Writing an Effective URS for Facilities, Services & Equipment

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PharmOut

Regulatory Knowledge, Practically Applied.

In this session

- Basics of URS
- URS in Regulations & Guidance
- Common failings in URS preparation
- The elements of a good URS
- Final thoughts on the future

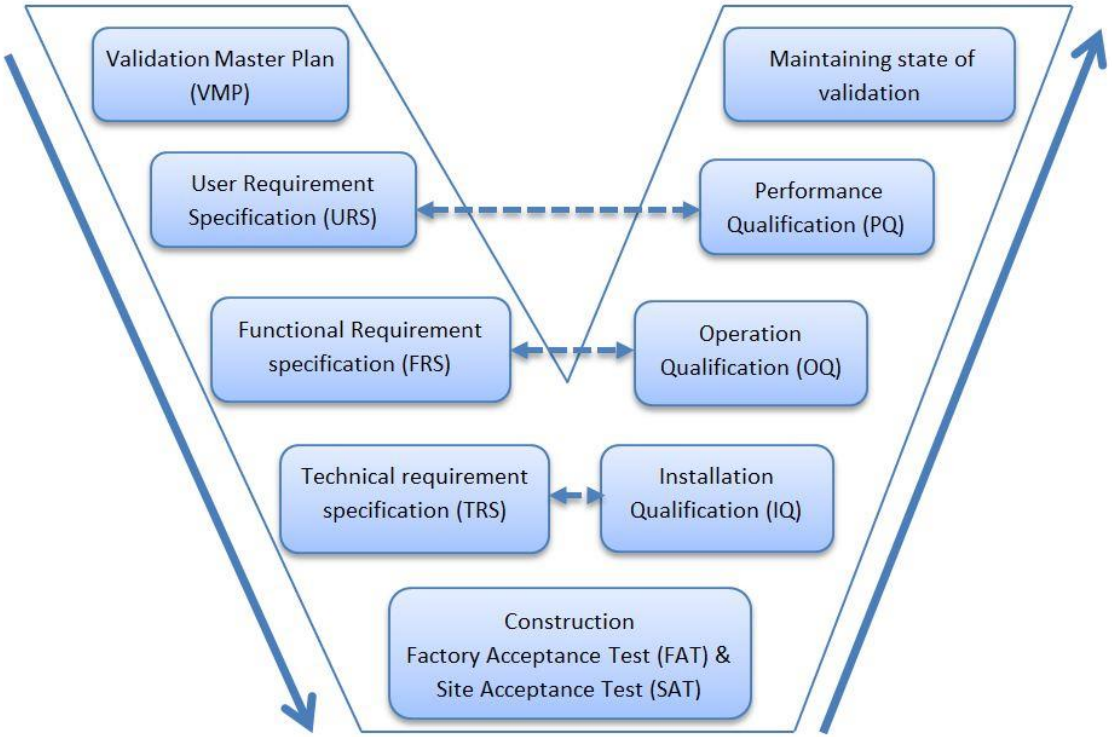
URS basics – what is a URS?

A User Requirements Specification is a document which defines GMP critical requirements for facilities, services, equipment and systems. A URS can be used to:

- Define the requirements for an entire project
- Define the requirements for a single, simple piece of equipment
- It is usually written in the early stages of FS&E procurement, after business case development and validation planning, but prior to purchase

URS basics – origins & historical use

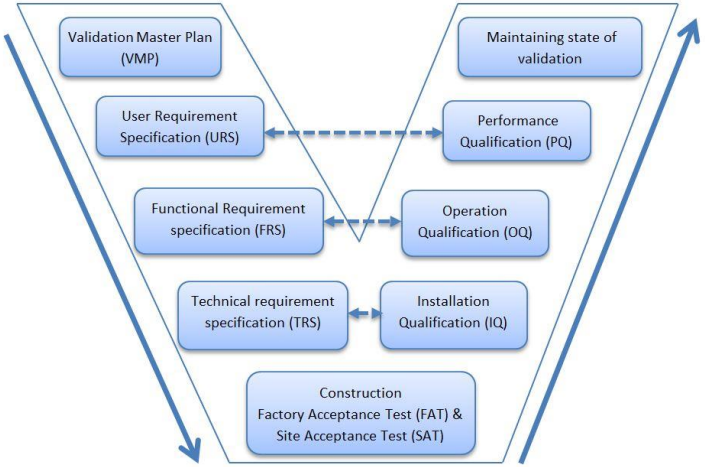
The use of URS in GMP arose from the early days of computer system validation, and the rise to prominence of the V-model across wider validation



URS basics – origins & historical use

The problem with the early V-model

- Demands an FS and DS, regardless of project complexity
- Early adoption resulted in superfluous documentation
- Increased perception of validation as red tape



URS basics – origins & historical use

The *perceived* inflexibility of the V-model led to the application of URS within a few distinct categories

- A URS, specifically, and only testable at PQ stage would typically be written for complex or expensive projects and systems, which lent themselves to multi-stage specification development
- A general "specification" may have been written for less complex projects, and been divided into User, Functional and Design requirements for specific testing across the phases of qualification. Primary focus was still to develop testing requirements
- Most commonly, for simple systems, no URS was written at all.

