CMC STRATEGY FORUM
ADVANCING BIOPHARMACEUTICAL DEVELOPMENT
NORTH AMERICA 2022

Celebrating 25 Years
WCBP
2022

Mini case study – Leveraging Analytical Prior Knowledge

WCBP January 2022

Facilitator: Kristi McKenzie, GlaxoSmithKline

Session Format

Objective	Discuss common approaches for establishing, assessing and leveraging analytical prior knowledge
Principles	• What is it? • How do we collect it? • How do we assess whether we can use it? • How do we decide if we are going to use it?
Case Studies	• Analytical Method Establishment • Analytical Technology Transfer
Open Discussion	• Share Thoughts and Experiences
Wrap Up	• Summary and Parting Thoughts

What is Prior Knowledge?

As a general concept “Prior Knowledge” is not new (e.g. referencing external publications). Referenced throughout ICH Q8, Q10 and Q11 documents and various US and EMA issued guidance

- ICH Q11: “Prior knowledge can include established biological, chemical, and engineering principles, technical literature, and applied manufacturing experience.”
- ICH Quality Implementation Working Group on Q8, Q9, and Q10 Q&As (R4): “Prior knowledge based on experience obtained from similar processes (internal knowledge, industry scientific and technical publications) and published information (external knowledge: literature and peer-reviewed publications)”

But there is no agreement on a systematic approach to managing and using prior knowledge

For our purpose here …

Prior Knowledge (PrK): Established process, product or method knowledge over multiple assets that, if demonstrated relevant, can be presented to strengthen scientific justifications in the regulatory submission for a specific asset

Where can we use Prior Knowledge?

ANALYTICAL METHOD DEVELOPMENT, VALIDATION AND TRANSFER

PROCESS DEVELOPMENT AND VALIDATION

CONTROL STRATEGY DESIGN AND DEVELOPMENT, STABILITY STRATEGY

How do we collect Knowledge?

The traditional model of knowledge management does not facilitate the use of prior knowledge.

- ❑ Knowledge is typically organized based on specific study and program
- ❑ Knowledge is typically unstructured, and data is segregated in various formats and systems

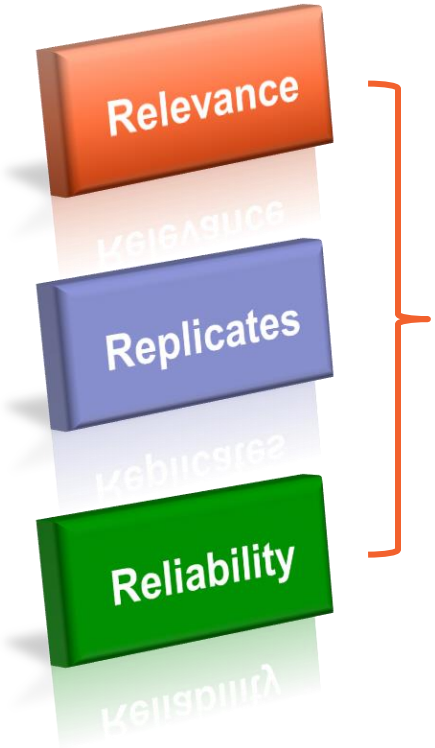
This clearly presents a challenge in presenting a prior knowledge justification to regulatory agencies.

ICH Q10: “Knowledge management is a systematic approach to acquiring, analyzing, storing and disseminating information related to products, processes and components.”

Building a good knowledge management system is the key enabler to efficiently use and soundly justify the relevance of prior knowledge in a QbD based development approach described in ICH Q8, Q9 and Q10.

How do we assess whether we can use Prior Knowledge?

