Enabling platform technologies: an industry perspective on enabling platforms and prior knowledge

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Overview

- What are platforms and prior knowledge?
  - *A look back and a look forward*
- An EFPIA perspective (using principles from the Nov EMA QIG L&L):
  - *The importance of platforms and prior knowledge*
  - *Tools and Enablers*
  - *Future considerations*
- Conclusions

Examples of Platforms

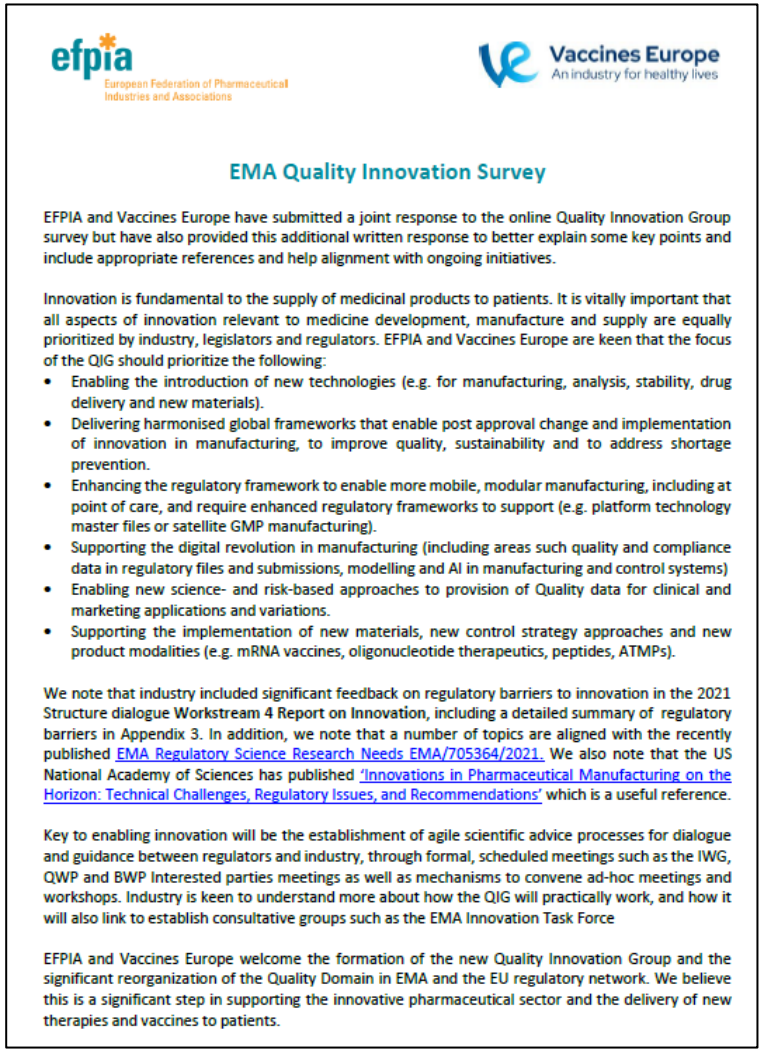
- **In Quality and manufacturing, platform is a diverse term:**
  - **Manufacturing platforms** (eg continuous tableting or continuous formulation) and their **control strategies** (eg parametric, analytical or model based controls)
  - **Analytical procedures**
  - **Active substances and excipients** (eg synthetic oligonucleotides, ADCs, conjugated vaccines, mRNA vaccines)
  - **Formulations**
  - **Devices**
- A platform can also include combinations of any/all of the above
- EFPIA support the EMA QIG principle that: ***a coherent body of prior knowledge data can be ring-fenced as a 'platform'***

Extract from 2022 EFPIA and Vaccines Europe Feedback on EMA QIG survey

- *"Supporting the **digital revolution in manufacturing** (including areas such as quality and compliance data in regulatory files and submissions, **modelling and AI in manufacturing and control systems**).*

- *…Enhanced regulatory frameworks to support (e.g. **platform technology master files** or satellite **GMP manufacturing**)*

- *…Delivering harmonised global **frameworks that enable post-approval change** and implementation of innovation in manufacturing, to improve quality, sustainability and to address shortage prevention."*



efpia
European Federation of Pharmaceutical Industries and Associations

Vaccines Europe
An industry for healthy lives

EMA Quality Innovation Survey

EFPIA and Vaccines Europe have submitted a joint response to the online Quality Innovation Group survey but have also provided this additional written response to better explain some key points and include appropriate references and help alignment with ongoing initiatives.

