Editorial - Special Issue on "Integrated Continuous Biomanufacturing: Industrialization on the Horizon"

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Continuous bioprocessing has the inherent advantage of higher productivity, which can facilitate implementation of small process trains resulting in cost-effective, lean, and agile manufacturing facilities. Impressive technological advances to enable continuous bioprocessing have been made in the recent past and were discussed at ECI's Integrated Continuous Biomanufacturing (ICB) III Conference (Cascais, Portugal, 17-21 September 2017) chaired by Suzanne Farid (UCL), Chetan Goudar (Amgen), Paula Alves (iBET) and Veena Warikoo (ex-Sanofi, currently Roche).

The ICB III conference brought together leading scientists and engineers from academia, industry and regulatory authorities that are actively engaged in continuous bioprocessing to debate how industrialized our sector can become and potential scenarios where continuous platforms will better serve our needs. The conference participants were surveyed on a number of questions related to continuous bioprocessing and a summary of some of the key responses is highlighted in Figure 1. The profile of the survey respondents were approximately 50% biopharma companies, 30% academia, 15% vendors, and 5% government organisations with the majority in process development, manufacturing science and technology (MSAT) or research roles.

The survey tackled the question of what a facility of the future might look like and the majority envisioned hybrid facilities with batch and continuous operations, with scale-out or numbering up principles rather than large scaled-up facilities and with ballroom designs. The survey aimed to assess also how many companies were serious about implementing continuous processes. The survey revealed that 40% of respondents were developing continuous and integrated platforms for products starting in Phase 1 and 20% in Phase II or post approval. This suggests a significant shift from previous conferences where there was a large effort in evaluating and demonstrating the potential of continuous processes without necessarily commitment in clinical programs.

Hurdles and challenges were addressed from two perspectives, the conceptual design phase and commercialization. During early decision-making, the top 4 hurdles to implementing continuous facility design concepts were complexity and risk (65%), lack of GMP technologies (50%), comparability or quality issues (30%) and management buy-in (28%). Moving towards commercialisation, the keywords that captured major challenges were validation, control, quality and definition as the sector comes to terms with new equipment and a greater need for automation and mechanisms to deal with deviations. Regarding the most important areas of Process Analytical Technologies needed for successful continuous and integrated bioprocessing, popular responses were online and inline sensors, monitoring, models for process understanding, and robustness capabilities. On the most effective mechanism for developing new processes and equipment for ICB, the majority of respondents indicated that collaborative ways forward were preferred with vendors or utilising open-source technologies developed in consortia.

This Special Issue of BTJ on the conference theme of "**Integrated Continuous Biomanufacturing: Industrialization on the Horizon**" captures some of the presentations and discussions from the ICB III conference across a range of topics from state-of-the-art technologies in continuous upstream, downstream, and drug product unit operations through to end-to-end continuous processes. Case studies for the implementation of continuous platforms were presented for these processes covering perspectives such as scale-down mimics, control strategies and cost of goods analysis.

On the upstream front, there are 4 articles on perfusion cell culture. More specifically, Sanofi (1) demonstrate reduced process and product heterogeneity in perfusion cell culture compared to fed-batch processes, ETH in collaboration with Merck Biopharma and Jagiellonian University Poland (2) illustrate how to improve perfusion performance by growth inhibition, Boehringer Ingelheim (3) tackle product retention issues using larger pore size membranes attached to perfusion bioreactors, and Merck KGaA (4) provide recommendations for comparison of productivity between fed-batch and perfusion processes.

On the downstream front, Pall Biotech (5,6) explore the productivities and cost savings with continuous chromatography setups. There are also 2 contributions providing insights on continuous virus inactivation from Boehringer Ingelheim (7) and MilliporeSigma (8) with additional commentary from BOKU (Austria) (9).

On the end-to-end front, MedImmune (10) share experiences implementing a fully integrated continuous antibody process with commentary on productivity and cost of goods impacts.

