Qualification of Temperature Sensitive Storage Areas

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PharmOut

Regulatory Knowledge, Practically Applied.

In this session

- Introduction to Temperature Sensitive Storage
- Regulations & Guidance
- Elements of a good qualification

Introduction

What do we mean by temperature sensitive storage (TSS)?

- The routine storage of any starting, intermediate or finished GMP materials which requires controlled temperature conditions. It applies to
  - 'Room temperature' (<25˚C) warehouses and store rooms
  - Low temperature storage cabinets (refrigerators/freezers)
  - Low temperature storage rooms (cool/cold rooms)
  - Could also apply to elevated temperature enclosures

Introduction

- There is a lack of explicit regulation on qualification and temperature mapping of TSS areas. But we know that we need to do it
- In recent years, there has been an increased focus on the product lifecycle, and what happens to materials before and after the manufacturing process
- Little consistency in approach between manufacturers, even in the same regulatory jurisdictions

Regulations

PIC/S and EMA

- GMPs

2.7. The heads of Production and Quality Control generally have some shared, or jointly exercised, responsibilities relating to quality. These may include, subject to any national regulations:

  - the designation and monitoring of storage conditions for materials and products;

3.19. Storage areas should be designed or adapted to ensure good storage conditions. In particular, they should be clean and dry and maintained within acceptable temperature limits. Where special storage conditions are required (e.g. temperature, humidity) these should be provided, checked and monitored.

- Guidances ... ☹

Regulations

FDA

- CFR 211

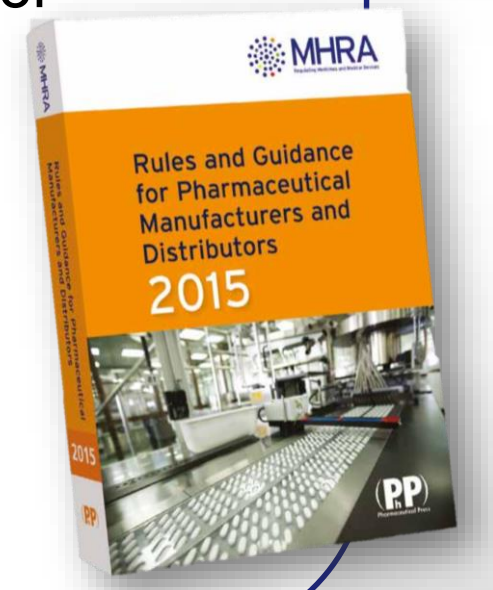
> Sec. 211.142 Warehousing procedures.
>
> Written procedures describing the warehousing of drug products shall be established and followed. They shall include:
>
> (a) Quarantine of drug products before release by the quality control unit.
>
> (b) Storage of drug products under appropriate conditions of temperature, humidity, and light so that the identity, strength, quality, and purity of the drug products are not affected.

- Guidances ... ☹

Guidances

MHRA

- Follows EMA/PIC/S GMPs
- Guidances …😐
  - 'Orange Book' was once the main source of information on storage qualification
  - Requires mapping on installation and seasonally
  - Does not mandate durations or locations



Guidances

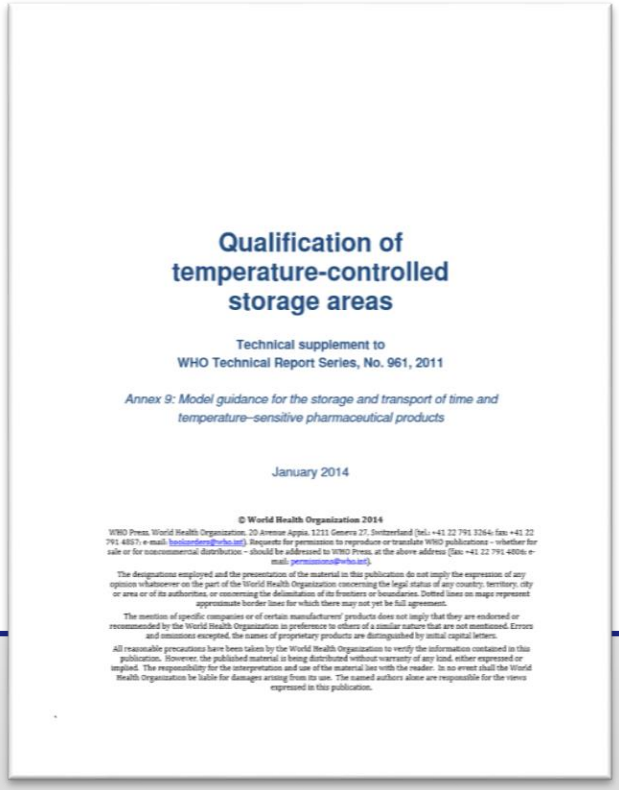
ISPE

- Have released a concept paper in 2012 … ☺
- The paper is being developed into a good practice guide, due late 2015.
- The concept paper alone is an excellent resource for temperature mapping exercises. It covers:
  - Probe numbers
  - Locations
  - Seasonal requirements
  - Analysis, and more

