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David Begg Associates 2008

Packaging Lines Control and Validation

Paul Osborne

Packaging Lines – Control and Validation

NEED FOR VALIDATION

- The Medicines Control Agency, author of 'The Rules and Guidance for Pharmaceutical Manufacturers & Distributors' defines validation as: 'The act of proving in accordance with Good Manufacturing Practice that machinery or processes operate as specified under all conditions.'
- Why Validate? Why go to all the expense?
- A death caused by a Septicaemia outbreak was traced back to a large Parenteral manufacturing practice. Blood banks in America spread AIDS in the early 1980's. Ariane 5 explosion on first flight 1996 – old software. NASA had the first disaster with a space shuttle, the STS107 in 2003.
- Lesson: Quality cannot be tested into the product: it has to be built into the system from the beginning.
- Need: To prove beyond reasonable doubt that equipment has been designed, built and is monitored to ensure that it is in consistent compliance with regulatory requirements.

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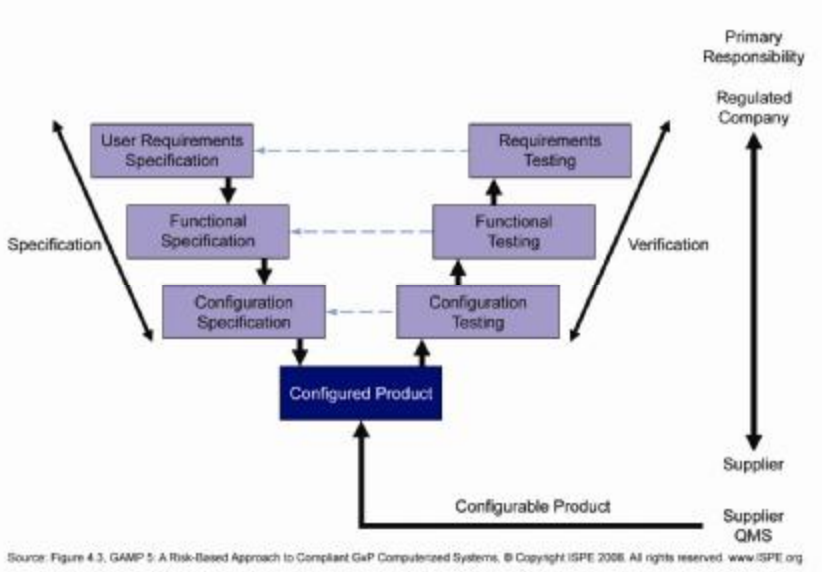
GAMP 5

- URS – User requirement Specification
- FS – Functional Specification
- CS – Configuration Specification (reference the manuals)
- Configuration Testing (was IQ)
- Functional Testing (was OQ)
- Requirements Testing (was PQ)



- We will be working through these phases
- How does this relate to our testing at the FAT and the SAT?

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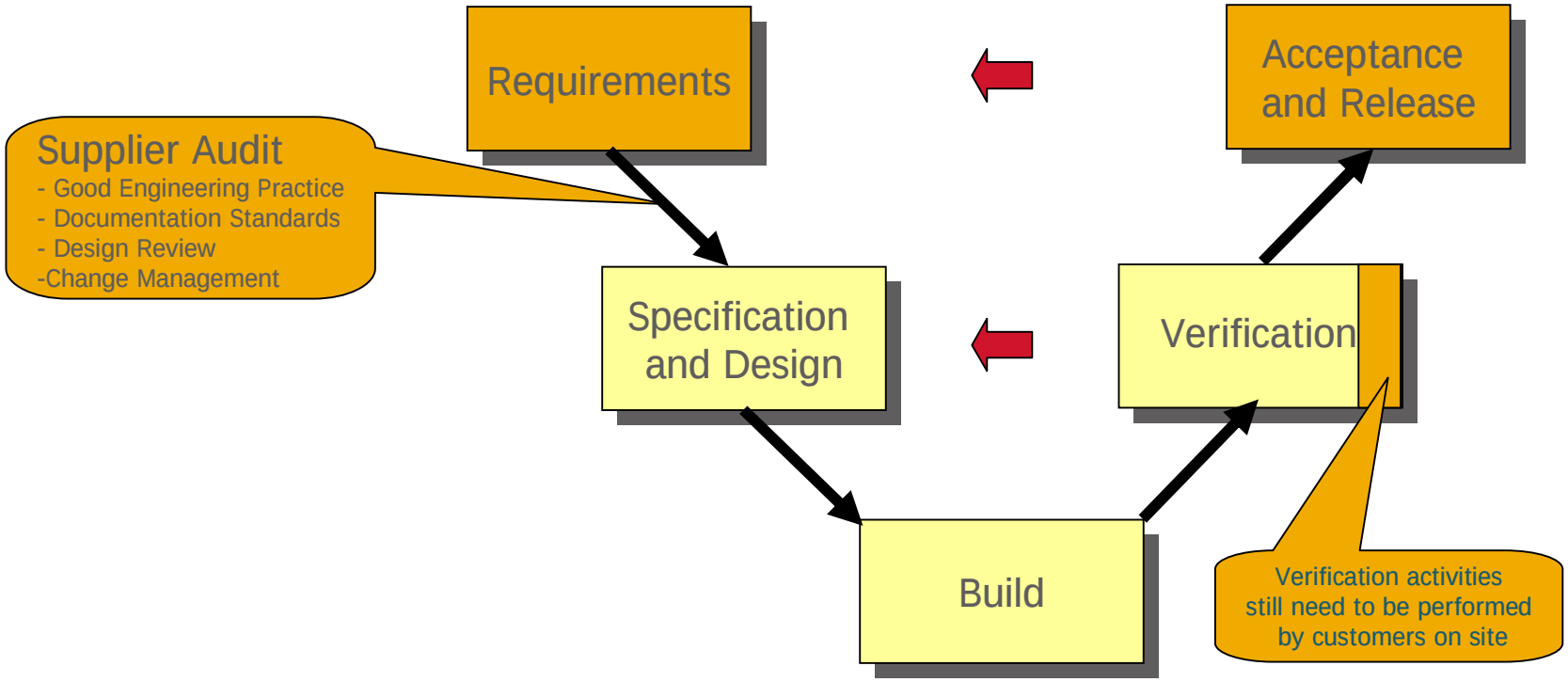
New Approach (ASTM Standard ASTM WK9864)



