



Commentary

Meeting commentary—“Medicines for older adults: Learning from practice to develop patient centric drug products”[☆]John Wahlich^a, Sven Stegemann^b, Mine Orlu-Gul^{c,*}^a The Academy of Pharmaceutical Sciences, Q House, Troon Way Business Centre, Humberstone Lane, Thurmaston, Leicester LE4 9HA, UK^b Capsugel, Bornem, Belgium^c University College London, School of Pharmacy, Department of Pharmaceutics, 29-39 Brunswick Square, London WC1N 1AX, UK

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ABSTRACT

A meeting jointly organised by the Academy of Pharmaceutical Sciences (APSGB), the Geriatric Medicine Society and the UCL School of Pharmacy took place on the 13th of March 2013, in Stevenage, UK. The meeting was attended by a number of experts involved with the treatment and development of drugs for the older adult, including clinicians, pharmacists, academics, regulators and representatives from industry. The event created the platform to discuss the provision of medicines for older adults from a pharmaceutical sciences perspective.

‘The use of medications in older patients is arguably the single most important health care intervention in the industrialized world’. (Avorn, 2010)

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1. Introduction

With the worldwide demographic shift and continuously increasing life expectancy, the old and very old patients are not only the major user group for medicines but are also the fastest growing population with a potential need for medicines. In contrast to the older adult population sub-group, the challenge of providing medicines for paediatrics is well recognised and there has been an increasing interest in the literature in particular since the introduction of the EU Paediatric Regulation in 2007 (Paediatric Regulation, 2007). The European Paediatric Formulation Initiative (EuPFI) is particularly active in this area with annual conferences, preconference workshops, webinars, newsletters, review papers and research studies. Consequently there are a significant number of publications relating to paediatric medicines including their formulations. However the literature and interest in medicines for older adults is much less well developed. This is a situation that needs to be addressed as people are living longer helped in no small measure by the achievements in the pharmaceutical sciences.

Data according to Eurostat suggest that the number of older adults (aged over 65 years) will increase in the EU from 87 million in 2010 to 123 million in 2030 (Giannakouris, 2010). In the UK for example older adults aged 80+ will represent 9% of the population in 2050 compared with 4.8% in 2012 (United Nations, 2012).

Paediatrics and older adults have similarities in their medicine requirements as both population groups lack suitable formulations, pharmaceutical packs and administration devices to meet their needs. While some of these needs are common, others are very different. For example, an individual’s impairments mainly shape the specific requirements of older adults, whereas immaturity has the major effect on the needs in paediatric medicine. Young children always have a carer, often their parents, whereas some older adults may live on their own or have carers who are as infirm as they are. On the other hand both groups can have problems in swallowing, even though in children it is due to an immature swallowing physiology and in the elderly it is due to age or disease related swallowing impairment (dysphagia).

Just as children cannot simply be regarded as smaller adults, older adults cannot simply be labelled by age. Paediatrics can essentially be regarded as a special, relatively homogeneous population sub-group whereas older adults represent a very heterogeneous group with many different sub-populations characterised by different sets of morbidities, co-morbidities and impairments. Compared to paediatrics, older adults are by far the main users of drug products and while individuals over 65 represent 16% of the population they consume 31% of all of the medicines.

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* Corresponding author. Tel.: +44 20 7753 5968.

E-mail addresses: john.wahlich@btinternet.com (J. Wahlich), sven.stegemann@capsugel.com (S. Stegemann), m.gul@ucl.ac.uk (M. Orlu-Gul).

The purpose of this meeting was to build on the discussions held by EMA in March 2012 (EMA, 2012), highlight the challenges and opportunities that exist for improving the provision of medicines to older adults, act as stimulus for future pharmaceutical meetings with a specific focus on geriatric medicine and to consider the potential next steps in this field.

The following text provides useful background reading (Wehling, 2013).

