VALIDATION ACTIVITIES: AN EXAMPLE OF CLEANING VALIDATION PROTOCOL

ISCT Lab Practice Committee
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Gloria Carmona Sánchez
Head of Quality Assessment and GMP Facilities.
Andalusian Network for the Design and Translation of Advanced Therapies

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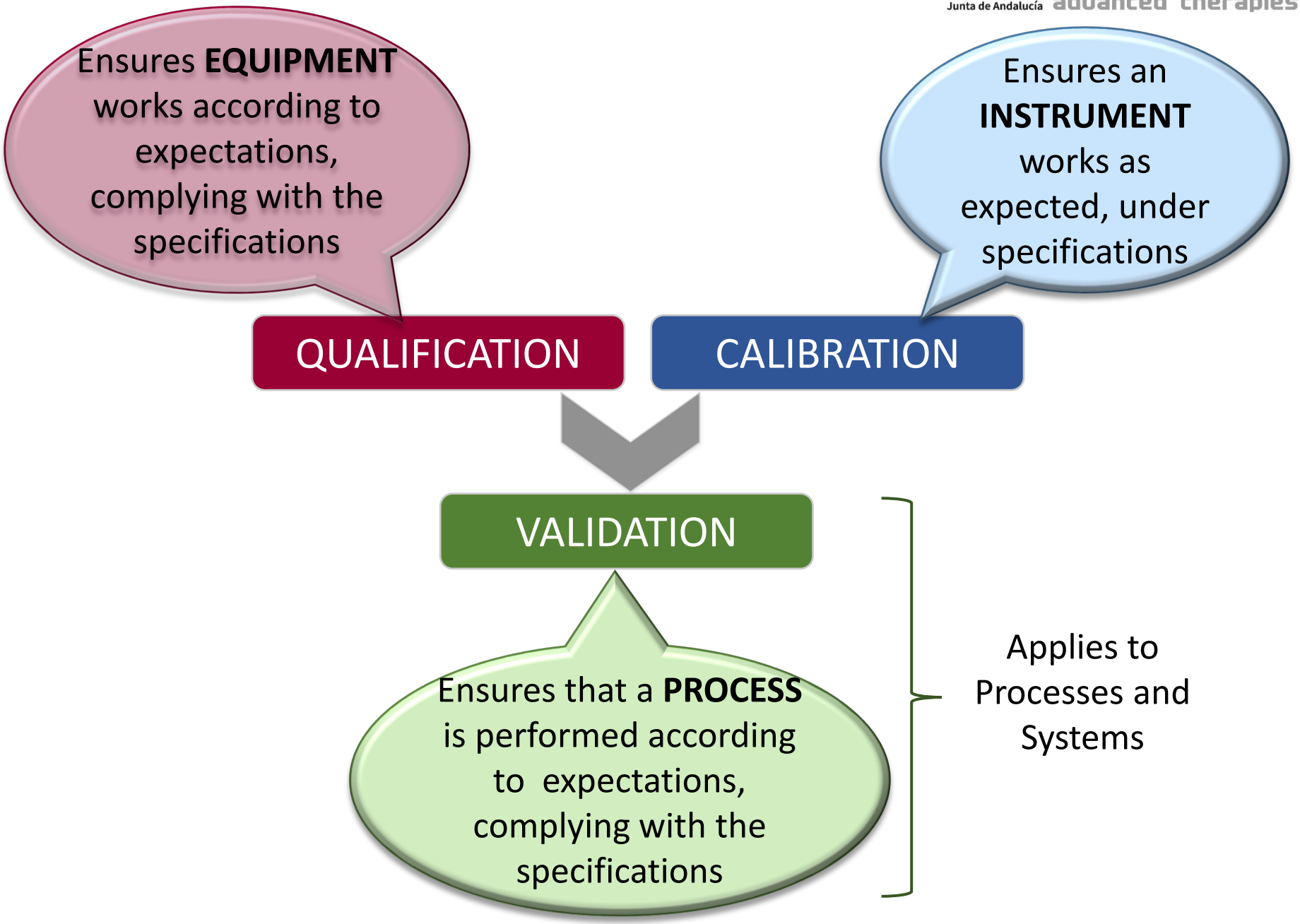

Ensures **EQUIPMENT** works according to expectations, complying with the specifications
Ensures an **INSTRUMENT** works as expected, under specifications
QUALIFICATION
CALIBRATION
VALIDATION
Ensures that a **PROCESS** is performed according to expectations, complying with the specifications
Applies to Processes and Systems

VALIDATION STUDIES

Should **reinforce** good manufacturing practices

Be conducted in accordance with **defined procedures**

Results and conclusions should be **recorded**

OBJECTIVE

to *demonstrate the ability to provide*, on a continuing and reproducible basis, *homogeneous products according to quality specifications*.