Guidance

WHO

- Released two technical report supplements in 2014 …☺ ☺

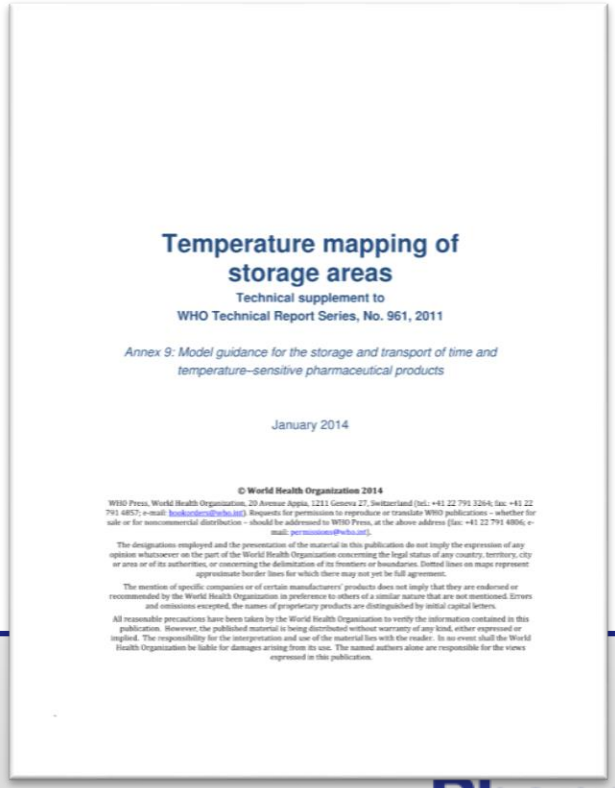


Qualification of temperature-controlled storage areas

Technical supplement to
WHO Technical Report Series, No. 961, 2011

Annex 9: Model guidance for the storage and transport of time and temperature–sensitive pharmaceutical products

January 2014



Temperature mapping of storage areas

Technical supplement to
WHO Technical Report Series, No. 961, 2011

Annex 9: Model guidance for the storage and transport of time and temperature–sensitive pharmaceutical products

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Guidance

- WHO Technical Supplement on qualification of temperature controlled storage areas
  - Intended as a one-stop-shop for warehousing agents who may have no other GMP experience
    - Explains in detail the purpose and requirements of each phase of qualification
    - States that OQ and PQ mapping should be at least 24 hours
    - Refers to companion supplement for further information
    - Excellent source of information on how to qualify a TSS area from start-to-finish

Guidance

- WHO Technical Supplement on mapping of storage areas
  - Intended as a companion to other WHO documents, including the qualification supplement
    - Explains the purpose of mapping
    - Provides guidance on the protocol and report contents
    - Provides limited guidance on frequency of periodic mapping and numbers of probes
    - Provides guidance on location selection
    - Excellent source of information the analysis of data