2. Physiological changes on ageing

There are important physiological changes that occur with increasing age and which have a direct impact on the use of drug therapy. Older adults vary in their degree of age-related changes (both physiological and cognitive), the number of co-morbidities they may have (which has not only implications from a disease perspective but also implications for the number of medicines they may be taking, so-called polypharmacy) and their medical and lifestyle histories. For this reason there is no such thing as a standard older adult. Unlike paediatrics there is no simple classification of older adults into different sub-groups. ICH simply refers to individuals over the age of 65. Another classification refers to the 'early old' (65–74 years old); the 'middle old' (75–84) and the 'late old' >85. A further physiological approach uses the classification of 'fit-elderly' and 'frail-elderly' (Stegemann et al., 2010).

Ageing is defined by a progressive change in the physiological and psychological characteristics of the human body coupled with a transient loss of cellular, molecular and physiological functionality of a tissue or organ.

Physiologically, the older adult has a different ratio of fat to protein to water in their body make up (30:12:54) compared to a younger adult (18:16.5:60) (Puig, 1996). This has consequences for the absorption and distribution of both lipid and water soluble drugs. In addition, older adults may have diminished receptor sensitivity and responsiveness; their ability to mount a compensatory physiological response is reduced and their normal homeostatic mechanisms are blunted (e.g. baroreflex, thermoregulation, posture, GI integrity and volume/electrolyte balance) and can sometimes produce an inappropriate response to a stimulus.

Absorption and distribution in the older adult can be affected by a number of physiological factors (Perrie et al., 2012) (Table 1).

The increased amount of fat in the older adult serves as a store for fat soluble drugs (e.g. amiodarone, desipramine, diazepam or haloperidol) and the decreased amount of water impacts water soluble drugs (e.g. lithium or aminoglycosides). These changes can have a significant impact on the pharmacokinetics of drugs and older patients can develop adverse effects for drugs which have a narrow margin between their therapeutic and their toxic doses, e.g. digoxin and warfarin.

Decreased protein binding (to albumin or α -1 acid glycoprotein) in older adults is more a consequence of disease rather than age and

Table 1
Absorption and distribution in the older adult.

Factors impacting absorption	Factors impacting distribution
Amount of saliva ↓	Cardiac output ↓
Gastric acid production ↓	Renal blood flow ↓
Gastro-intestinal surface ↓	Hepatic blood flow ↓
Active transport mechanism ↓	Albumin water levels ↓
	Volume of distribution for water soluble drugs ↓
Gastric pH ↑	Peripheral vascular resistance ↑
Gastric emptying time ↑	Body fat/water ratio ↑
	Volume of distribution for lipid soluble drugs ↑

↓, the factor is reduced; ↑, the factor is increased.

Table 2
Metabolism and elimination in the older adult.

Factors reducing metabolism	Factors reducing elimination
Liver function (through decrease in blood flow and hepatic mass) ↓	Kidney size ↓
Cyp P450 enzyme levels ↓	Renal blood flow ↓
Overall drug metabolism ↓	Number of functional nephrons ↓
	Tubular secretion ↓
	Overall glomerular filtration rate (GFR) ↓

↓, the factor is reduced.

can have an impact on the free fraction of protein bound drugs, leading to increased delivery to receptors and drug–drug interactions. For example, ibuprofen is 99.5% protein bound and any reduction in binding will increase the amount of free drug and consequently may require a reduction in dose.

Metabolism and elimination are also reduced by physiological changes on ageing (Perrie et al., 2012) (Table 2).

The reduction in drug metabolism particularly impacts lipid soluble drugs through changes in the Phase 1 and 2 metabolic pathways, while the reduction in the GFR is highly important for renally excreted drugs (which are typically water soluble). In both cases, this leads to an increase in the systemic drug concentration and is typically the major reason why drug doses are reduced (or intervals increased for b.i.d. dosing) in older adults. Renally excreted drugs which could be impacted include: atenolol, gabapentin, H₂ blockers, allopurinol and quinolones. From a clinician's perspective, focus must be given to the potential reduction in the GFR as this leads to greater variability as individuals vary in the extent of the reduction. One of the important changes with age might be the development of frailty, which can be defined as the condition of reduced capacity of multiple physiologic systems and occurrence of multiple organ dysfunctions (Woodhouse and O'Mohany, 1997) which consequently might require the adaptation of the drug therapy. Frail patients might also lose their ability to carry out important, practiced social activities of daily living when exposed to either psychological or stressful conditions (Morley, 2009) which might impact the execution of drug therapy.

