

Joint BWP / QWP workshop with stakeholders in relation to
prior knowledge and its use in regulatory applications

Subteam 3 –

How to Use Prior Knowledge in Process design and development - General Considerations

Ron Ogilvie , Director Regulatory Affairs, Pfizer

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Process Development Session Outline

Part I (25 min)

- Regulators Viewpoint (Dr. Sean Barry)-15min
- General Considerations, including small molecules considerations -10min

Part II (30 min)

3 Case Studies: 10 min each

- Prior Knowledge to optimize process characterization approaches, mAb (Amgen)
- Prior knowledge to optimize process validation approaches , mAb (Roche)
- Prior knowledge to streamline viral safety and resin lifetime studies (mAb and vaccine, EBE viral safety consortium & MSD)

Part III (30 min)

Q&A linked to case studies – 10 min

General Q&A and discussion – 20 min

Use of Prior Knowledge to Support Manufacturing Process Design and Development

- Prior knowledge is widely used in design and development of the manufacturing process for small molecule and bios entities
 - Prior knowledge of common DS and DP manufacturing operations and equipment
 - Underlying science e.g. of API chemical processes – kinetics etc.
- Development ‘risk assessments’ use prior knowledge and multi-disciplinary experience to inform experimental approach.

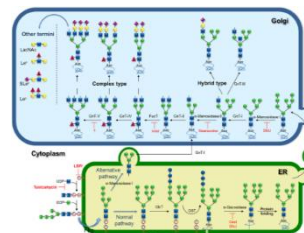
Technical Literature



Applied Manufacturing Experience Platform knowledge

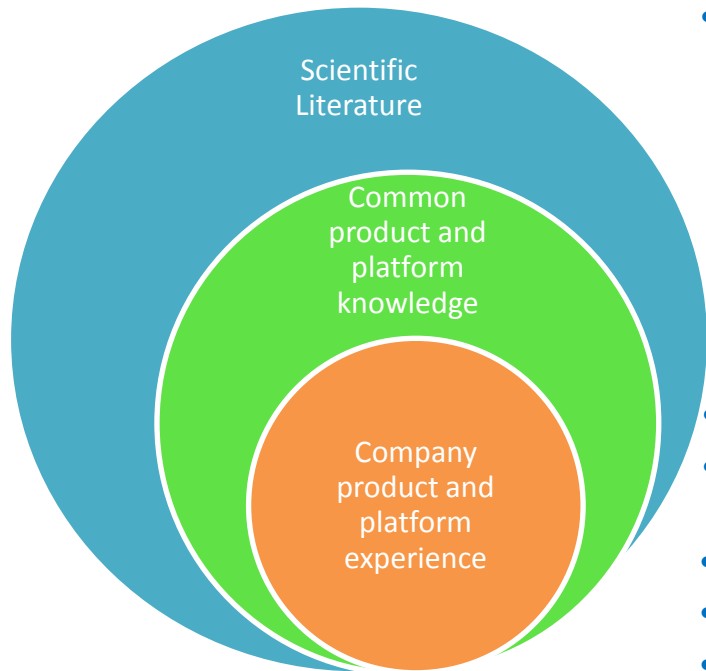


Common Scientific & Engineering Principles



Although prior knowledge is a dynamic concept, **developers and assessors need to share a consistent, scientific understanding of the available prior knowledge** in order to facilitate the development of products and the full implementation of ICH Q8-12

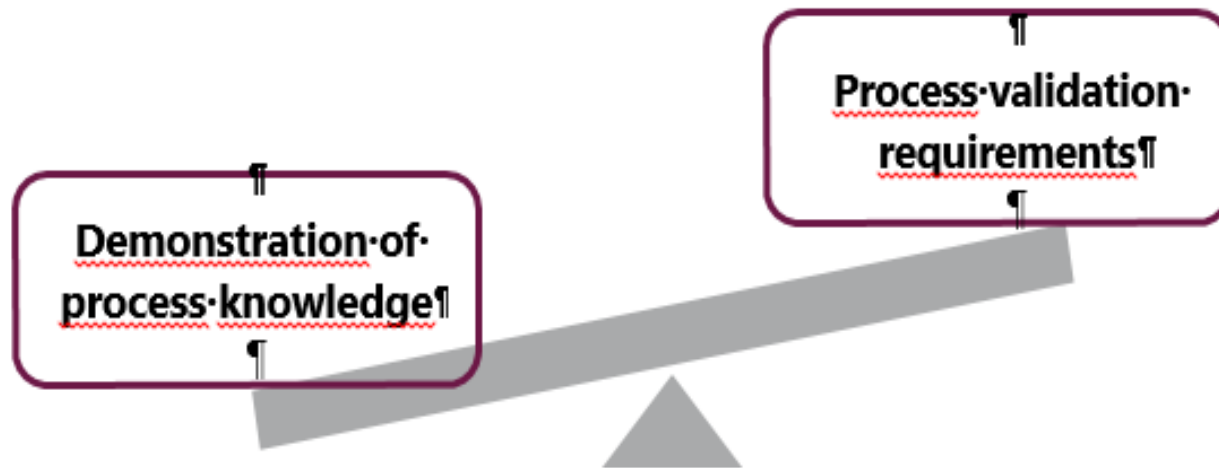
Knowledge from a variety of sources can be applied to support Process Design and Development