URS basics – current status of URS

In more recent times, independently of regulatory guidance, industry has realised the value of effective URS writing

- Not just for testing requirements
- Also helps convey the general GMP expectations which might not otherwise be testable
- Provides a mechanism to hold vendors (and site personnel) to account

URS basics – current status of URS

- Manufacturers started to set up their own systems and utilise URS as the primary GMP specification document for both procurement and subsequent testing.
- Not universal, and still often overlooked for simpler installations
- Still suffers from confusion about what is "permitted" in a URS.

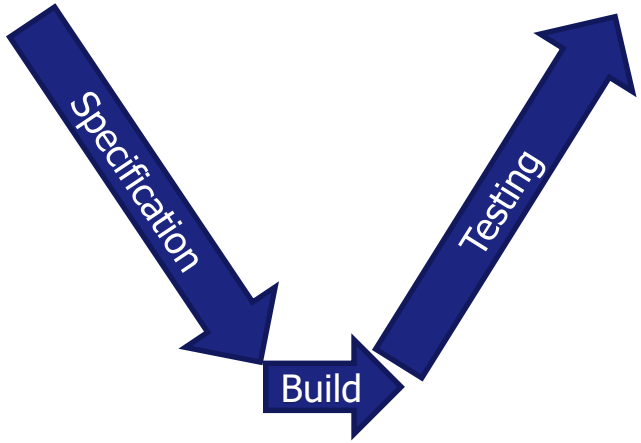
URS basics – current status of URS

ASTM E2500 (2007) was the first standard to document an approach with the same intent, but more flexibility than the original V-model.

- General concept of **specification** "to communicate requirement inputs, including product quality considerations, to those responsible for design"
- Links specification to verification (testing) through the concept of "critical aspects" (specification should focus on critical aspects → verification should confirm critical aspects are within acceptable limits.)

URS basics – current status of URS

- Other guidance's (both industry based and regulatory) have followed. (ISPE in particular)
- New Annex 15 (2015) specifically requires a URS (and/or FS) for all new FS&E and systems used in GMP manufacture
- Will become a mandated requirement in Australia



URS basics – current status of URS

Annex 15 New Requirement

User requirements specification (URS)

3.2. The specification for equipment, facilities, utilities or systems should be defined in a URS and/or a functional specification. The essential elements of quality need to be built in at this stage and any GMP risks mitigated to an acceptable level. The URS should be a point of reference throughout the validation life cycle.

- Essential elements of quality – GMP critical requirements
- GMP risks mitigated *prior* to URS writing
- Point of reference throughout lifecycle (living document)

Common failings relating to URS documents

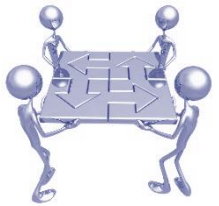
Late preparation

- URS often an afterthought, or seen as a burden
- Have seen examples
  - Post procurement – (late start to val. life cycle)
  - Post installation – (oops … we better specify what we're going to test!)
  - Post commercial use (oops … the TGA are coming …)
- Better late than never (maybe) … but:
  - Miss opportunity to influence design
  - May result in installations which are compromised

Common failings relating to URS documents

Lack of collaborative approach

- Quite commonly, URS written by one engineer, rubber stamped by manager and QA
  - Becomes more problematic with increasing complexity
  - Multi-disciplinary input required
    - Engineering
    - User
    - Validation
    - Quality
  - Involvement of other disciplines should increase with complexity and risk



Common failings relating to URS documents

Failure to communicate URS to vendor

- Even when a URS is written to kick off a project procurement phase, it can be overlooked as a procurement tool.
  - Should supplement or even replace a user brief for GMP equipment
  - Can and should be written with this in mind (provision to third party)
  - Inevitably saves time in vendor negotiations and provides a baseline of accountability

Common failings relating to URS documents

Under-utilization of URS

Traditional approach still lingers in URS preparation

- High level statements designed to be tested at PQ
- Even when more detail is known about requirements

Opportunity in URS to provide all parties with information on:

- GMP critical requirements (high level statements)
- Critical aspects (functional and design requirements)
- General requirements (expectations important to delivery but not GMP critical)
- Constraints (physical, policy, time, etc.)