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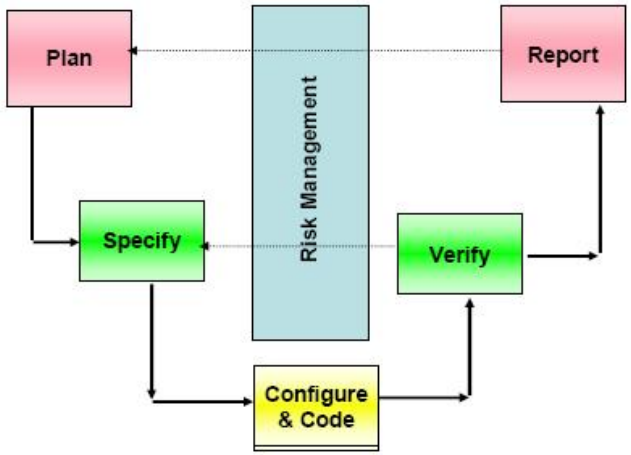
RISK

- The first question then is - What tests do we complete to validate the machine?
- The easiest approach is to rule out the things we do not need to test in order to complete the validation.
- Complete a Machine and System Risk Analysis, divided into three areas.

1. Ethical or GMP Risk (Items that would cause a product recall).
2. Business and Operational Risk (for example cosmetic defects and throughput of machine).
3. Safety or H&S Risk (injury to personnel, usually covered when the machine is CE marked).



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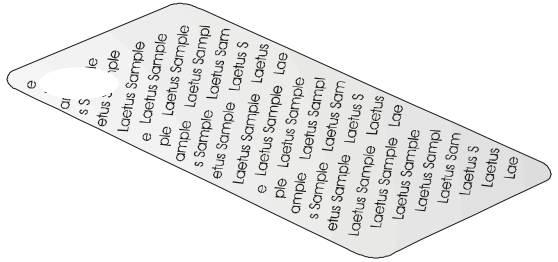
1. GMP risk

- Incorrect or contaminated pharmaceutical product
- Incorrect assembly of the ‘unit of dose’ carrier (blister, bottle, vial...)
- Incorrect packaging component in the final assembly (incorrect carton, missing or incorrect label, missing or incorrect leaflet…)
- Incorrect or illegible lot or batch identification

2. Business and operational risk

- Poor packaging quality (cosmetic defects)
- Excessive machine down time
- Machine damage or wear
- Excessive change-over times
- Slow speed of operation



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3. H&S Risk

- Guards not operating correctly
- Exposed mechanisms causing human harm
- Open electrical connections
- Human contamination by API's

- We must make tests 100% for all aspects of potential GMP risk!
- We can include such Business and Operational Risk as we see fit.