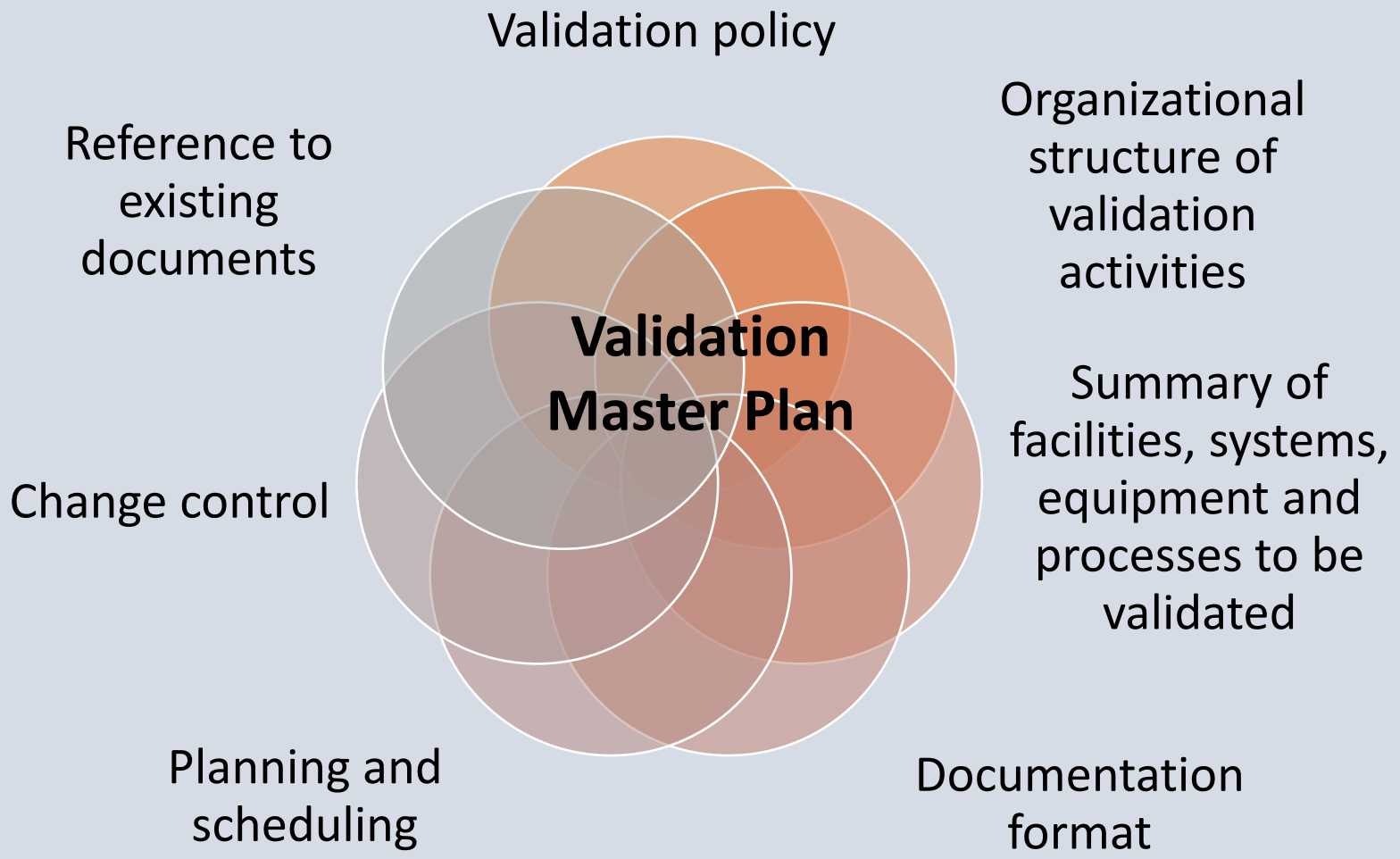
CONSIDERATIONS IN VALIDATION PROCEDURES

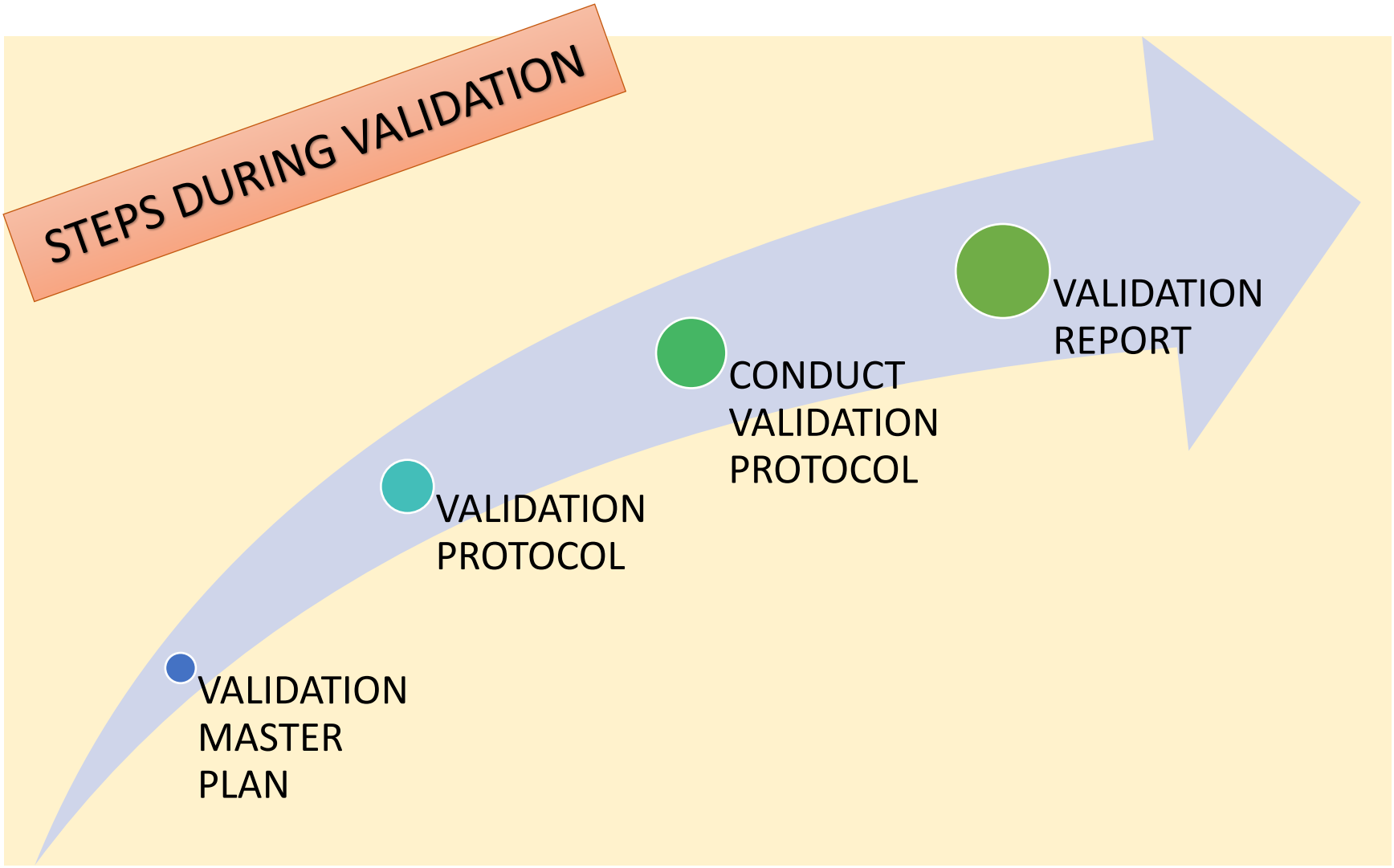
Significant *changes* to facilities, equipment and processes, *which may affect the quality of the product, should be validated.*

A **risk assessment approach** should be used to determine the scope and extent of validation.