A drug's half-life is proportional to its volume of distribution/clearance (hepatic and renal) and can be significantly affected by changes in these terms on ageing.

The disease state also has an effect on an individual's physiology (Table 3).

Pharmacodynamically the sensitivity of the body to benzodiazepines, warfarin and hypotensives may be increased while the sensitivity to beta-1 modulators in cardiac tissues may be decreased. Other drugs which are impacted and where effects are increased include phenothiazines (impacts most of their effects),

Table 3
The impact of the disease state on physiology.

Disease state	Impact on physiology
Renal failure	Reduced renal clearance Reduced protein binding
Cardiac failure	Leads to sodium and water retention Hepatic congestion (reduction in clearance)
Hepatic impairment	Leads to sodium and water retention Hepatic congestion Decrease in protein binding (increasing the volume of distribution and hence drug half-life) Decrease in pre-systemic metabolism
Acute phase response	Increase in alpha-1 acid glycoprotein (which decreases the volume of distribution and hence drug half-life)
Small bowel disease	Decreases the extent of absorption
Migraine	Decreases the rate of absorption

NSAIDs (impacts GI effects) and anticholinergics (impacts central effects exacerbating pre-Alzheimer conditions) while for calcium channel blockers the effect on the PR interval is reduced.

The route of drug delivery can also be impacted in older adults (Perrie et al., 2012).

The lung capacity declines due to age related changes in the lung structure with a gradual increase in the lung's residual volume (RV) and a gradual decrease in the inspiratory reserve volume (IRV). The pulmonary arteries thicken with age and from about age 60 the mucus layers also thicken and calcification of the cartilage occurs. All of these factors have an impact on the Forced Vital Capacity (FVC) which is typically reduced by 40% (compared with adult capacity) by age 85. The net consequence is a potential impact on the deposition and efficacy of orally inhaled drugs especially those for the treatment of asthma and COPD, which are most common in older adults.

Other age related changes that impact drug delivery are the potential changes to the skin (thinning of the epidermis) affecting transdermal delivery, the reduction of the tear film with dry eye being much more prevalent in older adults, as well as changes to the oropharyngeal system due to an impaired swallowing response and changed sensory perception for taste and smell.

3. Adverse drug reactions (ADRs)

ADRs can be idiosyncratic (usually unpredictable and unrelated to the wanted effects of the drug) or dose related (usually predictable and related to the desired effects of the drug). The former tend to be more serious while the latter have a much higher prevalence in older patients and are preventable. Reasons for this include pharmacokinetic changes in older adults (affecting distribution, renal function and liver volume in particular); changes in their sensitivity to drugs (caused by impaired functional reserve, e.g. blood pressure homeostasis); a higher prevalence of disease and most significantly by their greater concomitant drug consumption (polypharmacy). A particularly striking example is the ADRs experienced with nitrazepam (Greenblatt and Allen, 2004). Other drugs which are particularly prone to ADRs in older patients are: diuretics, analgesics, antihypertensives, neuroleptics, digoxin and NSAIDs.

4. Polypharmacy

Over the past 25 years new drugs have constantly entered the market allowing the more effective treatment of most of the chronic diseases appearing with age. As a consequence, polypharmacy, the use of more than 5 different drugs simultaneously, is very common in older adults. In one study, in a group of older adults with a mean age of 82.2 years, 51% took ≥ 6 medications/day (Hajjar et al., 2007). In another study of residents in care homes (mean age 82.5 years) approx. 12% were on 1–5 medicines, 35–41% on 6–10 and 46–54% on 10+ medicines (Patterson et al., 2010).