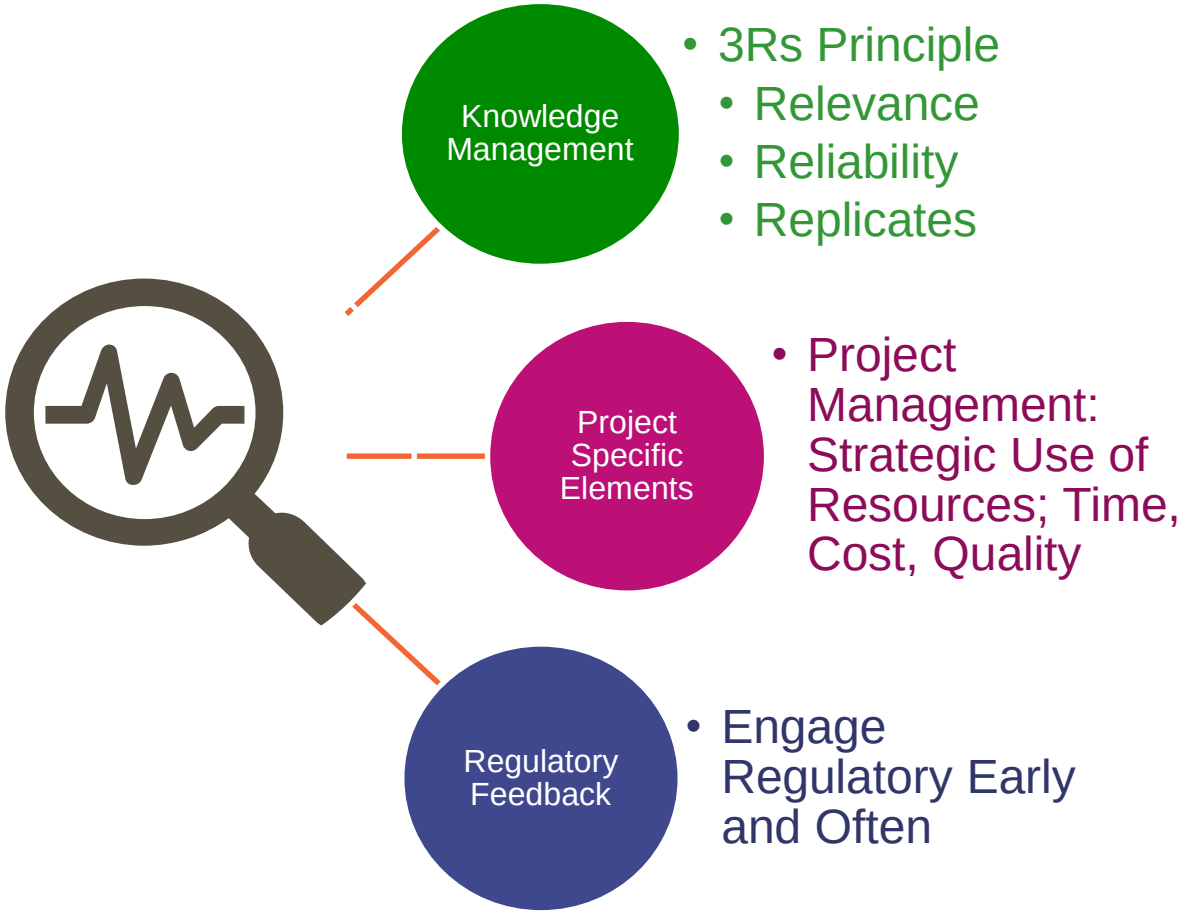
Applying the "3R's Principle"*



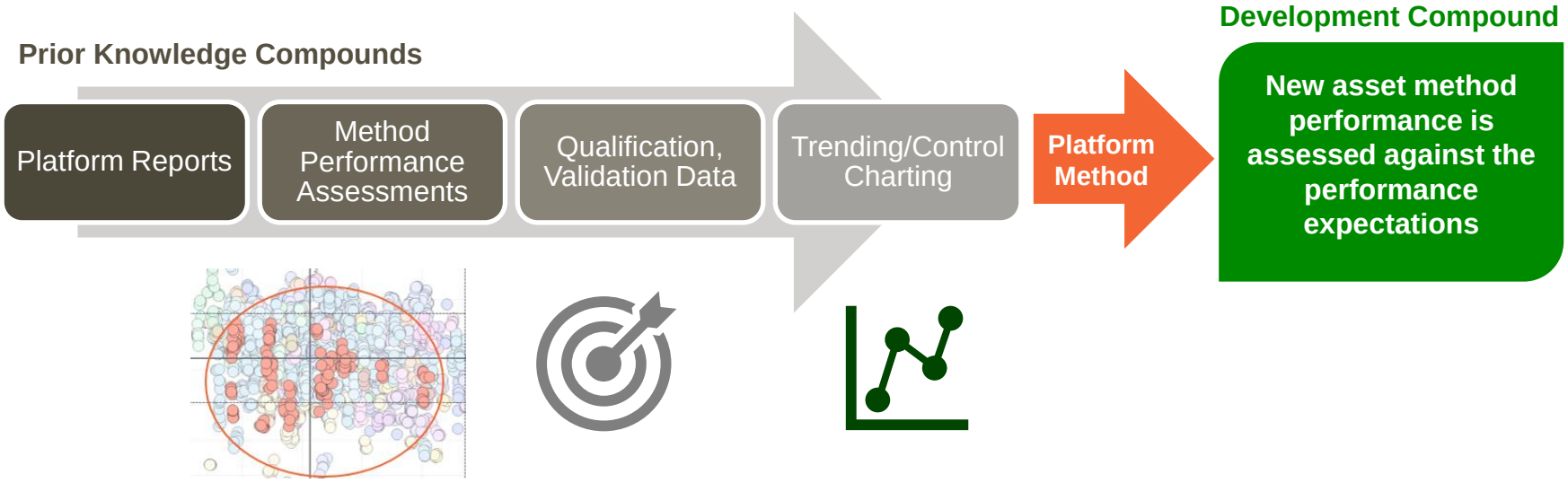
- *Method Relevance Assessment*: Establishing and documenting the similarity between the project method and the prior knowledge report
- *Method Performance Assessment*: Method performance is compared against prior knowledge examples with data visualization, control chart trending, and statistical assessments
- *Method Knowledge Matrix*: Summary of data and references for validation and transfer data for asset and prior knowledge examples allowing assessment of data integrity