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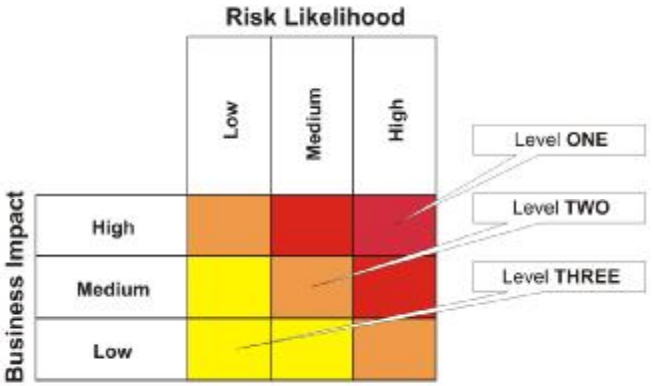
- Regarding Risk there is a procedure defined in GAMP 5
- First determine the chance of the adverse business risk event occurring:
  - Low – once in every 10,000
  - Medium once in every 1,000
  - High once in every 100
- Next – determine the business impact:
  - low – minimum impact
  - medium – moderate impact
  - high significant long term impact to the business



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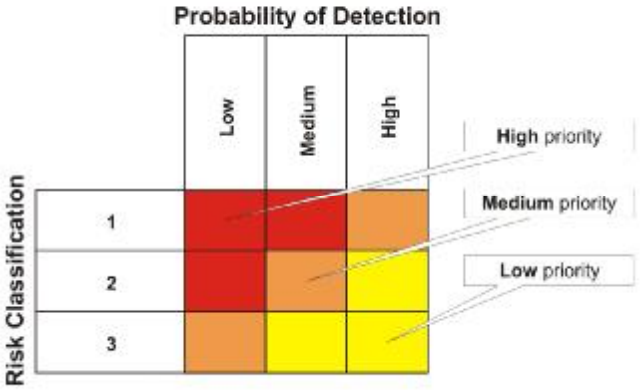
- Now assess the probability of detecting if the risk can be identified;
  - Low, detection of the event is unlikely
  - Medium, detection is possible
  - High, the risk is easy to see at each occurrence.

- By combining the risk classification with the probability of detection it is possible to prioritise the fault conditions and access how vulnerable you are.



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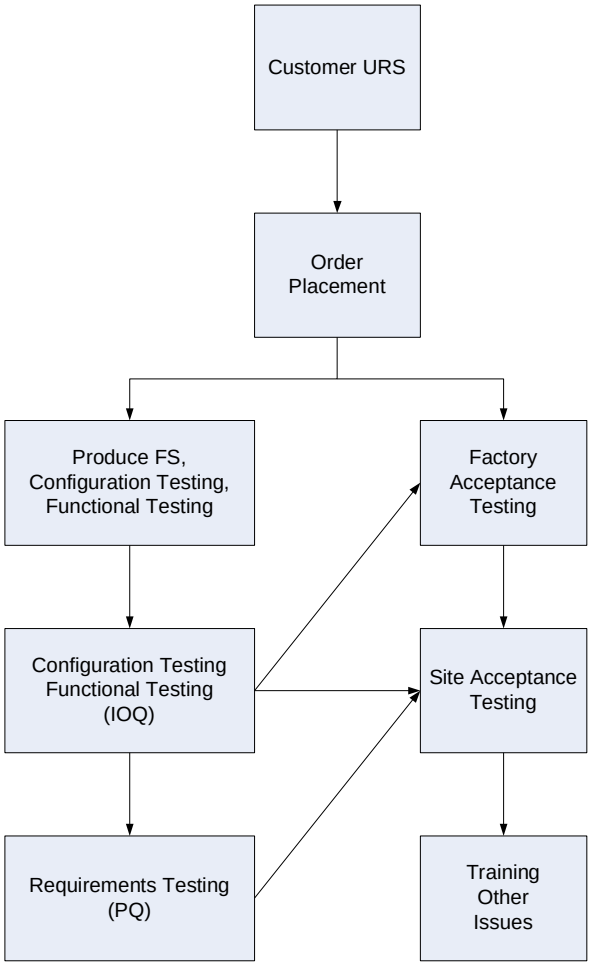
TESTING

- During factory acceptance testing most of the Configuration Testing (was IQ) can be completed if required. Also, some of the Functional Testing (was OQ) can be completed as required.
- The System Acceptance Testing FAT and SAT should be fully documented.
- The completion of Functional Testing for a system confirms that it is ready for use in the manufacturing process.
- The Requirements Testing step verifies system performance(was PQ). Requirements Testing is conducted under actual running conditions across the anticipated working range. Such testing documentation is created by the customer.



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SEVERITY OF VALIDATION REQUIREMENT

- The first step is to determine the severity of the validation requirement, with respect to packaging systems having computer or PLC control equipment.
- This is simplified today, with GAMP 5 having only three software Categories.
- The type of system supplied requires configuration to support specific business processes, then it falls into Category 4.

