed, issues surrounding rights and consent still centred on parental consent and decision making, as opposed to children.

Constructions were generally formed from a developmental perspective, with participants making assumptions of children's ability and understanding, based on age and personal experience.

Table 7.3.2 Key informants' ways of constructing children in interviews

	Theoretical construct	N° of Participants	% Participants	N° of References	% References
1	passive actors	15	83.0	30	13.9
2	guinea pigs	10	56.0	15	6.9
3	a medical discipline	9	50.0	24	11.1
4	reliable witnesses	7	39.0	12	5.6
5	therapeutic orphans	7	39.0	8	3.7
6	unreliable witnesses	6	33.0	12	5.6
7	social actors	5	28.0	7	3.2
8	precious possessions	5	28.0	13	6.0
9	different from adults	5	28.0	5	2.3
10	expert patients	4	22.0	9	4.1
11	active participants	4	22.0	4	1.9
12	attachment/kinship	3	17.0	7	3.2
13	an afterthought	3	17.0	6	2.8
14	innovative thinkers	3	17.0	6	2.8
15	crucial informants	2	11.0	6	2.8
16	stakeholders	3	17.0	6	2.8
17	capable others	3	17.0	5	2.3
18	joint decision makers	3	17.0	5	2.3
19	decision makers	3	17.0	4	1.9
20	developing adults	3	17.0	4	1.9
21	valuable asset	3	17.0	4	1.9
22	a vulnerable or at-risk group	3	17.0	3	1.4
23	Campaigners	1	0.5	2	0.9
24	Egocentric	1	0.5	2	0.9
25	a disadvantaged group	1	0.6	2	0.9
26	medical heroes	1	0.6	2	0.9
27	a burden	1	0.5	1	0.5
28	a minority group	1	0.5	1	0.5
29	bad practice	1	0.5	1	0.5
30	a priority	1	0.5	1	0.5
31	Public Relations (PR) tools	1	0.5	1	0.5
32	complex little people	1	0.5	1	0.5
33	dignified beings	1	0.6	1	0.5
34	equally important	1	0.6	1	0.5
35	Equals	1	0.6	1	0.5
36	Unimportant	1	0.6	1	0.5
37	an underserved sector of society	1	0.6	1	0.5
38	unpredictable entities	1	0.6	1	0.5
	a different species	0	0.0	0	0.0
	a revenue source	0	0.0	0	0.0
	adequately provided for	0	0.0	0	0.0
	Citizens	0	0.0	0	0.0
	incapable others	0	0.0	0	0.0
	a marginalised group	0	0.0	0	0.0
	real human beings	0	0.0	0	0.0
	<b>TOTAL</b>	<b>18</b>		<b>215</b>	<b>100.0</b>

**Key:** **Negative constructions** – for the top ten constructions; **Positive constructions** – for the top ten constructions; **Newly identified constructions**

### **7.3.3 Overview of constructions of involvement**

Constructions of involvement were polarised; ranging from a hindrance to essential. Generally, participants viewed involvement as potentially valuable, yet there was cynicism embedded throughout their utterances. This in part was attributable to involvement being constructed as an 'obligation' or a necessary obstacle to overcome, and a practice shrouded in uncertainty. The overriding construction of children's involvement was children as clinical trial participants. Children's views were only considered as valid when they could provide new insight into an issue that could not be answered without consulting children directly, e.g. how they feel about taking a particular drug.

The subject position of the professional being the 'expert' manifested in numerous ways. For example, participants expressed concern that patients do not understand the problems faced by pharmaceutical researchers, or are uninformed/misinformed about R&D. Therefore, researchers were reticent to share ideas before data is published and cautioned about the dangers of imparting snippets of information to unqualified minds.

The most positive construct to emerge was participation as innovation. In this instance children were considered able to contribute to the early stages of research to help generate ideas and assist with trial design. Though there were concerns that expectations had to be managed. When children's participation was constructed as a democratic process, this was about working collaboratively with patient advocacy groups and Young People's Advisory Groups, not directly with sick children.

Direct communication with children was limited, and only occurred with older children (over 12). For those who had communicated with sick children, it had a profound effect. Direct contact had little impact on

researchers who had encountered children but not communicated with them about their medicines. Participation as knowledge sharing focused on how children can disseminate information that is provided by pharmaceutical researchers to other children, or patients and a way for researchers to collect data.

## Chapter Eight: Constructing children and involvement

### 8.0 Overview

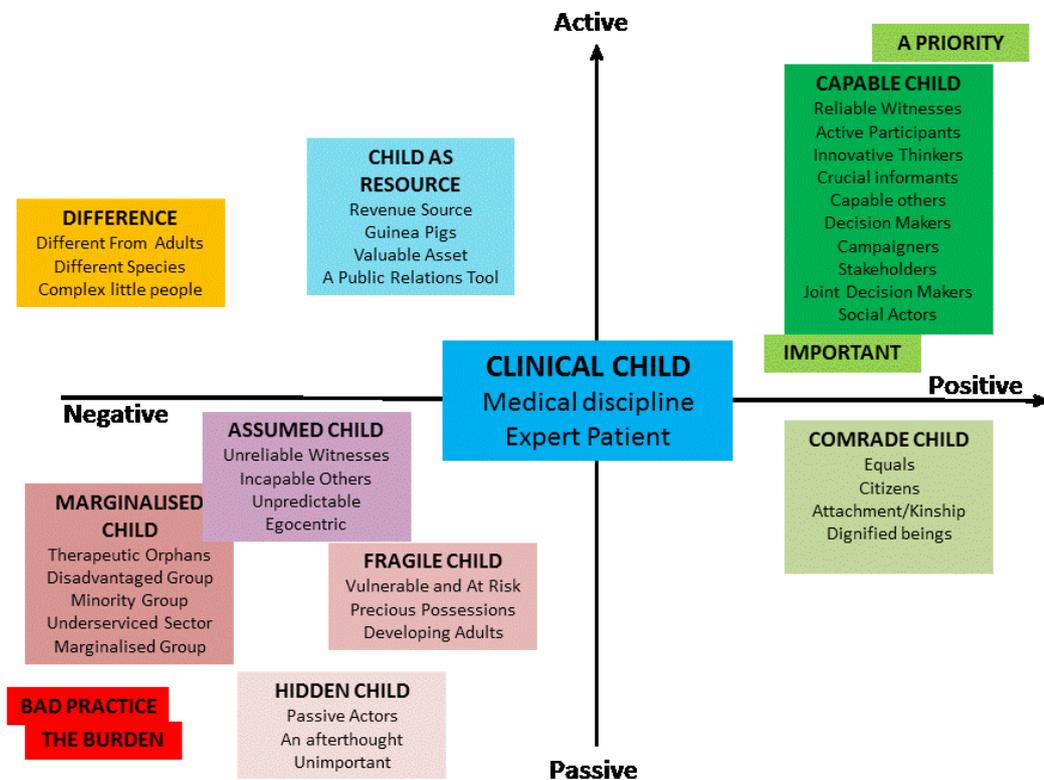
In the previous chapter, I presented an overview of the findings of interviewees' constructions of children and involvement. This chapter provides detailed findings presented thematically for their constructions of children and involvement.

### 8.1 Constructing children

There are differences as to how children are described depending on the professional genre of the participants. I identified 26 different ways of constructing children in the political genre (see Table 5.3.4), and from the interviews, I identified a further 16 new constructions (see Table 7.3.2). The predominant construction of children that emerged from the interviews was the same as that for the political speech analysis, where children were constructed as passive actors, with 83% (n=15) of participants referring to children in this way (see Table 8.1). Children were often constructed by participants as a medical discipline (50%, n=9), using cold, technical language. As with the data identified in the political speeches, when children were talked about as therapeutic orphans (39%, n=7) or guinea pigs (56%, n=10), they were positioned as being vulnerable and in need of adult protection or intervention. There was a fairly even split of participants constructing children as reliable witnesses (39%, n=7) versus unreliable witnesses (33%, n=6). Most of the constructions of children that emerged from the interviews formed noticeable groups. Figure 8.1 shows constructions of children plotted

on a dual scale axis. The groups are categorised, though arguably subjectively, in terms of whether they could be considered positive or negative constructs and whether they portrayed children as passive or active. I considered the constructions of the clinical child to be neutral and discuss my reasons for this in section 8.1.1.

**Figure 8.1** Categorising ways of constructing children



### 8.1.1 'Clinical' or 'medical' definitions of children

As suggested (see section 1.1.2, 1.1.2 and 8.1.1) medical sciences have very specific clinical definitions of children based on developmental assumptions and timelines (Williams *et al.*, 2012). It has been highlighted that in relation to children's involvement in clinical trials the age groups do not correlate with children's developmental maturation (European Union, 2008; Vohora, 2018). Further, there is inconsistency with the definitions that are used (see Table 8.2), prompting the International Conference on Harmonisation (ICH) to call for standardisation of these terms (ICH, 2001; ICH, 2017). The dominant medical voice, which influences and can prejudice the constructs of children. The ICH E11 report on clinical investigation of medicinal products in children suggests that chronologic age alone might be an inadequate categorical determinant to define developmental subgroups in paediatric studies. They reiterate the lack of scientific basis for what they describe as "the arbitrary division of pediatric subgroups by chronological age" (ICH, 2016) (ICH E11 (R1), line 135-138) and the potential delays that limit the study population by these age divisions could cause with regards to the development of medicines for children. Other than suggesting that, condition dependent, it is reasonable to include certain child subpopulations in adult medicines studies or adult subpopulations in children's medicines studies, there is still no suggested alternative for the categorisation of children. As discussed in the opening chapter, the constructions of children and childhood fluctuate over time, place and space. I see no clear resolution to this in a discipline where precision of dosage is calculated by physiological development compounded by risks of over or under-dosing.

**Table 8.1.1 Age stages defined according to NICHD paediatric terminology**

NICHD Stage	Definition	ICH E11 Stage	Definition
Preterm neonatal	The period at birth when a new-born is born before the full gestational period	Preterm new-born infants	
Term neonatal	Birth– 27 days	Term new-born infants	Birth-27 days
Infancy	28 days–12 months	Infants	1-23 months
Toddler	13 months–2 years		
Early childhood	2–5 years	Child	2-11 years
Middle childhood	6–11 years		
Early adolescence	12–18 years	Adolescent	12-17 years
Late adolescence	19–21 years		

Adapted from: NICHD, Eunice Kennedy Shriver National Institute of Child Health and Human Development. (Release Date July 6, 2011) (ICH, 2001; Williams *et al.*, 2012).

I categorised ‘clinical’ and ‘medical’ definitions as those utterances contextualising children within medical discipline using technical terminology. Using technical language is a potent way of indicating a professional identity but it can cause confusion (Doherty, 2013). Informants’ knowledge of my medical understanding, and so they spoke in a way in which they were accustomed. For these reasons I classed this construct as neutral in nature but not in terms of impact. In the first excerpt below M3, an academic translational researcher, refers to the new born child as a “neonate”, dominant utterance of medicalisation of a child unable to, in their opinion, express their views. When talking about the applicability of children’s rights in medicines R&D, he suggests the child’s views are not so important:

M3-TrA: *“Well I think they are applicable in cases, but they are not applicable in every case. Obviously, they are not applicable in neonatal medicine because you cannot ask a neonate their views on what is going to happen. Erm, even*

*under the age of, a child that can't talk for instance. (..) Once a child is able to understand simple things there is quite a lot more that you can do. (.) But how much they can understand but I don't think you should be asking for their consent before school age. But you can still talk to them about what is going on. To make note of it."*

M4, a translational researcher in the pharmaceutical industry, employed the use of the adjective "infantile" on several occasions: when talking about the importance of clinical trials in children; the amount of time and investment required and the impact of the paediatric regulation on resources. The implication of the use of such an adjective on the construction of children can create negative imagery (e.g. puerile) but this term had become part of his everyday technical language, as has paediatric population instead of referring to children.

*M4-TrP: "So tablets, for example, for certain specif-..(.) certainly for, for infantile patients, they are not appropriate, so put on your plan for a suspension formulation, which is suitable for paediatric patients."*

### **8.1.2 'Capable child' – constructions of children as proactive**

Within this category I included utterances of children as: social actors; active participants; reliable witnesses; crucial informants; capable others; decision makers; joint decision makers; innovative thinkers; campaigners; and stakeholders.

Children were often constructed as '*expert patients*' by the informants. When F2 an involvement specialist and funder talked about what children's views could add to medicines R&D, she constructed patient knowledge as a form of expertise and grouped children explicitly in with

patients, thus constructing children as experts. F2 did express a lack of desire to dedicate time to listen to individuals' views but preferred to have access to a large bank of qualitative or quantitative data from which to examine views.

F2-InvF: *“Exactly. From the most expert person because the experts in this field are not the key opinion leaders everybody talks about; the experts are the people who live with it day by day or maybe even their partners or their children or their parents... .. I would not like to have to listen to every person, give them an hour of my time to (.) constantly think about it.”*

Whilst opening the interview, and without prompting, a male academic translational researcher, M3, constructed children as capable in the context of a clinic where he used to work. He spoke about how he had talked directly to children and how they gave their views about *“All the things that you can imagine from a process/service point of view”*. He expressed his admiration that children gave up their free time waiting to be seen by doctors and how *“it never irritated them”*.

When asked about her experience of working with children F13, an involvement specialist, constructed children as capable of giving *“frank and honest”* opinions suggesting that this might make researchers nervous. She stated that working with children was *“the most refreshing part”* of her job.

Here we see the voice of the involvement genre influencing utterances. In the children's involvement genre, participation is promoted, and children are viewed as experts, but I also encountered this construction from participants in the research genre. M5, a commercial researcher, constructed children with epilepsy as capable when talking about his past experiences of working them, revealing his professional respect for them with use of the adjective "*honoured*" (see section 9.4.3.1 for full excerpt).

When talking with F6 about Article 12.1 of the UNCRC and its implications for medicines R&D, I encountered conflict with speech, she related this to the process of completing assent forms. Utterances were constructed that suggested that the participant believed that the children as **social actors** did have rights and should be involved in decision making. However, her conviction was weakened by the conflict present when parents and joint decision making was pulled into the mix.

F6-TrP: "... you know at the end of the day you know it is not just the parents' decision it's the child's decision as well, so they are they have the right make their own views as well. If the child decides she or he doesn't want to participate but the parents do: want their child to participate then that is something that needs to be dealt with between the parent and the child. But they do ultimately have their own, you know, the final say, the child, and erm, and that is the case for all clinical studies, so erm I think, you know article 12.1 does apply and it is something that this the company and even the pharmaceutical industry is doing."

F1, a female funder when talking about ways that children can contribute to R&D, constructed children as **active participants** when those who wish to involve children make the process engaging. She also talked

about children as creative thinkers and about children's openness and reliability. This utterance provides an example of the internal conflict often present in participants' talk. Bakhtin suggests that in dialogue we often talk to an invisible third listener, the superaddressee (Morson and Emerson, 1990). The superaddressee can be personified as a number of significant others, e.g., God, absolute truth, human conscience, the people, the universe etc., dependent on the time, the person, or the encounter (Holquist, 1990). In the following example we see the superaddressee as an arbitrator of thought between the superaddressee and the author (\*). This was dominant in F1's talk, as we can see in this closing of her argument on children's ability to contribute to R&D.

F1-F: *"Generally, they can, they often(..) they are often very open, they say what they think, erm ... and so: you know you can get an understanding of how they are feeling and also(.) erm They see things that sometimes, as you say, things that are very obvious to them like thinking outside the box and (..) erm (..) they are quite spontaneous and they like to be involved in things. You know if you give them a project to do, erm.... \*Then you know, as long as you are making it exciting and interesting enough, then they could really get involved and you could really use (,) they could contribute their brainpower to a topic and erm, often in a way that adults can't, they get very excited about things generally, erm."*

F2, an involvement specialist and research funder, constructs children as **reliable witnesses** in her talk about changes in the medicines R&D since the introduction of the Paediatric Regulation. Speaking from the involvement genre, her utterances often suggested that children are more reliable than their parents. During the interview, this participant had

complained that she was not allowed to talk directly to children due to legislation (see Chapter Nine). When talking about an asthma study, she stressed that children were a “valuable asset” and were able to rate their compliance to medicine taking because “*they were just so honest*”. The following example, talking about research into compliance with growth hormone treatment, provides insight into her construction of children as reliable witnesses:

*F2-IF: “So (.) the compliance to ask parents who have children of twelve about the compliance it’s very (.) strange because I am asking the parents about what happens in the bedroom upstairs when they’re not with their children (.) the compliance, the non-compliance is so big with these children with growth hormones. However, we never really find out why and how because we cannot talk to the children between nine and thirteen. So yeah, I do, (..) I think it’s a pity because I think children are quite savvy and strong to tell what they think and what they need.”*

A number of participants who had experience of talking directly to children stressed the importance of talking to and listening to children. When discussing areas in the drug development timeline where children’s involvement could have an input, children were talked about as being equal to or better than adults for providing ideas, as in the following examples:

*F3-OA: “If you spoke to them, if you talked to them, erm, kids may well have ideas, especially if there are living with a chronic disability, chronic condition they may well have an idea. Now it may not go anywhere, but (..) adults’ ideas don’t necessarily go anywhere either, erm, but I think they*

*may well have some erm, a role to play right at the beginning.”*

*F4-OA: “(..) And they could probably give their viewpoint on how they’re feeling as well. You know, if you ask a child a straight question, they are probably more honest than an adult who might just try to brush that under the carpet and say -oh was that a side effect oh, I just thought it was, you know, just me. So, so yeah maybe their honesty and integrity in the child is something that the researchers can rely. Because they generally know how to lie and make mistruths as much as children. Corrupted by society \$the way that adults might be.\$ <sup>12</sup>So ...”*

Talking directly to children featured heavily for M5, a commercial translational researcher. He said that being able to talk directly to children if the law allowed would give greater insight into conditions, thus constructing children as capable of contributing to the improvement of medicines.

*M5-OP: “[Yes:, ] because essentially by, by meeting young people who suffer from epilepsy, I gained a better understanding of epilepsy as a, as a , as a condition and as somebody involved in the industry=if I was in the right part of the industry it may give me an insight into ways that I could improve formulation or dosage form, in order to improve their life. So yes, I think, the more information we have, as an industry, the better we can make our products.”*

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<sup>12</sup> The \$ sign denotes that the interviewee was smiling or laughing while talking.

With regard to how children's rights are applied in medicines R&D participant F9, a funder, suggested that children are being given "*more of a say now*" but her utterance was littered with conflict suggesting that what will be listened to is dependent on the "age range", "level of ability" and "understanding" of the child. The capability of the child at different life stages was questioned and thus the child was implicitly constructed as the 'developing child', with growing capability.

M2, a clinician/academic researcher displayed overt conflict between his constructions of children when talking about where in the drug development timeline children's participation could be increased. Here he questions children's abilities, positioning them as unreliable witnesses, then continues by arguing that their views are suppressed and should not be as at they are "developmentally" capable of understanding at a young age.

M2-OA: *"Well I suppose in terms of the initial ideas, I mean we have to, to recognise just er: that in terms of erm: emotional and behavioural issues children aren't going to be er, the best reporters. I mean I work with kids erm in terms of, of depression and anxiety (..) and every time, almost inevitably, you come across a child who nobody, who nobody thinks has any problems (..) and then you actually meet the child and you ask them to complete a ratings scale, or you ask them for their symptoms and then you actually find that there, you have come across kids who have been suicidal and nobody knew anything about it er because nobody actually thought to ask them,... ... And so, I think, it's, it's vital that they're involved in terms of asking about symptoms. Erm, then at the pre-project er: I think kids should be (..) should be it's, it's like they need to be part of the team, or part of the*

*group obviously you need to consider age, you need to consider developmental level but I mean, when you get down to kids, you know, I believe that developmentally kids six and seven can understand most concepts (..) once you present them in the right way."*

Taking this a stage further some participants constructed children as **crucial informants** when talking about children's participation at various points along the drug development timeline. The construction of crucial informants was uttered on a number of occasions by F13, a female involvement specialist. When talking about how she was involving children in research and the process of children's participation by way of teaching/training young people. When talking about where and she thought children's input would be most useful, she said:

*F13-Inv: "I would definitely say (..) the ideas stage, so: (..) ... .. (..) The priorities have most likely been set (..) and it is the idea that comes next but unless the, the patients like the idea of that study (..) you are not going to get them involved in that study, so I think that's crucial at that point."*

Occasionally children were constructed as **stakeholders**, typically when participants were talking about involvement regarding access to information, as demonstrate in the following excerpt from the interview with M2.

*M2-OA: "... and erm I guess we will, erm: we're thinking about how best to disseminate that information obviously to relevant stakeholders, including er, young people and their parents. So, we'll probably end up writing our report which is slightly less academic and technical for parents and I think*

*we should probably seek to do something similar for young people.”*

The construction of children as **joint decision makers** and their potential to actively influence decisions about their medical care was highlighted by various participants. Children were constructed as a vital component of a decision group, usually consisting of children, parents, researchers and clinicians. In the following example, when talking about how to exchange ideas between children and pharmaceutical manufacturers, M2 suggests that parents should be involved as they are part of the decision-making process.

M2-OA: “*And I think it’s involving children and their parents it’s, er, you know, because parents clearly will have a big influence on their children ...”*

Children were constructed as **innovative thinkers** as illustrated by this example from a research funder. Within this utterance, we encounter fluctuations of thought when the superaddressee ventriloquates (takes over) the participant’s talk about children’s participation, which I mark either side with an\*.

F1-F: “*But I, realistically, unless the child is like, you know, really, really advanced scientifically and its knowledge of you know, molecular biology. I, I, I just... I just can’t, I just don’t see how they would be able to (..) yeah. Obviously like, you know, the child should be, definitely listened to and\* .... Although having said that, you do get kids who, you know, who come up with some really good stuff. I remember a story of a: guy who was looking into brain trauma and he was wondering why somebody had an injury in one*

*particular area of the brain. And it was his daughter that came up with the, you know, 'well the brain moves doesn't it so, you know, that, is why, why he got smacked there'. And it was the kid that actually gave him the answer, so you know in that situation well.... Yeah.... \*I mean I don't know if you could have you know a day, like a day of, like a talk on different, a certain like pathway, you know, in the brain and then the kids get in groups and discuss, ooh, how could we tackle that and what do you think we could do, or, you know that kind of thing. Erm, that would be nice to get them thinking along those lines and who knows [laughs] \$they could find [laughs]. Who knows? They could. They could\$"*

Talk of capability manifested in various forms in participant speech. In the following example the child is constructed as a **capable other** when F13 talked about support and competence in the context of children's views, but she also highlighted that these views are being concealed by gatekeepers.

*F13-Inv: "..., you know over the years it has been unethical to do research on children, now it's unethical not to. But you'd think that the barrier would be parents don't want to enrol their child onto a trial, (..) because that is the biggest decision that they will ever make in their life. But (..) it's not. It's the clinicians who are reluctant and they feel it's (,) they're overburdening that family by asking them to take part in that particular trial, for whatever reason ..."*

Finally, in this category, I found constructions of children as **campaigners**. F9 talked about an experience that she had had when taking children to talk to politicians in London to present their views on care and

support for children with epilepsy. One of the children was severely challenged by epilepsy but proved to be very capable of expressing his views.

F9-F: *"... when we got there, they were brilliant. And one was not very verbal but (..) he still got his point across. And (..) the young people, you could see how happy [they were.]"*

Stobo (1995, p. 565) suggests that researchers are 'chart-makers' that need three ingredients: commitment to intellectual curiosity; preparedness; and time to observe and think. Throughout the talk with the participants, these qualities were often attributed to children. The association of capability and innovation with children was a common construction but was often framed by conflict and apprehension. I encountered participants laughing after comments where they had constructed children as capable. This suggested that this was not a normative construction of children. Often participants argued openly with the superaddressee as if confirming where their response should be situated between the interview space, their professional role and obligations and their understanding of the participation genre. The qualities of researchers suggested by Stobo could be likened to the natural qualities of children. To guarantee the best medicines are created, it requires the best minds in the field allocating time and importance to the development of innovative drugs, formulations and delivery routes. The best minds, as opposed to the most academically qualified minds

### **8.1.3 'Assumed child' – constructions of children based on own beliefs**

This category encompasses utterances that implicitly or explicitly construct children as: unreliable witnesses and incapable others. Here participants 'assumed' children's capabilities influenced by the heteroglot and

discourse in the medical genre. One participant when talking about whether a three-year-old can express their views about not liking a medicine:

*F10-EA: "But they don't understand the implications of not taking the medication, so I don't think you can, you can't until a child is old enough to understand what the implications of taking the medication are, they can't really express a valid view (...) but once they get old enough to understand that it makes them better, erm (..) then I think their views are more valid. Because no child wants to take medication, do they? So, they always spit it out and say no, so that doesn't really help you."*

A female commercial translational researcher discussed the issue that children are often constructed by historical recollections of an adult's own childhood, or by an adult's perception of children. Despite berating the dangers of doing this, i.e. "adults might jump to conclusions" about how children will react, she herself assumes their capabilities in her saying:

*F12-P: "(,) children are actually very good at actually hiding and just dealing (,) well not dealing with, but I think that children can be encouraged to speak up about every aspect of their life (..) in a way that allows us to understand what we need to do to actually improve it (..) wherever possible (..)"*

Two participants, a female involvement specialist (F2) and a translational researcher (F3), talked about how information from children in their own words might prove useful from a very young age and the negative nature of assuming children's capabilities. F2 suggested improving communication methods with children, such as using drawings or cartoons and developing child specific questionnaires to facilitate children's

understanding of particular medicines focused issues. She also suggested that “[a]nother hurdle” was knowing how to ask young children questions, stressing the importance of adults learning how to frame questions for children:

*F2-IF: “so I think that you cannot ask directly, you can only ask indirectly, so how do you feel now? How do you feel now? And maybe not even how do you feel but like, how does your head feel? How does your tummy feel?”*

On several occasions, I found that whilst participants openly referred to their superaddressee, they were reticent to accept the superaddressee’s influence. F3 questioned the superaddressee influence and thus the construction of children as unreliable. When talking about her thoughts as to why children aren’t being involved more along this process, she raises the issue of adults’ caution about accepting the validity of children’s opinions.

*F3-OA: “... because people don’t know how to communicate with children, they don’t know (..) I think they would struggle perhaps to even, even if they felt that they ought to involve children, I think they’d struggle with just trying to word the question, to illicit the right information to create er, an environment and an atmosphere where the child felt able to (..) participate. I think they’d struggle with all of that. Erm (...) I think there are still (..) people who don’t think children have valid opinions (..) Erm, which is a great shame.”*

This ‘caution’ was highlighted in a number of utterances by participants. For example, M3, a male academic translational researcher, suggested caution when considering a child’s capability. He suggested that children’s views vary in credence, distinguishing between children who were

“logical” and “rational” and those who might be rebelling or in denial of illness. He suggested that these states will influence children’s responses, making their responses unreliable. In the following example, F2 reinforces the construct of children as being unreliable by repeated use of the adjective ‘unpredictable’. Ironically, if children’s responses were predictable the we would not need to talk to them.

*F2-IF: “Yes, let me think. Yeah, it is mainly about risk and feasibility and (...) I have to come back to feasibility because children are quite erm, erm unpredictable? In research that is quite annoying because you create hypotheses based on research and assumption really, and you are trying to validate them and so I think you should have really large sample size (.) to cover the unpredictability of children’s answers and behaviour and so again they need a lot of children, even more than maybe erm, so that’s again feasibility but yeah their unpredictability.”*

#### **8.1.4 ‘Marginalised child’ – constructions of children as needy**

In this category the ‘marginalised child’ includes constructions of children as: therapeutic orphans, a disadvantaged or minority group, or an underserved sector of society. Most participants constructed children as marginalised when talking about the introduction of the Paediatric Regulation, or motivations behind drug development. Unlike talk in the political genre, children were rarely constructed as therapeutic orphans and when they were, it was implicit as illustrated below. The issue of limited epilepsy drugs for children was raised on a number of occasions and was the utterance within which the construct of therapeutic orphan manifested. Whilst talking about how medicines development has changed since the introduction of the Paediatric Regulation, F6 highlights how studies into

children's medicines have increased but not for under 12s. Her utterance is loaded with medicalised talk demonstrating institutional dominance impacting on her construction of children.