Innovation is fundamental to the supply of medicinal products to patients. It is vitally important that all aspects of innovation relevant to medicine development, manufacture and supply are equally prioritized by industry, legislators and regulators. EFPIA and Vaccines Europe are keen that the focus of the QIG should prioritize the following:

- Enabling the introduction of new technologies (e.g. for manufacturing, analysis, stability, drug delivery and new materials).
- Delivering harmonised global frameworks that enable post approval change and implementation of innovation in manufacturing, to improve quality, sustainability and to address shortage prevention.
- Enhancing the regulatory framework to enable more mobile, modular manufacturing, including at point of care, and require enhanced regulatory frameworks to support (e.g. platform technology master files or satellite GMP manufacturing).
- Supporting the digital revolution in manufacturing (including areas such quality and compliance data in regulatory files and submissions, modelling and AI in manufacturing and control systems)
- Enabling new science- and risk-based approaches to provision of Quality data for clinical and marketing applications and variations.
- Supporting the implementation of new materials, new control strategy approaches and new product modalities (e.g. mRNA vaccines, oligonucleotide therapeutics, peptides, ATMPs).

We note that industry included significant feedback on regulatory barriers to innovation in the 2021 Structure dialogue Workstream 4 Report on Innovation, including a detailed summary of regulatory barriers in Appendix 3. In addition, we note that a number of topics are aligned with the recently published EMA Regulatory Science Research Needs EMA/705364/2021. We also note that the US National Academy of Sciences has published 'Innovations in Pharmaceutical Manufacturing on the Horizon: Technical Challenges, Regulatory Issues, and Recommendations' which is a useful reference.

Key to enabling innovation will be the establishment of agile scientific advice processes for dialogue and guidance between regulators and industry, through formal, scheduled meetings such as the IWG, QWP and BWP Interested parties meetings as well as mechanisms to convene ad-hoc meetings and workshops. Industry is keen to understand more about how the QIG will practically work, and how it will also link to establish consultative groups such as the EMA Innovation Task Force

EFPIA and Vaccines Europe welcome the formation of the new Quality Innovation Group and the significant reorganization of the Quality Domain in EMA and the EU regulatory network. We believe this is a significant step in supporting the innovative pharmaceutical sector and the delivery of new therapies and vaccines to patients.

Fourth listen-and-learn focus group meeting of the Quality Innovation Group

Event

November 2024

The focus of the Quality Innovation Group's (QIG) fourth listen-and-learn focus group meeting with representatives from academia and industry is on:

1. Platforms for medicinal products manufactured using prior knowledge, such as common manufacturing platform approaches (multiple MAs).
2. Platforms for medicinal products against agents which are or have a potential to cause serious cross-border threats to health e.g. pandemic/pandemic preparedness (one MA).
3. Platforms for the manufacture of personalised or individualised medicines ('one patient/group of patients-one product', one MA) e.g. covering different ultra-rare orphan indications.

The aim of the meeting is to discuss key points identified, outlining examples of platform technologies compliant with any of the three categories above and focusing on the scientific challenges and data required to corroborate the proposed 'platform,' in line with the considerations included in the linked call for case studies document.

How do platforms and prior knowledge connect?

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

22 March 2018
EMA/CHMP/BWP/187162/2018
Human Medicines Research and Development Support Division

Meeting Report:
Joint BWP/QWP workshop with stakeholders in relation to prior knowledge and its use in regulatory applications
23 November 2017, European Medicines Agency, London

Principles Agreed at the 2017 workshop are still applicable and widely understood:

"Concepts such as platform knowledge, platform technologies, platform design space can be used to apply such knowledge "