In addition, approx. 70% of older adults take OTC medicines along with their prescribed medicines and in most of the cases this drug use is not reported to the physicians.

It is not uncommon for one medicine to be prescribed to treat the ADRs resulting from a concomitantly administered drug, either prescribed by another physician or an OTC medicine used by the patient. Such situations can easily develop into what is called a prescribing cascade. This has been mentioned as a major concern as, for example in the USA, medicine related issues are the 5th leading cause of death. As prescription cascades develop over time, it is mandatory that medication reviews are performed on a regular base in older adults (Milton et al., 2008).

Reference to the 1976–1978 edition of the British National Formulary (BNF 1976–1978) helps put the treatment of older adults into an historical perspective: 'Most elderly patients have poor

memories and get confused. They may live alone, or with a partner who is no better. They find it difficult to follow even simple instructions, and the complicated schedules sometimes offered, with many drugs to be taken at different times. They are creatures of habit and once they have been on tablets for a long time it may be difficult or unkind to stop them.' This statement, even so simplified and probably not acceptable anymore today, is clearly an example of the challenges for drug therapy in older adults and the problem of professionals to understand the patient's perspective.

The medication reviews should ensure that the term 'polypharmacy' relates to a patient on 'many drugs' rather than its current negative connotation of 'too many drugs'. However, as the patients are getting older, regular medication reviews need to be performed. The reviews should be based on treatment priorities and the concepts of (1) avoiding treatments with no proven benefit or which have a contraindication (e.g. STOPP or Beers criteria) and (2) initiating therapies only where a proven indication exists (e.g. START criteria) (Gallagher et al., 2008). From the perspective of reducing adverse drug reactions, there are some items to consider during the review:

- Produce a prescription checklist
- Identify concomitant morbidity
- Anticipate PK and PD changes with age, disease and resulting from the use of other drugs
- Choose low doses of drugs with narrow therapeutic windows and use dose titration
- Consider a low threshold for the change of treatment
- Discontinue unnecessary treatments

From the perspective of maximising the treatment benefits the review should:

- Focus on primary and secondary prevention in particular for:
 - osteoporosis
 - hypertension, diabetes
 - stroke prophylaxis in AF, CAD
 - hypercholesterolaemia
- Consider mortality and morbidity reduction in particular for:
 - heart failure
 - malignant disease
- Address symptom control
 - analgesia
 - Parkinson's disease, Alzheimer's disease

It is critical that the patient understands and accepts the therapy and is involved in the decision making during the medication review. The prescriber's role during the review should be to give advice.

The importance of Shared Decision Making in the discussions with the older adult on their medication (Lally and Tullo, 2012) must be emphasised. This aspiration can be complicated due to the frailty of the patient (who may have difficulty seeing or hearing the information); their intellectual capacity to understand and contribute to what may be a complex decision involving polypharmacy, co-morbidities and medicines with unknown risks and benefits in the elderly; and their interest in being involved in the process. Older people would like to be informed on their medication and keep their autonomy. The process is assisted by the involvement of the patients' carers and an individual's knowledge about disease and medication with the latter being increased in recent years through the use of the internet.

5. Adherence

Adherence is a major factor in achieving the expected outcomes of a drug therapy in the older adult (but also any other patient no matter what age). The WHO has published on the five dimensions of adherence (see details included in the reference [American Society of Aging, 2012](#)) which highlight that adherence is a complex issue with social/economic; health care system; therapy; condition and patient related aspects, each of which have multiple contributory factors ([Krueger et al., 2005](#)). Different ways of improving adherence in older adults have recently been reviewed and offer some direction when dealing with such patients ([Stegemann et al., 2012a](#)).

Adherence is impacted by a patient's understanding of their disease(s) and why the medication is needed. They may be concerned about the adverse effects and whether they believe that the medicine will be beneficial to them. As an example, data have been presented ([Vrijens et al., 2006](#)) which show that the number of patients continuing to take atorvastatin after 300 days went up from 70% to nearly 90% when they received feedback from a pharmacist (helping them understand their medicine and disease) as part of an adherence review.