F6-P: *"Erm (exhales) I think in terms of the, the amount of studies that we do in children, I mean erm, before (,) so the past in other companies that I have worked on, they have always been in adults they've never really been many studies run in the adolescents or, or a younger paediatric population. I think now there's more and more studies, especially since I started here at [Company Name], you know, we have always, we always start with the twelve, twelve, twelve years and upwards, so we are including at least the adolescent population. I think now there is more and more focus on studies, doing (,) running clinical trials in, in the paediatric population. I mean we have still got a long way to go. The, the paediatric the very young population, you know, the neonatal population all the way up to twelve years. I think there still need to be more research done in that, in that area."*

When talking about his dissatisfaction with the industry's lack of desire to invest in trials in children, M3 constructs children as therapeutic orphans. This is particularly in the context of conditions that affect both adults and children.

M3-TrA: *"... we have all these medications that are licenced in adults and because (.) it is recommended that drug trials should be done in adults first, they get done in the adults and then they're used, and we don't have any evidence base for their use in children. And er, so all we can do is use them on*

*an unlicensed basis, which is very unsatisfactory, so we were very much in favour of any pathway that increased the ability to use, to try out those drugs in children. ...”*

The prospect of helping children was a motivator for participants chosen careers. Here the children were often constructed as a **disadvantaged group**. As seen in this example when F3 is talking about rights in respect to children’s medicines R&D.

F3-OA: *“Why would we not? Erm (...) you say article 24.1 erm, if you put, it you think about that as perhaps a learning-disabled child, or a child with complex er... epilepsy, erm, it still remains a post code lottery out there. Absolutely, not only to somewhere, to get a placement here perhaps to get access to our rehabilitation services our assessment service is most definitely a post code lottery, erm so yes absolutely they are, completely applicable.”*

Rarely did I encounter instances where children were constructed as a **minority group**. If they were, it was usually in reference to children being a “small population” (F3), or an **underserviced sector** by use of the term “overlooked” (F12).

### 8.1.5 ‘Hidden child’ – constructions of children as unheard entities

This category comprises constructions of children as passive actors or children as an afterthought. I found that although children were overtly constructed as **passive actors**, participants acknowledged that children’s abilities were hidden. For example, children being talked over in a doctor patient interaction or not being able to express their views. Participants also acknowledged that passiveness is sometimes attributable to physiological and

psychological challenges or that their views are 'hidden' by their parents either by choice or by gatekeeper dominance.

When participants talked about whether children's views could prove useful to those working in R&D, it was recognised that their views are often suppressed, as researchers might not actually listen to what was said. Even when children are involved, their views can be "completely hidden" (F13) as the supporting voice of their parents might be the only voice that is listened to, and that also some children "don't want to make that big decision themselves" (F13). Although F13 is strong supporter of children's participation, she constructs children as having passive tendencies. The following utterance supports children as able to respond as well as an adult but recognises that the industry regards children as passive.

*F4-OA: "I just wonder because of how sometimes children are you know, their views are there, they're dear, you know, what would you know about it, so their views might be swept under the carpet. So, it's whether they would actually listen, erm, but certainly I think the researchers could glean something from erm, working with young people in terms of you know, ..."*

The passive actor construction was often demonstrated by the exclusion of children when talking about decisions that should involve children, as demonstrated in the extract below from the interview with F1, when talking about the consequences of the introduction of the Paediatric regulation.

*F1-F: "There will be more steps involved in actually getting drugs: out there, because obviously the ethical approval will take longer and will be more rigorous and if you have to test*

*them on children themselves, it is not just the ethics of having the children involved, it is a whole issue about recruiting the children and the parent consent and parental attitude of y'know 'do I want my child in the trial?' That kind of thing."*

Another common manifestation of passivity was when the participants referred to children having actions performed 'on' them. As demonstrated in this utterance by an involvement specialist/funder when talking about the pitfalls of recruiting children into clinical trials. In the interviews, children were constructed as passive in terms of decision making, with gatekeepers controlling children's decisions to participate in clinical trials. There were many references to the control over children by clinicians and parents with regard to recruitment of children into clinical trials, such as: "relying on key opinion leaders to help us design the trial to the best abilities", "discussions with the physician for the child", "feedback mechanisms" that excluded the child, and in one instance the "child and the parent are being managed by the physician".

F6-TrP: *"... a lot of the time the decision is being made by the parents and maybe we need to educate the parents a bit more why these researches are being done and, you know, if it is, if it is a drug, for example, that we have done a lot of research in, it has a good spectrum profile then (..) that needs to be understood by the pa-.. (,) you know, the parent, you know, because sometimes they might turn round and say well, actually I don't know enough about this study, I don't want to enter my child and I'd be the same."*

Another participant talked about the importance of disseminating findings to the public but excluded children from mix throughout her interview.

F7-TrP: *“Awareness of what(.) everyone is trying to achieve I’d guess you know the individuals, and the parents, the guardians of children with, you know, certain diseases, would probably very much like to be fully informed of, you know, the drugs that their, their children could take erm, and the potential and the future and to understand the challenges. (...) I think that if I were a parent, I would want to understand that. ...”*

M1 constructed children as passive actors in the context of a clinical trial on pre-term babies. He discussed the issue of parents’ refusal to allow their children to be in the placebo group.

M1-A: *“... it is interesting actually, that the parents, they wanted their children to be in the treatment group and not in the placebo group (.) because there was so much pro probiotic publicity, they wanted their children definitely to be in that group. Erm, whereas we were very cautious, and we thought that we wouldn’t get parent compliance because they didn’t want their children experimented on, but it was the complete opposite and then having started the study, erm, professionally people were saying it’s unethical to do this because you don’t know what the effect would be on children. Erm, (.) and the parents were kind of ahead of the professionals for want of a better term and then it changed completely, and the professionals said it is unethical to do the study because \$everyone should be on probiotics\$ [laughs]”*

Children were sometimes hidden by implicitly being referenced as an **afterthought**. In some instances, there was explicit recognition as children not being considered in medicines R&D, as illustrated in this extract of F13 speaking about the current status of children's participation in research:

F13-Inv: "*... because obviously I'm a real advocate for real involvement but sometimes you just can't, it's not physically possible to do it because, or you just, 'cause you haven't got the time to do it because you've been given three days' notice to do it before some. ...*"

Conversely, when talking to another involvement specialist about participation in general, F2's speech action of tagging children on to the end of the sentence, provides an implicit example of children as an afterthought in action.

F2-IF: "*... so I think that involvement should only be the case if you have a plan, if that sounds logic. If you have a plan, so, yeah, so I, I am all for involvement because it aids responsibilities, may be also with children yeah.*"

This action of tagging children on to the end of an utterance focused on adults is demonstrated in the following extract when talking to M1 about sourcing people to be involved in clinical trials.

M1-A: "*So in breast cancer screening or prostatic or whatever is the specific antigen for men, ... people are told go and get screened, go and get whatnot and they are not really told what the disadvantages of the tests might be. Erm, I don't think it is any different for children really (..) it's the same kind of argument really, I suppose ...*"

### 8.1.6 'Fragile child' – constructions of children as dependent

Children were often constructed as 'fragile' in the participants' utterances. Here they were talked about as vulnerable and at risk. I have also included the construction of developing adults in this group as when children were talked about in this way it was associated with vulnerability.

The construct of vulnerability and risk is prevalent in participants' talk. When talking about children's rights in medicine F1 acknowledges recognition that children have "*more of a protection*" that she deemed to be "*absolutely right*", as people are "*looking out for their best interests*". However, she also recognises that whilst children are protected, this does not necessarily facilitate giving children a voice. The following utterance reinforces the construct of the fragile child, as it focuses explicitly on urgency, using phrases such as "vulnerable population" and "looked after" when talking about working with patient groups.

F12-P: "... I think that there's a definite sort of sense of urgency associated with people working directly with children (..) and again, (..) you know, as I have mentioned before, it's purely because I think there is an increased sense of urgency to make sure that children are being looked after and are receiving the best care that they can. Particularly in non-hospital environments and erm, you know, it's a very vulnerable population and very often the patient groups are, are very powerful in terms of having a very strong voice both in the political arena and the healthcare arena and erm, I see patient groups being a vital link between (..) erm, erm, erm, those who work on political agendas, working on erm, political guidelines and national health guidelines and erm,

*those who are perhaps working on local protocols and guidelines.”*

Explicit use of developmental constructs was employed in participants speak about children’s participation for insight into hidden symptoms. This was particularly evident when participants were talking about life-stage issues such as puberty and the complexities of creating medicines for children due to their physiological development. Constructing children as vulnerable through utterances centring on **developing adults** emerged mainly in the context of ability, as seen in this extract from the interview with F4 talking about involving children in developing new formulations.

*F4-OA: “(..) Well, they could be willing participants taking the medication and therefore we can look at the picture in that cohort. Erm, they would certainly perhaps get more information about formulation and about what’s acceptable. Erm and that’s, working in the industry I do, I see time and again that we don’t have a liquid formulation from the outset because it’s been researched in adults and adults can generally swallow tablets and so that’s a huge problem. I think and if they were actually considering children at a younger age, at younger stage of development of the drug, and coming out with a liquid formulation that would actually help manufacturers become more credible. Perhaps having a product that can be given to children under the age of being able to swallow the tables that would be about eight, nine, ten.”*

### 8.1.7 'Different child' – constructions of people not adults

In this category I present examples where participants construct children as being *different from adults*; or *complex little people*. In general, explicit reference to children as *different* was found using phrases that I had regularly encountered in medical and political discourse. Explicitly this would emerge with particularly popular phrase, children are “not small adults”. This construct and phrasing emerged in the interviews on numerous occasions or participants would refer to specific physiological differences, such as “their metabolism is different” (F1). Good examples of the emergence of this construct in talk can be seen in the following utterances by F12 and F8. These utterances emerged when participants were talking about the potential catalysts behind the creation of the Paediatric Regulation. Interestingly, F12 commences to suggest that children are not “peop”[le] but stops herself and adjusts the statement to say different from adults.

F12-P: “... , as I said, er, children can't be seen as just small adults therefore they do have a very different physiological profile to that of peop-, to that of adults and erm, you know, process and erm, (..) and process drugs in a different way so (..) I should imagine and this is just a guess, I don't know, I should imagine that with an increasing focus on patient safety that there has been a, you know, a consequential focus on children's safety and therefore it's been highlighted that children do require, specific (..) type drugs that have been specifically formulated for their physiology as opposed to that for adults.”

F8-TrP: “Erm, 'cause you know, I'm not, I don't think pre-legislation (..) there was a lack of intent, I think it's a case of formalise-=recognising the need, recognising that children

*are not just a big grown-up divided by weight and it's about formalising that need."*

The construct of **different from adults** was often framed by medical technical language, such as saying "the paediatric response" (F4) to medicines being different or referring to children as the "paediatric patient" (F6) followed by the adjective 'different'. The construct of **complex little people** also creates children as different from adults though less explicitly. In the following utterance, F3 acknowledges the institution wide acceptance of the construct of children not being "little adults". Her description of difference is insinuated but not implicit, as it is verbalised, albeit subtly.

F3-OA: "*..., children are not, I mean people say it all the time, children are not just little adults, children are very complex little people, sometimes little. Erm, (..) and (..) it's very easy to miss, to forget to communicate with them properly. Erm, and I think if we could get the ability to communicate with children better, it would make everybody's lives easier."*

#### **8.1.8 'Child as a resource' – constructions of children as tools**

This category contains constructions of children as a resource that emerged from the interviews and comprises children constructed as: guinea pigs, valuable assets and public relations tools. I had expected to find instances of children being constructed as a revenue source but found no examples of this. Instances where children were talked about as guinea pigs was used to highlight the need for medicines research, as opposed to viewing children as objects to be experimented on. On the one hand, the phrase "guinea pigs" was used explicitly to strengthen the mental imagery of the pharmaceutical industry viewing children's participation purely as a vehicle to access child clinical trial participants. As suggested by F3, an epilepsy nurse

specialist and academic research, who said: *“I think that they just think that they’re guinea pigs”*. On the other hand, F12, a commercial translational researcher used the term to highlight the potential elevation of children’s participation beyond that of clinical trial participants earlier in the drug development timeline by saying that involvement should not be *“necessarily \$in the guinea pig sense\$ but sort of in the design sense ...”*. The fact that she cringed and said the words in a jokey, laughing manner indicated her discomfort with the term. On the other hand, this construction emerged implicitly, as seen in the following extract when M3, an academic translational researcher talked about children’s views in medicines R&D

M3-TrA: *“But if you are doing research on a child who’s been given the diagnosis for the first time that’s a much more difficult situation. It has to be done because obviously there are instances when we need to do research right from the beginning, from the beginning of the illness but it is much more difficult.”*

F2 focused on the issues of problems of increasing participation, highlighting the conflict of fear versus the benefits for consumers of medicines.

F2-IF: *“I am not sure (..) whether that is feasible because I think there, there is not enough money to incentivise parents to put their children up for guinea pigs really. And also, with regards to some drugs, some drugs have gone really wrong in the last few years, you know like drugs that have caused death and all these things because of negligence or being too quick to go to market. I think people are quite scared ...”*

F9 and M1 talked about their past experiences of working with patients. They highlighted how the “anti-science” culture prevalent in the UK negatively impacts on the construction of medical research by laypeople. Here research is a process where people are used as guinea pigs.

F9-F: *“Because a lot of the time people think you’re (,) I have had someone say that erm(..) a mum says that to me - I don’t want you experimenting on my son (...) because she had just heard the word research.”*

M1-TrA: *“Yeah it is, and it’s a general (..) and it is also an anti-science thing that erm, people don’t like their children being experimented on.”*

Children were sometimes constructed as a **valuable asset** in regard to obtaining information. F11, an epileptologist and translational researcher talked about how much of asset information from children can prove to be, when she saw some of her patients being interviewed. They were aged six to ten years.

F11-EA: *“... And it was a real eye-opener how much they had to say. They have got an awful lot to say erm,...”*

In the following example we see a participant, F8, sway between implicit and explicit construction of children as valuable when talking about her feelings surrounding people’s participation in research.

F8-P: *“Erm, (...) I think (..) that (..) potential patients or (..) people close to those patients, so: potentially parents, caregivers, you know, depending on what type of patient population we’re talking about, people impacted by (..) patients with certain diseases. I think they have you know an*

*awful lot to offer in terms of erm, (..) helping form and formulate good, (..) feasible research."*

Later more explicitly, when talking about ways that children can contribute to medicines R&D, F8 argues that children's views are valuable. Although, unsure about the level of importance of children's views at the beginning of the interview, F8 is very clear in closing.

*F8-P: "Okay. Yeah, I mean, by participation full stop erm, (..) and (..) the child (..) you know any subject participating in any clinical trial is giving sh- valuable, valuable data. Erm, you know, we should never be (..) collecting any data whether we are talking about a measurement erm, a scale, a, a, questionnaire or samples of blood or urine if it is not to be used if it's not useful in the study itself. And paediatric studies are no different."*

I encountered utterances promoting the potential for children to be employed to communicate medicines-based issues to wider audiences. One participant when talking about laypeople's participation on panels, talked about children's potential to be involved in public relations to promote a particular medicine.

*F1-F: "Well, I think it is good PR to have a kid on board and everything but I think in that (.....) in those (....), in those circumstances then erm, I think you know children who are old enough to you know talk about how many seizures they have had and how they have dropped with this drug erm, I think that's probably their involvement but we do not have any kids on our panels at the moment."*

### 8.1.9 'Comrade child' – constructions of children as acquaintances

In this category I have grouped together: children as equals, children as citizens, children talked about in the context of attachment or kinship, and children as dignified beings.

The use of *kinship* as a construct could be viewed as spurious. Here participants referred to children in a familiar fashion. Unlike the use of the kinship construct in the political genre where adults want to display their allegiance with children for benefit, i.e. to win supporters and thus votes, in the interviews this construct was rarely employed. Indeed, the following excerpt provides the best example where M2 is talking about marketing medicines.

M2-OA: *"I think in terms of product launch, I mean, kids, if they go, I mean this is the danger, \$ you can't market, (laughs) you can't market an ADHD drug as in, as in, er: this is great for you kids and market sit to kids as in you know, kid friendly but you have to manufacture in a manner which respects, er: the views of kids I mean there is an advertisement up therefore an ADHA drug on the back on one of, the medical journals and it's something like -whose a stinky, smelly, something like this child and then this ADHD drug or whatever can sort of (..) , I just think it's a bizarre ad, and I think if you [see it you would be, ...]"*

### 8.1.10 Capabilities: assumed, measured and reconsidered

F3-OA: *"Children don't tend to whinge and moan about being sick. Kids are incredibly, incredibly resilient and put up with all kinds of stuff that would floor the rest of us (..) erm*

*and I love it, I love working with kids. Probably, \$I love the naughty ones\$”*

Despite the participants’ general reluctance to explicitly categorise children’s abilities by age, children’s capabilities were implicit in their utterances surrounding involvement. As demonstrated in the following excerpts from an epileptologist and paediatric neurologist talking about receiving feedback from children on research protocols.

F11-EPN, TrA: *“I think it depends on the age and what you call a child. I think teenagers are going to have more of an input than (.) the young children. The young children, all they want to know is where their next meal is coming from and can they participate in all the activities that their mates do? Erm:, and if they don’t actually understand what their epilepsy (,) you know, know that they are having seizures, many of them think well, I’ll just keep taking the drugs and do what my mum says. It’s when they get to teenage life and want more empowerment erm, and (..) possibly they could erm, (..) have an involvement of trials, knowing how often they can come for a review, and what they think is reasonable from an investigation point of view and erm:, you know:, why that, investigation is required and some understanding of how the (,) the investigation is required so that information can be disseminated and their (,) but much of their (,) but also on information sheets as far erm, information on the trial, I think that’s a key area where they could actually have helped \$I usually ask my own kids...\$ (laughs)”*

In the excerpt below F12, a translational researcher at a pharmaceutical company, stresses that children are treated equally but her utterance following suggests that this is not the case with younger children viewed as less 'capable'. This emerged in her utterance when talking about how to elicit feedback from children aged 3-17 years old about medicine use.

*F12-TrP: "The, the same questions are asked of all of them. ... Erm, although for those who perhaps aren't willing to answer themselves.. ..or aren't capable of answering themselves, then erm, they're asked by proxy. And that would normally be their parent or direct guardian. Erm, the, the doctor or nurse is able to answer erm by proxy also but we'd obviously prefer it if it was a direct family member because we don't want to erm (.) pre-empt any, \$any reaction from another vest, you know, a party with a vested interested.\$"*

Involvement specialists and funders were more overt about their how they talked about children's capabilities. One female involvement specialist's utterances drew regularly on the construction of children as capable. I located 15 examples in the interview. Most focused on the issue of age and capability, two concepts that were often discussed together by many participants. This suggests that these constructs are intrinsically linked within medicines' discourse. This participant, though aware of age, did not allow it to impact on children's ability, and remained open to assessing each child as an individual. F13 is later explicit that young people don't like age categories and assumptions about children's capabilities should not be confined by age but should be judged on an individual level; further highlighting the necessity for the medical industry to harmonise ways of categorising children (see section 8.2).

F13-Inv: *"..., so you could have a fourteen year old who could fit easily into the younger age group because of their abilities, so you could do that, you would make that conscious decision to do that (..) but then likewise you would have, you know, a, an eight year old who'd fit into the older group."*

In my interviews I found that capability was often conflated with maturity, as demonstrated in this extract from F6 a commercial translational researcher.

F6-TrP: *"... you can turn around and say well a ten-year-old child doesn't have the: maturity and understanding but then every ten-year-old child is different. (.) So: you know, some, some might be very mature and very intelligent, and you know and then there can be someone else who doesn't have the same level of maturity or the IQ, so I think it's difficult to: kind of (.) say a specific year, say a specific age because it really depends on the child. But for research you have to give them, you know, you have to assign them to a specific age group, so you have got the adolescent patient group, the you have got the paediatric patient, the very young patients, so erm you group them and that's the only way you can do it because everyone within that group will be different as well..."*

Social work professor Amy Rossiter (2007) suggests that professional discourses objectify patients and that official versions of their lives are constructed through documentation. She suggests that a lack of reciprocity is a concern, as professionals can describe patients from powerful yet intangible positions allowing them the opportunity to perpetuate assumptions about

ability. Rossiter (2005) suggests that we utilise findings from discourse analysis to develop an 'historical consciousness' in order to escape reproduction of historical traumas, by recognising the effect of historically located discourse on contemporary talk. In the case of children's participation, these traumas have included the historical blatantly oppressive consequences of medical dominance, such as experimentation, and the contemporary oppressions of paternalism and subconscious collective parenting, such as assumed capability and protection. This has resulted in reduced agency and limited involvement for children in medicines R&D.

Talking about very young children's capacity to express their views on medicine, F4 attempts to reject perpetuated constructions in the pharmaceutical industry looking for ways that children are capable of providing insight into medicine use by constructing the child as a composition of physiological and psychological traits.

*F4-OA: "Pt. Yeah, potentially. I mean, if, if, if you are doing it in a two-year-old and they spit it out \$it is a sure sign that they don't like the taste\$ (laughs). Yeah but I think comprehension is a big issue isn't it, it gets a bit tied up in lots of other speak erm, and , and if you are talking about working with people with learning difficulties you know then you get into questions about are they understanding to the same level as a normal adult that's in the trial. Erm, so, so yes I think there will be limitations based on the age of the child, but if we are looking purely at the symptom that might be being controlled, or the acceptability, you can still glean that from a two year old erm, by the clinical picture and the physical response, rejection of the medication, thinking about it with my pharmacy hat on. Erm:, So, so yes there*

*could be limitations, but I think you could probably see some picture.”*

Conversely, F5 displayed uncertainty about children’s capability with regard to making any decisions about medicine taking.

*F5-O: “Again that’s got to depend on the age of the child as to how you’d approach that too, would. (,) you know. (...) If an older child you can have a bit more of a reasoned to and fro conversation about that, with a younger child, I’m not so sure.”*

In one instance children abilities were constructed within the context of legislative governance.

*M5-OP: “It’s the parents that, you know, you can’t (coughs) excuse me, you can’t fill a prescription if you are under sixteen (..) parent or guardian has to go to collect the script. So, strictly speaking (..) children are not involved.”*

However, I also encountered participants displaying conflict with regard to children’s capabilities on decision making. Here M5’s utterance is loaded with conflict and expression of paternal dominance.

*M5-OP: “It depends on severity of the condition and the age and maturity of the child. Yes, you may have to (laughs) \$literally pin them down and force them to take it.\$ You know, if it’s a life-threatening disease and nobody wants to lose a child, so you are going to make that child take it. And I would happily give consent to a doctor who would inject that child against their wishes, should I be convinced that the*

*benefit outweighed the risk. And I think any parent, faced with that dilemma would do exactly the same."*

Key informants were polarised on whether they felt there was an age limitation for involving children in medicines research R&D. I found that 27.8% said that there were age limitations, 33.3% (n=6) said that age was dependent on the child as an individual; 33.3% (n=6) said that there was not an age limitation for involvement and 5.6% did not answer the question. Age limitations were wide, ranging from 3 to 16-year olds.

Interestingly, what emerged from the data was that children should be judged on cognitive age and not numerical age. As the following excerpt from F11's interview illustrates:

*F11-EPN, TrA: "So if you have a cognitive ability of a three-year-old but you're sixteen you can't give a consent form (..) and there are laws and guidelines that we have to follow for that, so that they give assent rather than consent. Erm and who has the legal rights ..., ... especially over the age, you know, when they get to over the age of sixteen depending on who has got legal (..) guardianship of them, erm, so, you know, it is cognitive ability erm, age of cognitive, you know cognitive age with actually is both."*

Some participants did not ascribe an age range but discussed how children could be looked down upon by doctors and researchers with regard to capability. One participant suggested that one "can't even put an age range" (F1) on when doctors would listen to children. In the following excerpt we witness F2 providing conflicting constructions in the same speech flow, initially suggesting that there should not be an age limit, to only wanting to do

research on people over eighteen for ease, punctuated with a smile and laugh.

*F2-Inv: "Three-year olds or four-year olds can be very opinionated (4.9) I think, well, I think er, I have, well I don't have children and I will not er, ... I think that there should not really be an age limit. However, the guidance should be different per year even. There are books that children read when they are three and there's other books for when they are four and I'm thinking (..), what is the difference but apparently they jump so much in one year and then the next year and so I think for every year the child's, you should have adaptive programmes, which brings in, which brings in another hurdle for the clinical trials. Because you have to implement different er, feed backs and therefore also different analysis and different outcomes. So, with eighteen plus you just give one questionnaire to everyone and get on with it. \$So another hurdle. (Laughs). Sorry.\$"*

Participants raised issues such as socioeconomic factors, type of medication and the setting as elements that might complicate and impact on the construct of children being defined by their age by the pharmaceutical industry. However, numerous participants stressed that age limits have to be set. The following utterance from M1-TrA who had within his interview derided the ability of children to contribute gave a preference for a higher age limit of sixteen years for any sort of participation other than as a clinical trial subject. He suggested that he would *"rely on what the parents or the guardians say, rather than what the child says under sixteen"*.

## Constructing involvement – talking about patient and public involvement

### **8.2 Constructing involvement – talking about patient and public involvement**

In the previous chapters I described how children's agency was absent in the context of children's medicines legislation (see Chapter Six) and presented the complex mix of constructions of children present in participants' utterances (See Chapter Eight). In this chapter I present the constructions of participation that emerged from the interviews. My aim was to understand how, within the rhetoric and growing discourse of PPI, children's involvement was constructed by those practising within children's medicines R&D. I open by providing a summary of the participants' views about involvement as a concept.

#### **8.2.1 Involvement: what it means**

*M2-OA: "I think you probably have to sell the idea to the pharmaceutical companies and show them examples of where collaboration can work I'm not so sure that you should legislate or anything like that but I do think that pharmaceutical companies once they see the benefits of, of children's involvement they can, they will involve them."*

F13-Inv: *"It's making sure those examples are out there for public knowledge to say look, this is the impact of young people's involvement on research..."*

I thought it best to start this chapter by summarising how participation was conceptualised explicitly by the participants. Through the course of the interviews, participation was constructed in various ways. Participants' explicit views ranged from participation as a type of public appeasement, to a way of accessing patient intelligence. Some viewed participation as a utopian practice that pharmaceutical companies would prefer not to have to execute, as illustrated in the following extract:

F1-Inv: *"... I think they would be able to see why it would be a good idea but in practice I think they would rather not."*

Positive views focused on participation as a way of engaging with patients, sharing knowledge and findings, accessing their expertise and intelligence in order to pre-empt potential problems with research. Here the focus was to facilitate clinical trial recruitment and improve compliance with medicine taking, as illustrated by the following extract:

F3-OA: *"My theory is that the earlier you include a child in decision process, in information giving around their epilepsy, the less likely you are as an adolescent to rebel and become non-compliant with medication, which is another risk factor."*

Participants who particularly supported participation were less concerned about increased access to patients to boost clinical trial uptake but focused more on the value of providing better support for patients and better medical outcomes as the benefits of participation.

More cynical views focused on participation as a "contrivance" (M1) or a trend, surrounded by uncertainty and a platform for patients to air

negative views. Here F2, an involvement specialist, whilst talking about the expert patient, describes her requirement for participation to be more structured to limit, what she views as, the growing boldness or rudeness of the online environment increasingly used for patient feedback. Interestingly, children's involvement is tagged onto the end, as an afterthought.