Elements of Good Mapping & Qualification

Follow the available guidance

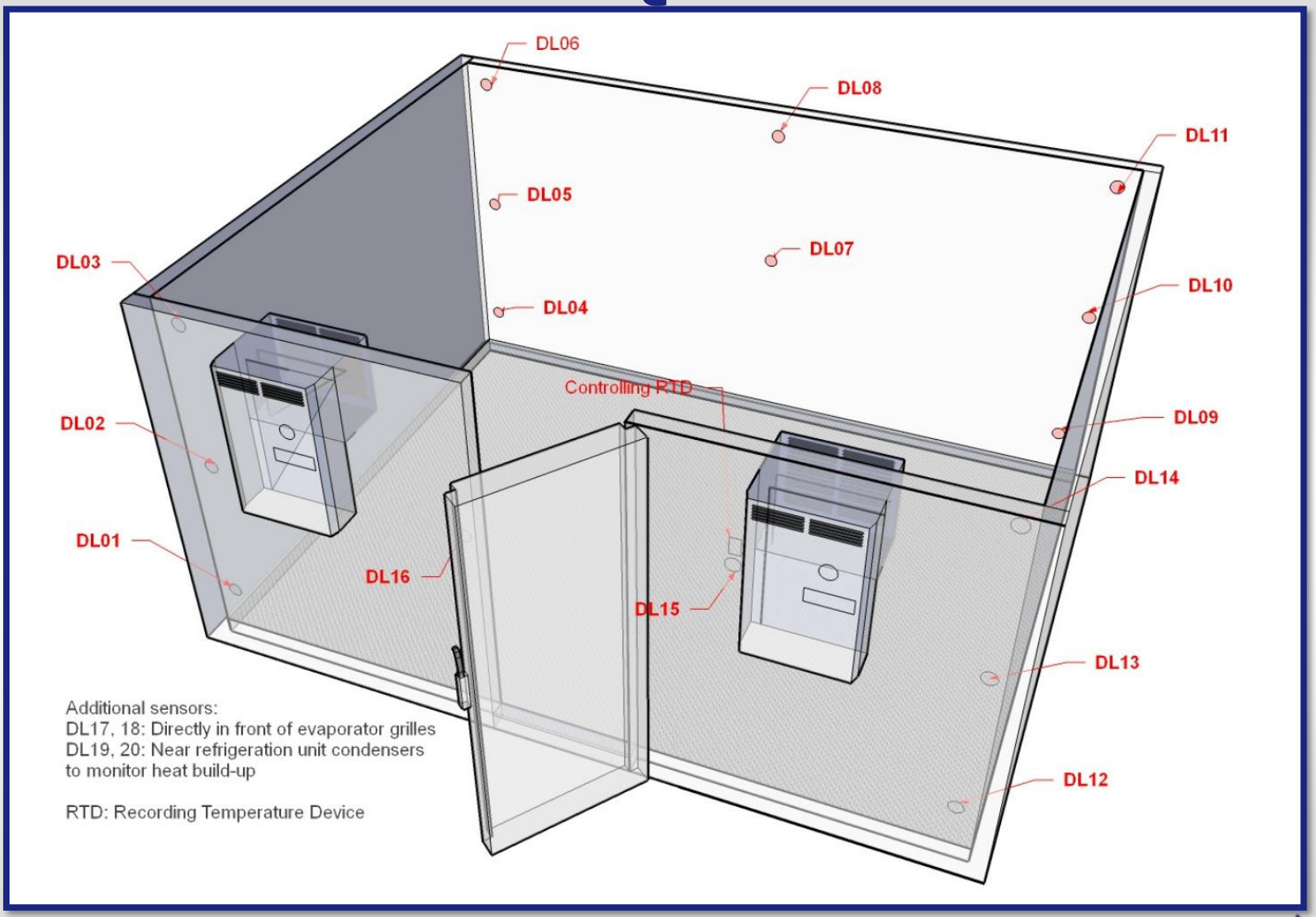
- Currently favour an approach of following WHO supplements, and using the ISPE concept paper to fill in the gaps when encountered
  - Simplifies the approach
  - Less justification usually required to inspectors

Elements of Good Qualification

Mapping layouts

- Not one-size-fits-all. Consider all information relevant to the space to be mapped
  - Size – select a number of probes appropriate to the space (for large warehouses, this can be a challenge)
  - Location of GMP materials within the storage space
  - Exclusion zones
  - Heating and cooling sources
  - Grid in 3D

Elements of Good Qualification



Elements of Good Qualification

Seasonal requirements

- Is the TSS area subject to seasonal fluctuation?
  - Not always the case
  - Warehouses with external walls almost always are
- Give consideration to the seasons at the site
  - Some tropical environments see little seasonal variation
  - Mid summer and mid winter may not always be extremes
- Seasonal testing should form part of PQ. Interim sign off at completion of first phase

Elements of Good Qualification

Duration

- No less than 24 hours for initial qualification. 72 hours recommended where capacity to control is less (e.g. larger spaces)
- Periodic requalification may be performed for reduced durations if tight control has been shown in previous qualifications

Elements of Good Qualification

Acceptance Criteria

- Mean temperature
- Overall temperature variation
- Individual location variation
- Excursions
- Stability
- Mean Kinetic Temperature

Elements of Good Qualification

Analysis

- Simple assessment/calculation against acceptance criteria
- Statistical analysis (i.e. MKT) where appropriate
- Consider WHO recommendations on data interpretation

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Thank you for your time.
Questions?

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