While the development, clinical testing, manufacture, distribution, prescribing and supply of medicines are highly controlled processes there is no control once the medicine is in the hands of the patient (and often limited control when it is administered by the patient or care giver). Consequently the instructions included in the patient insert, which need to be agreed with the Regulatory Authorities, are frequently not understood by the lay patient.

Likewise, operations to modify the dosage form, for example to crush or split tablets to facilitate swallowing, which would come under the strict control of GMP if performed in the pharmaceutical industry, are completely uncontrolled in the hands of the patient or care provider and hence ideally should be avoided.

Whether a patient adheres to their medication can be impacted by one or more stages in the therapeutic process. From the initial experiencing of the disease, to the diagnosis and involvement of a physician up to the resulting prescription and medication schedule to the preparation of the medication (removal from packaging, etc.) to the final dosing, requires several critical decisions by the patient and each step can result in adherence issues. Once polypharmacy is taken into account, the complexity, and hence chances of poor adherence, escalates.

Without acceptance of the disease and acceptance of the therapy, adherence is most likely not achievable and without follow up, on how the patient experiences the disease and the therapy, adherence will not be maintained. As professionals, we should not blame the patients for their non-adherence but instead try to understand their problem and attempt to resolve it to enable them to follow through their therapy independently and in an adherent manner.

Data ([Vrijens et al., 2008](#)) on individuals with different compliance 'schedules' showed patterns that ranged from the 'perfect' patient who always took their medication as prescribed to the 'random' patient who not only failed to comply with medication timings but also took drug 'holidays'. Variants of these were the patient whose compliance varied at different times of the week or who started off with every good intention and then, perhaps because they did not see an immediate benefit, gradually tailed off in their compliance.

Adherence can be impacted by the lack of disease threat or the severity of adverse events. For antihypertensives adherence was highest (approx. 70%) for the more modern drugs (such as ACE inhibitors or Angiotensin II Receptor blockers) and poorest (approx. 30%) for the older diuretic or beta-blocker drugs ([Kronish et al., 2011](#)) due to latter typically having a greater incidence of ADRs.

Some of the factors affecting adherence relate to the packaging, dosage form and/or dosing requirements and hence are potential targets for the pharmaceutical scientist to address. An example would be the contradiction between child-resistant packaging requirements and an easy-to-open need for older adults. Various considerations have been made to address this, for example the individual blistering/packaging by a community pharmacist or a dual cap that has a child resistant and an easy to open facility that can be used as appropriate. There is a British Standard on the ease of opening packaging which addresses the needs of the older adult ([British Standard, 2011](#)).

6. Formulation, administration and management of medicines with a focus on the needs of older adults

6.1. Swallowing considerations

There is a general perception that solid oral dosage forms are preferred across all patient populations as good swallowing functions are assumed as a life-long stable capability. A recent review provided evidence that there is an important age and disease relationship in the capability of safe swallowing. Problems with swallowing oral dosage forms occur in about one third of older patients and modification of the dosage form in terms of capsule opening and tablet crushing is considered as a common practice in nursing homes ([Stegemann et al., 2012b](#)). This has the following consequences:

- Uncoated or large tablets can be difficult to swallow
- Older adults may often resort to crushing, chewing or splitting tablets with the risk of not receiving the full dose or compromising a delivery system which requires that the tablet remains whole
- The contents of a capsule or a crushed tablet may be mixed with food to facilitate swallowing and this may lead to poor or inappropriate dosing or compatibility issues

6.2. Dosage form and pharmaceutical product design

The development of age appropriate drug formulations and products is still an area where there has been limited scientific research. Older adults are a very heterogeneous group of patients, however, they have some communalities with regard to specific problems that should be considered in the development.