*F2-IF: "... So that's how I see involvement. By always having, like erm, a structured way of getting the involvement because by giving everybody a voice that's great (.), but you have to structure it you have to make sure that it comes together somehow and that is also one of the reasons why I don't (..) also a lot of people don't think that it's good, but I think that it's good but that's why I don't let patients become a member of my platform. I don't allow them to talk to each other, because I don't want that involvement, so even though I'm Mrs Patient voice I don't give them a free voice really because I don't want to get into negative spirals of communications. So ...however you want to describe it (laughs) and erm, and negative and people are keeping, getting each other down all the time, so even though I'm, I like to hear from them and I like to, I want to hear from them in structured ways and so I think that involvement should only be the case if you have a plan, if that sounds logical. If you have a plan, so, yeah, so I, I am all for involvement because it aids responsibilities, may be also with children yeah."*

Throughout the interviews there was reference to researchers being obliged to involve patients or the public in research, which was often constructed as a tokenistic "box ticking" exercise. Some participants voiced concern that patients have nothing to add to improve research. M1's response to what public participation means to him provides an excellent example of the conflict and hostility researchers can have towards PPI. M1 is explicit about his feelings:

M1-TrA: “[Laughs]. *It means that there is always a box on the form that you have to tick to submit the grant, erm and if you haven’t ticked the box you have to say why you haven’t ticked the box (..) and in a lot of cases it’s completely inappropriate because the public erm, have absolutely no knowledge (..) and nothing to offer whatsoever* [laughs] *to the research question that you’re discussing, erm... And it’s a fashion thing, it’s just, it’s just increasing relativism, my opinion is as good as yours and all that kind of stuff, (..) which is just nonsense.*”

M1 then provided an example of a complex problem surrounding “the “16S subunit of the ribosome” and how little value public participation would have in similar instances. However, he did display conflict, suggesting that “*it is a good thing to have the box there*” as it forces researchers to consider whether there is “*a role for public involvement*” and how to recruit people. Throughout the interview M1 drifted between supporting and deriding participation. He suggested the necessity of PPI to secure funding from grant bodies.

M1-TrA: “[Long pause.] *No, (..) I think it’s worth considering on a case by case basis but generally I think, I think, that there isn’t, there is quite a limited role for it. ... But I think it is always worth flagging up and discussing seriously (..) but I don’t think, I mean at the moment. It can be done as a bar to research, if you haven’t got the right person.*”

However, he summed up his feelings about PPI in the context of a current sensitive and complex trial that he was running, which involved children. He could not recruit participants into the trial as the condition was rare and he considered that they could not possibly “*have an expert opinion*”. Despite his personal conflict trying to rationalise participation, M1’s overriding opinion was made clear at the end of the utterance.

M1-TrA: *"It's just meaningless, so erm you know, \$it's just bollocks really.\$"*

### **8.2.2 Personal experiences of working with children, patients and support groups**

Of the 18 key informants interviewed, half of them had experience of working with a patient or support group; all of which described their experience as being positive. However, over half of the participants (n=10) had not involved children in their own research. Four participants stated that children were often involved in their research endeavours but that these children were usually over 12 years old. The majority of participants (n=14) described children's participation in medicines R&D, as being essential or 'a good thing'. M5 referred to 'difficulties' regarding children's participation, where he constructed participation as problematic due to the *"ethical and scientific difficulty about involving children"*. However, he was one of only two researchers to recount a positive experience of talking directly to children (see section 9.4.3.1). Only M1 (see also section 9.1) stressed that children's participation was a bad idea. In the extract below, he openly constructs children's abilities negatively when talking about his view that children do not have rights.

M1-TrA: *"... I mean they don't have understanding or expertise, so (..) I just don't really see the relevance of erm (...), of asking them about \$anything [laughs]. I don't mind telling them about anything, but erm\$, or, I don't mind talking to them about anything (...) but I don't really see that it, I don't see that they have got anything to offer. And actually, I'm very sceptical about rights for children (..) 'cos I think it is a bit of an oxymoron. I don't think children do have \$any rights at all\$ [laughs]. Because they are not adults, rights are something you give to adults, intelligent or stupid (..) they all get rights. \$But I don't think children do\$ (..)"*

I generally, encountered polarised views of participation, where it was either constructed negatively framed by problems, or positively where participants expressed the benefits. In the following sections I present these polarised constructions using selected utterances from the interviews.

### **8.2.3 Negative constructions of participation: Involvement as a problem**

In this section I present the constructs of participation as: tokenistic, the interfering public; a resource intensive exercise, a bureaucratic minefield, an unwanted obligation, and a barrier to research. The majority of negative constructions that emerged appeared to arise from participants understanding from the industry as a whole (the pharmaceutical genre).

The issue of participation as **tokenistic** emerged in a number of ways by several of the key informants. Mainly this was explicit and presented in a way that suggests that the participants were comfortable using this term to describe children's participation. Examples of this emerged in the interviews with participants, who embraced the adjective openly. They described tokenistic participation explicitly as "*a paper exercise*" (F3-OA) or directly saying that it is "*very much tokenistic*" (F13-Inv) describing their cynicism about the levels of actual patient involvement in the medicines R&D industry.

Implicit constructions of involvement as tokenistic were also evident in participants' speak. This was sometimes framed by uncertainty, questioning current practices within the genre. F1 suggested that research into new treatments for children happen without the child "*having expressed much*" and that she did not think that children's "*input is given much of an opportunity*".

In the following extract, F7 draws on experience of the pharmaceutical genre to frame current practice of children's participation. We see a number of shifts in speak, from tailoring literature for children,

constructs of assumed capability and finally the passive child that has no final say, summing up tokenism.

F7-P: *“I think, yes, we do specifically (.) when children are involved, so under eighteens are involved, we do (.) tailor our, (.) we have assent forms instead of the adult version, so it’s tailored (.) the language is tailored to explain exactly(.) in, in the appropriate language for their age, what the trial is they can make the decision obviously by speaking with the physician. Ultimately the physician is taking the responsibility and obviously the children’s parent or legal guardian will also sign off.”*

### **8.2.3.1 The interfering public**

A negative construct emerged in the form of participation associated with the **interfering public**. Here patients and the public were constructed as uninformed, unknowing and unwelcome. For example, M5, a participant who was openly in favour of participation, responds with an utterance loaded with the pharmaceutical genre’s perception of trained professionals knowing more.

M5-OP: *“(6.1 second pause while considering the question). (Smiles). \$The uninformed getting involved in things that they don’t really know about\$ (laughs) to be honest. Erm (..) if you were, let’s say, Mercedes Benz (..) public involvement could be seen as them interfering in your ability to make a car that you can sell.”*

This construction was common within my interview with him. As demonstrated in the following utterances.

M5-OP: *“(..) uninformed pressure groups trying to affect the way that a science-based industry develops products ... .. Allowing people to interfere in early stage development in product... no ... not unless they’ve got the required*

*qualifications, no because it's (..) it, it doesn't make sense frankly."*

However, he clearly distinguishes between public and patients, where patients are viewed as experts, and wished to stress the importance of making a clear distinction between patients and *"the vast majority of the public don't actually understand the problem"*.

Several participants suggested that the public *"might not understand the challenges we [the industry] face ... in order to try and get a paediatric drug to market."* (F7-TrP). F9, another commercial translational researcher suggested that this perceived lack of understanding by the public is the very reason why pharmaceutical companies are *"careful about sharing research information"*. She justified this by saying that because the public generally view the pharmaceutical industry negatively, *"the public don't understand"* and there is a lack of trust *"so the researchers seem very distant. You don't think of scientists and think – ooh I could party with them. (Laughs.)"*

### **8.2.3.2 The misinformed**

From another perspective rather than uninformed the public were constructed as **misinformed**, as illustrated by F10 when talking about people's perceptions of medicines research.

F10-EA: *"... the idea of drug company research conjures up all these dreadful images to people of rats in cages. I mean, there are some rats clearly but they don't understand it and they don't have a voice so that would be helpful."*

The source of the misinformation was not explicitly stated but implicit utterances suggest issues of mass media information in the above extract and dangers of over-hearing information, as illustrated in the following extract:

F11-EA: *"I mean I saw a twelve-year-old erm, last (,) two weeks ago erm, and the parents obviously were really concerned and had brought her to see me and had been given some misinformation. But she had only obviously overheard the parents, nobody has actually sat down with her and she had misinterpreted half the information that she got ..."*

Or in this utterance the participant constructs misinformation in the context of mass media but infers the responsibility lies with the pharmaceutical companies to ensure that better information is disseminated to the public.

M2-OA: *"I think there's dangers, dangers about how one disseminates information I think you have to be always careful er, I think there are dangers of the tabletisation of science where you actually get people interpreting particularly abstracts and er, looking at and it get published in a newspaper and it's not always clear about the limitations of the research or the highlights, so you tend to get the headline..."*

### 8.2.3.3 An unwanted obligation

Participants from all sectors often constructed participation as an **unwanted obligation** that is *"the fashion"* (M2) which is met with reluctance and viewed as *"a necessary obstacle"* (M2) or *"necessary evil"* (F4-OA).

In the following extracts from my interviews with F11 and F13, when asked how participation is received by those working in translational research, F11 suggested that it is viewed as *"a pain in the neck"* by the pharmaceutical industry in general.

F11-EOA: *"\$Erm, I think they feel it's a pain in the neck\$. Erm, (..) it is difficult, oka:y, I think there is a willingness to work with us but there is, to be balanced against a huge expense of doing it."*

*Erm, the one concern, at the present time, is that the pharmaceutical companies are finding the UK too bureaucratic to involve centres and therefore they are finding it easier to recruit patients from eastern bloc countries, erm, developing countries, where diagnostic facilities won't be as good, diagnostic criteria will not be as good and there really is evidence that the placebo response is going up and part of that is thought because maybe misdiagnosis, it's not epilepsy in the first place (..) and the second issue is that there's still a view in those countries that the doctor is the best and they want to please the doctor."*

F13-Inv: *"I mean, there is, there is a bit of reluctance to involve, because I think, (.) personally, I feel that (.) they think that patients could hinder the process of erm, (...) like for example in the [Disease name] trials, for example over the years, you know, there's been patient groups who've advocated particular, you know, trials and drugs, and that could have delayed the process. So, I still think there is a reluctance to involve."*

However, she goes on to say that despite the reluctance more researchers are seeking the views of children:

F13-Inv: *"But I mean, for the one company working on the [disease name] study for example, (.) they have been unbelievable. I mean, they've been so: (..) erm, ke:en to be involved or get kids involved (..) in the whole process, that's unheard of. So, whether it's filtering through, whether it's the (,) the impact of involvement is filtering through, I don't know ..."*

#### **8.2.3.4A bureaucratic minefield**

Constructions of participation as a **bureaucratic minefield** emerged in numerous ways. Sometimes the utterances were laden with personal experience

Bureaucracy and box-ticking are generally linked in discourses about institutions in the public domain. When discussing the issue of involving

children in clinical trials, participants often discussed the increasing practice of funders requiring public consultation in research, and accountability to funders explaining how and to what degree patients were involved and if not, why not. Participation was constructed as a box-ticking exercise full of complexity from participants working in all the aligned disciplines involved in my research.

The construct of bureaucracy emerged implicitly in talk about access to children's views. Legislative practice does not permit the commercial pharmaceutical industry to talk to patients directly irrespective of age. This is highlighted in the following extract from my interview with F12, while talking about times when children have imparted their views about medicines to her:

*F12-P: "(...) Definitely, (..) although pharmaceutical industry that's something that I would, I would never encourage erm:, because we're not, by law allowed to talk to patients, however (..) people including children erm, saying children, I'm including those up to the age of eighteen, erm: have spoken to me and it's been very interesting erm, to have, you know, positive feedback (..) obviously where, you know, in a, in a situation where I can't actually \$say very much...\$"*

The pharmaceutical industry was positioned as being concerned about the bureaucracy of involvement and its impact on expenditure, time and profit, as seen in this extract from my interview with F1:

*F1-F: "Erm, I think, I honestly think, they think 'Oh no' because there is a whole new level of bureaucracy involved; bureaucracy is time, time is money erm, (..) I think that they would probably rather, I mean there is already enough, I mean it takes so long for a drug to come to the market and then by that time their patent has, you know, practically gone [laughs]. So erm, I think their view would probably, like, I think they would be able to see why it would be a good idea but in practice I think they would rather not."*

This is further illustrated in the following extract from my interview with F2, when talking about why children's involvement does not occur on a wider basis within the pharmaceutical industry.

F2-Inv: *"I think that they just see it as one big hurdle, like I am almost thinking. They just see it as a lot of, (..) not even cons, with regards to outcomes, but cons with regards to regulatory affairs. (..) I think, they would just think, huh that is a lot of work for something good. So, I think that you could have most success with pharmaceutical companies that really are in it for good will, for making a change, for idealist approach. I think pharmaceutical companies want to make innovations because they want to get more money so that they can make more innovations. I think that that they don't even take it up because of the time, the effort, the legalities, probably just have to hire somebody especially for children like the legalities and everything so I don't think that they are interested because of the hurdles."*

In the case of the following utterance we see the participant implicitly constructing the pharmaceutical industry's idea of participation as a way of generating revenue.

F5-O: *"I would probably feel, and I don't know that it's just a necessity as a means to an end (...)"*

### 8.2.3.5 Clinical trial subjects

Conversely, those working within commercial pharmaceuticals were often explicit in their support of participation but from the construction of participation as **clinical trial subjects**.

F8-P: *"(Laughs) \$I think (..) the pharmaceutical industry takes paediatric clinical research very seriously, it really (..) I see it as very high on (.) erm, the sort of priority status of all our... our clinical development programmes. It has to be now. And erm and (..) I genuinely think that (,) at least in my experience, those*

*designing the studies and running the studies are genuinely thinking about not only the subjects and the subjects participating in the studies but the wider patient population that their, that these studies are designed to hopefully help at the end of the day. I, I do genuinely think that."*

A commercial translational researcher constructs participation as clinical trial subjects and also as a means to recruit and retain study participants. While highlighting recent improvements in participation in the light of the potential risks of involving children, she suggests not knowing how to involve children is the main barrier to participation. She focused heavily on this construction of children's participation as **clinical trial subjects**.

*F6-TrP: "Actually, I think it's worthwhile, I think erm: we should speak to patients more often, we should speak to children more often and find out how do they feel about being part of a study, do they feel happy about taking part in studies, you know. What can we do to make it, to make it easier for them if they do participate? ... So, at the end of the day, you know, if we want to improve recruitment rates into our studies, then we need to understand what's stopping them from entering these studies ..."*

M5 also constructed participation as **clinical trial subjects** but whilst talking I noticed the participant, a commercial pharmaceutical researcher, announced a role switch. In the excerpt below, we see him switch from speaking as the industry to speaking "as a parent". This phenomenon arose regularly throughout the interviews where participants answered a question in more than one role, with each participant bringing a cast of characters and voices to the interview space. I discuss this in more detail in Chapter Ten.

*M5-OP: "I would say that children's involvement in trials is something that we as an industry, probably as parents fight until our dying breath. I think (..) you have to be able to extrapolate and say it works adults, if we reduce the dosage form, the dosage (..) amount, it's going to work in children."*

As I have suggested, within the medical discourse, children's involvement in research is viewed mainly as including children as research subjects in clinical trials. An editorial piece in the *Lancet* (Anon, 2006) stressed that undertaking clinical trials in children "... must be for the benefit of current and future generations. The key lies in identifying meaningful clinical questions, studying them in a robust manner and publishing the results fully so that findings actually inform practice". If the *key lies in identifying meaningful clinical questions*, then it can be argued that the medical researchers need to involve children beyond the level of clinical trial subjects. They need to involve children in identifying research questions, as potentially children are the ones holding the key to the answers. Communication is also a pivotal aspect of involvement as it is demonstrated to contribute to reductions in "drug related incidents" in children (Stebbing *et al.*, 2007, p. 443).

#### **8.2.4 Positive constructions of participation: hope and potential**

*"... you can involve children in every aspect of the research process so from the idea right the way through to dissemination."* (F13-Inv)

In this section I present positive constructions of participation. I found three major positive constructions of participation. These metaconstructs, as I refer to them, are participation as: innovation, democracy and a knowledge conduit.

##### **8.2.4.1 Innovation**

Despite constructing children as innovative thinkers, participation as **innovation**, although raised by participants, was not a general construction. There were contrary views regarding children's ability to generate useful information at the ideas stage of drug development. Participants often suggested that children have "*got ideas to contribute*" (F11-EA) from the early

stages of medicines research, such as helping to “*develop the research protocol*” (F9-F). Some participants expressed concerns that although the idea of including children to generate new ideas was good practice and could create innovation, caution was needed in its implementation, as illustrated in the following extract.

F9-F: “... *it’s ideas being thrown about (...) and it’s a difficult time to involve, even the general public who don’t have a scientific background, or a background in that specific area you are researching to then involve children, you could completely (...) erm, you could confuse them and there is always the con- (,) the worry as well that someone could latch onto one bit and just run with it.*”

M2 talked about his belief that innovation comes from patients, especially children and children’s ideas and how it can enhance research.

M2-OA: “*Erm, I might explain, my original rationale, I believe the idea of, for a lot of drugs and this may not be and commonly heard view, actually comes from patients including children and I believe this strongly from working with the parent s support groups. I believe that a lot of ideas, in terms of problems that, that, that, you know, need to be addressed actually come from parents because I think (...) er: particularly I have worked with a lot of genetic syndromes, and I feel that a lot of the progress has been made from parent support groups, parent putting up their hands and say my child has this particular problem, you know, has anybody else got that and a lot of the time the clinicians won’t be aware of that so that (...) drives my idea there. ... but I guess (...) all new research is enhanced by, you*

*know, the participants understanding what exactly what it's all about etcetera."*

#### **8.2.4.2 Democracy**

I present the democratic constructs of participation as stakeholders, having input, consensus, decision making, collaboration and access under the metaconstruct **democracy**.

##### **8.2.4.2.1 All stakeholders**

Participants recognised that ideas can be generated from a variety of stakeholders. When talking about innovation in children's medicines focus was on the parents, patients and professionals, as opposed to the children themselves.

*F4-OA: "Well, I hope it would mean involve more than just health professionals in the people taking the drug it would be, if we were talking about children, the parents of the young people may be taking the drug."*

*F5-O: "(2.5 second pause, whilst thinking) I think it means having input and ideas from a wide variety of people, from a different background so it's not just about, Joe Public as in parents, you know, it's professionals as well, to having wide, to get as many different [ideas]"*

Sometimes the stakeholder construct emerged less obviously with democracy or voice being afforded to the children through use of patient advocacy groups. This is illustrated below where F8 is talking about what participation means from her perspective.

F8-P: *"It probably means, patient groups, patient advocacy groups, consultation type groups to me."*

#### 8.2.4.2.2 Collaboration

Collaboration at the other end was constructed as the gold standard for children's participation. In the following excerpt F12's utterance announces her pride and allegiance to the pharmaceutical industry and the industry's commitment to collaboration:

F12-P: *"I am very proud to say that I work on the medical and clinical side, which is the non-commercial side, so (..) it's never been about just bumping away selling drugs, it's been more about making a real difference for patients because that's why we're here, so I can only say positive things about the, about pharma industry and er, and it does sadden me when all too often the press paints a very negative picture of pharma because erm, you know, it's, it's all about working hand in hand ultimately."*

And M2's suggestion of creating child or student councils:

M2-OA: *"I think they need to come together as an overall... (,) as a, as a group and decide upon policies around it and say actually (..) so the National Association of Pharmaceutical Companies or whatever, will say actually yeah we have in every organisation we will have a child council, or a student council or whatever it is and they will, you know, get involved in various stages, or whatever. And it's not through tokenism (..) it's about collaboration, it's about improving the development of the medicines, you know."*

#### 8.2.4.2.3 Decision making

Within this construct of democracy falls the process of decision making. In the following extract F3 displays conflict with use of the words “should mean”. Here she draws on the rhetoric of institutional discourse, but this appears to conflict with her own more implicit constructions. Her own views were not clear throughout the interview.

*F3-OA: “I think it should mean that we all are able to contribute to any decisions that have a bearing on our lives, be that transport, education, health, er, whatever (..) I think (..) it is possible to do that as a paper exercise (..) so that people think that they’re involved and contributing whether that actually then translates into their opinions actually developing erm, you know, being included in how things develop.”*

Constructing participation as decision making was explicitly used to democratise medicines R&D, as illustrated in this extract:

*F5-O: “[Yeah, I do think] it’s a good thing, I don’t think (,) you can’t just have one group of people making decisions, because (..) whether they mean to or not, their judgement could be clouded depending on what discipline they’re coming from.”*

Beyond decision making is the idea of reaching consensus. Participants that valued consensus were explicit in their talk, as illustrated in this excerpt from my interview with F4.

*F4-OA: “I mean, I actually probably having worked on committees with people, the more people you have on the committee, the more difficult it is to, kind of, come to a*

*consensus and therefore if you are saying, yeah it's open to 600 people from any walk of life then I think you could end up erm, it becomes it gets more restrictive because you never get to a kind of agreement but it is the kind of route we're going erm. but the concept of having some public involvement and it being representative of certain parties, I think is probably more beneficial than just having a free for all, let's have a public meeting and anyone can chip in."*

#### **8.2.4.2.4 Access to information**

Transparency and information sharing were a key construction emerging from the interview. This manifested in terms of open access to information, suggesting that the pharmaceutical industry needed to be "open and frank" (M5) and share information freely with the public in order to build trust, as in the example below:

*F9-F: "And I think for researchers it's important we get the message across and are as transparent as possible ... .. And when people come from that place, it's (..) it's the role of the researcher to give them all the information so they are comfortable enough and know their rights or else you're on a (,) it's tricky because as soon as anything goes wrong they will say well it's because of the research (...) and you don't want to start on a negative, on negative grounds."*

Or in terms of closed access where the public are subject to "information overload". M5 highlights the perception that the pharmaceutical industry withholds findings from clinical trials suggesting that this is not viewed as "public information".

M5-OP: “... *let’s say, you’ve got two indications that you’re testing the drug for. It’s failed for one, but it’s passed for the other. The public don’t need to know that it doesn’t work for Parkinson’s, but it does work in Alzheimer’s.*”

#### **8.2.4.3 A knowledge conduit**

The final metaconstruction of participation is as a **knowledge conduit**. Here participation was constructed as: data collection, talking to patients, feeding back information, and disseminating data.

##### **8.2.4.3.1 Talking directly to children**

The concept of knowledge exchange featured highly with the majority of participants. The issue of talking to children and listening to children to obtain “direct” insight, such as by employing scales such as patient reported outcomes, was considered to be hampered by third parties such as doctors and parents. F8, a commercial translational researcher, said that they “*rely very much on the physicians, on the investigators*” to obtain inform but that it would “*really help to get to the patients*” directly. Access to children is greatly restricted by legislation and this was often raised by the participants. One participant talked about the development of patient reported outcomes to obtain information directly from patients (M4), which he viewed as “*a key area*” in terms of direct involvement of patients.

Only two participants, one academic translational researcher (M3) and one commercial researcher (M5), had experience of talking directly to children about the medicines they had made or were researching. When I interviewed M3 he was in the process of setting up a study for a pharmaceutical intervention to treat a digestive disorder. He lauded the experience of involving children in their clinical trial, as their input helped them to design the trial.

M3-A: *“So we had, we had a research group day in which I was the:re (.) and my research fellow was the:re and our research nurse was there, and it was attended by children, or teenagers I would say, with (..) ... but also parents of the children who were there. So, this was a really excellent forum. I was delighted by how well and how easily everybody grasped the explanation of the trial the different arms ... .. we directed them in particular areas that we wondered about: the idea of the placebo (.) group, the idea that the placebo group should never have any treatment or whether they should have treatment later (.) and the general length of the trial. So, we had really important information about all those aspects, erm, a:nd (.) in fact we took minutes and we’ve incorporated those ideas. Some of them we haven’t finalised on because the trial hasn’t finished being designed yet, but their input has really made a big contribution to the design of that trial.”*

M5 talked directly with children who were potential users of their medicines when he went to visit children living with epilepsy. Their company manufacture AEDs that are used by children and he was part of a company delegation invited to talk to children who were extremely challenged by the condition. He described his involvement as “fortunate”. When talking about this experience in the interview, M5 displayed deep emotion, acknowledging the level of insight this experience gave him.

M5-OP: *“(..) actually, it, it (,) honoured is not too strong a word. We started off interviewing care givers, administrators, we were actually producing films for [Institution] and there was a young lad who was being monitored twenty-four seven with electrodes on his head (..) all linked up back to the*

*computer. Where they were studying the impact of seizures?  
... .. And (..) I interviewed that young man, who was sixteen?  
seventeen? ... He knew what was going on (..). He (..) was  
incredibly (..) knowledgeable about his disease and the impact  
it had on him."*

M5 did not meet with trial participants, however, the experience of direct contact with children had a profound impact him both in terms of considering the impact of the medicines his company manufactured on children's lives, and the way that he viewed the ability of children to contribute to pharmaceutical knowledge, thus recognising a gap in his knowledge.

In both instances the children were teenagers, as opposed to young children, suggesting that professionals are either more receptive to communicating with older children, or that access to young children is more difficult.

#### **8.2.4.3.2 Data collection**

The data collection construction was closely linked to that of children as clinical trial participants. In this instance, participation was viewed as a way of collecting information about a condition or a treatment, as shown in the extract where M4 is talking about the importance of children in clinical trials.

*M4-TrP: "You do, you do a specific test like a laboratory examination and you get a reading you do an ECG a:nd but you can do that for efficacy data as well you do a very specific and you say okay this is the reading and this is the response and then you measure the response. Or the other way that we do that is to, we ask physicians, (..) how do we, you know, how do you think the patient is doing?"*

#### 8.2.4.3.3 Feeding back information

A continuation of the construct of participation as talking to patients emerged when participation was constructed as children feeding back their views to researchers and researchers feeding back their findings about their research to children where possible.

F12-TrP: “[<sup>13</sup>Children] have spoken to me and it’s been very interesting erm, to have, you know, positive feedback (..) obviously where, you know, in a, in a situation where I can’t actually say very much...”

However, language and understanding were a concern for one participant, but that participation should take place whenever it is “feasible” (F11). However, one participant suggested that it was difficult to know whether this feedback “had an impact on the study development” (F11).

#### 8.2.4.3.4 Dissemination

A continuation of feedback, and by far the most commonly used (39% of participants) construction within the metaconstruct of knowledge conduit, was that of participation as **dissemination**. Dissemination is viewed as a shared responsibility between researchers and children. When the construct of dissemination was discussed as children helping to disseminate information, it was viewed as important that children feel that their participation in a trial was worthwhile and appreciated.

F1-F: “And they you know they are good people to have on board. And also, they will talk about stuff too, so if you want

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<sup>13</sup> Added by GS to clarify topic of discussion

*the word to be spread about something [laughs] \$you know the playground\$ [laughs].”*

*F9-F: “... how I see it, I’d say is be helping you develop the research protocol then they are also participants of the study. You are feeding back the findings to them and they are helping you disseminate.”*

When talking about researchers disseminating information to children, issues of lack of available research findings was raised. This was suggested to be due to researchers’ reticence to share findings with unqualified minds, raising the issue of transparency. There was concern that children and parents might misinterpret findings and apply them inappropriately. When talking about product marketing M5 felt that dissemination did not occur for information that was considered unnecessary.

*M5-OP: “... but it’s not really public information it’s, it’s kept under the table because until (..) that point there the general public know nothing about the product.”*

Despite this, participants suggested that there was an increase in researchers talking to patient groups about their planned research and their findings. M2 further suggested that researchers must carefully consider the format and language that is used to present findings.

*M2-OA: “Erm and this is something we are thinking about at the moment with regard to our current project which is coming to an end how best to disseminate the information given the fact that the majority of audiences we probably want to reach are lay as in parents, teachers, young people, you know.”*

Some participants suggested that dissemination should be viewed as a two-way process. The MHRA are candid about the processes being their policy creation and implementation and their inclusion of stakeholder consultation. On their website under the 'Policy development and delivery' section they state that "the Agency seeks to develop and successfully deliver new policies and look critically at existing regulation and procedures to improve them wherever possible. In doing this we consult with our stakeholders<sup>14</sup> to ensure that policy and practice protects public health, is transparent, proportionate and deliverable, and does not place unnecessary burdens on industry. They further emphasise the importance of evidenced based policy and that stakeholders are actively "engaged" in policy proposals via compliance with the Government Code of Practice on Consultation (MHRA, 2009). HM Government suggest that any stakeholder consultation should consider the following seven criteria: when to consult; duration of consultation; clarity of scope and impact; accessibility of consultation exercises; burden of consultation; responsiveness of consultation; and capacity to consult (HM Government, 2008). However, I question who comprises these stakeholders and how are these stakeholders selected. Working with "interested stakeholders" is a noble endeavour but stakeholders can only be interested if they are made aware that policy proposals that affect them are in existence and also if they understand them. In the case of paediatric medicines, this excludes the children who are directly affected unless the information is relayed to them, regularly, by a patient organisation that truly represents the children views.