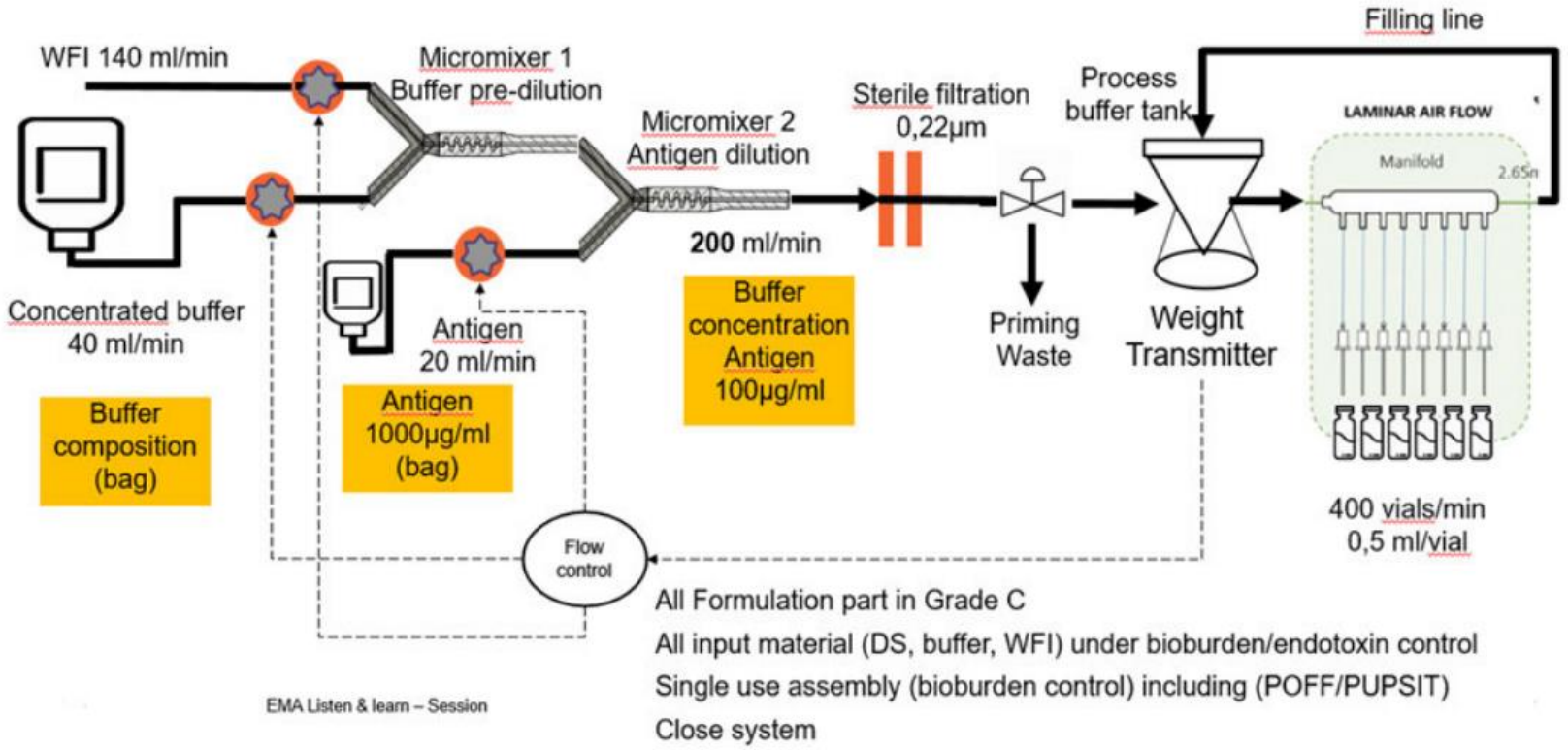
In such cases, the applicability, or qualification, of a platform to a new molecule is a key consideration."

"There may be a need to adapt a product's development (i.e. 'trade-off') so that the prior knowledge remains relevant. In particular, in order to maintain the robustness and applicability of the platform, it may be necessary to exclude certain products which do not fit the platform."