- Dosage form design
 - The size, shape, surface structure, taste and smell of the product should be considered to improve the ease of swallowing
 - If the tablet is too small then it may difficult for the visually impaired patient to see and pick up the tablet
 - Most tablets are white making differentiation difficult where polypharmacy is an issue
 - The use of trans-dermal formulations is an attractive option avoiding oral dosing issues and using a route where absorption is less subject to ageing, however, they can be difficult to administer by older adults independently
 - Orodispersible tablets may be perceived as easier to swallow, however, dehydration and xerostomia in older adults should be considered as contra-indications
- Packaging and labelling
 - Child resistant containers and peel back or push through foil packs can often be difficult for elderly adults to open and they

may resort to re-packaging the medicines into other containers with the risk of medication errors, unknown stability, poor or no labelling and easier access by children. Dosette boxes and compliance blister packs are an example here. The design of these packs may not always be helpful to older people when taking their drugs, in particular when these packs are filled with a number of different medicines each with a similar appearance

- Labelling can be difficult to read (due to the choice of a small font size and or unclear type, poor text contrast with background, use of inappropriate colours, etc.)
- Varying the manufacturer of generic products included in prescriptions can cause frequent changes in packaging, colours and labelling which often causes confusion

6.3. Medication schedule and management factors

Older age is often linked with multi-morbidity and use of polypharmacy, which significantly increases the complexity of the medication schedule and has a direct impact on the patient adherence. Following considerations can be made:

- Dosing frequency
 - Adherence is significantly impacted by dosing frequency. Modified release dosage forms requiring once daily dosing are much preferred
 - It may be possible to alter the drug release of a dosage form to reduce the incidence of PK related ADRs
 - Dosing requirements should be kept as simple as possible and fixed dose combination products should be considered
 - It is important that the patient establishes a medication implementation plan to get into a regular habit of when to take their medicines

- Dealing with polypharmacy

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- It may be difficult to schedule and comply with the different dosing requirements of multiple medications (with or without food, different dosing frequencies and timings, etc.)
- Compliance aids (e.g. alarms) may or may not help (e.g. can the patient hear the alarm or remember what it means? or they may get stressed with the sound, especially patients with cognitive impairment)
- There is an opportunity for more combination products to reduce the pill burden.

7. Care of the older adult

Another important area to improve the treatment and therapeutic outcomes in older adults is the treatment of older adults in care homes. In respect of recent news about poorly performing UK care homes, the US had experienced similar issues in the past and Congress asked the Institute of Medicine to investigate the concerns in 1986. Their report (Hughes and Lapane, 2006) (summarised here from a medicines perspective) found: medication errors; failures to provide prescribed drugs and excessive use of chemical restraints (including anti-psychotics (used in 20–50% of residents), hypnotics and anxiolytics). The report was enacted by the US Government in 1987 through ‘The Omnibus Budgetary Reconciliation Act, OBRA 87’. This specified that ‘‘The [care home] resident has the right to be free from any psychoactive drug administered for purposes of discipline or convenience and not required to treat the resident’s medical symptoms’’. Pharmacists are required to monitor the use of these drugs and challenge their unjustified usage. The Act had the

effect of reducing the use of antipsychotic drugs in US care homes to around 14.5% although by 2005 this figure had crept back up to 28% (Chen et al., 2010).

Data from various countries and homes suggested that there is a marked variation in the use of anti-psychotics in different care homes. The culture within the home appears to influence the prescribing habits. Homes can be classified as ‘resident-centred’ (focussed on the resident, use multi-disciplinary collaboration and avoid the use of physical and chemical restraints – ‘would try other things first’); ‘traditionally-centred’ (culture is one of custodial care with behavioural control and the use of restraints and little multi-disciplinary collaboration – these homes treat residents ‘for their own good’ which includes the use of psychoactive medication). Homes falling somewhere between the two extremes were classified as having an ‘ambiguous’ culture. (A study in New Zealand and Northern Ireland used a quantitative instrument to evaluate the cultures and most homes had an ambiguous culture (the scores were similar in the two countries).)