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<sup>14</sup> The author has added the bold effect to this text to highlight the phrase.

### 8.3 Constructing children's involvement in medicines R&D

I looked at what children's participation meant to the participants and how this fitted within children's rights and evaluated the implications of the discursive constructs on potential of children's agency. In 1969 Sherry R. Arnstein constructed her "ladder of citizen participation", a time known to produce some of the great political activists and when human rights were high on the public agenda. Arnstein's ladder consisted of eight rungs ranging from manipulation, on the bottom rung, to citizen control at the top. This ladder was then further divided into 3 levels: at the lowest level (rungs 1 and 2) non-participation, tokenism sitting in the middle (rungs 3-5) and at the highest level (rungs 6-8) citizen power. There have been several adaptations of Arnstein's ladder over the years but despite its original application of town planning, this theory has maintained its relevance and is still applicable to most disciplines including community participatory health research (Cornwall, 1996; Rifkin and Pridmore, 2001), government health programmes (Feingold, 1977) and, most relevantly, setting of NHS R&D agendas (Involve, 2008; Oliver *et al.*, 2004). Thompson (2007, p. 1299) discusses the relevance of the levels/ladders of participation to the "four most discussed models of treatment decision-making". These models are, going from the lowest level of power to the highest: *paternalism*, *shared decision-making*, *professional-as-agent* and *informed decision-making* (Thompson, 2007, p. 1299). The process of involving children in healthcare decisions can be argued to fall within the three degrees of tokenism: informing at the lowest level, consultation in the middle and placation at the upper end, based on Arnstein's (1969) model. However, the models of participation are constructed, the current level of children's involvement in medical research paradigm is constrained to the lower levels. If children cannot progress up the ladder of participation within the medical R&D paradigm, then it can be argued that the medical

interventions that are being created for children, not only run the risk of being poorly informed and irrelevant, but consequently, less likely to be effectual.

The UK Government recognised the requirement for patient involvement in relation to healthcare decisions which directly affect them, with its creation of the *Patient Partnership Strategy* back in 1996 (NHS Executive, 1996). The rise of patient-centred medicine evolved as a partial response in opposition to doctors making value decisions on behalf of their patients (Hope, 1998, p. 291). This opposition to making value judgments contributed to the more recent rise of patient-centred medical research (Harper, 1998). Involving lay-people can be central to identifying patient-important outcomes for medical researchers to assess and is vital in helping design patient information leaflets and aiding recruitment for clinical trials (Hope, 1998, p. 292). Since the early 1990s there has been growing interest in how patients can be involved in medical research. The work of Oliver and Entwistle identified key stages that lay-involvement could contribute to the medical research process: deciding research priorities; identifying problems and formulating research questions; identifying research funding priorities; research design; interpretation of findings and systematic reviews (e.g. Entwistle *et al.*, 1998; Oliver, 1995). The extent to which 'involvement' exists for children within the medical R&D process has been demonstrated, by engaging with the literature, to be ambiguous. Many children are challenged by chronic illness or physical disability and are frequent and long-term users of pharmaceutical interventions and health services so have much to contribute to inform service development (Lightfoot and Sloper, 2003).

### **8.3.1 Benefits and pitfalls of involving children in research**

Focusing on service user experiences produces a different type knowledge, experiential knowledge (Sweeney, 2009, p. 26). Perspectives elicited from qualitative inquiry are personal and often unrepeatably,

therefore subjectivity is introduced into the mix. Angela Sweeney in her chapter of a book entitled *This is Survivor Research*, focused on how an epistemology for service user research is emerging, highlighting the key writers in this field (Armes, 2009; Beresford, 2003; Rose, 2009). Each author approaches service user research from a different perspective but all agree that the knowledge produced from users is likely to be more authentic, 'better' and more 'complete' because, as Peter Beresford (2003) explains, this knowledge brings experience, interpretation and knowledge closer together.

Children have important and valid contributions to make with regards to contemporary medicines research and to public health policy (Bernays *et al.*, 2017; de Graaf *et al.*, 2017). Although generational issues will be manifest, the exclusion of children's perspectives is myopic and ignorant. Children are the true 'experts' on what it is like to be a child. Adult medical researchers can reminisce about childhood, sympathise and even try to empathise with children in a bid to elucidate data to help them understand the implications and impact of health challenges in childhood but to truly understand the impact, the researcher must listen to the voices of children.

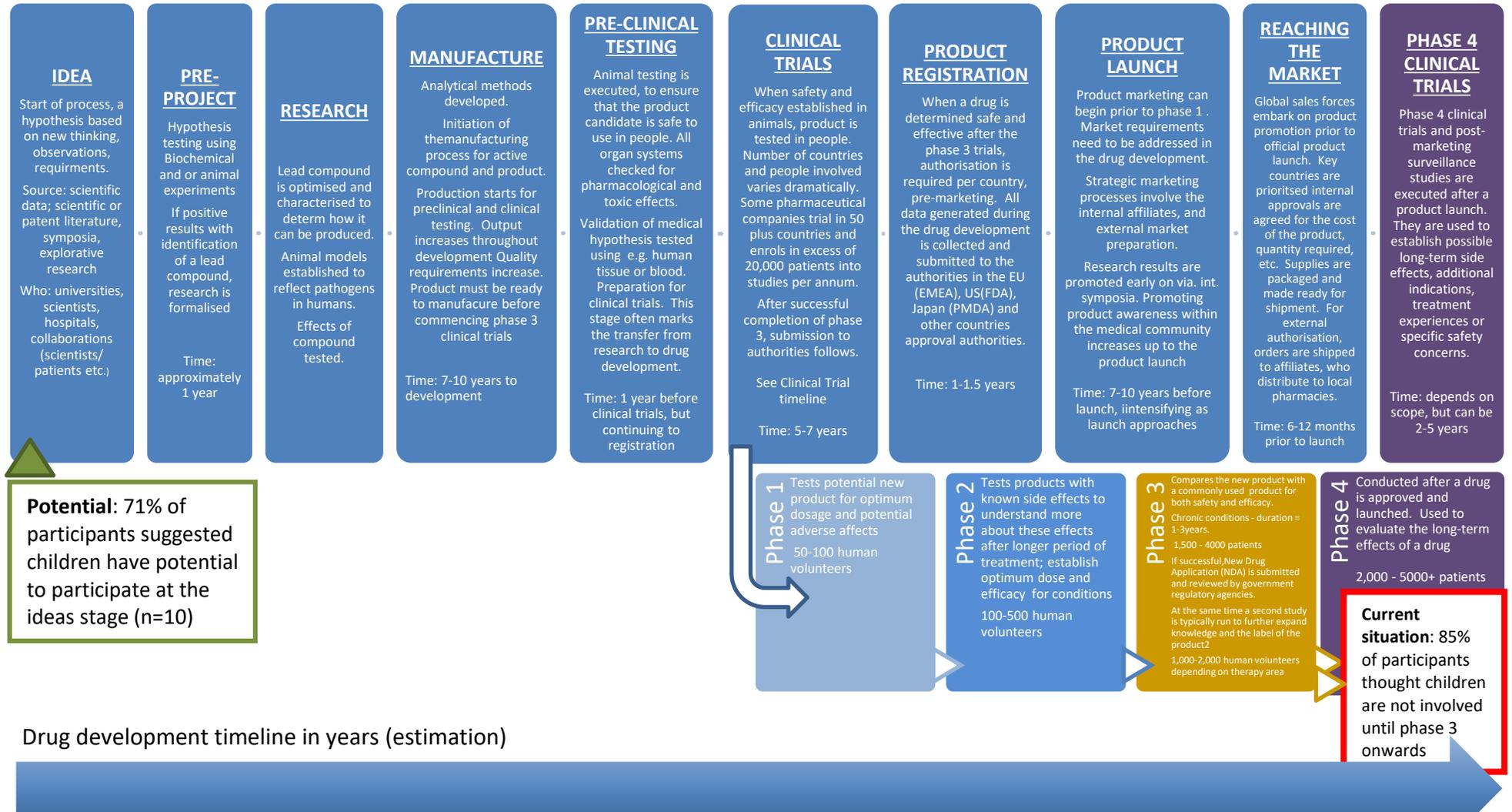
There are established organisations that actively involve and seek patient-consumer input into, among other aspects, research design and priority setting (James Lind Alliance (JLA); INVOLVE; NHS Health Technology Assessment; HTA and the Cochrane Collaboration). However, the JLA and INVOLVE place a more equal approach to children's input.

Involving children in research activities does not come without its pitfalls, e.g. in terms of the increased efforts required by the researchers. Over recent years partnerships with children has had mixed success. Although, children are generally motivated to be involved and have been shown to be motivated by altruism – for others suffering from similar conditions and for those who care for them – this has been shown to be

conditional. It is based on the belief that their opinions are listened to and valued and that they should have feedback and therefore reassurance by staff is paramount (Lightfoot and Sloper, 2003, pp. 284, 286). Successful working partnerships with children will, in part, depend upon the development of appropriate methods to involve children (Dixon-Woods, Young and Heney, 1999, p. 779).

The majority of the participants suggested that children could have an input early on in the drug development timeline but suggested that the current status quo is that children participate mainly in the later stages (see Figure 9.6). With any problem the best place to start is the beginning and the beginning in research is 'blue skies' or basic research, then on to translational research to find practical applications for these entities. If children were involved at the beginning, there is a greater chance of producing a better product. Whereas blues skies research is generally described as 'pure' science, exploratory, innovative, curiosity-driven and fundamental, translational research is evidence-based and goal-driven research. It has however been suggested that innovative research has moved away from being "curiosity driven" due to increased central funding and peer review processes that prioritize research based on worthiness (Rees, 2004). There are various definitions but all essentially focus on the exploratory nature of blue skies research and its goals to "advance knowledge and understanding – driven by researchers who are curious, open-minded and interested (Linden, 2008). Most participants constructed children as curious, open-minded and innovative, therefore children's involvement could fit within the remit of translational research. However, with regards to medical research this requires researchers to design methods to engage children and maintain their interest.

Figure 8.3 Drug Development Timeline - from concept to patient use – potential for participation



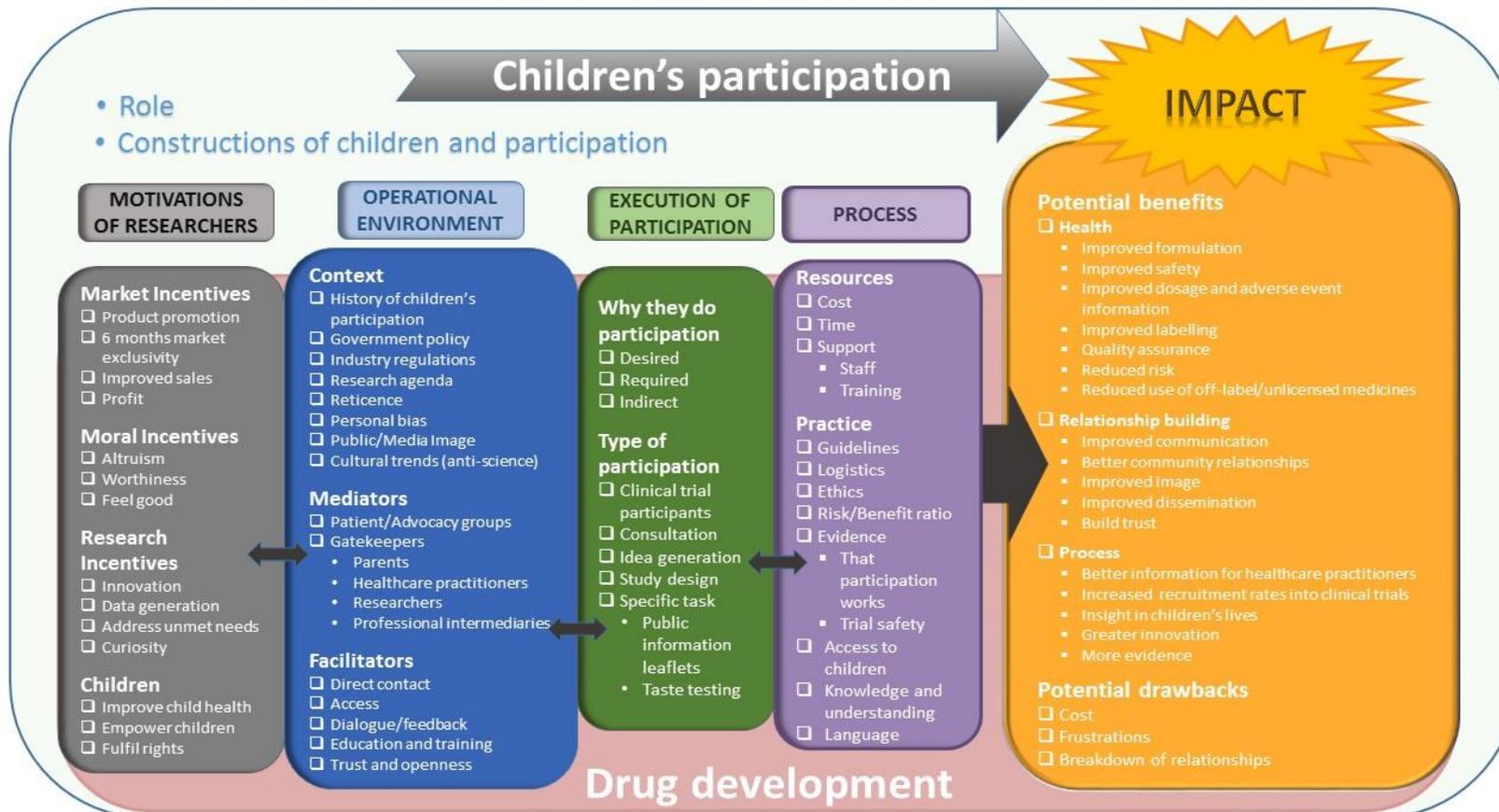
## 8.4 Conceptualising children's involvement in medicines R&D

Oliver *et al.* (2015) suggest a framework of three interrelated dimensions of involvement: the drivers; the processes and the impact. This framework provides solid foundations to help understand public involvement as an activity, and the intricacies of the interactions that occur in participatory processes, therefore I discuss my findings in the context of this framework. They cite similar barriers to participation to those that I found in my research including: lack of motivation, inability to identify appropriate people, inappropriate involvement methods, lack of resources, time and training to name but a few. This concurs with other research conducted in this field (Domecq *et al.*, 2014; Forsythe *et al.*, 2014; Hubbard *et al.*, 2007; O'Connell and Mosconi, 2006; Shippee *et al.*, 2013; Thompson, 2007; Thompson *et al.*, 2009)\*. Whereas the cited supporting research focuses on the participation of patients in general, my framework differs in that it specifically focuses on children's participation and is not constructed from my experience of participation, or from research within this genre, but is compiled purely from the emergent utterances elicited in the interviews and constructions presented in Chapters Eight, Nine and Eleven. The conceptual framework I present (see Figure 9.6) consists of: motivations, operational environment, execution of participation, and processes, all of which can affect the impact of children's participation. These factors rest within the constructions of children and participation, be they positive or negative. The motivations of professionals suggested by the participants, fall within Oliver *et al.*'s (Oliver *et al.*, 2015) 'drivers of involvement', with commercial levers emerging as the predominant motivation for children's participation. Commercial levers suggested were product promotion, market exclusivity, improved sales, and profit. Falling under the banner of 'process of involvement' (Oliver *et al.*, 2015), are my categories of operational environment, execution of participation and process. Participants' focuses within the operational

environment were both drivers and processes. For example, the mediators were suggested to be: patients, patient advocacy groups, parents, healthcare practitioners, professional intermediaries, and the researchers themselves. These are often the drivers of involvement, however the motivations of some for driving involvement, may be resisted by others. Therefore, not only are the mediators drivers, they can also prove to be preventers of participation. Mediators were viewed as people, or more specifically, social interactions between various people. Conversely, facilitators were viewed as actions or practical processes, mainly centred on enabling contact between researchers and child patients. However, trust and openness emerged as an area where researcher participants felt much work was needed. This was partly confirmed by the non-researcher participants who often intimated that they viewed the pharmaceutical industry with caution. Execution of participation also partially consists of drivers (why professionals do participation) and partially processes (type of participation). Why professionals undertake participatory research was related to their professions, i.e. involvement specialists desired participation; funders required participation; and researchers were mixed, suggesting that sometimes it happened indirectly in that clinical trial participants might impact on the course of the research by contributing knowledge, thereby having greater involvement, and indeed impact than initially expected. The type of participation (process) also was predictably constructed differently. To researchers' participation was predominantly children as clinical trial subjects, and occasionally being given specific tasks such as helping to create public information leaflets, or taste testing. For involvement specialists or funders there was a greater emphasis on consulting with children and accessing children's ideas early on in order to help inform study design. The specifically process driven elements that emerged were either resource or practice based and are in line with those found in other literature quoted above\*. Impact is conceptualised as how "outsiders influence research" (Oliver *et al.*, 2015, p. 48). The impact of

children's participation emerged as polarised, either beneficial or problematic. The health benefits suggested were mainly based on experience of working with children in either an advisory capacity on patient information leaflets, or from the result of children participating in clinical trials (i.e. improved: safety, labelling, formulation, dosage, and adverse event information). However, participants aspired to participation that would reduce the use of off-label and unlicensed medicines, for which evidence is not currently available. Relationship building was purely from an aspirational perspective, in that the participants hoped that participation would help to improve: communication, community relationships, and the image of the pharmaceutical industry, and also to build trust. Aspirational ideals were also identified within the process benefits, where professionals hoped that participation would result in greater innovation and better health outcomes. However, participants required evidence of the outcomes of participation to verify this. The potential drawbacks of participation emerged mainly from the perception of those who had no experience of conducting research that involved lay people. These participants were concerned that costs would be unworkable, and imagined a process that was convoluted and frustrating, and that could result in the breakdown of relationships between researchers, patients and the public.

Figure 8.4 Moving children’s involvement in medicines research and development forward: a conceptual framework



Compiled from: Participants constructions of children and involvement

## Chapter Nine: Constructions, multivoicedness and roles

### 9.0 Overview

Identifying emergent constructions of children and involvement provided an overview of professionals' views of these discursive objects (Chapter Eight) but applying the Bakhtinian filter, offered fresh insight into the tenuous relationship between medical research and children, and illuminated the multivoicedness of the participants. This multivoicedness suggested conflict in participants' mind-sets, or 'roles' in the interview space.

In this chapter, I present the roles that emerged; instances where the participants spoke from different perspectives. Exemplar utterances from the interviews are used to explore the metaphorical 'hats' that comprised the interviewees' apparel and I introduce the concept of the *dramatis intrapersonae*, the list of players present in the interview, Bakhtin's heteroglossic scene. I contextualise my findings by combining role theory and role conflict theory with Bakhtin's heteroglossia and polyphony, to examine both the external and internal influences on role adoption and role conflict. Further, I discuss the influence of role when employing these particular discursive constructs and their impact upon practice; facilitating or blocking children's involvement.

## 9.1 The concept of participant epistemological heterogeneity

*“All the world’s a stage*

*And all the men and women merely players;*

*They have their exits and their entrances;*

*And one man in his time plays many parts.”*

(Shakespeare, 1623, p. 894)

As the above quote suggests, one person plays many roles throughout their life. Indeed, throughout the course of a day people transition between a variety of roles, consciously or subconsciously, seamlessly drawing upon their role experiences to present their ‘self’ within social encounters. Shakespeare introduced every play with a *dramatis personæ*, a term generally used to denote a character list, those involved in a play, novel or narrative (Oxford, 2002, p. 433; Webster's, 1991, p. 283). The literal translation is the “masks of the drama” – *persona* (Latin) meaning mask as well as, personage, character, or part (Oxford, 2001). Not only is this term used in the literary/theatrical genre but also in the disciplines of law, anthropology (notably Clifford Geertz (1973) in his *Deep Play: Notes on the Balinese cockfight*) and more rarely, sociology. I even located ten references to it in the medical sciences, although utilised rather randomly in the context of genetics (Berg, 2001; Pappas, 2005), anaesthesiology (Aronson, 1992), immunology (Orihara *et al.*, 2010), metabolic science (Sorani *et al.*, 2015; Tarasov and Rorsman, 2016), psychology (Bertman, 1980; Grier, 2011; Ringstrom, 2009), and, in one instance, purely as a superficial title with no clear utilisation in the text (Anon, 1985). This concept is employed to contextualise the persons contributing to a situation, legal proceeding, ethnography or a study. In the interview, I suggest that one should not just consider the people involved as players but also consider which roles they are playing; roles that can change depending on the situations encountered. Roles can alternate at any given time, e.g. clinician, to researcher, to parent and to advocate. Perspectives can also change as we absorb the emotions

associated with memories acquired whilst occupying our particular roles. People's physiognomy may appear as oneness, but it is constructed from a complex meshwork of implicit characters, each with differing perspectives that seamlessly flow into and out of each other. I am not suggesting that people's characters can be elicited via a simple socio-anthroposcopy exercise – this would be immeasurable and subjective, but I propose that as qualitative researchers, before evaluating the perspectives of others, one needs to address the potential motivations and perspectives contained within the person. I believe that these various motivations are more likened to *dramatis personæ*, but more specifically they are the inner actors, a person's unique *dramatis intrapersonæ*.

## 9.2 Discovering the *dramatis intrapersonae*

What 'self' is presented and how a person positions the 'self', is dependent on multifarious factors. Children learn to see themselves the way that others see them (Mead, 1934), and it also posited that the 'self' is a 'looking glass self' (Cooley (1902) as cited in Potter and Wetherell, 1987, p. 98) where "it comes to reflect social expectations". Individuals learn to 'refer' to their social groups and, through a process of 'social comparison', adjust their identities (Festinger (1954) as cited in Potter and Wetherell, 1987, p. 98). Potter and Wetherell (1987) present the metaphorical elements of three models of 'self' in discourse analysis: trait theory (self as an 'honest soul'); humanistic theory (the romantic image of 'self') and role theory (the theatrical image of 'self'). Role then is suggested to be a "means of reconciliation", a 'set of activities, qualities and styles of behaviours that are associated with social positions', between individual self-expression and society and social determinism (Ibid, 1987, pp. 97-99).

I referred extensively to the work of Michael Banton when considering the roles that were presented in the interviews. Banton (1965, p. 138) suggested that an actor's behaviour is a response to the need of others,

so the 'self' is the product of one's ability to see themselves as they consider others see them.

However, throughout Banton's work he positions role as being a conscious endeavour. The existence of the idea that we can consciously choose or manipulate which 'self' we present to the world, raises questions about whether the responses in the interview were genuine. If we consider this in the context of Bakhtin's heteroglot, roles that are adopted ventriloquate voices and utterances differently. Each role is loaded with personal history and each utterance is loaded with 'others' history. This combined makes for a complex presentation of talk within any social interaction.

Potter and Wetherell (1987) suggest that people become performers and therefore theatrical metaphors become appropriate. They suggest that people act in ways that are expressive of their role rather than their unique personality, and thus present a "multiple set of possibly discordant identities" (ibid, 1987, p. 98), which can create conflict. Bakhtin (1984, p. 295) suggested that personality is a manifestation of an individual's consciousness conveyed employing every aspect that a person uses to externally express, or unveil themselves to and for others. He positioned personality as a way to approach language as artistic representation. I consider that personality is a form shaping process of the matrix of the individual and offers insight into how people view their 'self'. Different roles may require a different 'self' and, therefore, the self runs the risk of becoming fragmented. Role theorists generally hold that people conform to roles because of "subtle mechanisms of socialisation" and that over time roles become 'habitually assumed' (Potter and Wetherell, 1987, p. 98); as an innate response to social interactions; feeling a situation. One could also argue that it is because of self-preservation. For example, when talking about children's choice in medicine taking, I encountered several situations where the speaker presented the role

of parent as justification for extreme action and dissolution of children's rights in the home environment. This leads me to suggest that roles are activated by triggers and emotions. In the interviews, participants sometimes created their own triggers whilst answering a question, and thus self-activated a change of role.

### 9.3 Introducing the *dramatis intrapersonæ*

Analysis of the roles that manifested in the heteroglossic space produced a list of *dramatis intrapersonae* that can be summarised as: the Scientist, the Employee, the Parent, the Father, the Aunt, the Adult, the Friend, the Role Butterfly and the Chorus<sup>15</sup>. I will now discuss the individual aspects of the *dramatis intrapersonae*, and their potential impact on constructions of children and participation.

#### 9.3.1 The Qualified Professional

I found 11 examples of utterances spoken from the role of the qualified professional most commonly emerging as the Scientist and the Employee. Both M3 and M4 engaged with medical terminology when answering questions about children and neither had entered into any process of negotiation about whether this terminology is acceptable in the interview setting. M3 employed dramatic language referring to a baby as a "neonate", a term that would not be employed in speech outside of the medicines' genre. Although both participants are translational researchers, M3 works in academia a factor that could be impacting on his use of language and thus impacting on the construction of the child as a medical discipline. Both informants constructed children as incapable and in the case of M4, problematic. Both informants associated themselves strongly with their constructions, rarely employing the passive voice. M4 in the opening

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<sup>15</sup> In keeping with the concept of the *intrapersonæ* as actors, I capitalised the words as I am positioning them as character names.

statement stopped and rephrased his response to ensure that he was specific about the children he was talking about. The role of the Scientist was adopted when participants considered how to communicate with children. For example, when talking about: disseminating research through mass media or peer reviewed journals (M2), their feelings about the Paediatric Regulation and the perceived differences between children and adults (M5).

F2, an involvement specialist, consciously engaged her Scientist persona without announcing herself as a scientist. She talked about thinking “*from a scientific perspective*” when talking about children’s participation in clinical trials and her reticence for coordinating trials with children.

One participant (F9) subconsciously transitioned into the Scientist role when she expressed a fear held by scientists of people taking their ideas in order to rationalise why scientists don’t like to communicate their research ideas:

F9-F: “... a lot of the time erm, you don’t talk about your research until it’s done (..) you, you can only say a little bit erm, and with, you know, going for funding, you don’t want someone else to take your ideas, you don’t want to talk about your (,) the data that you have been gathering because once you get to the end and actually analyse them statistically \$you know, it might not tell you what you thought six months ago\$.”

Later she consciously engaged with the Scientist persona when asked about ways to improve relationships between children and researchers captured in the utterance: “\$Having cool scientists like me!\$ (Laughs.)”

I found 15 examples when five participants transitioned into the role of the Employee. These were occasions when a collective role was expressed in the utterance speaking as “we” or “us”. In some instances, there were more

explicit collective roles adopted. I categorised this as occasions when participants were speaking as “*we as a*” in association with an organisation. F11 adopted the collective role when talking about PPI development and approval processes involving children. F11 and F13 presented their role allegiance, by use of the pronoun ‘us’ and ‘we’ in their utterances.

The Employee role was usually adopted when participants were talking about policy or practice issues. When talking about burden and fear of epilepsy and its impact on families, F12 transitioned into the Employee role from an earlier individual (‘I’) stance with the repeated use of the pronoun ‘we’ throughout her utterance.

F12-TrP: “... we are only able to target a certain age group but erm, it is, again from the sort of soc-, the social side of the child’s life, (..) it is so important for us to be able to understand what’s affecting them and in what way their condition affects them, and with something with like epilepsy which too often has (.) ... and it’s important for us to be able to understand what support children not in terms of medication but in terms of the education and support of those around them, so that they can lead a more normal life and it might be something as simple as educating you know their fellow student, their families, their friends ... ..., it’s important we can (,) that we not only support the child themselves in every aspect of their: of their environment from schooling to other social activities , erm:, to coping with their friends, explaining their condition to their school mates, and you know, enabling them to have as mean, as normal a life as possible but also alleviating the burden for the direct caregivers, so that they don’t feel that they’re the only ones that are bearing the, the brunt of care in:: in a community setting, so away from the hospital. ...”