**Melody Schmidt, Genentech, 2020 Biophorum CMC consideration for expedited development and WCBP presentation*
Frank Zettl, Roche, 2017 Joint BWP/QWP workshop on prior knowledge
Josefine Persson, Roche, 2018 CMC strategy forum presentation

How do we decide if we are going to use Prior Knowledge?

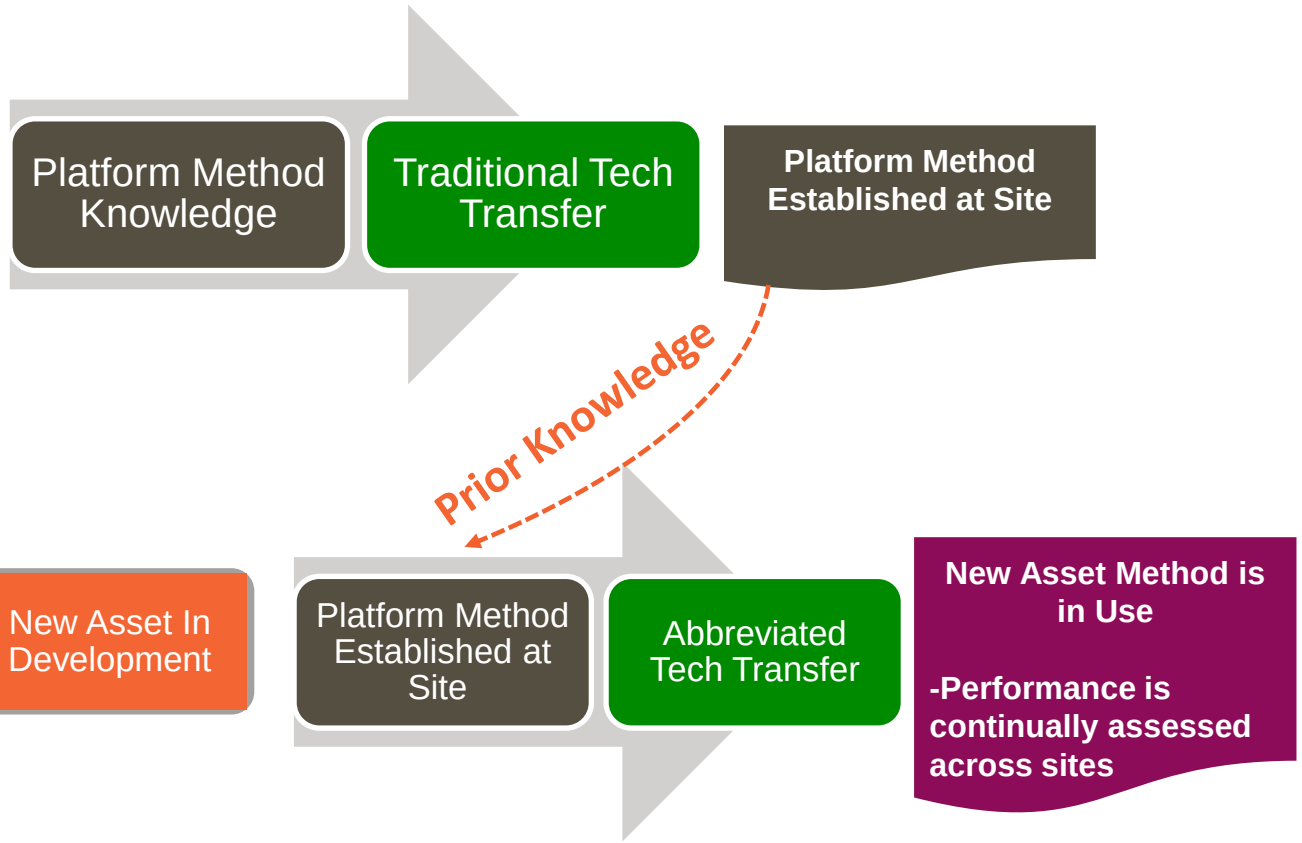


Case Study: Analytical Method Establishment

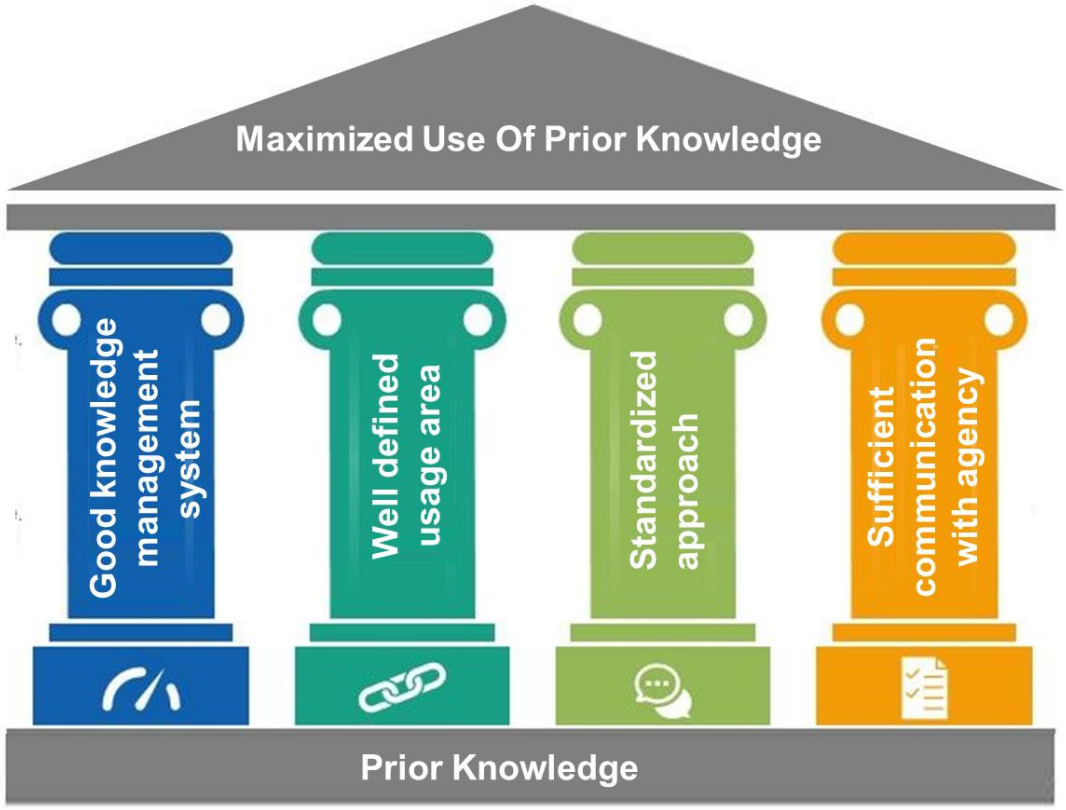


Case Study: Analytical Technology Transfer

- Size Exclusion Chromatography
- Capillary Gel Electrophoresis
- Capillary Isoelectric Focusing
- Residual DNA
- Residual Protein A
- Protein Concentration
- Residual Host Cell Protein



Benefits of Maximized Use of Prior Knowledge



Resulting in …

- Increased and more accessible product and process understanding
- Knowledge and data that can support accelerated development timelines
- A potential reduction in the amount of product specific wet lab work during analytical and process development, validation and transfer

Pitfalls to Avoid

Missed Timing

- Failure to plan as part of the integrated project plan
- Failure to engage regulatory early and often

Not using a systematic process

- Not going through a rigorous justification of relevancy
- Not maintaining justification throughout the process

Narrow focus

- When the justification to use prior knowledge becomes more difficult than executing the study, just do the study!

Open Discussion - What is your Experience?

- Have you considered establishing prior knowledge process? If not, what is holding you back?
- What are some challenges and benefits associated with establishing a knowledge management system?
- What are some challenges and benefits associated with establishing a systematic assessment process?
- Have you had success in leveraging analytical prior knowledge justification for:
  - ❑ Clinical Files?
  - ❑ Commercial Files?
- Regulators - do you have any examples of what to do? What not to do?

Summary and Parting Thoughts

There is the opportunity for significant long-term benefits through establishment and use of prior knowledge, including, but not limited, to strengthening analytical scientific justifications

Establishment of a knowledge management and standardized assessment process is an investment. This investment may translate to time and resource savings over time.

Establishing a PrK process is not about just reducing testing it's about maximizing the impact of scientific efforts and providing a comprehensive analytical package. One-off analytical exercises do not ensure real-world performance

Prior Knowledge assessments (e.g. historical method performance assessment) may become an expectation, especially in the context of accelerated analytical strategy