Platform technologies and Prior Knowledge in Quality and CMC

- EFPIA welcomes the focus of the QIG on platform technologies and prior knowledge for manufacturing and quality.
- The significance of these concepts to patients and the modernisation of manufacturing cannot be overstated:
  - Rapid development, scale up and supply
  - Enabling innovation in manufacturing (eg continuous, DCM, model-based control strategies, advanced analytical methods, combination products….)
  - Enabling development of new, complex active substances, finished products and devices
- At the 2017 EMA prior knowledge workshop, EMA and industry agreed on the fundamental value of prior knowledge and the significance and complexity of presentation and approval in regulatory dossiers
- **EFPIA believes advancement in regulatory science and processes enabling the use of prior knowledge are essential to the further development and deployment of platforms & use of prior knowledge**

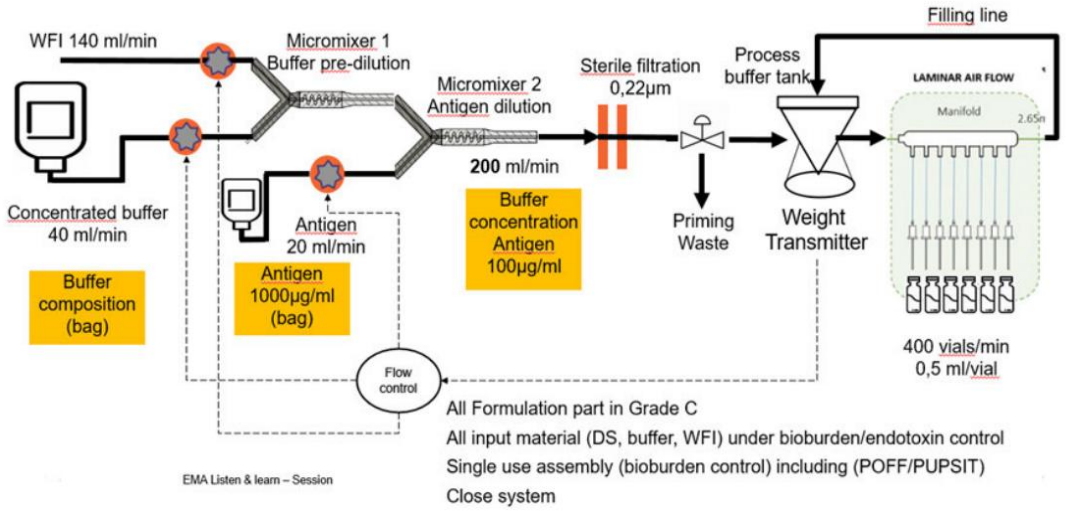
Example: Continuous Formfilling Platform



- *Control of CQAs (eg concentration of antigen)*
- *Can be controlled via hybrid models comprising derived via empirical studies, CFD simulations, multiple sensor inputs ....*
- Differing degree of parametric and analytical controls, options for RRT