When F2, and involvement specialist, talked about the legalities of communicating with patients and the dangers that it creates in terms of not providing insight into people's conditions, she adopted the Employee role throughout.

F2-Inv: *"but from a professional point of view I worked in pharma company and we, we were very scared to always to talk to patients to think to patients to do whatever with patients because we were scared that we would go over the threshold of, not the threshold the barrier of legalities with regards to what is legal or not and er, I always never really understood it. We were, we knew everything about the doctor, what the doctor wanted, what the doctor thought, what the doctor wanted in terms of helping their patients. However, we never knew how it was to live with the disease, or to cope with the illness or condition, so I never really understood the logic behind that (.)."*

M5 provided an example of being more explicit in adopting the collective role. When talking about improving top-down communication from research to the public, he said:

M5-OP: *"I think we (,) what we have to do as an industry is be more open about side-effects and improve communications. ...Yes, we as an industry have to publish side effects. It has to go into the patient information leaflet. ... .. I don't think, as an industry, (..) this is particularly well known. I'm speaking as somebody from the (..) far end of the process."*

### 9.3.2 The Parent

The most commonly encountered and most influential roles that participants adopted were those of paternal/maternal origin. I categorised

this as when participants adopted the role of: parent, mother, father, aunt, uncle or adult in order to justify decision-making on behalf of children. Half of the participants adopted this role during the interview from whom I located 35 examples. This role was adopted either implicitly or explicitly.

When talking about industry motivators for creating the paediatric regulation M5 explicitly announces his role as a parent and detaches himself from the collective industry role he had previously adopted.

M5-OP: *"I think (,) speaking as a parent, rather than someone in the industry, it's to ensure that the same range of treatments available to a child, as is available to an adult. ... But as a parent, luckily (Note: knock table twice, indicating touch wood) my children have not suffered too greatly with, with childhood illnesses."*

In the interview with M5, he had earlier described his daughter, now legally an adult, as being "naïve" and not able to "fully understand" the implications her actions. In the following example we encounter M5 talking about whether children can make informed decisions and how the paternalism encountered above makes the adult want to make decisions on the child's behalf, thus suppressing children's freedom. Indeed, M5 is explicit about his assumptions about children's capabilities.

M5- OP: *"I'd like to think that the industry can make products available to children in a controlled and efficacious way. But my concern, more from a parent's point of view, is (..) when is that child able to make a decision about what they are going to take. I think that that is the role of the parent, is to make the informed decision on behalf of the child and yes you can argue that in, in a modern society with communication the way it is, children become much more,*

*let's say, streetwise at a much earlier age. I think my son at the age of probably thirteen or fourteen, I'd have been happy for him to make that decision on his own, ..."*

Talking about children's decision-making capabilities M5 verbalises his assumptions of children's capabilities suggesting that this is more of an issue for the parent than for the professional.

M5-OP: *"They are still learning to read and communicate so they don't have the depth of knowledge that we as adults have, hopefully, gained over a number of years, so I think (..) I'd like to think that the industry can make products available to children in a controlled and efficacious way. But my concern, more from a parent's point of view, is (..) when is that child able to make a decision about what they are going to take."*

When discussing talking to children about medicine use, F5 implicitly adopts the Parent role, transitioning mid-sentence when describing her use of paternal persuasion to get her child to take medicine.

F5-OA: *"... my son well, you know he's occasionally said well I'm not going to take it and I say yes okay but if you don't take it you are going to have a seizure and you are going to end up in hospital, so he ends up taking it."*

When talking about medicine taking, the Parent role was sometimes implicit, identified by referring to 'my daughter', 'my son' and 'my own children', as demonstrated in the following example.

F13-Inv: *"Yeah. Oh God, my daughter hated taking tablets (.), she couldn't take tablets and erm, you know, it was a matter of well you either take them or you know, (.) you just*

*don't get better. I'll always remember there was one (,) there was a dissolvable mixture that they had to take that was like Dioralyte for example, which was quite vile at the time, we are talking twenty odd years. Now, (..) they just refused to take it, they just refused to have that medicine."*

F13, a strong advocate of children's involvement, when talking as a parent, assumed a paternal 'right' to use force. It appears that, in the case of the participants interviewed, this is embedded in the ethos of being a parent and is used here to justify actions as not being cruel behaviour but an accepted norm.

*F13-Inv: "\$Quite a lot of force and bribery\$. Erm an:d, I think in those situations though, you just have to dilute it with some sort of, you know, (.) juice of some sort, you know, or disguise it or something, you know. But tablets wise you had to either crush them or go and find a, you know, liquid form so the majority of it was, you know, paracetamol, so that was quite easy but (.) anything to do with antibiotics (hhh), tablets wise, even now she still can't take tablets properly. She hated taking tablets (.) but, you know, now it's not so much of a problem. My son never really had a problem, he just used to do it, you know, \$whatever was necessary\$ you know."*

In another example of paternal persuasion, M5 suggests giving children medication against their wishes, later justifying his response as something that "any parent" would do. He later brought the two roles together, suggesting that professionals and parents have a shared objective to get children involved in clinical trials.

M5-OP: *"It depends on severity of the condition and the age and maturity of the child. Yes, you may have to (laughs) \$literally pin them down and force them to take it.\$"*

F3 also demonstrated paternal dominance when she talked about her personal struggles with her own son in the context of Ritalin taking. Implying that she might use force:

F3-OA: *"He had been on the medication probably about (..) three months ... .. yeah, we did discuss it but at the end of the day, I said, pt you're gonna take it. And funnily enough he never actually refused."*

The most extreme example of parent M1 adopted the role of the Parent while discussing medicine taking and children's views, as illustrated in the following example:

M1-TrA: *"No.... \$he has got to take it or leave it, no he hasn't got to take it or leave it. He has got to take it.\$ No, I mean it hasn't.... If it is unpleasant, so what. Yeah... injections hurt, so what... and that's it."*

Three participants adopted a less forceful stance as the Parent on the subject of medicine taking. For example, F4 when talking about her own children takes a more professional approach.

F4-OA: *"... how we are going to get it down. Reasoning but actually saying this is, this is the medicine that the doctor's prescribed that will make you better, so let's see if we can find a way of taking it. Er, however I have never experienced side-effects, but I think I would think differently if the child said it is making me sick all the time, or it is giving me a really bad tummy ache, or any of those things I think I would*

*probably be doing something about stopping. Seeking to stop the medication erm, by contact with the GP or whatever."*

Indeed, F11 explicitly stressed that you cannot hold somebody down and force them to take medicine, as this might exacerbate the situation. She said that this needs to be overcome as illustrated in the following excerpt:

*F11-EA: "I mean, nobody should have a nasogastric tube or rectal administration because they actually refuse to take the medication\$ we have to find ways of doing it, erm (..) you know, occasionally we have had food refusers, where you have ended up with a gastrostomy tube for the food- (,) for the nutrition and then you end up putting the drugs down it. But, you know, you should be able to get around it with behavioural therapy and working round it."*

F13 talked about instances when other parents had told her of occasions when their children had refused medicines and the potential dangers that accompany this. She gave an example with potentially lethal consequences when a child with nephritic syndrome after a kidney transplant who had refused medicine and her mother had mixed the medicine within jam sandwiches. However, the child was adamant that they would not take the medicine and the mother found the sandwiches hidden behind a speaker in their living room.

Here, M3 talks about listening and understanding what children want while he adopts both the Professional role and that of Parent.

*M3-TrA: "I mean it has happened. I mean we have given medications to my daughter that she didn't want. Erm, but we*

*through rational discussion got her to be able to take them.  
(..) So that to me was fine really."*

F5 talked as a parent in the context of the parent-doctor relationship when a child is particularly sick. Demonstrating the vulnerable nature of being a parent. Later in the interview F5 suggested that "*as a parent, your beliefs will cloud your judgement*" in the context of medical decisions.

F5-O: "*... and I think, as a parent, when you go into hospital and your child's acute, erm, and the treatment you are trusting that they're doing the very best, the thing that's right to help your [child]*"

F6, a translational researcher, displayed internal conflict when talking about entering children into clinical trials. Firstly, she adopted the professional role and then one minute later she adopted the Parent role where she feels decision making should be done on behalf of the child.

F6-TrP: "*... but me: \$working in clinical studies, personally would never enter a child into a study (laughs), so just (,) which goes against completely why (,) what we try to encourage in the studies that we are working on encourage\$ but you know what we are trying to get from our studies, and obviously without these children without the patients, we wouldn't, we wouldn't have the drugs on the market but, you know, with the safety profile of the drug and with what they have to go through and that,\$ I don't know if I would ever enter my child, into, into a study\$ (laughs)... ... I think if it was my child I wouldn't\$ but if there was no, nothing else available and I had no choice then I probably would but if there was another treatment available, then I definitely wouldn't enter*

*my child into a clinical study. \$So, it completely goes against what I, what do as a job.\$ (laughs)”*

Here we see an explicit example of the impact that being a parent had on the execution of a research task, where M5 discusses the emotions of interacting with child participants

M5-OP I was interviewing subsequently, I, I, I had to, I had to stop because the emotions came through thinking (...) you know, my, my son’s studying civil engineering at university, and speaking to this lad, who at the time was roughly the same age as my daughter and looking at the impact it had had on his life.

In another instance discussing children who refuse medicine M4 starts by explicitly announcing his role as a father. Later, when asked about giving medicines to children that they might not like, asks whether he can speak as a father and shortly after uses his “*personal experience*” with his children to justify forcing his children to take medicines that they had refused.

M4-TrP: *“I am a father of two children ....”*

M4 TrP: *“... well I can talk as a father, ...”*

M4-TrP: *“From personal experience with... my children \$have been incredibly negative about er, about them anything they had to do with the medicines it was a disaster, disaster (laughs). I ended up with, this sounds terrible out loud, but I ended up with syringes (laughs) and pushing down. Immobilising them\$ and this was even for simple things like Calpol. Very, very complicated issue, er, about convincing (,) generally my experience is that it is incredibly difficult to convince a child to take a medicine”*

Later in the interview with M4 he explicitly announces that his response is formed from within his Father role and, as with M5 earlier, we see an example of detachment from a professional role.

M4-TrP: *"I think there is, as I said, I am thinking a bit as a father here, rather than somebody who works in the pharmaceutical industry or a physician. I think there is er, a line,(.) and that line can change (..) quite substantially from child to child."*

### 9.3.3 The Aunt: or second-degree relative

In instances where participants were not parents, I looked to see if other maternal/paternal roles were adopted. Only one participant drew on a second-degree relative role. I found that this role carried with it similar constructs of children's abilities, as demonstrated in the following example where F2 talks about her niece.

F2-Inv: *"My niece is five years old, and she doesn't see the connection of taking a tablet and then five hours later having diarrhoea or something. She would not see that connection and she would not feel if she is drowsy or, if she gets really tired, she would not make that connection. So here comes already one... quite... you would just have to monitor her on hourly basis and ask her how she is feeling. She would not say oh I don't like this tablet because it makes me sick in (.) five hours, so I think, I think niece would be able to say oh mum I don't want to take this drug because it tastes horrible. If she puts it in a like nice jelly or whatever she probably won't complain about it."*

F7-TrP: *"(...) I think that if I were a parent, I would want to understand that."*

#### 9.3.4 The Adult

The role of adults was often adopted to discuss involvement in clinical trials, specifically when talking about issues of decision making. In the following example, F13 is explicit about her role as the Adult.

F13-Inv: *“But as an adult we can make those decisions for ourselves but for the young people, (.) even if they want their mum and dad to make that decision for them, I still think it needs, those patient information leaflets to be designed appropriately to meet their needs.”*

Later the adoption of the role was implicit, where F13 uses collective association with adults using the pronoun “us” to differentiate between adults and children.

F13-Inv: *“Although it might seem small to us, to a child who has got to have these injections on a daily basis is, you know, is ground-breaking for them if they don’t need to have that, you know.”*

When M3-TrA considered his interaction with children he recounted a story that had occurred 30 years previously when he was a research fellow at a Saturday morning clinic. He talked with passion about how the children and he would “*talk about everything*”: diagnosis, investigations, waiting times and service provision. He was struck by the children’s resilience and willingness to give up their Saturday afternoons. He remembered that the “most important thing” to the children was that they wanted people to understand their disease and find treatments.

Talking about children’s abilities to express an opinion, M2’s utterances suggest in closing that he would consider other methods to give medicine to his child if he could not take it conventionally.

M2-OA: *"... I had this situation with regard to, to my son, when he was born he had a (..) number of issues and er: I wasn't happy with the advice that I was receiving so I (..) did try to inform myself, it didn't seem to make them very happy but it didn't really bother me erm yeah I mean, I would have to say that at that point, I'm not sure that his view, is (..) informed enough (..) I would think in that sit, in that, at that, at that, for his age I would might have to try and encourage him to er, to take the medication (..) and if he, if obviously physically can't take it, he can't take it, you know, well I might would have to look at a different way of giving it to him."*

### 9.3.5 The Kinship Actor

The Kinship Actor emerged when the speaker assumed the role of a family member or close friend but not in a paternalistic manner. This included: son, daughter, friend, sibling, spouse or partner. I found that the role of the Friend was adopted by participants to recount stories and their perspectives where they did not have personal experience. For example, M5 talks of a friend's daughter challenged by epilepsy when talking about off-licence medicine use in children.

M5-OP: *"Friends of mine have a daughter who's epileptic ... and it severely constrains their lifestyle because they have to consider the impact on her, on things that they do."*

One participant (F2) took the perspective of a sibling when she transitioned into the role of the Sister during a discussion about people's lack of awareness of the extent of the use of untested drugs in children:

F2-Inv: *"Society you know for people like, for (Jxx- name excluded) like my sister, (..) she would not even know that there's that if my niece, God forbid, would get ill, my sister*

would not even think about better this drug was tested or not in children. She would probably just think make my child better, whatever, so er.....”

Participants often spoke from the role of first- or second-generation offspring: son, daughter and grandson. None of the participants announced their role explicitly by stating ‘as a son’ or ‘as a daughter’ etc. but rather this emerged by reference to my mum, my dad, my father etc. The following example shows how readily M5 adopts his roles as son and grandson while talking about prioritising medicines for the older population over children and talked about how Alzheimer’s disease impacted on his family

M5-OP: *“For example, my father has is suffering from fairly advanced Alzheimer’s, he’s happy in his own little world. He takes his tablets. He is actually remarkably healthy for a man who turned eighty-two yesterday. The strain is all on my mum. ... So it’s (,) I guess, growing up in the sixties, being brought up by my grandmother a late-Victorian really, basically you just make the assumption the doctors are going to get it right. Now we know that’s not the case but it’s too ingrained in me to question it, I suppose. ... My grandfather’s generation di:ed before Alzheimer’s manifested. My grandfather died when he was in his mid-sixties. My dad (..) has survived two heart attacks, at eighty-two he is physically actually quite robus:t, but Alzheimer’s has manifested.”*

### 9.3.6 The Role butterfly

The transition displayed by M5 led me create a new category that captured participants who flitted from one role to another, either consciously or subconsciously. I looked for other examples of participants transitioning between various roles within the interview and found only two further

examples (F11 and F8). F11 kept switching between her professional role as the Scientist and the collective institution of Research to respond to a question about discovery new aetiologies of epilepsy. When talking about communicating with children about medicine use, F8 explicitly transitions between the Employee, Kinship actor and the Patient, as can be seen in the following extract:

F8-TrP: “... *not with my work hat on, no. ... Okay, so a close friend’s... son who is asthmatic, I’m asthmatic, and so we have spoken about asthma medications and inhalers and the best way (,) and the use of spacers and spacing devices and things like that.*”

However, the best example was again from M5 when in one 3-minute-long response to a question about informed consent. M5 switches between the Scientist, the Parent, the collective Industry, back to the Parent, then the Qualified Professional, the Patient, collective Industry, reverts to the Parent, collective industry the Qualified Professional and the Kinship Actor.

M5-OP: “.... *However, the scientist in me (..) doesn’t see how it can be made to work at the same level as it can in adults, simply because it’s, it’s (,) I guess it comes down to informed consent of the individual because (,) er my daughter’s nineteen, she still can’t take tablets. ... We: (,) as somebody who worked in the industry, we have always discussed things like, and yes, it is inevitably as a parent the conversation start off with the abuse of drugs ... .. recreational drugs. My, my children understand what I do, erm (..) do they understand side effects? (...) I’m not sure, (..) it’s, it’s something that even as somebody who has been working in the industry as long as I have, I am currently suffering from hearing loss in one ear potentially as a result of taking statins. I have to take the statins to reduce my*

*cholesterol, so it's (,) I think we (,) what we have to do as an industry is be more open about side-effects and improve communications. Now if you think, my children grew up in erm, a northern European environment where education at least of an acceptable standard. ... Yes, we as an industry have to publish side effects. It has to go into the patient information leaflet. ...Speaking as somebody who's run packing lines, it would make my life easier because the most frequent breakdown on a tablet packing line is often the patient information leaflet. ... If, if you like I use (,) a friend of mine is a carpenter, is he actually going to understand the PIL when he reads it? (..) If he reads a PIL and it says may create hypertension, does he know what hypertension is? ..."*

### **9.3.7 The 'anOther perspective'**

Four participants readily adopted the role of a third-party answering questions from the perspective of another. Here the participants state the assumed feelings or actions of others. For example, F2-Inv starts talking about sister's reactions from the perspective of her sister: "*She would probably just think make my child better, whatever, so er....*", and later as her niece: "*I think my niece would be able to say oh mum I don't want to take this drug because it tastes horrible*". Then finally, when talking about drug development, she talks from the perspective of the pharmaceutical industry:

*F2-Inv: "If I were erm a pharmaceutical company and I wanted to develop a new drug, an innovative drug, a new area, I would start thinking about adults because I that my, that my barriers are much lower there. So that, that the rate of success is much higher if I just go for adults for all... for legal battles, I already probably am going to have a lot of legal battles to prove that my drug is erm, economically better than all the others. So: I*

*am going to probably have a delay of three, four years to get reimbursed by governments, so let alone (.) children. So, with children clinical trials and, I would probably think, phew, if I want to have a success let's think about children may be (..) at the end \$when I have some time left.\$"*

Another example from the interview with F3-OA is when she adopts the an'Other perspective of clinicians, when talking about drug discovery: "*So, pt, new anticonvulsant comes on board some clinicians think oh yeah, we ought to try that..*"

### **9.3.8 The Chorus: activist, expert patient and the stakeholder**

There were a variety of other roles that arose in the interview space. I have grouped these roles/*intrapersonæ* together as, although they are significant, they did not manifest on many occasions.

The three participants that engaged with the Activist *intrapersona* usually announced this role and provided a qualifying statement in close proximity. In the case of F13, the activist could be argued to be innate due to her role as an involvement specialist. Here we encounter her talking about involvement methods.

*F13-Inv: "Yeah. I do. \$ I do now. I'm quite, I'm quite\$, I quite sceptical now in terms of you know in everything that I read I always have my patient and public involvement hat on an say that's absolutely rubbish that."*

For F9, she engaged with the Activist voice early in the interview and embraced this role in each utterance when talking about the UNCRC.

*F9-F: "\$Ooh gosh\$ As a young child I was very (...) very outspoken about my views and speaking up for people who I*

*may have felt were less fortunate than I was, so I got very involved in environmental clubs and human rights clubs at a very young age and erm (...) my parents actually sent me to school in [Country], boarding school in [Country], and I did more of that because in a place, in [Country] you can see more of erm (...) environmental degradation and you can see more of children whose rights have been (...) (laughs) have been neglected completely. ...”*

All people can be argued to be Stakeholders and, though an integral role, it was rarely engaged. There was only one explicit use of this role when F9, a funder, was talking about “*what we as end-users*” might think of the paediatric regulation.

The *dramatis intrapersonæ* can be described as a list of characters that are integral components of human identity, which might be adopted or activated at any time, depending on the situations encountered. Examining the multivoicedness of the participants’ utterances in the interview, revealed a complex meshwork of *intrapersonæ*, one dominating another at various points during the process. The *dramatis intrapersonæ* were triggered by the nature of the questions but also helped to provide shelter from participants’ decisions. In particular with regard to forcing children to take medicine against their will; this was justified within the voice of the parent but never emerged in the voice of the qualified professional.

#### **9.4 Role, role conflict and intrapersonal conflict**

*“The idea of role is an intellectual tool, ... remarkably illuminating when brought to bear upon many facets of social life”* (Banton, 1965, p. 3)

Every person has expected roles. In role theory these are suggested to be duties or obligations that come with certain rights, norms and responsibilities “an abstraction to which the behaviour of people will conform

in varying degree” (Banton, 1965, p. 21). Roles can be genetically predetermined at birth, e.g. man or woman; inherited (e.g. born into poverty or royalty); allocated by one to another (e.g. getting promoted due to performance or intellect); or elected (e.g. the Prime Minister). Further, role is a way to study co-operation, which led to its use in economic conflict and business (Biddle, 1986; Leischnig *et al.*, 2016). Role theory is filled with abstract concepts, for example the idea of a hierarchy of prestige in roles, e.g. medical researcher versus patient. Status or prestige can be ascribed to issues of power, especially within the subject matter of this thesis.

Banton (1965) suggests that role systems vary in intricacy from simple, such as in tribal systems where roles are decided at birth, to complex. In complex and progressive societies, capability means more impact and there are various roles or social positions to be adopted via choice or designation. Roles can be distinct (e.g. researcher and parent) or subtle (e.g. junior researcher and senior researcher) and not only a form of self-expression but a representation of the self. Thus it is argued that roles determine a person’s personality, therefore people’s natures fluctuate (Potter and Wetherell, 1987, pp. 97-99).

One-to-one encounters can be analysed in terms of the relationships between roles and customary behaviour (Banton, 1965, p. ix) or social norms. Roles have limits or boundaries and these can cause conflict due to difference between the ideological standpoints associated with certain roles (Banton, 1965, p. 1). This was manifest in the interviews. Banton (1965) suggested that one reason for analysing social interactions in terms of roles was the “social bargains” that underpin interactions, which require at least two parties, for example: doctor and patient, parent and child, or researcher and funder. However, I identified dichotomous relationships between participants’ own roles. The six paired relationships that emerged were: company-employee, parent-child, policymaker-practitioner, researcher-practitioner,

practitioner-parent, and practitioner-patient. These pairings were often the site of intrapersonal conflict emerging within the heteroglossic space, as utterances filled with changes in demeanour, attitude, tone and language.

I was surprised by the way in which the interviewees switched between roles and the impact that these shifts had on their responses to the questions. Banton (1965, pp. 93-94) suggests that role changing and behaviour modification creates problems for social relations. I identified examples of this when participants were talking about medicine taking. The disregard of children's rights was attributed to being a 'right' of the role of the Parent and the justification was suggested by their talk to be due to their parental 'obligation' to protect their child. When I listened to the interviews repeatedly, it became apparent that the interviewees were not always conscious of their shift in role. This role transitioning presents a problem for children's participation; as professionals, the majority of participants recognised children's rights but as parents they did not.

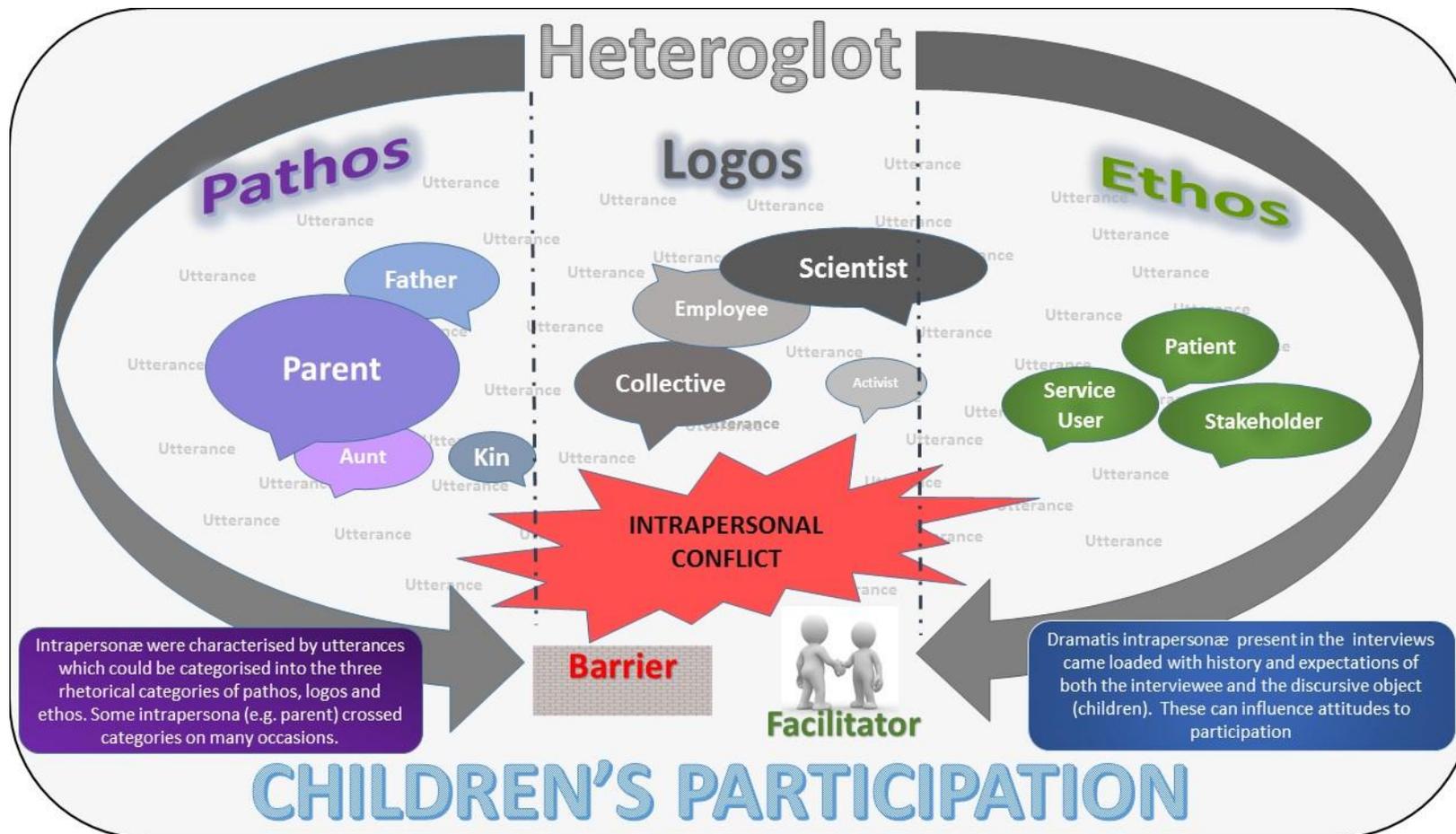
From a Bakhtinian perspective predominant voices prevailed when talking to professionals about children which was loaded with 'other' voices from different genres. By combining role theory with Bakhtinian theory I have attempted to add another dimension to understanding the discursive objects by identifying: the multiplicity of actors that were present in the heteroglot, the *dramatis intrapersonæ*, and their conscious or subconscious role adoption. The complexity of history that is attributable to each 'utterance' and the potential for 'other' characters to ventriloquate the speaker was manifest in the interviews. On reflection, participants were not always willing to proffer particular roles in the interview space and the majority of role switching was performed seamlessly. Occasionally participants actively searched for their other roles to interpret the questions. This was demonstrated by fluctuations between voices and constant referral to the superaddressee to act as a personal mediator. In one instance a participant

(M4) vocalised his transition moving further towards the role of the Father throughout the interview. First, he announced that he was a father, then that he said that he was thinking as a father, and finally he said that he was talking as a father. This stratified transition into his role suggests that answering questions on children's participation resonated with his paternal role eventually capitulating to its dominance. Banton (1965, p. 150) suggested that roles may influence a person's perception of others. However, role theory has been criticised as only being used when suited for particular analysis, with social anthropologists and sociologists choosing examples to fit particular arguments, whilst "evading the task of formulating general and testable propositions." (Banton, 1965, p. 22). Also, roles are often considered in isolation. Further, how roles enact with other roles and role adoption is positioned as being a conscious act (Ibid, 1965, pp. 149-150), however I found this to be a predominantly subconscious act.