The Fleetwood Project (Patterson et al., 2010, 2011) (a model of care developed in the US in which pharmacists work with doctors to improve the quality of prescribing with the aim of reducing the use of inappropriate medication and adverse drug events and to promote evidence based practice) was applied to care homes in Northern Ireland and the prescribing results compared to control homes which were not subject to the intervention. The baseline measurements before intervention suggested that approx. 66% of residents were receiving psychoactive medication with between 72 and 81% of these having been prescribed inappropriately. Twelve months after the intervention the number receiving inappropriate psychoactive drugs had dropped to 22% in the intervention group while remaining high at 58% in the control group (Patterson et al., 2010).

In conclusion, the use of inappropriate psychoactive drugs in a care home can be linked to a culture of control (so-called ‘traditionally-centred’ homes) and can often be at odds with a resident’s autonomy. In part this may reflect the residents’ generation (a quote from a nurse in one of the homes highlights this: ‘I think they’re of a generation that would be very compliant’). Only time will tell if the next generation of residents are as compliant and whether they will stand up to this type of control!

8. Regulatory perspective

The European Medicines Agency (EMA) has recently initiated a process to review the future regulatory pathways for geriatric medicines. ICH7 (ICH, 1993) requires that a representative number of patients should be studied pre-authorisation and for some medicines the main users will be older adults. A population PK or specific PK study including patients of 75 years and beyond should be performed to understand the impact of potential age related physiological changes. Older adults are often under-represented in clinical trials relative to the disease prevalence. The view at the meeting was that the situation was improving since this issue has gained greater visibility (EMA, 2006; Cerreta et al., 2012).

‘‘Seniors are either taking drugs in the absence of evidence-based trials on their age groups, or are denied drugs because they are untried on the age groups’’ (Godlovitch, 2003)

The background to the Paediatric Regulation of 2007 and the associated requirements for Paediatric Investigation Plans (PIPs) provide indications on how government involvement could be necessary to address the shortfall in medicine provision for one patient sub-population (namely children and younger adults aged 0–18). One aspect of this was the availability of funds through the

European KP7 initiative to develop medicines for this population sub-group.

However, there are certain difficulties in addressing the older adult sub-population in a similar way as there would almost certainly be calls for other groups (the obese, the pregnant, etc.) to be given the same focus and it would clearly be impractical to respond to all groups in the same way. The consequence is that *at this time* there are no plans for a Geriatric Regulation or Geriatric Investigation Plans for the development of medicines for older adults. However EMA has recently published on the need for a reflection paper on the quality aspects of medicines for older people (EMA, 2013). This would provide an overview of the aspects requiring special consideration in the pharmaceutical development of a medicine. The strategy is to identify where the licensed pharmaceutical products do not specifically meet with the needs of older people and revise the existing guidance accordingly. The intention is to harmonise the already available tools and use them more effectively. To assist this, an EMA road map to 2015 on the geriatric medicine strategy has been published and a quality reflection paper for public consultation is also due shortly (EMA, 2011a).

The roadmap ensures that the lessons learned from paediatrics are applied and that the Agency will undertake “specific efforts to ensure that the needs of older people are taken into account in the development and evaluation of new medicines”. The strategy has two guiding principles:

1. To assure that medicines used by older adults are of the same high quality, and appropriately researched and evaluated for use in this population
2. To improve the availability of information on the use of medicines for older adults

In addition to ensuring that the requirements laid out in ICH E7 are adhered to, the strategy calls for a definition to be developed for ‘frailty’; a Geriatric Needs Survey to identify geriatric activities and instruments (or lack of) at national and European level; a workshop on Geriatric Medicines and work on geriatric medicine formulations and adherence. A CHMP Geriatric Expert Group (GEG) has been established (EMA, 2011b) and will “provide advice to applicants on regulatory requirements for the development of products likely to be used in the elderly”.

Work on the reflection paper is due to start in Q3 2013 and to be finalised Q3 2014 with external consultation planned for Q1/Q2 2015 and issue due by the end of 2015 (EMA, 2013)

The intent is to analyse the relevant scientific literature and post-marketing data; liaise with stakeholders on practical issues and perform a gap analysis on whether or not existing marketing authorizations are fully meeting the needs of elderly patients.