In addition to biologics drug substance manufacture, the Special Issue also includes a review article from Insmed and UCL (11) investigating how some of the biopharma continuous concepts might apply to liposomal drug products.

We sincerely thank all the authors and reviewers for their contributions to this Special issue as well as all those that contributed to the success of the ICB III conference. We look forward to the upcoming ECI ICB IV conference (Brewster (Cape Cod), Massachusetts, October 6-10, 2019) to bring together the community once again and advance the adoption of continuous bioprocessing in the sector.

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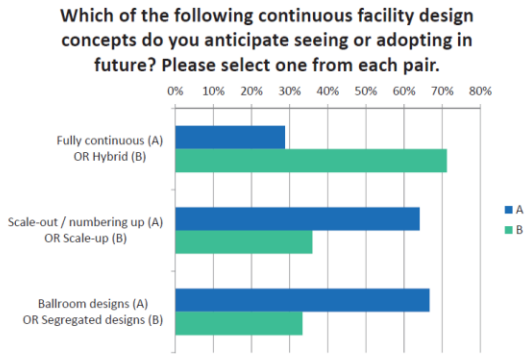

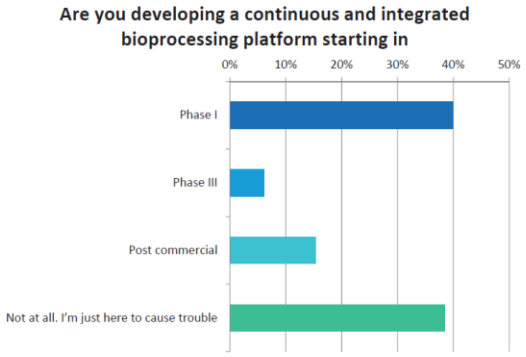

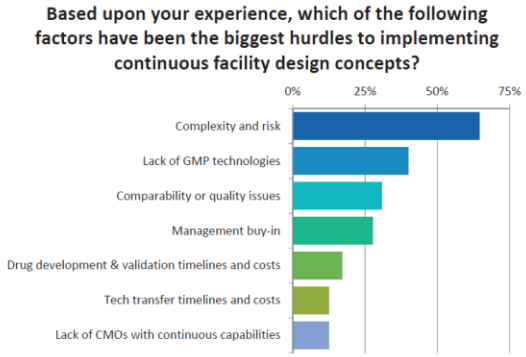

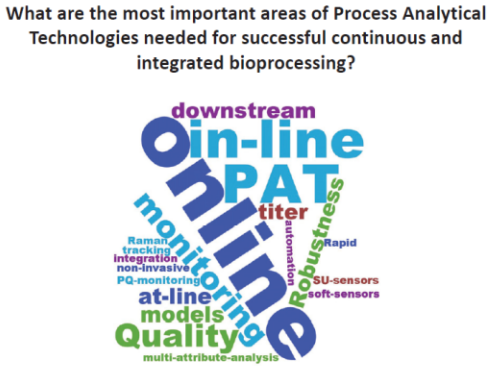

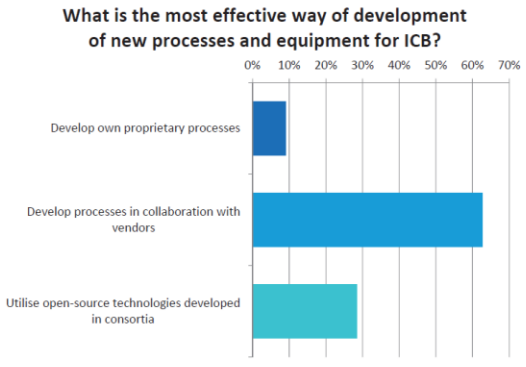

Figure 1. Summary of key survey responses from the ECI Integrated Continuous Biomanufacturing III (ICB III) Conference, Cascais, Portugal, Sep 17-21, 2017.