All validation activities should be **planned**.

Key elements should be clearly **defined** and **documented** in a **validation master plan**.


Validation policy
Organizational structure of validation activities
Summary of facilities, systems, equipment and processes to be validated
Documentation format
Planning and scheduling
Change control
Reference to existing documents
Validation Master Plan


STEPS DURING VALIDATION
VALIDATION MASTER PLAN
VALIDATION PROTOCOL
CONDUCT VALIDATION PROTOCOL
VALIDATION REPORT

VALIDATION PROTOCOL
a *written protocol*

specifying

how validation will be conducted

critical steps and acceptance criteria need to be included

reviewed

approved

CONDUCT VALIDATION PROTOCOL

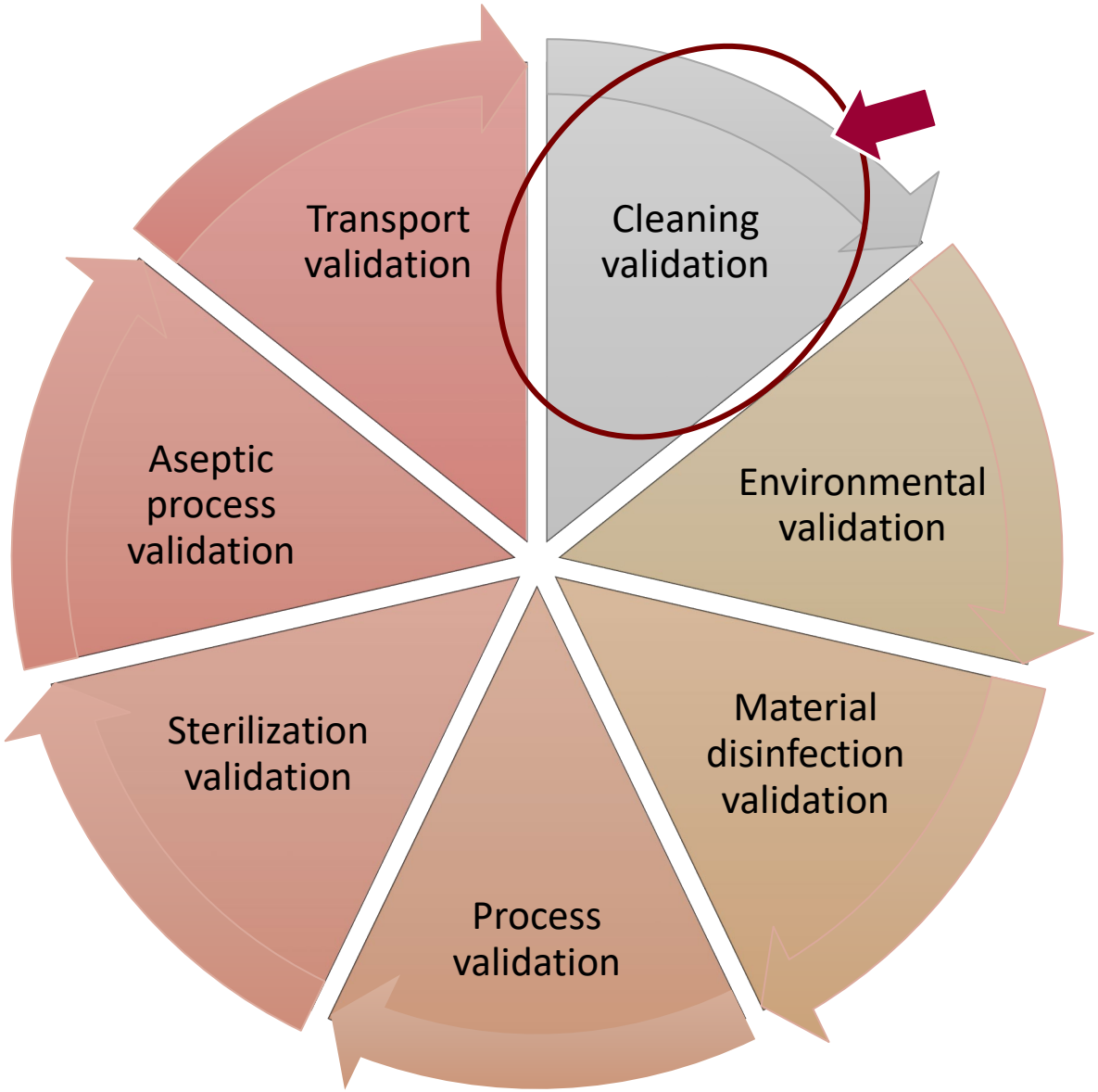
VALIDATION REPORT: Collect all data obtained after developing validation protocol