The following organisations are also of interest:

- Ephor: Expertise centre PHarmacotherapy in Old peRsons (EPHOR): <http://ephor.artsennet.nl/English-website.htm>
- Geriatric Medicines Society: <http://www.geriatric-medicine.org/>
- European Union Geriatric Medicine Society: <http://www.eugms.org/>
- AGE Platform Europe: <http://www.age-platform.eu/en/about-age>
- NCA Expert Groups (Dutch): <http://www.cbg-meb.nl/CBG/nl/over-ons/netwerk/expertgroepen/default.htm>

9. What does the future hold?

Developing age appropriate products has to be seen as an opportunity for the pharmaceutical industry. A polypill technology originating from GSK was presented as a case study for such innovation. This novel tablet design addresses one of the factors leading to

poor adherence by combining appropriate medications into a single tablet. Put simply the individual tablets are stuck together to produce a single tablet. Assuming that the dosing schedules for the individual components are compatible and that the overall tablet size is not too large, then this approach could effectively reduce the pill burden for an individual on polypharmacy.

The technology is capable of joining together tablets to create a single entity and GSK has developed a prototype bench top assembly device to do this. The individual components are not restricted in terms of their formulation and once combined the performance in terms of drug release should be unaffected. While capable of working with existing tablet formulae, reformulation to produce smaller tablets and/or shapes more amenable to being fitted together, would result in a more acceptable final product.

The concept is more than just the technology as it would require a different approach to how medication is prescribed and dispensed and potentially impacts the existing supply-chain process. One way in which it might be used is in a pharmacy where a pharmacist could process a prescription containing multiple drugs by producing a single combination tablet using the assembly device to fill all or part of the prescription. The individual components for the final product could be supplied by the innovator companies in the correct size and shape to be combined into the final product.

The approach is not limited to combination products. For example different strength components of the same drug might be combined in different ways to produce a wide range of strengths without having to manufacture every option (e.g. 1 mg and 3 mg tablets might be combined 1 mg+placebo; 1 mg+1 mg, 3 mg+placebo and 1 mg+3 mg to cover the range 1–4 mg using only two manufactured tablet strengths). This has obvious attractions to the manufacturer and makes it easier to produce a final product personalised to the patient.

GSK have taken the technology as far as they are able and are now looking at an open collaboration between companies, patient-representative bodies and other groups to develop the concept further.

10. What are the next steps?

Ageing is a natural phase of the life span. Getting older brings along physical and cognitive impairments but it should not be recognised as a disease. The perspective should be in the positive direction, even by considering terminology and the use of words such as ‘older’ (rather than ‘old’) and ‘appropriate prescribing’. Similarly by treating older adults with dignity. The positive moral perspective is crucial. Motivated older patients can do better. The researchers should be inspired by consumer friendly products in other industries to develop older friendly dispensing systems with reminders.

The strategies towards improving the medicine for older people should cover all age ranges in the older adult population, in particular the critical age groups that are likely to have impairments. The regulatory approaches should be valued and the relationship between industry and the authorities should be strengthened by sharing opinions on draft regulatory guidance documents. The pharmaceutical industry should apply for scientific advice on planned initiatives at an early stage.

The Geriatric Medicines Society has been a successful initiative with the aim of serving as a multidisciplinary network to address the challenge of medicines for older patients from a holistic perspective. The members meet twice a year to discuss the strategies for better medicine and practices for older people. More not-for-profit consortiums working on geriatric medicines should be established in order to raise awareness and accelerate the quality of older people's life. In the UK the Academy of Pharmaceutical

Sciences (APSGB) plans to establish a Focus Group on age appropriate medicines to share ideas and encourage collaboration.

The clinical research networks can play a crucial role to improve the quality of medicines for older people. The clinical study portfolio should grow to include studies with a specific focus on developing appropriate formulations with senior friendly packaging and adherence systems for older people.

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