Common failings relating to URS documents

Failure to manage the URS as a live document

- Common to see URS signed off and then filed away
  - Loses power of accountability
  - May allow design changes which negatively impact project
  - Likely to cause problems during testing phase
    - Document can be ignored and testing may not be reflective of requirements
    - If it is dusted off, some requirements may be out of date

Common failings relating to URS documents

Failure to verify design/deliverables against URS

- Even if the document is kept live, it is common to see qualification protocols prepared independently of URS
  - Extra testing is not normally a problem
  - Required testing may not be captured
  - Tests may not reflect original intent
- Highlights importance of requirements traceability

Elements of a Good URS

Regulatory requirements

- New Annex 15 requires* a URS for all new GMP related facilities, services, equipment and systems
  - Must define quality critical requirements
  - All defined requirements must already be risk mitigated
  - Must remain live for the duration of the subject life cycle
- FDA process validation guidance references ASTM E2500, but does not directly mandate user specification

Elements of a Good URS

Well defined scope and limitations

- It should be clear what the document is and is not to be used for
  - Cross references to related documents (validation plans, risk and impact assessments, relevant SOPs)
  - Where more than high level requirements are provided, the use of those requirements should be clear (mandatory vs nice to have)

Elements of a Good URS

Traceability

- URS is a great opportunity to integrate the fundamentals of a traceability matrix

Ref.	Requirement	Regulatory Reference	Verified at:
U1.	Grade A, B & C classifications shall be achieved through the use of terminally mounted HEPA filtration, class H14, or similar pre-approved filtration, to filter supply air.	Annex 1 Section 1	IQ

- This assists with clarity and with developing detailed RTM

Elements of a Good URS

GMP critical requirements

These are the types of requirements associated with the traditional URS approach

ISPE Good Practice Guide: Applied Risk Management for Commissioning & Qualification defines two types of GMP critical information:

> Process User Requirements (PURs): Requirements related to product/process output quality and/or GMP regulatory compliance. PURs must be qualified (verified as present and operating per design, and documented in Quality Unit approved documentation). The identification of PURs is described in detail in the sections below.

Elements of a Good URS

1. Process User Requirements
   - Usually high level statements which shouldn't evolve through the life cycle (typically testable at PQ/PV)
   - In simple terms, "what" the system needs to do
2. Critical Aspects
   - Detailed statements which may change through the design phase as the design evolves (typically testable at DQ/IQ/OQ
   - In simple terms, "how" to achieve the PURs

Elements of a Good URS

PURs	Critical Aspects
Are "process" based, linked to support of CPPs and CQAs	Are facility or system based, linked to prevention, mitigation or detection of quality risks, risks to PURs
Are the "what" a system must do or provide in order to assure that product meets all applicable specifications	Are "how" a system will meet or support the applicable PURs
Can and must be identified by users and associated SMEs and are best determined using a multi-disciplinary review based on science and process knowledge	Are typically identified or designed by Engineering SMEs in accordance with Good Engineering Practices (GEPs) and are best determined through risk assessment (formal or informal)
Validated as part of PQ or PV	Qualified through a program of physical and functional verification
Quality Unit should be involved in development and must be included in approval, typically as part of a VRB, and documented in a standalone URS, DQ, or other VRB approved format	Are developed as part of the engineering design and must be listed along with acceptance (design) criteria in some Quality Unit/VRB approved format (C&Q Plan, DQ, IQ/OQ protocols, etc.)
Are generally "fixed" by the process, and not typically subject to frequent or significant changes once approved (change control required for already approved PURs)	May be iterative and change as designs and/or control strategies are developed and modified (change control required for already approved Critical Aspects and associated criteria)

Elements of a Good URS

PURs vs CAs

1. In a complex system requiring Functional and Design specification, the URS should be limited to PURs, CAs can be developed through the detailed specification phase
2. For simpler systems (more common), the CAs can be integrated in the URS
3. All should be traced and qualified

Elements of a Good URS

Constraints

- Small or large projects can include constraints which will have an impact on a vendor's ability to supply. Constraints are rarely GMP critical, but might include:
  - Physical constraints
    - facility size
    - access size
    - availability and capacity of utilities
    - weight bearing capacity of the installation site
    - And so on …

Elements of a Good URS

Constraints

- Policy constraints
  - Global (company wide) quality policies
  - Engineering policies and standards
  - Social responsibility policies (e.g. green policies)
- Time
  - Site operating hours
  - Project timelines (including co-ordination issues)

Elements of a Good URS

Expectations

- Sometimes vendor assurance alone is not sufficient to have confidence that a supplier understands the nuances of GMP
  - Often useful to layout expectations that might seem obvious to some, but are not always well understood
  - Particularly recommended for facility construction and other vendors who do regular non-GMP work
  - Incorporation of expectation statements may depend on what other supporting specification is available

U1.	**Exposed insulation inside the air handling units should be avoided if possible. If internal insulation is exposed it must be used it must be a non-shedding material.**	**NA**	**Commissioning**

The Future of URS

- URS will now be a regulatory requirement
  - There is an expectation of follow through (URS → Verification)
  - Will become as important as Validation Plans in validation document life cycle
  - The importance of URS to design review and qualification will ensure we get better at it

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Thank you for your time.
Questions?

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