Use of Prior Knowledge and Platform Approaches: an EU regulatory perspective

CASSS meeting 21-23 October 2024

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Overview

What is Prior Knowledge?

- Prior knowledge includes company knowledge from development and manufacturing experience (e.g. experience based on similar compounds, products and processes) as well as reference to scientific and technical publications or application of established scientific principles e.g. within chemistry.

- References to Prior Knowledge and/or platform approaches appear throughout ICH guidelines Q8-Q14 and in various EMA guidelines.

Prior knowledge- EMA workshop 2017- Meeting Report

Prior knowledge

External & internal knowledge, evolution & transition of prior knowledge, extrapolation & justification of applicability

Using Prior Knowledge

Justifying use

Presenting prior knowledge in the dossier


EUROPEAN MEDICINES AGENCY

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

EMA Toolbox guideline on scientific elements, regulatory tools - PRIME MAs

EMA–FDA joint Q&As on Quality and GMP aspects of PRIME/Breakthrough therapy applications (europa.eu)

EMA Toolbox guideline on scientific elements, regulatory tools - PRIME MAs

- General
- Process validation (incl. concurrent validation)
- Control Strategy
- GMP
- Stability
- Comparability
- Regulatory tools

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

2 February 2021
EMA/CHMP/BWP/QWP/IWG/694114/2019
Committee for Human Medicinal Products (CHMP)

Draft toolbox guidance on scientific elements and regulatory tools to support quality data packages for PRIME marketing authorisation applications

Why use Prior Knowledge?

- **Knowledge gains:** opportunity for systematically building a large data package for a specific area
- **Efficiency gain**: accelerate dossier development of related dossiers especially for rare conditions
- **Efficiency gain**: assist the assessment process
- **Accelerate patient access** to medicinal products e.g. emergency situations

How to justify use of prior knowledge?

- **Context** and **relevance**

  Show applicability of the prior knowledge to the new product

- Explain and **justify**

  Clearly describe the extent of prior knowledge

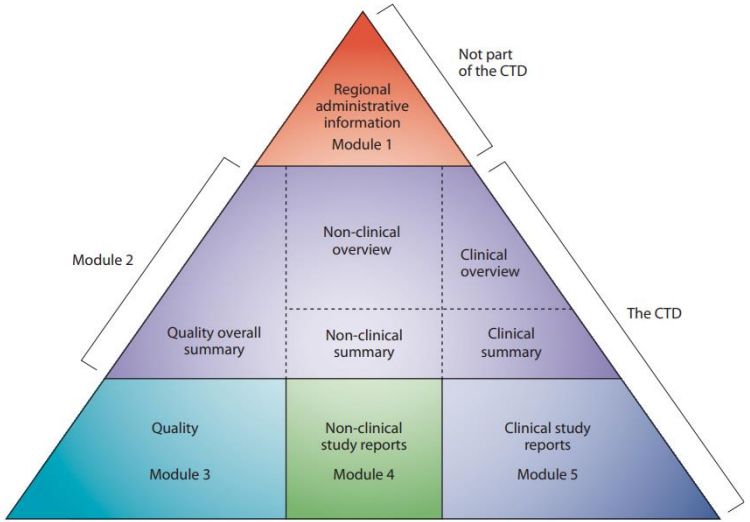
Use SA if needed*

*Scientific advice and protocol assistance | European Medicines Agency (EMA) (europa.eu)

How to present prior knowledge in the dossier?

- The information should be in the **appropriate dossier location**

- Consider the **level of granularity** needed.
  - *Inclusion of large data sets out of context are not beneficial to review-summary discussion useful*
  - *Differentiate between prior knowledge and new product data*



Examples of use of prior knowledge

- **Seasonal influenza vaccines** – degree of prior knowledge accepted, relies on relatedness/ prior knowledge of related authorised strains & minimises data required for annual updates

- **COVID Vaccine MAs -** first four initially approved vaccines had legally binding specific obligations (SOs) for deferred data (post-approval) in the context of the emergency benefit/risk. For one of these products however, use of prior knowledge avoided SOs for control strategy, specifications and stability.

- **COVID vaccine updates** - several variant updates approved for mRNA vaccines and one update for a recombinant vaccine; use of prior knowledge reduced submission requirements.

Key CMC flexibilities + manufacturing experience /GMP during COVID-19 vaccine MAA	Vaccine A	Vaccine B	Vaccine C	Vaccine D
Sufficient manufacturing experience for MA in view of B/R	√	√	√	√ Prior Knowledge, platform data
GMP issues during rolling review	√ GMP (sites)	√ GMP (sites)	√ GMP (sites)	√ GMP (sites)
Control strategy/specifications flexibilities	√ some outstanding data, incl. for excipients, impurities. Additional characterisation data required –SO	√ some outstanding data incl. characterisation data required –SO	√ additional output parameters agreed-for review after PV completion- REC. Spec to update-SO	√ limited remaining data-confirm criticality of assigned CPPs-> REC
Comparability flexibilities	√ limited commercial data & characterisation issues- SO	√ limited commercial data-> complete package-SO	√ complete the package-> review comparability ranges post-auth -SO	√ complete the finished product package- SO
Process validation flexibilities	√ concurrent-SO	√ concurrent-SO	√ concurrent-SO	√ concurrent-SO
Stability flexibilities **SO= specific obligation** **REC= recommendation**	√ limited real-time & commercial-SO	√ limited real-time & commercial-SO	√ limited real-time & commercial, review spec-SO	√ limited real-time & commercial-but platform data- REC

What is a Platform Approach?

