Regulatory Perspective on the Applicability of Platform and Prior Knowledge in Product Development

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The Wonders and Woes of Biological Platforms

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Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

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A quality product of any kind consistently meets the expectations of the user.




Drugs are no different.


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Patients expect safe and effective medicine with every dose they take.
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FDA
Pharmaceutical quality is
assuring *every* dose is safe and effective, free of contamination and defects.
www.fda.gov


It is what gives patients confidence
in their *next* dose of medicine.
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Disclaimer

Please refer to any cited guidance, as this talk only refers to them at a high level. Specific regulatory issues need to be addressed with the relevant assessment team.

PLATFORM AND PRIOR KNOWLEDGE

Platform Technologies

General Platform Definition

- *A group of technologies that are used as a base upon which other applications, processes or technologies are developed (techopedia)*
- *A set of actions or ideas that form the basis for future development (Cambridge dictionary)*
- May be considered a subset of "prior knowledge" per ICH Q10
- May include "modular" unit operations where the considerations are independent of connection to other operations
  - ➢ Individual companies may develop their own platform(s)

Examples of Platform Approaches- mAbs

Discovery, Design & Optimization

- Target development & engineering
  - Lead selection (e.g. screening platforms)

Control Strategy

- Specifications (methods and acceptance criteria)
  - e.g., process-related impurities

Pharmaceutical Development

- Formulation & stability

Manufacturing Process

- Downstream Purification Design
- Modular impurity clearance
- Modular viral clearance

ICHQ11: 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)*

- A-mab case study applies the concept of platform and prior knowledge
  - e.g. Molecule design, formulation, manufacturing (upstream and downstream) process deign

CASE STUDY:

COVID-19 NEUTRALIZING ANTIBODIES

Examples of Platform Approaches Applied to COVID-19 Neutralizing mAbs

Lead identification

- e.g. collection of fully human antibodies generated by using humanized mice and convalescent plasma

Formulation & stability

- Most sponsors leveraged their own formulation studies from other antibodies
  - e.g. studies from previous molecules of the same isotype (e.g. IgG1)
  - Used a "platform formulation"
  - Accelerated stability studies (product-specific and other mAbs) were used to assess degradation profile and support real-time stability

Hansen et al., *Science* **369**, 1010–1014 (2020)
Taylor et al., *Nat Reviews Immunology* **21**, 382-393 (2021)
Kelly B. *Nat Biotechnol* **38,** 540–545 (2020)

Examples of Platform Technologies Applied to COVID-19 Neutralizing mabs

Manufacturing

- Most sponsors used mab platform manufacturing with little optimization
- Modular viral and modular impurity clearance was applied

Control strategies

- Most sponsors used a combination of product-specific and mAb platform methods
- Generally accepted acceptance criteria (e.g. process-related impurities) were applied
- Specs justification & risk assessment considered low probability of off-site target effects because the spike protein is a foreign target

Hansen et al., *Science* **369**, 1010–1014 (2020)
Kelly B. *Nat Biotechnol* **38,** 540–545 (2020)

How Did Platform Technologies help expedite development?

- Sponsors applied their own in-house technologies, platforms & knowledge in formulation, manufacturing processes, and analytical methods
- Platform manufacturing processes were used with little additional optimization
- In some cases, platform manufacturing processes start from in-house cell line to platform unit operations – no cell-line specific process development was applied
- In some cases, limited new technologies were created & applied for COVID - no time to experiment

How Did Platform Technologies help expedite development?

- Some sponsors conducted parallel development "at risk, up-front investments" - **no risk to patient safety**
  - e.g. using parallel processes expanding clonally-derived cell banks and non-clonal cell pools
  - Scale up and transfers were conducted in parallel
    - Worked closely with CMOs with experience manufacturing mAbs
  - High business risk tolerance

- Process optimization was not intended, or it was deferred for the BLA

  ➢ Agency's flexibility is contingent on this adequacy of the knowledge provided; not merely "less information"

Opportunities for drug development?

Yes, platform approaches were possible and worked for COVID-19 because we have been applying them already!

But

- Applicability of platform and prior knowledge is limited by the data and information submitted in an application
  - Industry should provide scientific rationale of the applicability of such knowledge to a particular product
- There are opportunities for leveraging industry's knowledge and this should be provided in the application
  - It is not sufficient to just say e.g., it is the same formulation or same process, etc.
- Platform and prior knowledge have been and can continue to be applied; however,
  - Industry needs to be willing to do the work up front and willing to share it (we don't know what you don't tell us)

THANK YOU FOR YOUR ATTENTION

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