- **General Scientific knowledge, engineering principles and published literature**
 - Improve & harmonize processes – SME knowledge
 - Design & execute workplan (LCM & Projects) and performance dashboard
- **Common “understood” CQAs and CPPs for similar product/Process**
 - Equipment and engineering knowledge
 - Modeling and simulation
- **Data from Product Design and selection**
 - Early Process Design studies
 - Small scale and Clinical manufacturing
 - Modeling and simulation
 - Prior knowledge from similar product/platform
 - Process characterization

General Considerations – Prior Knowledge & Process Development

How knowledge and control approaches impact on process validation -



Whilst ICH Q8(R2) recognizes that the level of knowledge gained and not the volume of data provides the basis for science-based submissions and flexible regulatory approaches, ... the accumulation of prior knowledge, innovative technologies and platform process raise the need for a **common understanding of the level of demonstration** that is required.

Prior Knowledge in Small Molecule Process Design (DS)

Use of prior knowledge to design in chemical quality from the manufacturing process

- Exploit chemical knowledge to select route and process (efficiency, safety, environmental)
- Design of conditions and isolations to control side-reactions/degradation/ incompatibilities
- Prediction of GTI risks and their purge*
- Structural diversity can mask that underlying science is well known / predictable (mechanism and kinetics)

Use of prior knowledge to design in physical properties

- BCS class/bioavailability, polymorphism (predicting) and the Drug Product dosage form complexity
- Processes can be designed to control crystallisation kinetics – and hence the solid state, particle shape and size
- Prior knowledge / modelling used to understand particle size requirements and milling, conditions

Prior Knowledge in Small Molecule Process Development (DP)

Use of prior knowledge in manufacturing process development (platform knowledge)

- Platform understanding of similar products (types of dosage form, properties of excipients, API characteristics) manufactured using similar processes and equipment – Granulation, drying compression, coating - prediction of scale up etc
- Greater consistency in process and control strategy for continuous platform tablet manufacturing process

Use of prior knowledge to determine validation approaches

- Experience with selected manufacturing processes and equipment
- Link number of batches for validation with prior knowledge and manufacturing experience (small scale, development studies)

Prior Knowledge in Small Molecule Manufacturing + Lifecycle Management

Use of prior knowledge (engineering principles) to inform changes to scale & equipment

- Modelling of chemical reaction and mass transfer kinetics – prediction of scale up risks for certain reactions (heterogeneous, biphasic, hydrogenation) and scale up parameters
- Definition of the control strategy through scale dependent (e.g.) and independent (e.g.) parameters and controls
- Engineering understanding of scale-up drug product manufacturing processes - flow, blending, compression etc

Use of prior knowledge in life cycle management of changes

- Understand and model changes to the process conditions (parameters, input material attributes)
- Determination of the assessment strategy for implementation of changes (what to test and what to model).
- Prior knowledge to manage stability evaluation of a changed product – inc. predictive packaging science
- Use prior knowledge to manage change of analytical methods (e.g. critical method operating parameters)
- A PACMP is an example of use of prior knowledge

Summary: Use of Prior Knowledge in Process Design and Development

- Prior knowledge is widespread in small and large molecules development, for DS&DP
- Less experimentation to support process design and development may be appropriate when working in a well-understood and well-precedented areas
- Optimal use of platform and prior knowledge is of benefit to applicants and stakeholders
 - Rapid, efficient, consistent and science based approach to medicines development
 - Applicability of prior knowledge to product specific case needs to be justified
- Prior knowledge can be leveraged together with small scale manufacturing experience to optimise approaches to validation and post-approval change
- **Developers and regulators need assured scientific understanding and sharing of available prior knowledge in order to facilitate development and maintenance of products**