#### **9.4.1 Role and construction of children's participation**

Role-changing considers different factors when it comes to children, for example in terms of capability in the Anglophone world. Strains occur when young people insist that they are physically and psychologically mature. Outside of the home children might be being treated like adults, yet inside the home their parents still treat them like children. In the context of role theory, Banton (1965) suggests that the parent role conceptualises the child differently in terms of the stage when it is appropriate to treat them as 'adult'. Emotional stressors further complicate how children are perceived, e.g., moral obligations or unwillingness to relinquish the parent role (Ibid, 1965, pp. 99-100), which was manifest in the interviews. The dominance of the Parent in these interviews suggests that the potential for children's participation in medicines research does not rely solely on the researcher in the room, but the Parent that is waiting off-stage, ready to enter and make judgements about their capabilities.

Figure 9.4 Role conflict within the heteroglot characterised by pathos, logos and ethos



## 9.5 The impact of the paternal/maternal role adopter

In the examples above, participants adopt a paternal role to justify and exert power over children in order to get them to take medicines that they might not have wanted to take. Paternal status and love are presented as justification for certain behaviours, i.e. forcing children to do things for their own good.

In the role of the Parent, participants experienced emotional conflict. Intrapersonal conflict between their role as the Scientist might contend with their maternalistic/paternalistic impulses as the Parent, which may impact on work-based decision making. Being a parent has a more integral part to play over the protection of children. A desire to conduct research into children's perspectives might be attributable to the Mother/Father *intrapersona*. For example, Tracy Jensen (2008, p. 384) on 'speaking as a mother', focuses on the inclusion of the researcher's self as being "foundational to knowledge itself".

Jensen argues that we all speak from somewhere - and where this is should be examined, used and unpicked (2008, p. 384). She questions whether she should silence the 'I' and 'me' from her research analysis but questions whether imagining "different facets of my Self are open to such separation" and furthermore, whether anything can indeed be gained from examining these "facets". Jensen talks of the authority often given to those who "speak as a mother". Indeed this 'mother status' often permits the right to speak on a subject at all - for example when experts on parenthood qualify their expertise by printing the number of children they have alongside their qualifications (2008, p. 385). Jensen questioned where research ends and 'real life' begins, concluding by arguing that the emotional politics of research should be considered as an approach to autoethnography. I suggest that participants' research lives and 'real life' experiences are synchronous and to separate out emotions associated with these roles will be near impossible. All

that is possible, is to recognise that they exist and be aware of the potential impact this can have on children's advocacy in the context of children's medicines R&D.

## 9.6 Issues of paternalism

"Paternalism might be thought of as the use of coercion to achieve a good that is not recognized as such by those persons for whom the good is intended"(Dworkin, 1983)

Using the above statement as a definition, paternalism is evident within the medical and healthcare paradigms, particularly with reference to healthcare practitioners who are motivated to operate in the patients' 'best interests'. As I have demonstrated in the research (Chapter 6 and 8), acting on behalf of children regarding creating policy, therefore, is positioned as justifiable if individuals (i.e. parents, carers, healthcare practitioners, etc.), organisations and the Government are acting in the children's best interests.

Identifying why the practice of exclusion of children is continuing within the medical research paradigm is complex, as is quantifying or assessing the degree to which children's participation is exercised. As previously outlined, the UNCRC and various other national and international initiatives encourage patient-consumer involvement but factors challenging children's participation are heterogeneous. Issues such as: reduced political impact, limited access to information, lack of representation, paternalism and lack of established *fora* within which children can present their views, all impact on children's agency within the medicines R&D paradigm. Of the above issues, one of the most critical factors suppressing the voice of children with the medical genre is the continued paternalistic attitude apparent within medical culture in general and the interviews conducted for this research. Arnstein (1969, p. 217) cites 'paternalism' as one of the significant roadblocks

to attaining “genuine levels of participation” on the side of the power-holder, yet it remains manifest in public policy.

One of the dangers of not hearing children’s perspectives is that the ‘real interests’ of the children remain hidden, are misinterpreted, or massaged to comply with the perspective of those who are representing them for the ‘greater good’. In the UK, neo-liberal administrations have targeted the issue of paternalism in order to promote a more entrepreneurial culture with regards to healthcare provision (Winkler, 1987). Limited paternalism is defined as

“...when an individual in a position of superior knowledge has an active duty to explain the consequences of a decision. Here the “father-like” individual does not make the decision for the other” (Ebejer and Morden, 1988, p. 338)

This type of paternalism would be more acceptable within children’s medicines R&D, as although children are not necessarily experts on the intricacies of pharmaceutical intervention design, they often have expert opinions on the effects of these interventions, and they are definitely experts on their own emotions and lived experiences.

Increased awareness of children’s rights in the context of healthcare services should be generated from local to international levels, in order to emphasize the current and potential value of children’s participation in public policy and health services research. One of the greatest challenges for children’s participation is in the field of medicines R&D, an arena traditionally reserved for adults. Children must be treated as experts and have their perspectives integrated earlier in the R&D process in order to help to identify priorities and inform decisions that can affect change. Every healthcare consumer has the basic right to make an informed choice about the pharmaceutical interventions they receive, but I would further argue that every patient, child or adult, has a right to impart their views on the

development of the pharmaceutical interventions intended to manage their conditions.

## 9.7 Chapter summary

Participants commonly spoke with a variety of 'other' voices. It is crucial when considering how people construct discursive objects, to be aware of the *dramatis intrapersonæ* that individuals bring to the interview heteroglot. Children and children's agency are constructed very differently by the Parent and the Scientist, which has implications for implementing policy and the uptake of children's participation in medicines R&D. These *intrapersonæ* are not always easily discernible, or even coherent but their presence can have a significant impact on the way people view the world. Most common to emerge from the heteroglossic scene was the voice of the Parent. Paternal dominance highlighted issues of internal conflict regarding children's rights on a number of occasions. Adopting the subject position of the Parent changed participants' responses to aspects of medicine taking, in that this role was used to justify giving medicines to children by force. However, when talking as the Scientist participants valued children's right to refuse treatment and have a say.

Although the roles of the Parent and the Scientist generated different responses to children and medicine taking, both are protector roles, and both are paternalistic. This causes a problem in so far as knowing 'who' we are we addressing within the discourse of children's participation in medicines R&D. Academic papers target professionals, but how do we know that the person reading them is in the role of the Qualified Professional at the time they are exposed to the information. One participant suggested that we talk to professionals as parents to promote the uptake of children's involvement. Yet this same participant conformed to the role of forceful Parent with regard to medicine taking, which suggests that this would be the wrong approach. The mind-set of the Qualified Professional is one that, in the majority, accepts children's involvement; it is the professional we need to reach to facilitate children's involvement.

## Chapter Ten: Discussion and conclusions

### 10.0 Contextualising the findings

Advantages of multimethod research are suggested to be: triangulation – validating data and results by merging a range of data sources, methods, or observers; creativity – learning new or inconsistent factors that inspire further work; and expansion – broadening the scope of the study to encompass contextual aspects of the phenomenon (Tashakkori and Teddlie, 1998). The three components of this research: speech analysis, scoping review and Bakhtinian analytic methods (see Chapters Five to Seven), converged to validate my findings from the perspective of three sets of professionals; political actors talking around the research (political speeches; researchers who had involved children in clinical trials research (scoping review); and gatekeepers to early research. This enabled me innovative ways of understanding children's involvement in medicines R&D. Information gained has problematised the changeable 'self' in constructions of children and involvement, and how this might impact on the progression of children's involvement in medicines R&D.

Findings from the speech analysis suggest that children's views are not recognised in the regulations that govern children's medicines R&D. I could find no evidence in the political speech analysis, or in the documents themselves, that children were consulted (European Union, 2006a; European Union, 2006b; US Congress, 2002; US Congress, 2007). However, it must be noted that the main purpose of the speeches was to provide context to the interviews. The speech analysis contextualised the diachronicity of talk in the interviews and provided a historical dimension to the study. Children's agency in political processes and the evidence of their interaction with those creating

the policies was not evident. The speech analysis suggested that the regulations for improving children's medicines stem from protective paternalistic tendencies, yet it can be argued that all political speeches are paternalistic regardless of the subject matter (Tan, 2001). Orators of speeches adopted the rhetoric of pathos to frame their arguments (see section 5.3.3.1), relegating children to the realms of helpless individuals. Though elevating the need for legislation in the minds of the listeners, this use of rhetoric only serves to undermine children's agency (Mullin, 2014). This, combined with the lack of any consultation with children about the legislation, further cements the construction of children as beings who have things done for them, not citizens who do things for themselves. More than this, I found that alongside legislative policy, medical academic, and professional literature also do not include children's voices or views. Indeed, evidence of the benefits of children's involvement in medical research, as opposed to health research, is hard to find. Despite being 'talked about', there is no evidence of consultation or engagement with children to obtain their views on ways to improve research into children's medicines. The focus of the speeches was on methods of encouraging research into children's medicines and the technical issues associated with marketing authorisations, from the offset. I do not, however, deride the politicians' efforts in creating legislation that has attempted to encourage pharmaceutical trials for children. My concern is that the lack of consultation suggests a perceived lack of value of children's input, which could result in policies that are based on adult understandings and could potentially miss the needs of children.

Children were generally referred to or positioned as passive, under-serviced and vulnerable, I found that 46% of references to children positioned them this way (see Table 5.3.4). When talking about children, politicians shifted their use of rhetoric from logic (*logos*) to emotion (*pathos*). The prevailing rhetoric of pathos to frame the arguments to improve children's medicines, combined with the employment of popular patronising

phraseology, such as therapeutic orphans, further perpetuated the construction of children as a vulnerable, or at-risk group. Children were rarely talked about in the context of capability.

Children's views were considered in terms of ethics, rather than being considered in policy making. The absence of reference to children's views is a worrying finding from this study, in that politicians whose remit is to create policies for the benefit of their constituents, might only be considering their own views (Stadelmann, Portmann and Eichenberger, 2013). This raises questions about the motivation of the regulations for children's medicines.

Three key findings emerged from the scoping review that inform this research. Firstly, that children have views on a variety of topics that could prove useful to researchers allowing access to 'new' types of knowledge (Staley, 2017). Secondly, the review revealed that researchers who had actual experience of involving children, constructed them positively, speaking of the crucial nature of children's input. One author suggesting that children's involvement should be published in journal articles (Bernays *et al.*, 2017). Thirdly, I conducted a broad search, as I positioned that all children's views on medicines could potentially inform research. Of the 19,243 studies identified, only 21 matched the inclusion criteria, equivalent to 0.1%.

Constructions were varied ranging from passive to active (see Chapter Eight). As with the data from the political speeches, children were predominantly constructed as passive, positioning children as vulnerable and at risk, with little influence in medicines R&D. However, unlike the political speeches, children were also viewed as capable. Despite children's views being positioned as valuable, participants were reticent to open communication pathways with children directly. This research suggests that this reticence is a product of regulatory controls and industry demands on profitability.

The Bakhtinian analysis focused my attention on voice in the interview; who was talking. It emerged that not only were the words spoken in the interview the words of 'others', they were carried by the voice of a variety of 'others' that comprised the participant's cast of characters. I examined this in the context of the various genres that impact on children's medicines: medicine, translational research, legislation, practice guides, patient groups, and involvement specialists. The language from these genres has its own values and constructions of children that have filtered into participants' talk and ways of seeing children. Focusing on the tensions further revealed that participants constructions of children were challenged by who was speaking, which 'self'. Considering the interview space as a platform, or stage, for exchanging meaning drew me to reflect on the variety of participants' roles. Banton (1965) suggested that roles will have influenced participants' perceptions of children. I found that the expected duties and obligations assigned to participants other life roles (see section 9.3) were actualised in the interview space and heavily impacted on their constructions of children. Through reflecting on utterances in the context of role theory, I was able to identify the presence of hierarchical life roles, which came into play. The conceptualisation of the *dramatis intrapersonæ* battles between monoglossic influence and heteroglossia, it also assumes a total interconnectedness with all aspects of 'self' (the authorial surplus). Assessing an individual's *dramatis intrapersonæ*, and their dominance within professional practice has not been proven. Therefore, understanding professionals' 'true' perspectives may never be achievable, as these perspectives will be coloured by the adopted characters that may come into play at any point during a research exercise.

Roles were triggered by different queues, i.e. questions or memories. The conflict and competing nature of these roles, particularly between the Parent and the Professional, in children's medicines has implications for the realisation of children's involvement. The expected role of the Parent is

generally accepted to be that of protector, someone who shields their children from harm, often acting on children's behalf, thus often silencing children's voices. The role of the Adult suggests that the participant had more knowledge, due to chronicity and thus would be best placed to make decisions for children. I do not suggest that parents stop protecting their offspring, or that adults are not knowledgeable, but in the context of children's medicines we, as adults and parents, need to give children space to contribute to the discourse and impart their knowledge. In section 2.1, I discussed how over-protection has precipitated the current state of play within children's medicine and the 'therapeutic orphans' that have been created, have arisen due to restrictive ethical codes, which are under the guardianship of scientists who might often be parents. Conflict between these ideological standpoints, i.e. the Parent and the Professional, are problematic for children's agency with medicine taking (see section 9.5). This could impact on the credence given to children's input. Subconscious role transitioning and the internal conflict this has upon professionals is problematic in that another dominant role might prevail. If the Parent dominates, there is potentially suppression of children's involvement (Schoeman, 1980) in situations where the Professional role is expected.

The issues of defining children's physical and psychological maturity further complicate the process, in that views were suggested to be more valid when they were provided by older children, with participants having only 'listened' to children who were 12 years old or over. In the absence of an arbitrary line denoting transition from childhood to adulthood, children are at the mercy of the cast of roles that constitute the individuals with whom they interact, as to how they will be viewed. The reflexive response to this revealed that participants' roles, their various *dramatis intrapersonæ*, can influence their decisions, actions and constructions of children and thus affect their perceptions of and receptiveness to children's agency.

In the remainder of this chapter I discuss my findings in the context of other research, drawing on the Johari window and diffusion of innovations theory. I discuss the: implications for practice; issues for improving children's involvement; implications for the future; study limitations; and final conclusions.

### **10.1 Reticence towards children's involvement**

Evidence of patient involvement in biomedical research is limited (Barber *et al.*, 2011; Staley, 2009), with the majority of accounts of involvement being anecdotal. A qualitative study identifying examples of the use of patients' experiential knowledge in biomedical research (Caron-Flinterman, Broerse and Bunders, 2005), identified 21 cases. The authors reported that involvement was predominantly decision-making in policy, research programming and prioritisation, occasionally research topic identification and formulating research questions. No cases of patient involvement were identified in the "core" stages of biomedical research: research design, execution and data interpretation. Three types of output from involvement were suggested: demands (research priorities), ideas (aetiology or therapeutics) and judgements (research relevance) (Ibid, 2005). None of their included examples involved children; they consisted of patient organisations and parents.

The scoping review conducted for this thesis also located no evidence of children's involvement in early stage research, rather all the included studies were situated within T2 translational research or later. What emerged from the review was the broad range of topics where children shared their views: health condition, impact on their lives; medicines; medicine taking; research and development; knowledge and information sharing; clinical trials and emotion and agency. Often professionals who had involved children in

research had valued their input and lauded the benefits of the children's expert knowledge.

Though several interviewees talked about the crucial nature of children's involvement in research design, they were pessimistic about the practice of involving children. They felt that the pharmaceutical industry required encouragement to involve children in research. The barriers to involvement are well-documented (e.g., Boote, Baird and Beecroft, 2010; Boote *et al.*, 2014; Domecq *et al.*, 2014; Forsythe *et al.*, 2014; Oliver *et al.*, 2015; Parsons *et al.*, 2016). In the following section three of these barriers to children's involvement are discussed; the ones that featured highly in my research and on which little has been reported.

## **10.2 The 'mythical' legislative barrier**

Participants from the commercial sector constructed children's involvement as a "huge mountain" (F10-EPN) to climb, complicated by legislative hurdles, an emergent construction across the interviewees talk. Indeed, T1 translational researchers, believed that they were not able to talk to children about their medicines due to legalities that prevent direct communication. One stated that they are "not, by law, allowed to talk to people" (F12). Of those interviewees who conducted research later in the translational process, T2 researchers, such as clinicians, who had the opportunity to talk to children, the majority did not. Commonly this was because interviewees felt like they did not know how to conduct research with children, or how children could practically participate in their research endeavours. Although there is uncertainty whether PPI enhances the value of information earlier in the translational continuum (Drolet and Lorenzi, 2011), collaboration is being actively encouraged in early stage research (ABPI, 2016a; ABPI, 2016b; Dobbs, 2016). Dispelling the myth of legal barriers to collaborate with children, Participants felt that the difficulty of navigating

through regulatory and legislative processes was further complicated by the process of involvement itself being unclear.

Poortman (2007) suggests that patient and consumer organisations “highly favour the proposed incentives [for researching medicines for children], regulatory requirements<sup>16</sup>, research funding suggestions and the attention for greater transparency and expert regulatory, ethical and clinical supervision”. Furthermore, patient and consumer organisations are contributing more to the children’s medicines agenda: providing information, inspiring patients/families, and adding to other valuable processes. Though Poortman talks about the influence on national and international health policy, this is not quantifiable and there is no mention of the children’s involvement, solely how they will benefit from the work of the patient and consumer organisations.

### **10.3 Organisations advancing children involvement**

As discussed (section 1.1.3), there are number of organisations dedicated to advancing children’s involvement. For example, INVOLVE since its inception in 1996 to support public involvement in the NHS, public health and social care has been encouraging PPI, though its promotion of children as expert contributors to research is more recent (INVOLVE, 2018). The NIHR now funds INVOLVE along with GenerationR in the UK (James Lind Initiative and NIHR, 2016). There various resources to support children and young people’s involvement in health research from the Nuffield Council and the Royal College of Paediatrics, which include structured guidelines on how to involve children in research (INVOLVE, 2012; Kirby, 2004; Pear, 2010), iCAN

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<sup>16</sup>These included: the creation of a European level paediatric fund to support additional research on existing medications and potential for use by children; extension of market exclusivity; development of a central database; formation of an EMEA paediatric expert advisory group; creation of a pan-European network of clinical paediatric and pharmacological experts.

and GenerationR (Hunter and Greenough, 2018; iCAN, 2019; James Lind Initiative and NIHR, 2016; Nuffield, 2015). Most participants did not appear to be aware of any published guidelines, and the few that were felt that these were not specifically targeting them, rather health care and social research as opposed to pharmaceuticals specifically. Indeed, interviewees were rarely aware of these organisations, let alone the resources on offer. Ironically one research funder suggested the creation of a “Children’s Medicines for Dummies” book (F2-Inv-RF). Another participant suggested that patient groups could help to construct guidelines to bridge the gap between political agendas, national health guidelines and those “working on local protocols and guidelines” (F12). Their preference was for a step-by-step guide that highlighted what needs to be done at each stage, timings and regulations. A couple of participants went as far as to say that the guidelines should incorporate moral tenets to instil the “feel good factor” as a benefit to conducting research.

## 10.4 Diffusion of Innovations and children's involvement

Evidence from the speech analysis suggested that children were not involved in the design of the paediatric legislation governing the development of children's medicines. The interviews examined whether this absence was evident at a practice level, and if children were involved, how early in the R&D process. Participants' responses reveal that on the rare occasions when children are involved in medicines research, it is mainly as clinical trial participants. Children are also consulted by researchers to review patient information leaflets, but I found no evidence of children's involvement beyond these two elements. As I expected, involvement specialists who work with T2 researchers, consult with and involve children in research design. Further, children who had been involved in research other than as clinical trial participants were older children, twelve years and over. The scoping review did identify studies where children were actively involved in research and their views were being recognised. What emerged from the scoping review was the idea of a spectrum of researchers from those readily accepting and utilising children's involvement, to those who were actively resistant to the idea. I categorised these professionals as:

- **Advocates** – professionals who are actively engaging with children's involvement, embracing involvement techniques and publishing research (Identified in the scoping review)
- **Reticent advocates** – those who externally consider children's involvement as beneficial but have many reservations about the process and impact of children's involvement – (Identified in the interviews)
- **Contrary advocates** - are those teetering on hypocrisy in that they speak a good game surrounding children's involvement but when encounter opportunities to talk with children, take the stance of adult knows best. (Identified in both the scoping review and the interviews)

- **Silent critics** – those who object to children’s involvement, because they are conflicted with their views being controversial within the rhetoric of children’s involvement, so remain silent (I don’t know if encountered any of these)

This bears relevance to diffusion of innovation theory. Diffusion of innovation seeks to explicate how, why and how quickly a technology or innovation spreads through particular populations (Berwick, 2003; Greenhalgh *et al.*, 2004). Diffusion of innovation theory suggests three clusters of influence over the rate of uptake of an innovation: 1) perceptions of the innovation; 2) people’s characteristics; and 3) context (Berwick, 2003).

Children’s involvement is the innovation in this instance and the context is medicines R&D. However, this study is looking to understand if how children are viewed might impact on professionals’ acceptance of children’s involvement in medicines research. According to Berwick the most powerful factor is the perceived benefit. Professionals are more like to adopt innovations if the benefit is tangible (Berwick, 2003). In this study, I have suggested that exposure to sick children changes perceptions due to researchers gaining ‘new’ knowledge, as highlighted by Staley (2017). The knowledge professionals gain about the expected consequences of the innovation leads to a “reduction in uncertainty”, therefore the professionals are more likely to adopt. To speed diffusion of an innovation, it should be compatible with the belief systems of those to whom it is aimed (Berwick, 2003; Stadelmann, Portmann and Eichenberger, 2013). Thirdly, the level of difficulty to use the innovation is key (*ibid*, 2003). In the context of this research the innovation, children’s involvement, is viewed by many as complex and convoluted, thus causing the innovation to be rejected.

The characteristics of the individuals who will adopt started to emerge from this study. The original study was on the rate of adoption of a new type of hybrid corn seed back in 1943 (Rogers, 2003). Five categories of

adopters were identified: the innovators, early adopters, early majority, late majority and the laggards (Berwick, 2003; Greenhalgh *et al.*, 2004). The innovators, the first to adopt and the early adopters, I suggest were identified in the systematic review. Not only are they employing children's involvement but are also writing about it and acting as advocates for its practice. In the interviews I encountered a broad spectrum, however it was only possible to speculate where professionals fell on the scale, as this was not planned for in my research.

Once the context is known and the nature of the professionals (adopters) is known, we can consider how to encourage uptake. There are six suggested 'rules' to the success of an innovation: 1) locate sound innovations; 2) support innovators; 3) invest in early adopters; 4) make early adopter activity observable; 5) trust and enable reinvention; 6) create slack for change; and 7) rule by example – this refers to identifying innovations through, for example, research journals or meetings. As encountered through the systematic review, children have views and professionals are supporting their involvement. These then are the innovators to be supported.

Involvement is increasingly the suggested method to facilitate better, safer and more appropriate services for various populations (Bird, Culley and Lakhanpaul, 2013; Stewart *et al.*, 2011). As the title of the thesis suggests, it could be argued that children's involvement is an oxymoron in the context of children's medicines.

Oliver *et al.* (2015, p. 50) suggest that the debate around involvement "needs to move on" and that further work is needed to look at inequalities in involvement and whether structures in place to encourage participation, simultaneously exclude some groups. In the case of the mythical legislative barrier, my research suggests that for children this appears to be the case, in that participants felt that legislation was preventing access to children and therefore their views. The conceptual framework for

children's involvement from the perspective of professionals that I present in this thesis (see Figure 8.4), suggests that there are four elements impacting on participation (motivation of researchers, operational environment, execution of participation and process) and that these are juxtaposed between professional and personal, and aspirational and evidenced.

The barriers and facilitators to involvement that have emerged in a recent study by Parsons et al (2016) who investigated professionals' views of PPI, share some similarity with the findings in this thesis. Their study focused on participants from UK, Poland and Spain. Four of their participants were from the UK and though they all worked in aligned professions to medicines R&D, none were translational researchers. Yet the similarities serve to strengthen the data produced in thesis, in that their findings extend to market research, regulatory affairs, public affairs and communication. I discuss the similarities where they have arisen in the context of responding to the above question.

Participants suggested that children should be consulted as experts and can provide unique insights into some of the challenges existent in children's drug development that could prove valuable to pharmaceutical R&D discourse. Indeed, published research identified in the systematic review support this (Bernays *et al.*, 2017; de Graaf *et al.*, 2017). Despite these positive perspectives of children's ability to contribute to R&D and the increased requirement for researchers to demonstrate that they are involving patients and the public in research<sup>17</sup>, interviewees collaborating with adult professionals and parents, as opposed to children. Habitually, researchers had an adult-centric approach to conducting children's involvement. Researchers talk to gatekeepers of children's views: patient advisory groups, parents, doctors, carers, psychologists, or play specialists (Coyne, 2010). Patient

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<sup>17</sup> NIHR require evidence of public involvement for publicly funded research and provide guidelines (NIHR, 2014).

groups, rather than acting as facilitators could indirectly be suppressing the progression of children's involvement, as generally adults act as the point of contact for research committees and advisory groups, therefore reducing children's agency. The results of this thesis revealed that participants made assumptions about children's capabilities (see section 8.4), this might also be true within the wider context of research focussed on professionals. Nevertheless, if participation involves adult representatives who make assumptions about children, it could result in important information about children's lived experiences of medicines being missed.

Evidence from this thesis suggests that participants who have direct communication with sick children were surprised by the level of understanding children had about their conditions. Direct contact altered professionals' perceptions about children's ability to contribute to the R&D process. Lack of this direct contact is therefore a barrier to children's involvement, and has been suggested to be the case for participation in general elsewhere (Parsons *et al.*, 2016). Superficial contact with children, which did not facilitate in-depth discussions, did not appear to impact positively with participants' mind-sets. Indeed, participants' mind-sets were only positively affected when they were speaking as professionals. Without direct contact, children's ability to understand and contribute to medicines R&D risks being underrated. When talking about knowledge, the misinformed, and the uninformed (see section 8.2.3.2), participants were concerned that children and their carers did not understand children's medicines. This was also found by Parsons *et al.* (2016) who suggest that professionals working in R&D wanted those involved in research to have medical knowledge. This then is problematic in that it suggests that professionals are not acknowledging child patients' experiential knowledge. Young children, particularly the very young, cannot acquire even very basic medical knowledge, this would take years, at which point they would no longer be children. Evidence from data elicited from the participants in this

thesis suggests then that fundamental changes in attitudes towards children's knowledge is needed.

The type of knowledge that professionals understand in this instance operates within the old paradigm of scientific knowledge, known as Mode 1. It characterised by the domination of experimental science; by an internally-driven taxonomy of disciplines, where autonomy lies with scientists (Veit et al., 2017). The new paradigm of knowledge production known as 'Mode 2', is socially distributed making it application-oriented, trans-disciplinary, and subject to multiple accountabilities. I would argue that socially distributed knowledge (Mode 2) can be identified through the Johari window if collaborative encounters with children are conducted (Oliver and Duncan, 2019; Stokes and Sutcliffe, 2018; Veit et al., 2017). This issue of facilitating collaborative encounters with participants is particularly important. Staley (2017) suggests that little is written about the process of involvement. As suggested, the experiential knowledge that patients bring during the process of involvement is not always known and new insights and perspectives can emerge. This knowledge is considered new as it has not previously been accessed by researchers (Rose, 2013). Staley's (2017) narrative review on what researchers learn from involvement and ways that they applied their 'new' knowledge revealed that there are four ways. Researchers: 1) acquired new or enhanced knowledge; 2) changed their preferences/priorities; 3) increased their communication skills with lay people; and 4) changed their attitude to involvement. She concludes that involvement changes what researchers 'think' and 'do' (ibid, 2017). This finding concurs with my findings, as interviewees who had direct contact with sick children valued children's abilities more than those who did not.