VALIDATION REPORT

- A report that *cross-references* the validation protocol should be prepared, *summarising the results*, *commenting on any deviations* observed, and *drawing the conclusions reached*, including recommending changes necessary to correct deficiencies.

- *Any changes to the plan* as defined in the protocol should be documented *with appropriate justification*.

PROCESSES THAT COMMONLY NEED TO BE VALIDATED



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CLEANING VALIDATION

the documented **evidence** that a given cleaning procedure removes contaminants, residues from previous product, and cleaning agents below a pre-defined threshold.

OBJECTIVE

to demonstrate that the **cleaning** process consistently **meets** the predefined **acceptance criteria**

CLEANING VALIDATION PROTOCOL

Cleaning validation protocol should be described in a document which should cover:

Detailed cleaning procedure

The selection of the equipment should be representative of the ***worst case scenario***

Sampling procedures

By swabbing and/or rinsing or by other means depending on the production equipment

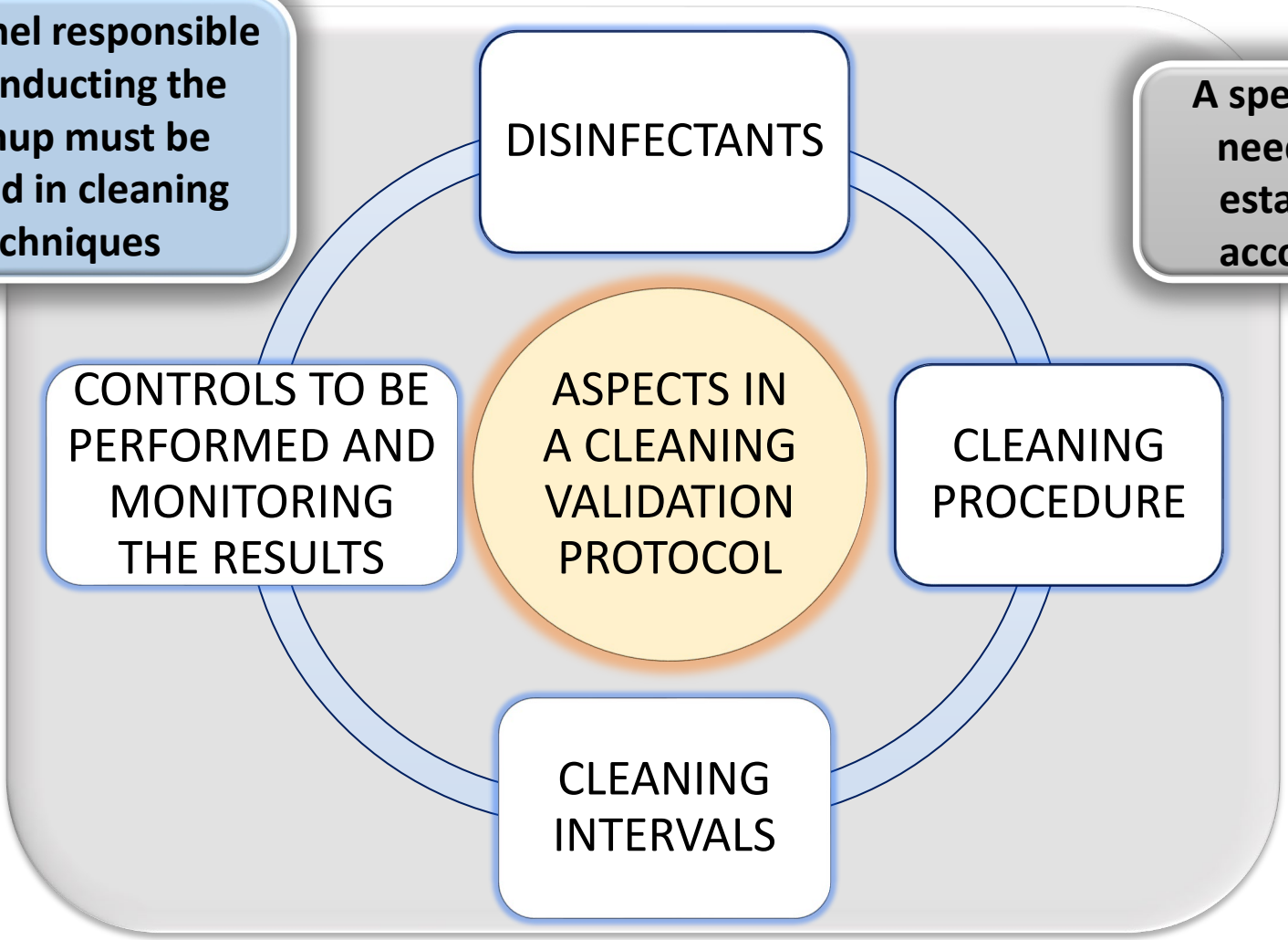
The sampling materials and method should not influence the result

