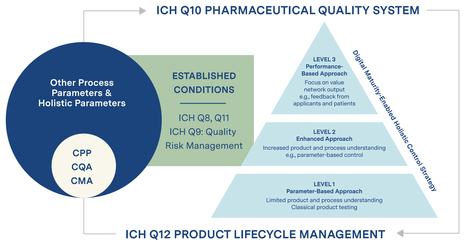
VALIDATION 4.0

As a work group within Pharma 4.0™ Special Interest Group (SIG) we work with GAMP SIGs, other ISPE groups, and the industry at large to develop and publish validation guidance for the pharma and biotech industry to allow us to maximise the digital innovation space while maintaining acceptable control and compliance.

The goal of Validation 4.0 is to develop a holistic, harmonized, risk-based approach to validation that incorporates the Pharma 4.0 working model, enabled by Digital Maturity and Data Integrity by Design, to align with, support, and facilitate timely utilization of current and future innovations in the pharmaceutical industry. To enable this, we need to break down the silos among computer system validation, facility, equipment qualification, product and process qualification, and the overall quality systems – and silos between manufacturers and regulators.

WHY NOW? NEW PARADIGMS

Control Stretegy



Process PPQ

Continuous vs Batch Processing
- Oral solid/liquid dose manufacturing has made progress
- Other processes, e.g. aseptic fill-finish, likely to follow suit

Distributed vs Closed Processing
- Shift from finished product testing prior to release to bedside manufacturing/delivery

Bulk Manufacturing vs Personalized/ Individualized Medicine
- How do we handle AQL/sampling with a batch size of one?

CPP-Based vs Holistic Risk Control
- Understanding non-CPP-related process risks (Data Integrity, etc.)
- Validating as verification of the Holistic Control Strategy

Algorithm-Based Process Control vs Heuristic Process Control
- Monitoring/adapting to changes to inputs (CMAs, CPPs) to deliver outputs (CQAs)
- Using machine learning to predict, self-adjust for process variability

DATA/CSV/CSA

Closed vs Open Data Flows
- Ensuring Data Integrity must include sanitization, validation, and consistency of data collected from open/uncontrolled sources
- Software as a Service (SaaS), Big Data, direct patient data (medical devices, etc.)

Siloed vs Connected IT Systems
- Validation assumes closed system (silo) containing combined manufacturing system and computer system
- HMI/data interactions are validated in discrete, extract-transform-load (ETL) model that rejects data from unknown sources
- How do we validate use of Big Data, distributed systems, uncontrolled source data (patients, etc.)?

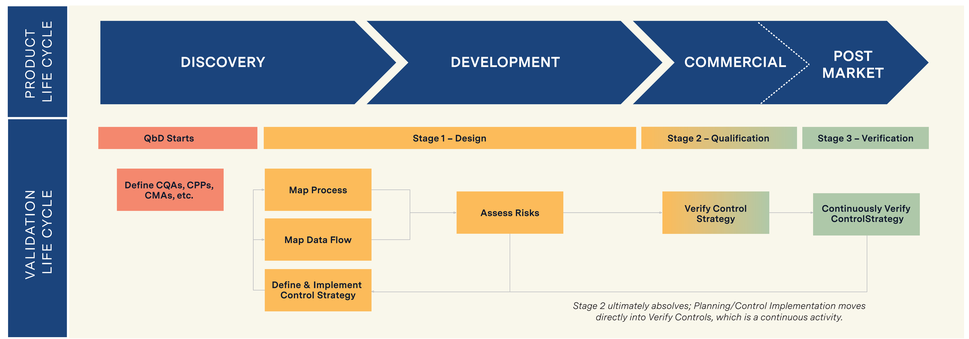
Waterfall vs Agile Software Development Lifecycle (SDLC)
- Validation methodologies are not well-adapted to frequent, iterative software release
- GAMP5 is more than the V-Model!
- How do we fully embrace – and validate – iterative/agile SDLC already supported by GAMP5?

THE FOUNDATION

QbD
Know the product/process requirements

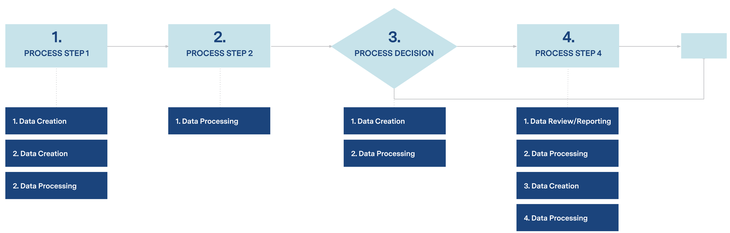
QRM/KM
Know the risks/important aspects to monitor and control

Validation
Know and demonstrate you can control it, continuously!



APPROACH

1. Process Flow – map out process steps
2. DataFlow – map out all data - whether it's created, processed, transacted, an output, etc...
3. Risk Assessment – assess risk on the data in the context of the process. Data is the fundamental element that needs to be evaluated.
4. Control Strategy – Define controls that decrease the risk. Demonstrating that the control strategy (culmination of all controls) is in place and effective essential becomes the validation package!



KNOWLEDGE ASSESSMENT	CRITICALITY Dependent upon impact on patient safety or product quality	VULNERABILITY Dependent upon the system setup (source) and data transfer (mode/technology)	DETECTABILITY Dependent upon immediate, downstream, or no controls for realizing issue before harm	OVERALL RISK	CONTROL STRATEGY	DEMONSTRATION OF EFFECTIVENESS (QUAL/QUANT)
1.1 Data Creation	High	High	Low	Med	...	
1.2. Data Creation	High	High	Med	High	...	...
1.3. Data Processing					...	...
2.1. Data Processing						

KEY TAKEAWAYS

- Risk Management leads to Knowledge Management when you move to holistic/continuous approach
- Control Strategy
  - Iterative starting in design stage
  - Holistic by engaging data from all parts of the product lifecycle and value chain.

CONTINUOUS PV LIFECYCLE, QBD LIFECYCLE, AND HOLISTIC CONTROL STRATEGY

System design, delivery, C&Q process moved from "series" to "parallel" process to PV process.

Focus system PQ as demonstration of system performance to deliver CPP(s).

Change process validation from three stages to a single stage / continuous process.