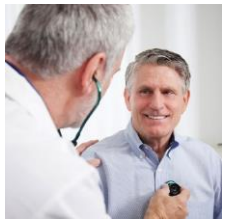
European Federation of Pharmaceutical Industries and Associations

Vaccines Europe

Establishing Platform Technology Master Files for human medicinal products in the EU/EEA

Mihai Bilanin (GSK) on behalf of the PTMF WS






Update of EFPIA MQEG BioManufacturing WG/VE
CASSS Oct 17, 2022

Problem statement

- In EU/EEA there is ***no regulatory mechanism today to protect the proprietary confidential information*** between collaborating parties (e.g. the IP owner and MAHs) for biologicals, platform technologies, materials used in biological manufacturing, novel excipients or ATMP products as exemplified by challenges recently observed for the co-development of Covid-19' therapies.

- There is further ***no regulatory mechanism to avoid re-submission or re-review of same data used in multiple regulatory applications***.
  - EFPIA proposed in 2017 at the BWP/QWP Prior knowledge (PrK) workshop [1] *"to consider the Use of a 'Master File' (DMF-type approach) as a way to gather prior knowledge information, where the relevant information can be reviewed and approved once by a competent authority and then cross-referenced in subsequent submissions. As the information needs to be kept current, use of a DMF would also facilitate lifecycle management through ongoing data maintenance and exchange with regulators."*

- Only a ***few MF options today*** in EU/EEA like the ASMF (*small molecules – excludes biologics*), VAMF/PMF (*limited use due to full disclosure needed*) for human medicinal products

- PTMF introduced for Vet Vx … innovative technologies only, ***no PrK data, complex EMA procedure***

Scope and expected deliverables

In scope:

- Focus on ideas/approaches for improving the current MF-based approaches in EU/EEA.
- Use as starting point for PTMFs the best features of current EU/EEA and global mechanisms

Primary objective:

- Advocate for the expansion the EU MF concept to a comprehensive MF system (e.g., FDA DMFs)
  - Extend and expand recent EU VetVx PTMF guideline to Human Medicinal Products (including PrK data)
  - Expand the use of EU ASMF for other type of materials, including Biologicals and others
  - Implement the industry recommendations made at the 2017 QWP/BWP prior knowledge (PrK) workshop

Deliverables:

- Gather input from industry and regulators, e.g. via a presentation at international conferences (CASSS) and interaction with EMA via QWP interested parties meeting (May 3 2022)
- Provide industry comments in support of new guidances (e.g., CVMP procedural PTMF guidance)
- Publish a position paper focusing on EU/EEA regulatory pathways to introduce the use of PTMF incl. best practices from other jurisdictions and MF compliance related aspects (e.g., Biologicals).

Regulatory position paper (focus)

- This paper is proposing:
  - the ***extension of veterinary' Vx Platform Technology Master File*** (vPTMF) to also apply to human medicinal products (not only Vx) and to also include platform (PrK) type data
  - that the existing ASMF should apply to other types of medicinal products (e.g. human medicines, including materials, components, DS intermediates, biologicals , excipients…
    - No regulatory impediment to introducing MFs for a biopharmaceutical (similar to API) has been identified except for the MAH' certification for the DP quality in the absence of full access to Restricted Part (*i.e.*, basis of ASMF exclusion of biologicals)
    - Discussion ongoing on certifications of MF or as part of the 1.6.1 QES certification
  - ***Case studies outlining briefly how a more flexible EU/EEA legal framework*** could allow for and facilitate an extended, flexible and modular use of Master Files are provided.
  - In Annexes, ***a summary analysis*** of
    - Challenges and limitations of the current EU/EEA MF approaches
    - Global (USA focus mostly) flexible/best approaches on MFs (content & procedural).

Regulatory position paper (proposed approach)

Existing EU/EEA MFs →	Proposed elements and applicability of updated MF approach in EU/EEA	← *Desired* EU/EEA MFs
	Procedural and legal aspects (to apply to all master files types)	
Legend: (***existing***) ✓ (***partially existing***) ✓	MAH takes full responsibility for the medicinal product, including any use/reference of MF ***Usage during the CTA*** (Clinical development) stages as well beside the MAA registration ***3rd party IP protection*** (e.g., Open and Closed parts of the MF, independent MF Holder possible) ***Avoid inclusion of the same information*** in the MAAs as in the MF (already certified) Same MF data ***Reviewed and Certified only once*** at 1st use (EMA or NAT but recognized by ALL) MF updates and of related MAAs by MAH, as applicable based on the Q, S, E impact ***Consistency of data and simplify the complexity*** of maintaining the MF and MAAs information	**Flexible, modular MF approach with different MF types like:**
PTMF (***Vet Vx***, 2022) ✓	***Manufacturing and Process Capabilities*** ***Platform to not be defined only as an innovative technology or manufacturing process*** ***Innovative and emerging technologies*** (3D printing, NGS, mRNA, viral vectors etc) ***and materials*** ***Platform***: synthesis and purification process ***and data*** : cell lines and/or culture conditions for multiple biotech DP : continuous manufacturing (chemical and biologics) : viral inactivation and purification steps : coupling procedure of a linker or payload for an antibody-drug conjugate ***Product Attributes type data (use of PrK) like*** ***Platformization of PrK data*** for specifications, novel analytical technologies data and method validation (e.g., HCP ELISA when the same parent cell line is used, see ICHQ14) ***Sets of data (PrK) applicable to multiple products***: stability data (profile, models & degradation patterns of like molecules), validation or qualification type data, ***facilities or CMO information, platform integral devices*** constituent parts of drug-device combinations	- ***PTMF***
ASMF (2003) ✓ **P/VAMF**(2004/05) ✓	***Materials and components like*** ***Biologics (including ATMPs)*** Small molecules (API) Blood and or Vaccine products ***Novel or non-compendia Excipients, Packaging or CCS*** ***Others***: linkers/payload used in manufacture of an antibody-drug conjugate, starting materials, parenteral cell lines, DS intermediates, conjugates, complex media, WFI supplied as DP, adjuvant	- DS (API ✓, ***biologicals, DS intermediates and materials used in their preparation, or DP*** - ***Novel Excipients, including Adjuvants*** - ***Packaging/CCS***

Regulatory position paper (conclusion)

- This paper is also highlighting the benefits of a platform and flexible MF approach, such as enabling industry and regulators to
  - leverage PrK gained from a particular platform/material and apply it to other products
  - have a central, "*one review*" of MF and reliance of its assessment and certification
  - enable the review and implementation of such platforms in a coordinated manner across all impacted products and support rapid innovation in new product development.
  - streamline and accelerate the review and approval by HAs in the subsequent use of such platforms for other products and/or for PACs to already approved platform technologies.

Final position paper expected submission for publication by end of 2022

Acknowledgement to the Working Group Members

13 participants, 11 Companies

Andrea Ruggiero, Merck,

Andrew Lennard, Amgen,

Carsten Amuel, Bayer,

Christina Juli, Boehringer-Ingelheim,

Helen Louise Newton, MSD,

Olga Sarnowska, Novartis,

Markus Goese, Roche,

Michele Schulz, Bayer,

Mihai Bilanin (*lead*), GSK,

Nadia Beaudoux, Lilly,

Nicky Tasker, AstraZeneca,

Sandra Hennig, Bayer,

Yves Bobinnec, Ipsen,

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Q&A and Discussions

Thank you