2023 EMA QIG listen and learn: Link to Meeting Report

Example: Continuous Formfilling Platform

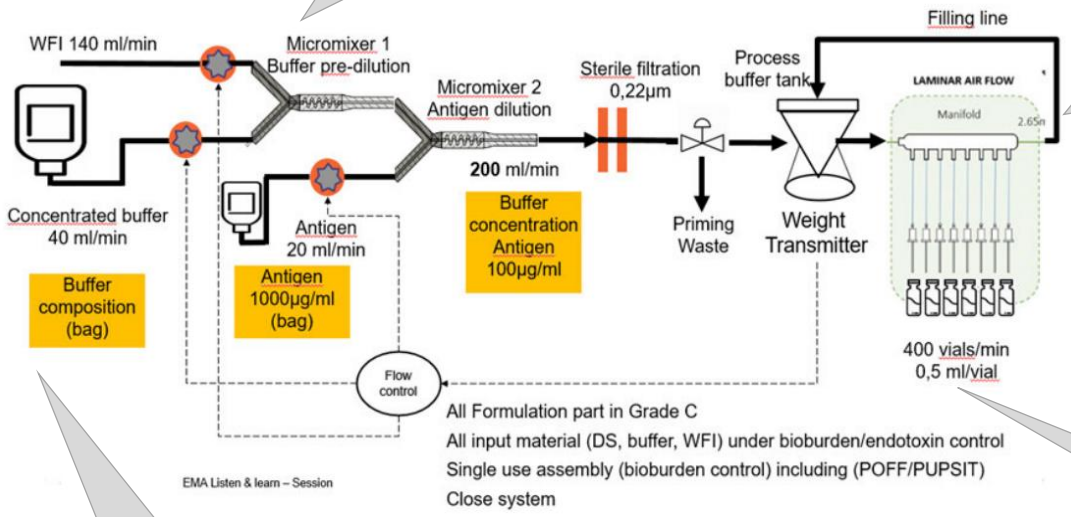


- Continuous biological manufacturing platforms are being widely developed
- The manufacturing equipment is applicable to many products
  - Basis of applicability considers pre-defined criteria (eg concentration, dosage volume, antigen amount, viscosity…)
  - GMP principles are standard
    - Sterility, cleaning, start up, shut-down, facilities
  - Control strategies can be standardised product to product
    - Product CQAs
    - Process control strategy (CPPs, IPCs, PAT, RTD/divert to waste….)
    - Model based controls may differ but be broadly applicable
  - Manufacture could be decentralised
- Development and validation could be highly streamlined: focused on verification of the prior knowledge

Example: Continuous Formfilling Platform

New sites, buildings facilities

Additional material feeds



Equipment improvements and adaptations

- Similar platform could be developed by many companies
- Individual platforms will also evolve

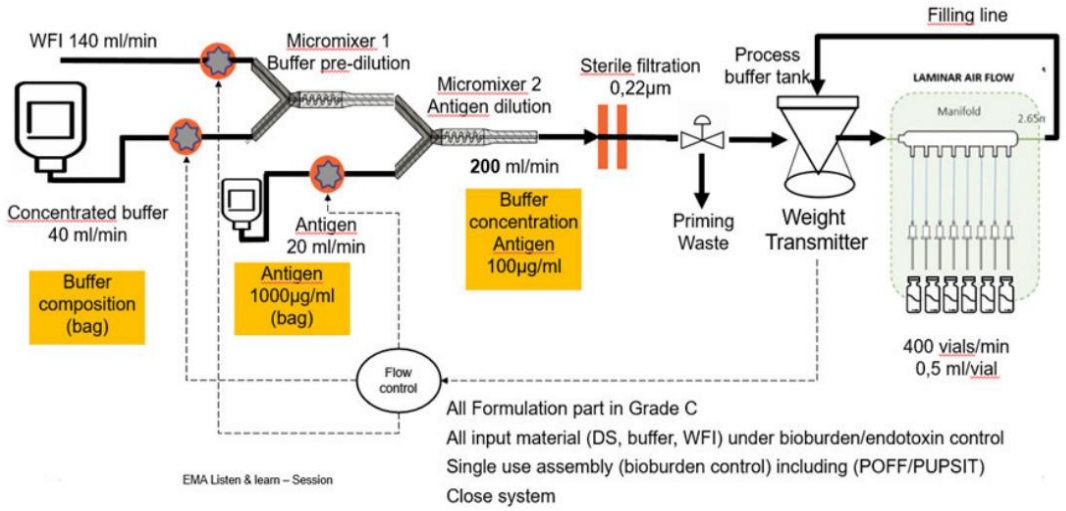
Refinement of process model controls (eg digital twin)