ICH Q11 glossary;

- "**Platform Manufacturing:** The approach of developing a production strategy for a new drug starting from manufacturing processes similar to those used by the same applicant to manufacture other drugs of the same type (e.g., as in the production of monoclonal antibodies using predefined host cell, cell culture, and purification processes, for which there already exists considerable experience)"

- Platforms make more widespread and systematic use of prior knowledge.

- However, in the EU, legislative provisions for 'platforms' are being drafted.

Platform Technologies in new EU pharma legislation proposal

EC proposal part of article 15 with fixed dose combination medicinal products:,

"a medicinal product comprised of a **fixed component** and a **variable component** that is **pre-defined** in order to, where appropriate, **target different variants** of an **infectious agent** or, where necessary, to **tailor the medicinal product to** characteristics of an **individual patient or** a group of **patients**"

ENVI COMPROMISE AMENDMENT - Article 4 -paragraph 1- point 30 (new)

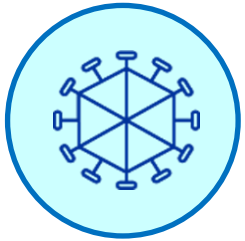
'platform technology' means a **technology or collection of technologies that is comprehensive, well-characterised, reproducible and used to support the development, manufacturing process, quality control, or testing of medicinal products or their components** that rely on prior knowledge and are established under the same underlying scientific principles.

Article 4 -paragraph 1- point 30b (new) introduces the notion of a '**platform technology master file'**

prepared by the owner of the platform technology, that contains data of a platform technology for which the underlying scientific principles, under which the platform technology is established, have reasonable scientific certainty to remain unchanged across products and to apply regardless of components added to the platform for a medicinal product;

EMA to prepare scientific guidelines on the requirements for an additional platform technology master file

Platforms: Using prior knowledge to establish a platform*



Can we use prior knowledge to approve **multiple viral vector-based therapeutics** targeting ultra-rare indications (personalsied medicines) in a **single platform MA**?

Can we utilise **prior knowledge** to establish an **siRNA platform** linked to **multiple MAs**?

Can we use prior knowledge to approve **multiple vaccines** containing different target sequences against an adapting pandemic virus in a **single platform MA**?

Can we utilise **prior knowledge** to establish a monoclonal antibody **platform** linked to **multiple MAs**?

* Note that EU legislative 'platform' definitions surrounding are currently being developed and these slides do not prejudice the outcome, nor do they confirm where platform data will be accepted.

Example: mRNA vaccine platform*

Can fixed and variable components in drug substance and drug product manufacturing process & control be defined to justify platform registration?

Which platform data are relevant?
Demonstrate & justify

Will the platform remain reproducible during lifecycle and for future linked products?

DS

Could include starting & raw materials, plasmid-platform but with adapted sequence?

Platform methods with specific adapted identity & expression assay?

Could platform stability model be useful, based on other relevant mRNAs - plus confirmatory data?

DP

Platform methods with specific adapted identity & expression assay?

Platform stability model useful, based on other relevant mRNAs plus confirmatory data?

* Illustrative example only; does not define data requirements for an mRNA platform

Analysis of 'platforms' from company requests from EMA SA, ITF* and company meetings 2017-2023**

- SAs, ITFs and BPMs of the last 5 years 2017-2023
- 29 uses of platforms were identified (15 from SA, 9 ITF, 5 Cy. meetings)
- Most frequently used for CMC/quality followed by NC and Clinical
- COVID-19 was the most common disease targeted
- 30% were for an ORPHAN designation
- Viral vector (particularly AAV) most frequently referred to

*ITF Supporting innovation | European Medicines Agency (EMA) (europa.eu)

**Information provided by Riccardo Saccà , Innovation and Development Accelerator (TRS-INO) office, EMA

Platforms- issues and future directions

- All companies and regulators don’t have the same understanding of what a platform is; very broad concept currently.
- Should a platform be restricted as to what can be registered & should there be limitations on access e.g. same MAH for a bio?
- How to permit cross-referencing of data across linked MAs?
- Will platforms be applicable to non-clinical and clinical data?
- A platform definition should not restrict the use of prior knowledge-> are we harnessing opportunities for more systematic use of prior knowledge
- What will be the format and location of platform data in the dossier?

Platforms- issues and future directions

- The robustness of the data needed to corroborate a platform (as for use of prior knowledge) requires understanding at company and regulator level- may be case specific.
- How will the lifecycle of the platform be maintained and how will it link to multiple products with their own lifecycles?
- What is the boundary between platforms and master files/ additional master files?
- Discussion can start now on **scientific challenges** in anticipation of future EU legislation.

Quality Innovation Group - Listen & Learn focus group meeting on Platform Technologies (19-20 November 2024)

Understand the landscape

Open dialogue with stakeholders, discuss **general/specific scientific challenges** with the use of platforms and **possible solutions**

Discuss case **studies** reflecting on level of **scientific data maturity**

comprising sufficient data of the active substance and/or finished product manufacturing process and control.

What are the fixed and **variable** components that define the platform?

How can the platform remain reproducible for linked (including future) products even during their lifecycle (i.e. there is reasonable certainty that the 'platform' can link to multiple products).

How should the platform **lifecycle** be managed to permit the platform to still apply to all linked products?

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Any questions?

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