Participants from all disciplines involved in this study suggested financial gain was indeed a big motivator for pharmaceutical industries, as the challenges of working in a capitalist market meant that monetary incentives

would always be influential. This thesis reveals that with participants operating under the prerequisite of profit, there needs to be proof of the financial benefit of children's involvement. Lack of this information is problematic in that it prevents the uptake of children's involvement. The impact of financial incentives generated by the US and EU regulations (European Union, 2006a; European Union, 2006b; US Congress, 2002), have marginally increased clinical trials in children. However, my research suggests that some participants were reticent about the need to increase clinical trials when unlicensed or off-label use is sanctioned by doctors, thus negating the need to prove clinical efficacy in children and the requirement for additional financial outlay.

Reticence behind children's involvement is further blocked by the perceived simplicity of the box-ticking approach to participation. Discussions with participants revealed that the process of 'box-ticking' did make them think about involvement, but that this was relative in that it was not improving participatory practices. However, when participants were talking about involvement, they were mainly speaking from the perspective of general PPI, which involved patients that were not specifically children. An investigation into the level and extent of PPI was completed in September 2015 (Wilson *et al.*, 2015). Findings from their study confirmed elements of this thesis in that PPI was most commonly executed in form of lay people reviewing patient information leaflets, and adults on steering committees. However, regarding providing evidence for those reticent of including PPI as part of their research, little was provided due to information about PPI not being accessible, or indeed collected. They suggest six "salient actions" to generate positive outcomes and impact (ibid, 2015, p. xxvii). These can be summarised as: shared understanding of PPI; a PPI co-ordinator; strong link between the lay representative and the study population; positive attitudes to and engagement with PPI; developing and maintaining relationships; and proactive and systematic evaluation. They suggest areas for further research

including: evaluation of the mechanisms and outcomes of PPI; engaging young people in PPI; identifying researchers' training needs for PPI; impact evaluations; and cost analyses, with which evidence from this thesis concurs.

Interest in participation has been growing over the last decade (Boote, Baird and Beecroft, 2010; Boote, Wong and Booth, 2015; Boote *et al.*, 2014; Domecq *et al.*, 2014; Forsythe *et al.*, 2014; Hoos *et al.*, 2015; Houyez, 2004; Oliver *et al.*, 2015; Parsons *et al.*, 2016; Pollard *et al.*, 2015; Pollard and Evans, 2015; Smits and Boon, 2008). However, as suggested above, published data on how to execute PPI is rare, which perpetuates uncertainty. This 'uncertainty' ran throughout participants' talk in the interviews. Not surprisingly, uncertainty focused on the implementation of involvement, potential difficulties regarding access to children, cost implications, and the benefits of involvement. Parsons *et al.* (2016) found that there was uncertainty about where patients could be involved. In response to this, this thesis uncovered that professionals often positioned children as a source of valuable information (see section 8.3) who could help to identify issues of importance to address in the ideas stage of research, pre-ethics. This stage potentially is more accessible to child participants, as it is a phase in the research that benefits from insight into a condition, or effects of particular drugs, thus experiential knowledge, rather than medical knowledge would be the prerequisite.

#### **10.4.1 Role was both a barrier and facilitator to children's participation**

Applying the Bakhtinian lens brought into focus the shift in voice and alerted me to role changes expressed through talk (see section 9.3). These changes in roles can act as both facilitator and barrier to children's involvement. The role of the Scientist (Qualified Professional) emerged receptive to children's rights and children's abilities and recognised the insight that children might bring to a research project. The roles of the Parent and the Adult served to block children's involvement by protection: acting in children's

best interests, speaking on behalf of children, and overriding children's rights (see section 9.3.2-9.3.4, 9.5 and 9.6). Consultation with children when professionals adopt these paternalistic protector roles is therefore limited, as the responsibility to protect appears to give the Parent the final say.

#### **10.4.2 Following the diffusion of innovations**

This thesis revealed that participants were optimistic about the potential value of children's input in terms of insight and feedback, yet this was offset with pessimism about the practice of involvement itself. Though not included in the main body of this thesis, participants provided a range of methods and vehicles to increase children's participation. Suggestions were born from the need to improve pathways to involvement from a practice perspective or, to a lesser extent, a patient perspective. Some suggestions were even born from activism with a focus on empowerment and campaigning, however altruistic tendencies were often tempered by professional rationalisation, evident in the commercial levers that were prioritised over end-user benefit. Despite the foundations of participants' suggestions, the evidence suggests that there is potential to apply involvement methods, and professionals would be open to their application with the proviso that appropriate support and evidence are available.

#### **Rule 1: Find sound innovations**

The thesis uncovered that collaboration was viewed as the preserve of adults; the collaboration between parents, carers, or patient groups and professionals. This suggests that collaborations are viewed as relationships between participants of equal standing, and the professionals in this study did not regard children as equals. Collaborating with patient groups has potential because operationally it is established, however, this is problematic in that adult-to-adult conversations silence, or at the very least, temper children's voices. Yet we must proceed with caution if this route is followed in that

children can have passive roles and for more satisfactory participation, collaboration needs to be child-centric. The Nuffield (2015, p. 172) report suggests that children, young people, and parents should be recognised as “genuine partners”, with their status being moved from passive subjects to active participants, using their experiential knowledge to inform development of research from the very beginning. However, evidence from this research found that the active participant is a phenomenon that exists in the rhetoric of professionals’ talk but the dominant paternalistic protector roles that were identified, relegated children to passive clinical trial subjects. Direct communication with children, such as the children’s forums, workshops, and focus groups suggested by the participants, encourage knowledge exchange, rather than prioritise top-down communication. These formats also assign children active roles and, as suggested in this thesis, will be more likely to facilitate positive changes to professionals’ understanding of children’s ability to contribute, thus encourage future involvement. Training is required to conduct knowledge exchange sessions properly. For example, inviting children to join panels that have an adult-centric format would be problematic in that it is unlikely that children will wish to sit for long-periods of time focusing on a single issue. Therefore, there is a need to design interactions around children. However, I would suggest that ‘top-lining’ summaries for children can prove to be patronising, as the researcher acts as a gatekeeper of knowledge by means of: a) selecting which information to reveal to children; and b) employing often unnecessarily complex language in the full reports to explain often simple issues. These practices exclude not only children, but any untrained readers from research findings.

**Rule 2: Find and support innovators**

The innovators are the clinicians and researchers who worked with the authors of papers indicating children's views presented in the systematic review. Innovators are suggested as being difficult individuals, possibly abrasive but provide novel answers and approaches (Berwick, 2003).

**Rule 3: Invest in early adopters**

This research suggests that with increased education for professionals, children, and parents, potential for children's involvement will increase. For professionals, the focus of training emerging from this research should centre on how to execute children's involvement. With regard to training for children, participants suggested that they should be trained in what happens in clinical trials. Projects such as GenerationR and Participation Works Partnerships are actively training children in aspects of clinical trials. Despite the existence of numerous guides on methods and processes for involving children in research (e.g. INVOLVE, 2012; Kirby, 2004; Participations Works Partnership, 2009), participants were uncertain where to access these and other resources, suggesting that training should include orientation in this area.

**Rule 4: Make early adopter activity observable**

A key factor surrounding reticence towards children's involvement was that participants did not have access to enough evidence that children's participation works in medicines R&D. Participants provided me with three examples of when children's views had positively affected the course of a research project in terms of providing insight into medicine use, helping to design successful clinical trials and thus secure funding (see Case Study boxes in Chapter Eight). The construction of participation is predominantly based on perceptions as opposed to evidence (see section 8.2). With increased

publication of evidence of successful and unsuccessful participatory exercises, professionals will be exposed to the possibilities and practicalities of children's involvement (see section 8.4 and Figure 8.4). The debate about evidence is entrenched within a vicious cycle; more evidence is required by professionals about the benefits of children's involvement, yet children's involvement must first be executed (and published) by researchers for there to be more evidence. Further, evidence of the processes, benefits and challenges of children's involvement, needs to be given a more visible platform in order to reach researchers who do not actively seek out papers on participatory practice.

**Rule 5: Trust and enable reinvention**

Innovation needs to come from outside of current practices (Berwick, 2003) and can be considered in terms of strengthening capacity for children's involvement in medicines R&D. Cooke (Cooke, 2005) suggests that there is a need to nurture skills, build relationships, invest in infrastructure to ensure sustainability and continuity. In the context of this, it can then be viewed as strengthening capacity for children's involvement. The early adopters should be supported, and ideas disseminated, encouraged and not forced (Greenhalgh *et al.*, 2004; Greenhalgh *et al.*, 2005). Networking ideas and new standards builds both intellectual (knowledge) and social capital (relationships) and builds trust between different groups, which is beneficial to the whole research process (Cooke, 2005).

**Rule 6: Create slack for change**

Changes in practice regulation to enable access to talk to children is needed. In section 10.2, I discussed legislative barriers. Changes are required to pharmaceutical research regulations to encourage information exchange between children and researchers. Participants were receptive to change and open to talking directly to children, but this research revealed that, even

when clinician researchers had the opportunity to communicate directly with children, the majority abstained. This revealed further uncertainty as to professionals' understanding of how children might be able to contribute to their research endeavours. I would argue that this is in part due to lack of 'the right type of' evidence being provided to researchers. Although organisations such as GenerationR (James Lind Initiative and NIHR, 2016) produce literature, and have a strong presence on the web, publications targeting translational researchers with evidence of involvement, or involvement methods such as Pollard et al (Pollard *et al.*, 2015) is scarce. Further it is questionable whether researchers in children's medicines are actively seeking out this research (see above), which is also in part attributable to lack of structured training.

This theory goes some way towards a vision of children's involvement where researchers are aware of the benefits, encouraged to involve children, are supported to do involve children from the laboratory to the bedside, where involvement or participation becomes 'participatory science' and where participatory science is recognised as a discipline in its own right as opposed to an 'add-on' to other research. The ABPI and other pharmaceutical organisations are taking huge conceptual steps, actively encourage participation (ABPI, 2016a; ABPI, 2016b), which is heartening.

**Role transitioning** – Role transitioning between participants' *dramatis intrapersonæ* presents a problem for children's involvement. As professionals, the majority of participants recognised children's rights, but as parents they did not. I argued then that these paternalistically grounded roles, the Parent, the Adult and to a lesser extent the Qualified Professional, might act as facilitators or barriers to children's involvement in medicines R&D (see section 9.4). As the dominant role adopted by participants in this research was that of the (protective) Parent, receptiveness to embracing children as capable beings who should be listened to lessens, and might prove problematic with respect to improving children's advocacy in medicines R&D.

I argue then that potential exists when discourse about children's involvement is aimed at the Professional and communicated in language that avoids the rhetoric of pathos. Use of the terms 'therapeutic orphans' and 'vulnerability' needs to be avoided to help create a platform for a new discourse in medicines R&D that positions children as capable and knowledgeable.

Innovations are born from the process of being innovative. To be innovative, there must be a desire and ability to think outside of our differing boundaries. Translational researchers aim to think outside of the confines of their scientific learning. However, children's boundaries have not been set by the convention of scientific rules, meaning that they think in relation to their own experiences. Potential for applying involvement methods exists, but this requires fundamental changes to policy, practice, culture and mind-sets. Bridging the gap between researchers and children could be initiated to inspire innovation if: the myth of regulatory barriers are dispelled thus encouraging researchers to talk directly to children, and community relationships are improved. Creating a culture of openness by improving community relations and reducing trepidation, or even fear, of medicines R&D will not be a quick fix, as media cooperation is needed to change the image of an industry with links to a chequered past. Training, support, and resources for all involved parties are also needed. Involvement specialists and those who have experienced PPI need to publish evidence, detailing the: procedures and methods employed, benefits, challenges and how to overcome them. Further, I argue that participation itself needs to be recognised as a scientific practice to raise the kudos of children's involvement. None of these elements are unsurpassable but require time, investment and a willingness from all parties involved.

## **10.5 Original contributions of the research**

This thesis provides new insights of potential benefits to a variety of stakeholders in children's medicines R&D. Knowledge gained will be

disseminated to any interested parties, in accessible language, process and utilise and not to ‘privilege some uses and actors over others’ as has been highlighted by Barker (2013, p. 79). Those involved in children’s medicines R&D who read this thesis, or the future literature that I produce, will benefit from gaining insight into how children’s involvement is perceived by the spectrum of informants. This research will also help to inform children who take medicines and their families, about the state of children’s agency within the R&D arena. Not only will the direct stakeholders (children, clinicians, researchers, policy makers, funders, and patient advocacy groups) benefit from this research, but people from other disciplines who are looking to involve children in projects, and/or are interested in understanding attitudes towards involving children. Those working within the disciplines of children’s rights, ethics, or education will also find this research of use. I list my original contributions as:

- This is the first study to investigate professionals’ views of children’s involvement in medicines R&D.
- This is the first attempt to conceptualise children’s involvement into a framework for children’s medicines.
- This is the first time that a Bakhtinian approach has been used to examine professionals’ views about children’s involvement.
- The first comprehensive scoping review on children’s views in medicines R&D
- This thesis provides a novel theory about the impact of intrapersonal role conflict and the concept of the subconscious activation of an individual’s *dramatis intrapersonae*, as a barrier to children’s participation. Most notably, the negative impact for children on capability and agency when informants adopted the Parent role, revealed through the application of Bakhtin’s theory of multivoicedness.

Suggestions for further research focus understanding on the power struggles between professionals and children, elevating the profile of children involvement in medicines research and supporting innovators and early adopters who promote children's involvement. Such as: how to involve children in preclinical research or how to generate ideas with children on complex pharmaceutical problems

## **10.6 Issues and limitations of this research**

This study combined theories of grounded social constructionism and contemporary theories of childhood. These *a priori* theories provided a framework for understanding how current processes and practices have arisen and helped me to understand the dynamics at play within the medical and pharmaceutical R&D paradigms. Had I employed different theoretical tools, I might have produced a very different thesis, but suggest that my findings would ultimately have been the same.

Due to the extent of the data that I acquired, I was only able to include excerpts from the interview transcriptions. The process of selective quoting and its potential to bias findings is an issue with discourse analysis in general. However, I present a well-balanced study by consciously rejecting position-taking and refraining from considering my own moral, political and personal opinions. I have quoted informants verbatim providing exemplars, or longer excerpts, to contextualise the data. When multiple informants discussed an issue, I selected the most illustrative examples; ones which I felt best represented the nature of the data as a whole.

The data presented represents a very specific set of participants, and although I tried to be representative of professionals that work in various sectors within children's medicines R&D, the professional occupations are by no means exhaustive. Also, as the participants were acquired by snowballing method (see Chapter Seven), the findings are not suggested to be generalizable.

## 10.7 Concluding remarks

This thesis has presented an in-depth insight into children's involvement from the perspective of professionals working within children's medicine in the UK and is the first piece of research to investigate this area. Based on the interpretation of the data herein, an argument is made that children's involvement is an underutilised practice that is beset by professionals' protective and paternalistic tendencies, and commercial pressures to generate revenue. The insight provided highlights the predominant construction of children as passive, vulnerable actors, and involvement as problematic and resource heavy. This research suggests a foundation for understanding the factors at play delaying the uptake of children's involvement in medicines R&D.

This research suggests that paternalistic tendencies can negatively impact children's involvement and similar constructions of children are present within the political and medical discourse. Further it suggests that the industry is cautious about the competencies of child patients to understand the complexities of translational research and their usefulness to help develop medicines. Indeed, scientists' predominant construction of involvement was passive, children as clinical trial participants, which not surprisingly differed from involvement specialists who regarded children as active participants, or consultants. However, no participants constructed children as equals, especially regarding making decisions about medicine taking. This suggests that adults, regardless of their profession, are overriding children's decisions and thus suppressing children's agency, which could manifest in suppression of children's involvement in medicines R&D. Indeed, the deep-seated beliefs about children's capabilities and the need for the adult to protect, be a major obstacle in the progression of children's participation in medicines R&D. The route to changing these deep-seated constructions requires further investigation. Encouragingly, there is evidence that children are being

involved by research innovators and that their involvement is very much valued, with children providing insight into a wide range of medicines related topics from lived experiences to views on basic science.

Furthermore, participants were revealed to have limited experience of communicating with children. For participants who had communicated with children, the interaction centred on the protection of mildly unwell children being treated with mild medicines and not seriously ill children, or those who would take the medicines made by them. I argue that exposure to children is not sufficient to have an impact. This requires direct communication, where children affected by particular conditions can talk to researchers about their medicine taking or illness experiences, and where the researchers can witness first-hand the impact that their medicines are having on the children's lives. The consequence of this combination of passive constructions and lack of exposure to sick children, serves to perpetuate children's reduced agency, both in helping to inform medicines R&D, and in making medicines-based decisions that affect them.

Protection and paternalism are related not only to the verbal and written discourse that surrounds children and involvement but has fundamental roots in the cast of roles that comprise the professionals' 'self'. Professionals' constructions of children varied dependent on the predominant role present at that time in the interview. This dominant role within the interview setting, was revealed to be the Parent or Adult in the majority of cases. This research revealed, not only the roles which were adopted, but the tensions between the many roles that professionals involved in children's medicines R&D might have. There are many challenges regarding improving professionals' attitudes towards PPI, which are compounded by how they view, or construct, children and involvement. Professionals' working in children's medicine are suggested, to be influenced by many factors that might not be specific to the pharmaceutical industry (Parsons *et al.*, 2016).

This thesis goes some way to address this by identifying the influence of the heterogeneity of the professionals' 'self'; the Parent, whose innate response is to keep children from harm, thus negatively affects involvement processes and rights, and the Adult, who claims greater knowledge, therefore making and taking decisions on children's behalf. The changes in mind-set and culture that are required then are further complicated by the presence of the of professionals' *dramatis intrapersonæ*. Therefore, changes in mind-set will take time and investment is needed to understand the impact of roles further. Heterogeneity has credence as an epistemological theory for participatory medicines research, as this phenomenon may go some way to explain the slow uptake of children's involvement and reticence to seek children's views.

The rhetoric favouring children's involvement in the development of medicines is undermined by political, commercial and social structures. I suggest that it is further undermined by the *dramatis intrapersonae* and the tensions between them vying for dominance. This thesis suggests that despite the historical rhetoric of children's involvement, children's participation in the early stages of children's medicines R&D only has potential, with a fundamental change in the mind-set of professionals involved in medicine R&D, improved resources and education for medical researchers, and improved access for those developing medicines to communicate directly with sick children exposed to risky medicines.

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# Appendices

## **Appendix 1: The United Nations Convention of the Rights of the Child – Information Sheet**

What follows are extracts from four Articles in the United Nations Convention of the Rights of the Child (UNCRC) that I would like to briefly discuss with you in our interview session.

### **Background**

The United Nations Convention of the Rights of the Child of 1989 was the final stage of a process that had evolved from a draft convention submitted by the Polish Government during 1979, the International Year of the Child (UNHROHC, 1993). It has subsequently been amended and expanded extensively. This convention was born out of the requirement by some member States of the United Nations for an official document of children's rights that would be binding under international law (UNHROHC, 1993). It is the most extensively ratified human rights agreement ever (193 countries) (Coyne, 2008, p. 1683).

### **Key articles**

All children are entitled to receive good health care provision irrespective of age, social status, mental capacity and physiological capability (United Nations, 1989). Four articles are particularly relevant to children's rights in healthcare (Article 5, 12, 13 and 24).

#### **Article 5:**

“State parties shall respect the responsibilities, rights and duties of parents or, where applicable, the members of the extended family or community as provided for by local custom, legal guardians or other persons legally responsible for the child, to provide, in a manner consistent with the evolving capacities of the child, appropriate direction and guidance in the exercise by the child of the rights recognized in the present Convention.”

#### **Article 12.1**

“State parties shall assure to the child who is capable of forming his or her own views the right to express those views freely in all matters affecting the child, the views of the child being given due weight in accordance with the age and maturity of the child”.

#### **Article 13.1**

“The child shall have the right to freedom of expression; this right shall include freedom to seek, receive and impart information and ideas of all kinds, regardless of frontiers, either orally, in writing or in print, in the form of art or through any other media of the child's choice.”(United Nations, 1989)

### **Article 24.1**

“State Parties recognize the right of the child to the enjoyment of the highest attainable standard of health and to facilities for the treatment of illness and rehabilitation of health. State Parties shall strive to ensure that no child is deprived of his or her right of access to such health care services.”

### **Article 24.2**

“State Parties shall pursue full implementation of this right and, in particular shall take appropriate measures:

- a. To diminish infant and child mortality;
- b. To ensure the provision of necessary medical assistance and health care to all children with emphasis on the development of primary health care;
- c. To combat disease and malnutrition, including within the framework of primary health care, through *inter alia*, the application of readily available technology and through the provision of adequate nutritious foods and clean drinking-water, taking into consideration the dangers and risks of environmental pollution
- d. To ensure appropriate pre-natal and post-natal health care for mothers;
- e. To ensure that all segments of society, in particular parents and children, are informed, have access to education and are supported in the use of basic knowledge of child health and nutrition, the advantages of breastfeeding, hygiene and environmental sanitation and the prevention of accidents
- f. To develop preventive health care, guidance for parents and family planning education and services

## Appendix 2: Example letter to key informants – with prior contact made

Dear X

Firstly, let me thank you for taking the time to talk with me at the 10<sup>th</sup> European Congress on Epileptology. I hope that, like me, that you found the Congress extremely exciting and beneficial.

To refresh your memory, I am the PhD student that is working on a study being undertaken at the Institute of Education and the UCL School of Pharmacy regarding children's involvement in medicines research and development. As I discussed with you, I am trying to gather the insights of those with relevant expertise in the area of medicines research and development.

I hope to develop a set of recommendations that will benefit both children and researchers and contribute to a greater understanding of the potential for children to be involved in research. The results from this research will help to identify ways of improving communication between those who make and those who take medicine, in order to suggest a workable platform for the exchange of ideas, experiences and views and improve children's medicine taking experience in the future.

I believe that your expertise in this topic will play a vital role in understanding this area and so I would like to invite you to participate in an interview.

This would involve me meeting up with you for a one-to-one confidential discussion, of around 40 minutes. The aim of the discussion is to find out more about your views regarding the involvement of children in the children's medicines research and development process. As I am seeking insight into the potential for children's involvement, I am interested in all views on this matter whether you have involved children or not.

The discussion will include questions regarding your experience or knowledge of children's medicines research. I hope to briefly explore topics such as the research process, funding priorities, children's capabilities and children's rights. I have included a summary of the research being undertaken to provide you with more details about the study.

Please note that if you decide to take part in this research project, you have the right to withdraw at any point and the right not to answer a question or discuss a topic.

I will contact you shortly to arrange an appointment at a time that is convenient for you. I will be available to answer any questions regarding the study prior to interview by email at [g\\*\\*\\*\\*\\*@ioe.ac.uk](mailto:g*****@ioe.ac.uk) or alternatively by telephone on either 0\*\*\*\* \* or 0\*\* \* \* \* \*.

I see this project as an important contribution to the field of children's medicine and your opinions will be extremely valuable and greatly appreciated.

Thank you for taking time to read and consider this request.

Yours sincerely

Gillian Stokes (PhD Student)

Encs. Reply slip, S.A.E., Research summary

### Appendix 3: Example letter to key informants – first contact

Dear X

I am a PhD student working on a study being undertaken at the Institute of Education and the UCL School of Pharmacy regarding children's agency and involvement in medicines research and development. I am trying to gather the insights of those with relevant expertise in the area of medicines research and development.

I hope to develop a set of recommendations that will benefit both children and researchers and contribute to a greater understanding of the potential for children to be involved in research. The results from this research will help to identify ways of improving communication between those who make and those who take medicine, in order to suggest a workable platform for the exchange of ideas, experiences and views and improve children's medicine taking experience in the future.

I believe that your expertise in this topic will play a vital role in understanding this area and so I would like to invite you to participate in an interview.

This would involve me meeting up with you for a one-to-one confidential discussion, of around 40 minutes. The aim of the discussion is to find out more about your views regarding the involvement of children in the children's medicines research and development process. As I am seeking insight into the potential for children's involvement, I am interested in all views on this matter whether you have involved children or not.

The discussion will include questions regarding your experience or knowledge of children's medicines research. I hope to briefly explore topics such as the research process, funding priorities, children's capabilities and children's rights. I have included a summary of the research being undertaken to provide you with more details about the study.

Please note that if you decide to take part in this research project, you have the right to withdraw at any point and the right not to answer a question or discuss a topic.

I will contact you shortly to arrange an appointment at a time that is convenient for you. I will be available to answer any questions regarding the study prior to interview, should you decide to take part, by email at [g\\*\\*\\*\\*\\*@ioe.ac.uk](mailto:g*****@ioe.ac.uk) or alternatively by telephone on either 0\*\*\*\*\* \*\*\*\*\* or 0\*\* \*\*\*\* \*.

I see this project as an important contribution to the field of children's medicine and your opinions will be extremely valuable and greatly appreciated.

Thank you for taking time to read and consider this request.

Yours sincerely

Gillian Stokes (PhD Student)

## Appendix 4: Consent Form

Working title: The rhetoric, reality and realisation of children's involvement in medicines research and development: bridging the gap between those who make and those who take children's medicines

Researcher name: Gillian Stokes

Academic Institute: Institute of Education and UCL School of Pharmacy

Please Initial Box

1. I hereby confirm that I have read and understood the information sheet for the above study and/or the researcher explained the purpose of the research to me.
  
2. I understand that my participation in this interview is voluntary.
  
3. I understand that I am free to withdraw from the study at any time, without giving reason.
  
4. I understand that I have the right not to answer any question that might be asked, if I so choose and that I can halt the interview and withdraw my responses at any point in the interview, without giving reason.
  
5. I agree to the use of my statements or comments being used as anonymised quotes in the publication of this research, under the condition that I cannot be identified and that my name, or anything that will identify me, will not appear in any research reports.

6.I understand that all information obtained from and regarding the interview will be kept confidential by the researchers and will be used only for the purpose of research.

7.I agree to the interview/discussion being audio recorded.

Yes / No

8.I would like to be provided with an edited copy of my interview transcript.

Yes / No

9.I would like to receive a summary of the key findings from this research.

Yes / No

Declaration:

I, ..... agree to be interviewed for this research.

Signature: ..... (Participant) Date: .....

Signature: ..... (Researcher) Date: .....

## Appendix 5: Search String

S1 child\* OR children OR infant\* OR preadolescent\* OR prepubescence OR prepubescent OR puberty OR pubescence OR pubescent OR schoolchild OR schoolchildren OR teenag\* OR toddler\* OR minors\* OR paediatric OR paediatrics OR pediatric\* OR pediatrics OR "pre adolescent\*" OR "pre pubescence" OR "pre pubescent" OR "school pupil" OR "school pupils" OR "school student\*" OR "young people\*" OR adolescent OR adolescents OR adolescence OR boy\* OR girl\* OR juvenile\* OR "school child\*" OR "school children" OR youth\* Or tween\* OR "nursery school" OR preschool OR "pre-school" OR "primary school" OR Kindergar\* OR "secondary school" OR "elementary school" OR "high school" OR highschool OR kid\* OR student

AND

S2 Medicine\* OR medicat\* OR drug\* OR pharmacon\* OR pharmakon OR pill OR pharmaceut\* OR prescription\* OR cure\* OR remedy OR remedies OR medicament\* OR tablet\* OR injection\* OR dosage OR dose OR lotion\* OR potion\* OR serum\* OR treatment\* OR restorative\* OR medicinal\*

AND

S3 View\* OR perspective\* OR standpoint\* OR attitude\* OR aspect\* Or ideolog\* OR idea\* OR understanding\* OR knowledge\* OR input\* OR outlook\* OR belief\* OR believes OR mindset\* OR opinion\* OR "community engagement" OR "public engagement" OR "consumer participation" OR "patient participation" OR lay OR consumer OR user\* OR participant\* OR participat\* OR involv\* OR engag\* OR consult\* OR collaborat\* OR contribut\*

## Appendix 6.2 ENTREQ statement checklist

No	Item	Guide and description	Check	Location
1	Aim	State the research question the synthesis addresses.		
2	Synthesis methodology	Identify the synthesis methodology or theoretical framework which underpins the synthesis and describe the rationale for choice of methodology (e.g. <i>meta-ethnography, thematic analysis, critical interpretive synthesis, grounded theory synthesis, realist synthesis, meta-aggregation, meta-study, framework synthesis</i> ).		
3	Approach to searching	Indicate whether the search was pre-planned (comprehensive search strategies to seek all available studies) or iterative (to seek all available concepts until theoretical saturation is achieved).		
4	Inclusion criteria	Specify the inclusion/exclusion criteria (e.g. in terms of population, language, year limits, type of publication, study type).		
5	Data sources	Describe the information sources used (e.g. electronic databases ( <i>MEDLINE, EMBASE, CINAHL, psychINFO, Econlit</i> ), grey literature databases (digital thesis, policy reports), relevant organisational websites, experts, information specialists, generic web searches (Google Scholar) hand searching, reference lists) and when the searches conducted; provide the rational for using the data sources.		
6	Electronic search strategy	Describe the literature search (e.g. provide electronic search strategies with population terms, clinical or health topic terms, experiential or social phenomena related terms, filters for qualitative research and search limits).		
7	Study screening methods	Describe the process of study screening and sifting (e.g. title, abstract and full text review, number of independent reviewers who screened studies).		
8	Study characteristics	Present the characteristics of the included studies (e.g. year of publication country, population number of participants, data collection, methodology, analysis, research questions).		