Additional, improved PAT controls, soft sensors

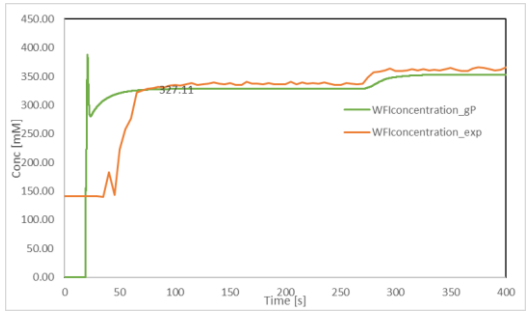
Changes to input material criteria

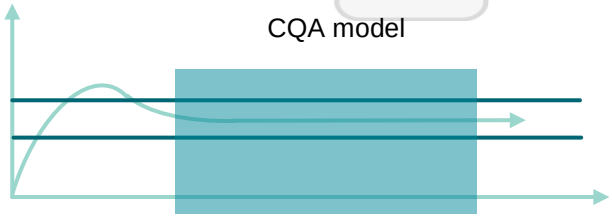
Platform enables digital approaches

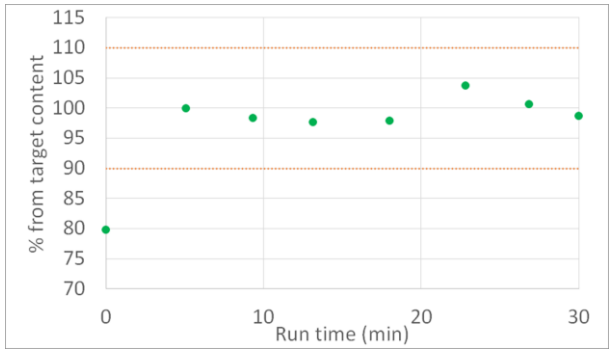
- Digital tools are being developed to augment process development and rapid development, scale up and supply



***In silico* tools to augment process development and platform digital twin to further reduce empirical development work and plant time**







- How to enable the use of the platform and its continuous evolution ?
- The regulatory framework and certainty will be critical - **regulatory science is a key factor for success.**

Regulatory Tools and Enablers

Innovation in regulatory-science is critical to enable industry to exploit the potential of platform's and prior-knowledge

Actions for the EU regulatory framework:

- Develop a scientific platform technology' guidance, considering the opportunities afforded by the new Platform Technology Master Files approach
- Aligning to other global platform technologies' initiatives, like the US FDA Platform Designation, in the spirit of enhancing global harmonization
- **Leveraging the industry's expertise and willingness to support regulators efforts***
- Transitioning to an assessment approach that is a mixture of platform and product specificities
- Authorizing platforms and not only products

* EXPANDING MASTER FILES FOR HUMAN MEDICINAL PRODUCTS IN THE EU/EEA

EFPIA/Vaccine Europe

Principles of a PTMF

EFPIA/VE believe the following principles regarding content and procedure are applicable for the new EMA(Quality) Platform Technology Master Files fulfilling the legislative definition of a platform under the EU GPL.

Enable implementation of use for platform's prior-knowledge in the regulatory framework as:

- Most platforms will be company own/specific
- In some cases, regulatory mechanisms for ensuring confidentiality between companies might be needed, similar to the ASMF
- The PTMF should work for all types of platforms
- The PTMF should be useable for MAAs and CTAs
- A PTMF would use sections from the CTD, but be a standalone document
- Initial PTMF authorization can occur as part of a marketing authorisation or variation – no need for separate, prior approval
- A PTMF can be updated via variations over the lifecycle (and changes enabled via a dedicated PACMP)

* EXPANDING MASTER FILES FOR HUMAN MEDICINAL PRODUCTS IN THE EU/EEA

Other Considerations

November 2024 EMA QIG Listen and Learn

- Examples and feedback from industry, academics and regulators

Revision of the EU General Pharma Legislation

- Initial draft focused on expanding the concept of the ASMF
- Industry feedback has focused on PTMF
- Next steps?

EU Variations framework, ICH (M4Q and Q12)

- Need to future-proof the regulatory framework (different CTD structure, cloud based….)

Reliance and recognition

- Platform technology, prior knowledge, PTMF recognition internationally

Summary and Conclusions

Regulatory science is a critical enabler for the use of platforms and prior knowledge

Innovation can be enabled or disabled by the regulatory frameworks and expectations

Global Harmonization and reliance are essential for industrialisation

Collaboration is the key enabler

Back-ups

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Meeting Report:
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The concept of master files as a tool for presenting prior knowledge was suggested by industry, in order to avoid redundant assessments. It was highlighted that an extended use of master files (e.g. for biologicals, excipients / packaging materials) is not possible under current EU legislation. If dossier content is identical to earlier submissions, the same full information (e.g. on excipients, packaging material) must be submitted within the new dossier. While it was agreed by regulators that the use of master files can avoid redundant reassessment of the same documentation in certain situations, it was noted that the master file concept alone cannot support the design of products, processes and control strategy. A challenge to the master file concept is that prior knowledge needs to be presented in the context of the application under assessment and not in isolation.