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GAMP 5 Computer System Categories

Category	Software Type	Validation Approach
3	**Non - Configured Product**	Provision of documentation, training, support and maintenance. The product should be developed and maintained by the supplier in accordance with good practices of GAMP5.
4	**Configured Product**	The product requires configuration to support specific processes. Provision of support with specification, configuration, verification and operation of the system. The product should be developed and maintained by the supplier in accordance with good practices of GAMP5.
5	**Custom Software**	The regulated company contracts the supplier to develop an application based on defined requirements. The supplier will be involved in the full project life cycle of the system and provide support during system operation as required. The product should be developed and maintained by the supplier in accordance with good practices of GAMP5.

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- In Category 4, the supplier should be encouraged, if he has not done so already, to produce a Functional Specification protocol, with a Configuration Specification (may be part of the manuals), a Configuration Testing documentation (was IQ) and a Functional Testing documentation (was OQ).
- The Requirements Testing (was PQ) is usually for the customer to provide.
- If aspects of the system becomes unique in terms of the computer system development, consider a full computer system validation approach to Category 5.
- With Category 5, for a full system computer validation strategy is required. The regulated company contracts a supplier to develop the application based on defined requirements. Therefore, the supplier will be involved during the full project life cycle of the system, and also to provide support during system operation as required. Procedures to follow should be agreed between the regulated company and the supplier and be documented in the appropriate plan.

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TRACABILITY

- Traceability may be achieved in a number of ways, including a Requirements Traceability Matrix (RTM), automated software tools, spreadsheets, or embedding references directly within documents.
- An RTM may be generated as a separate deliverable or as part of an existing deliverable, such as the requirement document URS or Functional Specification FS.

Requirements URS	Design Functional Specification	Testing Functional Testing
U1 1.1	F2 4.1	T1.1
U1 1.2	F2 4.5	T1.2
U1 1.3	F3.1	T1.3
U2 1.1	F3.2	T1.4
U2 1.2	F3.3	T1.5

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COMPANY AUDITS

Company audits will fall usually into the following categories:

- *Supplier Organisation*
- *Viability*
- *Quality Management System*
- *Systems Lifecycle Procedures*
- *Document Control*
- *Requirements and Design*
- *Electronic Record and Electronic Signature*
- *Programming*
- *Security*
- *Testing*
- *Change Control*
- *Support*

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21 CFR PART 11

- Data Security – Files on computers are not as secure as printed files locked away. The requirement is to apply the same security to a networked data file as to a printed document, the prevention of unauthorised access.
- Data Integrity – To alter an electronic document and to hide this alteration is easy compared to a printed document. The requirement is to show that an electronic networked document has not been altered, affording the prevention of unauthorised alteration.
- Audit Trail Integrity – Where alteration is permissible by an authorised person, the emphasis here is to show a historical trail of – Who? altered the document, When? was it altered, What? was altered. Please note that not a consideration here is Why? Legitimate reasons are assumed for legitimate users.
- Electronic Signature – The requirement to show a connection between the stated user and his legitimate identity.

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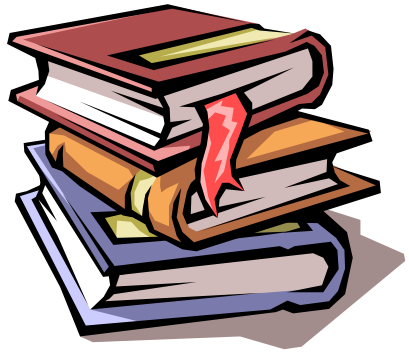
TRAINING

- The supplier should identify training needs and provide appropriate training. They should consider the specific methods, tools, techniques, and hardware to be used. Records of relevant training and experience should be maintained and should be available as part of the project documentation.
- The requirement is for classroom training with notes and a test to be made at the end, in both theory and practice.



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MAINTENANCE

- Procedures must established to ensure that backup copies of all software and other relevant data are taken, maintained, and retained within safe and secure areas. Backup and recovery procedures should be verified.
- Identify and define system components. Record and report the status of items and modifications to items. Ensure the completeness, consistency, and correctness of items of the machine. Control storage, handling, and delivery of items.

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- All changes proposed during the operational phase of an automated system should be subject to a formal Change Control process, and should be reviewed, impact and risk assessed, authorised, documented, tested, and approved before implementation.
- Consider that some elements of the machine must require routine maintenance - This is a planned activity.
- Periodic review – at routine intervals, once per year, review the status of the above.
- Document the review.

Thank you for your attention.