9	Study selection results	Identify the number of studies screened and provide reasons for study exclusion (e.g. for comprehensive search, provide numbers of studies screened and reasons for exclusion indicated in a figure/flowchart, for iterative searching describe reasons for study exclusion and inclusion base on modifications to the research question and/or contribution to theory development).		
10	Rationale for appraisal	Describe the rationale and approach used to appraise the included studies or selected findings (e.g. assessment of conduct (validity and robustness), assessment of reporting (transparency), assessment of content and utility of the findings).		
11	Appraisal items	State the tools, frameworks and criteria used to appraise the studies or selected findings (e.g. Existing tools: CASP, QARI, COREQ, Mays and Pope [25]; reviewer developed tools; describe the domains assessed: research team, study design, data analysis and interpretations, reporting).		
12	Appraisal process	Indicate whether the appraisal was conducted independently by more than one reviewer and if consensus was required.		
13	Appraisal results	Present results of the quality assessment and indicate which articles, if any, were weighted/excluded based on the assessment and give the rationale.		
14	Data extraction	Indicate which sections of the primary studies were analysed and how were data extracted from the primary studies? (e.g. all text under the headings "results/conclusions" were extracted electronically and entered into a computer software).		
15	Software	State the computer software used, if any.		
16	Number of reviewers	Identify who was involved in coding and analysis.		
17	Coding	Describe the process for coding of data (e.g. line by line coding to search for concepts).		
18	Study comparison	Describe how were comparisons made within and across studies (e.g. subsequent studies were coded into pre-		

		existing concepts, and new concepts were created when deemed necessary).		
19	Derivation of themes	Explain whether the process of deriving the themes or constructs was inductive or deductive.		
20	Quotations	Provide quotations from the primary studies to illustrate themes/constructs and identify whether the quotations were participant quotations of the authors interpretation.		
21	Synthesis output	Present, rich compelling and useful results that go beyond a summary of the primary studies (e.g. new interpretation models of evidence conceptual models, analytical framework, development of a new theory or construct).		

Source: Table adapted from Tong *et al.* (2012, p. 4)

**Appendix 6.3.1: Table of studies excluded on title and abstract**

<b>Exclude number</b>	<b>Description</b>	<b>No. of excluded studies</b>
1	Publication date before 1988	60
2	Language – not English	705
3	Not empirical evidence	745
4	Research protocol	78
5	Development/validation/evaluation of a research tool	24
6	Subject under study was not human	190
7	Focus – training, knowledge or education of professionals or students	1483
8	Focus – substance abuse/misuse or risky behaviour	3340
9	Focus – not on children’s medicines	8824
10	Case study/series/report	94
11	Focus – not on views/attitudes etc. or involvement/participation	1007
12	Focus – new-borns, infants or elderly	581
13	Focus – not on children’s views	923
14	Duplicates	164
	<b>Total number of studies included on title and abstract</b>	<b>346</b>

### Appendix 6.3.2: Table of studies excluded on full text

<b>Exclude number</b>	<b>Description</b>	<b>No. of excluded studies</b>
1	Publication date before 1988	0
2	Language – not English	1
3	Not empirical evidence	14
4	Research protocol	0
5	Development/validation/evaluation of a research tool	6
6	Subject under study was not human	1
7	Focus – training, knowledge or education of professionals or students	4
8	Focus – substance abuse/misuse or risky behaviour	0
9	Focus – not on children’s pharmaceutical interventions	163
10	Case study/series/report	0
12	Focus – new-borns, infants or elderly	0
13	Focus – not on children’s views	14
14	Focus – medication adherence/compliance	61
15	Focus – contraception	4
16	Focus – medicine use/knowledge/control/risk/preferences	38
17	Systematic review (used to harvest studies)	9
18	Not received or not available	10
<b>Total number of studies included on title and abstract</b>		<b>21</b>

**Appendix 6.3.7: Data analysis methods used by study (n=21)**

<b>Data analysis method</b>	<b>Subcategory</b>	<b>No. of Studies</b>	<b>Study</b>
Thematic analysis	Deductive	3	de Graaf et al. 2017; Kosse et al. 2018; Parsons et al. 2017
	Inductive	11	Bernays et al. 2017; Cuenca et al. 2015; de Graaf et al. 2017; Gallagher et al. 2011; Kosse et al. 2018; Mukattash et al. 2012; Parsons et al. 2017; Sandler et al. 2008; Townsend et al. 2010; Veinot et al. 2006; Webster 2017
	Unspecified	6	Barnard et al. 2008; Low et al. 2005; Maroun et al. 2018; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Pradel et al. 2001
Content analysis		4	Barnard et al. 2008; Cuenca et al. 2015; Low et al. 2005; Pradel et al. 2001
Quantitative evaluation		2	Barnard et al. 2008; Townsend et al. 2010
Descriptive analysis		1	Doherty et al. 2000
Not specified/Unclear		3	Carpenter-Song, 2009; Hodes et al. 2018; Williams et al. 1998

**Appendix 6.4.0: Table - Descriptive themes discussed with study details by number of studies**

Theme	No. of Studies	Study details
Medicines	20	Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; de Graaf et al. 2017; Doherty et al. 2000; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Low et al. 2005; Maroun et al. 2018; Mukkash et al. 2012; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Parsons et al. 2017; Pradel et al. 2001; Sandler et al. 2008; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Medicine taking	20	Barnard et al 2008; Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; de Graaf et al. 2017; Doherty et al. 2000; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Low et al. 2005; Maroun et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Pradel et al. 2001; Sandler et al. 2008; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998;
Emotion and agency	15	Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; Gallagher et al. 2011; Hodes et al. 2018; Low et al. 2005; Maroun et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Parsons et al. 2017; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Impact	14	Barnard et al 2008; Bernays et al. 2017; Carpenter-Song, 2009; Doherty et al. 2000; Low et al. 2005; Maroun et al. 2018; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Parsons et al. 2017; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998;
Knowledge and information sharing	14	Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; de Graaf et al. 2017; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Parsons et al. 2017; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017
Health Condition	9	Cuenca et al. 2015; De Graaf et al. 2017; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Murphy et al. 2015; Parsons et al. 2017; Townsend et al. 2010; Webster, 2017
Research and development	5	Cuenca et al. 2015; Gallagher et al. 2011; Kosse et al. 2018; Murphy et al. 2015; Parsons et al. 2017
Clinical trials	5	Bernays et al. 2017; de Graaf et al. 2017; Mukattash et al. 2012; Parsons et al. 2017; Sandler et al. 2008

**Appendix 6.4.1: Table - Children's views on medicines (n=20)**

<b>Sub-theme</b>	<b>No. of Studies</b>	<b>Study details</b>
Adverse events/ side-effects	11	Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; Doherty et al. 2000; Kosse et al. 2018; Maroun et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Physical characteristics	8	De Graaf et al. 2017; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Low et al. 2005; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Costs	5	Low et al. 2005; Parsons et al. 2017; Pradel et al. 2001; Veinot et al. 2006; Williams et al. 1998
Quality	5	Doherty et al. 2000; Hodes et al. 2018; Kosse et al. 2018; Low et al. 2005; Webster, 2017
Safety	5	Hs Low et al. 2005; Mukattash et al. 2012; Townsend et al. 2010; Williams et al. 1998
Acceptability	4	Bernays et al. 2017; Murphy et al. 2015; Parsons et al. 2017; Sandler et al. 2008;
A support tool	3	Maroun et al. 2018; Murphy et al. 2015; Townsend et al. 2010; Webster, 2017
Choice	2	Low et al. 2005; Murphy et al. 2015; Veinot et al. 2006
A sign of disease severity	2	Maroun et al. 2018; Murphy et al. 2015
Dosage form	2	Lindstrom Olinder et al. 2007; Webster, 2017
Caution	1	Cuenca et al. 2015; Mukattash et al. 2012
Efficacy	1	Kosse et al. 2018
Packaging	1	Hodes et al. 2018
Off-licence/ Unlicensed	1	Mukattash et al. 2012

**Appendix 6.4.2: Table - Children's views on medicine taking (n=20)**

<b>Topic</b>	<b>No.</b>	<b>Study details</b>
Practicalities	12	Bernays et al. 2017; Cuenca et al. 2015; Gallagher et al. 2011; Kosse et al. 2018; Low et al. 2005; Maroun et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Sandler et al. 2008; Townsend et al. 2010; Webster, 2017
Negative aspects	11	Carpenter-Song, 2009; Cuenca et al. 2015; de Graaf et al. 2017; Hodes et al. 2018; Low et al. 2005; Lindstrom Olinder et al. 2007; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998;
Adherence	11	Bernays et al. 2017; Carpenter-Song, 2009; Cuenca et al. 2015; Hodes et al. 2018; Kosse et al. 2018; Low et al. 2005; Mukattash et al. 2012; Murphy et al. 2015; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017
Positive impact	9	Barnard et al 2008; Cuenca et al. 2015; Low et al. 2005; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Pradel et al. 2001; Sandler et al. 2008; Townsend et al. 2010; Webster, 2017
Stigma	7	Barnard et al 2008; Carpenter-Song, 2009; Hodes et al. 2018; Murphy et al. 2015; Townsend et al. 2010; Veinot et al. 2006; Williams et al. 1998
Compliance	6	Doherty et al. 2000; Gallagher et al. 2011; w Maroun et al. 2018; Murphy et al. 2015; Veinot et al. 2006
Frequency and duration	4	Bernays et al. 2017; de Graaf et al. 2017; Low et al. 2005; Sandler et al. 2008
Purpose and value	4	Barnard et al 2008; Carpenter-Song, 2009; Maroun et al. 2018; Veinot et al. 2006
Difficulties taking or using	4	Cuenca et al. 2015; Low et al. 2005; Veinot et al. 2006; Williams et al. 1998
Ambivalence	3	Kosse et al. 2018; Murphy et al. 2015; Townsend et al. 2010
Pain or discomfort	1	De Graaf et al. 2017

**Appendix 6.4.3: Table - Children's views on Emotion and agency (n=15)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Fear	9	Carpenter-Song, 2009; Gallagher et al. 2011; Hodes et al. 2018; Low et al. 2005; Maroun et al. 2018; Pradel et al. 2001; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Feeling different	6	Barnard et al 2008; Cuenca et al. 2015; Low et al. 2005; Murphy et al. 2015; Veinot et al. 2006
Risk	3	Maroun et al. 2018; Mukattash et al. 2012; Parsons et al. 2017
Ability	2	Maroun et al. 2018; Mukattash et al. 2012
Age	1	Mukattash et al. 2012
Altruism	1	Mukattash et al. 2012
Assent/Consent	1	Mukattash et al. 2012
Honesty and reliability	1	Webster, 2017
Autonomy	1	Townsend et al. 2010

**Appendix 6.4.4: Table - Children's views on how medicines impact on their lives (n=14)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Independence	10	Barnard et al 2008; Bernays et al. 2017; Low et al. 2005; Maroun et al. 2018; Murphy et al. 2015; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006; Webster, 2017; Williams et al. 1998
Family and home	7	Barnard et al 2008; Low et al. 2005; Murphy et al. 2015; Lindstrom Olinder et al. 2007; Parsons et al. 2017; Pradel et al. 2001; Veinot et al. 2006
Friends, friendships and peers	7	Barnard et al 2008; Carpenter-Song, 2009; Doherty et al. 2000; Low et al. 2005; Murphy et al. 2015; Parsons et al. 2017; Townsend et al. 2010
Quality of life	5	Barnard et al 2008; Doherty et al. 2000; Low et al. 2005; Lindstrom Olinder et al. 2007; Veinot et al. 2006
School and learning	5	Barnard et al 2008; Doherty et al. 2000; Low et al. 2005; Murphy et al. 2015; Townsend et al. 2010
Food and diet	3	Barnard et al 2008; Low et al. 2005; Lindstrom Olinder et al. 2007
Freedom	2	Barnard et al 2008; Low et al. 2005
Support	1	Murphy et al. 2015
Sport and exercise	1	Pradel et al. 2001

**Appendix 6.4.5: Table - Children's views on knowledge and information (n=14)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Children's knowledge of medicines	8	Carpenter-Song, 2009; de Graaf et al. 2017; Gallagher et al. 2011; Hodes et al. 2018; Kosse et al. 2018; Pradel et al. 2001; Townsend et al. 2010; Veinot et al. 2006
Information provision	6	Cuenca et al. 2015; de Graaf et al. 2017; Kosse et al. 2018; Mukattash et al. 2012; Murphy et al. 2015; Veinot et al. 2006
Children's understanding of condition	6	Carpenter-Song, 2009; Gallagher et al. 2011; Kosse et al. 2018; Pradel et al. 2001; Townsend et al. 2010; Webster, 2017
Truth, trust, transparency	4	Cuenca et al. 2015; Parsons et al. 2017; Townsend et al. 2010
Knowledge of professionals, parents or carers	3	Cuenca et al. 2015; Parsons et al. 2017; Townsend et al. 2010
Training	1	Gallagher et al. 2011
Medicines licencing	1	Mukattash et al. 2012

**Appendix 6.4.6: Table - Children's views on their health condition discussed (n=9)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Diagnosis	3	de Graaf et al. 2017; Hodes et al. 2018; Townsend et al. 2010
Accessing or receiving specialist care	5	Cuenca et al. 2015; de Graaf et al. 2017; Gallagher et al. 2011; Kosse et al. 2018; Murphy et al. 2015
Seeking treatment	1	de Graaf et al. 2017
Finding a cure	2	Parsons et al. 2017; Webster, 2017
Outcomes of recovery	4	De Graaf et al. 2017; Murphy et al. 2015; Parsons et al. 2017; Townsend et al. 2010
Aetiology and genetics	1	Parsons et al. 2017
Developing predictive tests	1	Parsons et al. 2017

**Appendix 6.4.7: Table - Children's views on medicines research and development (n=5)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Ideas for medicines development	4	Cuenca et al. 2015; Gallagher et al. 2011; Kosse et al. 2018; Murphy et al. 2015
Research priorities	2	Gallagher et al. 2011; Parsons et al. 2017
Health services research	1	Parsons et al. 2017
Factors influencing research priorities	1	Parsons et al. 2017
Ways to improve treatment	1	Kosse et al. 2018
Basic science	1	Parsons et al. 2017
Clinical medicine research	1	Parsons et al. 2017
Psychosocial research	1	Parsons et al. 2017
Public health research	1	Parsons et al. 2017
Research funding	1	Parsons et al. 2017

**Appendix 6.4.8: Table - Children's views on clinical trials (n= 5)**

<b>Topic</b>	<b>No. of Studies</b>	<b>Study details</b>
Being a trial participant	4	Bernays et al. 2017; de Graaf et al. 2017; Mukattash et al. 2012; Sandler et al. 2008
Trials as progress	1	Bernays et al. 2017
Talking about RCTs	1	Parsons et al. 2017

## **Appendix 7: Interview protocol – Guide Schedule**

This schedule is to be used as a guide only. I intend to pick up cues from what the participants say and follow their lead and order of topics/issues.

### **Prior to the interview**

- Design the research questions
- Identify interview participants
- Research their background
- Send out contact letter of invitation to participate, with summary of the research
- Stress confidentiality/anonymity of data and provide example questions
- Arrange the date and time of the interview
- Send out a pre-interview pack

### **Immediately prior to the interview**

- Gain written consent to record the interview
- Explain that I want to hear their views on patient involvement and specifically that of children's involvement, either positive or negative views

### **At the start of the interview**

- Run over the background information about the study
- Verify permission to record the interview and to use the data
- Stress confidentiality and anonymity
- Stress that they may stop the interview, not answer questions, withdraw from the research at any point
- Ask if there are any questions about the project
- Check how much time they have available
- Check to see if there is a possibility of a follow-up interview if time does not allow completion
- Check to see that the recording device is working properly
- During the interview
- Conduct the interview covering issues to be included
- Take notes throughout the interview
- Maintain professionalism throughout the interview
- Be receptive, attentive, polite, non-judgemental and respectful
- Maintain control over the timing
- Collect consent forms

### **At the conclusion of the interview**

- Thank the participant and ask if there are any further request regarding supplying them with more details or data
- Request permission for possible follow up by telephone or email

**After the interview**

- Write up interview notes as quickly as possible
- Transcribe the recording using Nivo9
- Check and edit the transcript
- Send the transcript to the interviewee and ask them to confirm/amend accordingly
- Arrange follow up if required/agreed by phone
- Save information
- Ensure all data is kept confidential and anonymity is upheld.

## Appendix 8: Interview Guide

This interview schedule is to be used as a guide. I do want the interview to be organic, so when conducting the interviews, I will pick up cues from what the interview participants say and follow their lead and order of topics/issues that arise. However, there are specific areas that I want to address that are important to the research questions and will introduce these questions if need be during the interview process.

### Actions

- Initial introductions – talk through the research project again
- Ask participant to sign the consent form for recording and using information gained during the interview
- Clarify with the participant that I am interested in **all perspectives** with regards to children's involvement in research and development and therefore interviewees can be candid
- Re-iterate confidentiality
- Stress to the participant that they do not have to answer questions and that they may withdraw from the interview, and from participation in the research process, at any point.
- Give the participant an opportunity to ask any questions before officially starting the interview
- Use prompt sheet to initiate interview and make interviewee feel comfortable talking to me
- At end of interview, check issues covered
- Thank interviewee for taking part

### **Introduction**

Can you tell me a little bit yourself?

How long have you worked in children's medicines research?

What inspired you to become involved in medical research?

Can you tell me about the motivations and factors that are behind drug development in your experience?

### **Paediatric Regulation**

I have read about the introduction of the paediatric regulations in the US and the UK. Could you talk me through how conducting children's medicines research and development has changed for you since the introduction of the EU paediatric regulation?

What or who do you think were the catalysts for creating the EU PR?

From your perspective, could you talk me through the consequences of introducing the EU PR, the benefits and problems and how they have arisen?

### **Patient Involvement**

Could you talk me through your past experience of working with/within patient or consumer groups as part of a medicines research project?

There is currently a push for public involvement; could you tell me what public involvement means to you?

What are your feelings about patient/consumer involvement in research?

I have been looking into the drug development timeline and was curious to understand where in the R&D process you feel that patients/consumers are currently involved? [Show timeline]

### **Children's Involvement**

How do you think children are currently involved in children's medicines R&D?

I am interested to know how you are involving children in you research, if at all?

a) **If SO**, please give examples.

How would you describe your experience of working with children?

How would you change this experience for future R&D projects?

Can you talk me through the points on the timeline where you think children's input would be most useful, if at all? [show timeline]

Could you please explain your reasons for choosing these points?

Can you think of reasons for children not being involved more in medicines R&D?

How do you think that children could become more involved in future R&D projects?

### **Rights**

I have been reading a lot about children's rights and the UN Convention of the Rights of the Child. I included this in the pre-interview information document for your perusal. I was wondering whether you have ever encountered this convention before?

Within the Convention there were two articles that stood out to me, articles 15 and 23. (Show copy and read them again together.) Can you tell me how you think that these articles affect children's medicines research?

Can you describe whether you think that these articles are implemented in children's medicines research and in particular your research, and if so how?

Could you tell me whether you believe these rights are applicable, or not, to children's medicines R&D, and if so why?

Can you tell me where within the R&D process you think the rights of children are or may be considered, if at all?

### **Abilities**

In what ways do you think that children have the ability to contribute to medicines R&D?

Do you think that there are age limitations for the capability of children to contribute to, or have a valid opinion about medicines R&D? And please give your reasons.

Can you tell me about a time where a child has talked to you about the medicines they use?

(If yes,) Could you describe how useful the information was or could be to you or your company's R&D practices?

How do you think the insight into the child's/children's views proved to be useful to you, or could prove useful to you?

How did this insight/knowledge change anything regarding the R&D process, or how could it change anything?

May I ask if you have children?

A. **If yes:** If your child was to express an opinion on a particular medication (they may already have) that they disliked taking for reasons such as: taste, texture, appearance, frequency of dosage, stigma, pain or side effects, would this affect your decision to administer this medicine?

How do you think this might influence your research practices in the future, if at all?

B. **If no:** If a child was to express an opinion to you on a particular medication that they disliked taking how would this affect your research practices?, if at all?

How would you say the pharmaceutical industry really feels about the involvement of children in research?

What do you think could be done to create a good working relationship between children that take medicine and those involved in medicines R&D?

In what ways do you think that drug development companies could be motivated to involve children in research?

**Appendix 9: Interview prompt sheet**

Use as a guide only. N.B. Pick up cues from what the participants say and follow their lead and order of topics/issues.

**Checklist**

- Prior to meeting send out consent form; stress confidentiality/anonymity
- Explain that I want to hear their views on patient involvement and specifically that of children's involvement – this does not matter if it is positive or negative
- Gain written consent to record the interview
- Ask if there are any questions about the project
- Check how much time they have available
- Check to see if there is a possibility of a follow-up interview if time does not allow completion
- Conduct interview covering issues to be included
- Thank the participant and ask if there are any further request regarding supplying them with more details or data

**Interview Record**

Interview number:	
Interview name:	
Code name: (unidentifiable name)	
Gender:	
Ethnicity??	
Date of meeting:	
Time of meeting:	
Venue:	
Name of those present:	
Duration of interview:	
Participants occupation:	
Number of years in post:	
Background information: (i.e. work history...)	

**Appendix 10: Example of an interview record**

**Interview Record**

(Please note that all information provided will remain anonymous in any publication, will be kept confidential by, and only known to, the researcher.)

Interview number:			
Participant name:			
Code name: (unidentifiable name)			
Date of meeting:			
Time of meeting:			
Venue:			
Name of those present:			
Duration of interview:	:hrs		:mins
Participants occupation:			
Background information:			
Job title:			
Years in post:			
Job description:			
What attracted you to this profession?			
Gender:	M		F
Parent:	Yes	No	Prefer not to say
No of children:	M:	F:	Prefer not to say
Notes:			

**Appendix 11 Example of a reply slip for participants**

**Reply slip**

To: Gillian Stokes

Bloomsbury Scholar

Institute of Education and UCL School of Pharmacy

Email: [g\\*\\*\\*\\*\\*@yahoo.com](mailto:g*****@yahoo.com)

Tel: 0\*\*\*\* \* (mobile)

0\*\* \* (landline)

I would like to take part in an interview for the research project entitled:

Working title: The rhetoric, reality and realisation of children’s involvement in medicines research and development: bridging the gap between those who make and those who take children’s medicines

Title: .....

Name: .....

Job Title: .....

Company/Institution: .....

Address: .....

.....

.....

Contact me: Directly  Via secretary or alternative contact

Alternative contact name: .....

Telephone number: .....

Email: .....

Thank you.

**Appendix 11: Contact slip used for 10<sup>th</sup> European Congress of Epileptology**

Gillian Stokes (MSc. Dist.; BSc. Hons., NIMH)

PhD Student and Bloomsbury Scholar

Studying at Institute of Education and UCL School of Pharmacy

Email: [g\\*\\*\\*\\*\\*@ioe.ac.uk](mailto:g*****@ioe.ac.uk) or alternatively [g\\*\\*\\*\\*\\*@yahoo.com](mailto:g*****@yahoo.com)

Mobile: 0\*\*\*\* \*\*\*\*\*\*

Thanks so much for talking to me today at the 10<sup>th</sup> European Congress on Epileptology, London 2012.

You are a really important contact and your views and ideas would prove invaluable to my research.

I will contact you shortly by your preferred method to arrange a one-on-one discussion.

If in the meantime you have any questions, please feel free to contact me any time.

Once again, thank you.

**Appendix 12: Table summarising ways that participants feel that children can contribute to medicines research and development**

<b>Findings</b>	<b>Examples</b>
Openness	Insights
Be active participants	Projects Enthusiasm Think outside the box Help with research design – feasibility, planning, interview schedules, questionnaires, satisfaction surveys, PILs Analyse qualitative research
Experts	Insight How to improve experiences Ideas
Speaking out	Championing research in their condition Disseminate data
Children's traits	Reliable Honest Frank Direct – don't beat around the bush Dedicated Have integrity Enthusiastic
Children's views	Feedback on tastes, how they feel, dosage, formulation, acceptability, impact, ethics QOL
Morals	Acceptability of products, manufacture
Giving their bodies	
Different perspective	
Outcomes	

**Appendix 13: Table of example thematic categories of children’s participation: positive, negative and neutral constructions**

<b>Finding</b>	<b>Construction</b>	<b>Examples</b>
<b>Positive</b>	Vital	To produce good quality research
	Valuable	
	Worthy	
	Children	Reliable witnesses  Active thinkers  Media impact - positive
	Achievable	
	Ideas	Brainstorming  Filter into gatekeepers (parents, carers, healthcare professionals)
<b>Negative</b>	Fear	Of children (safety, risk)  Of litigation  Of parents
	Impractical	Feasibility
	Uncertainty	Don’t know if it works
	Contrivance	Bend things to make it look like there’s involvement when there isn’t
	Age limitations	What is a child?  Understand of the implications/meaning of research
	Children	Protection
	No proof	No involvement worked
<b>Neutral</b>		Commitment is needed by the researchers and the children

## Appendix 14: Participant information sheet

Gillian Stokes, PhD student

Lead Supervisor: Professor Sandy Oliver

Joint Supervisor: Professor Ian Wong

Institute of Education, University of London and UCL School of Pharmacy,

Email: [g\\*\\*\\*\\*\\*@yahoo.com](mailto:g*****@yahoo.com) Tel: 0\*\*\*\* \*\*\*\*\*

My research is entitled: The rhetoric, reality and realisation of children's involvement in medicines research and development: bridging the gap between those who make and those who take medicine. I am looking in the nature of children's involvement in children's medicines research and development (R&D), with a specific interest in medicines for conditions that require regular pharmaceutical management. It is well documented that there are inequalities in the standards and provision of safe, efficacious and high-quality medicines for children. There are also inequalities in the participatory process for children in medicines R&D, who are currently not being given the same opportunities as adults.

Currently, no research exists that is aimed at understanding why children are not more involved in the R&D of the medicines designed for their use. This is where my original contribution to knowledge will be; to understand why children views are currently situated at the periphery of children's medicines R&D and the discourse that surrounds it and to identify how and where children can become more involved in the future.

My aims are to investigate the attitudes, ideas, and beliefs of those involved in medicines R&D with regards to children's involvement in the medicines R&D process. Furthermore, to identify the barriers, facilitators and potential opportunities for involvement, in order to suggest ways in which children and those involved in medicines research can share ideas, expertise and experiences.

For the interviews, I am interested in your views, whatever they might be regarding children's medicines R&D.

You can leave the study, or request a break, at any time.

This study has been subjected to and passed ethical review and follows the Institute of Education ethics procedures.

As a participant, I ensure that you have the right to withdraw at any point without penalty and I have provided details on the enclosed Consent Form.

I anticipate that the findings from this study will be written up for a thesis, for publication in a peer reviewed journal, may appear on the internet and presented at international conferences. All results will be anonymised, ensuring that it will not be possible to identify you from what is published.

If you have any questions at all regarding this, please contact: Gillian Stokes. (Details above.)

If you are willing to participate, please sign the enclosed Consent Form.