Acceptance criteria

Specific rationale for setting limits should be included

CLEANING VALIDATION PROTOCOL

Personnel responsible for conducting the cleanup must be trained in cleaning techniques



A specific plan needs to be established accordingly

CLEANING PROCEDURE AND CLEANING INTERVALS

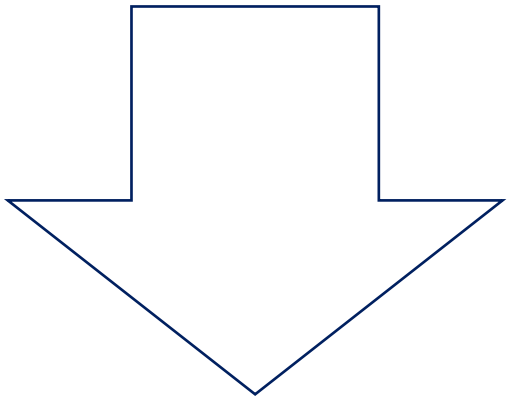
The following considerations apply when designing the strategy:

The **influence between manufacturing and cleaning** should be taken into account *to define dirty time* for cleaning procedures

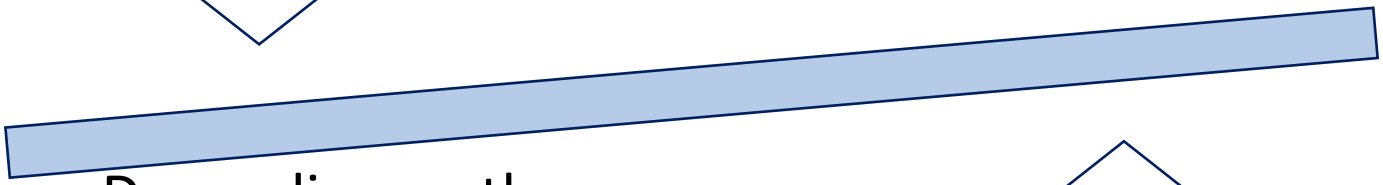
The **influence between cleaning and use** should be taken into account *to define clean hold times* for cleaning procedures

DISINFECTANTS

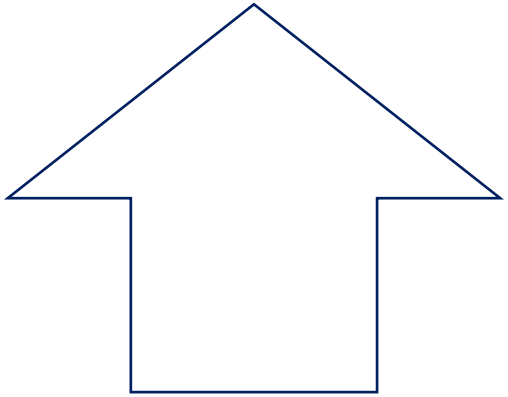
A. HOW TO SELECT THE ADEQUATE BIOCIDE TO DISINFECT



The selection of an adequate biocide to disinfect surfaces of aseptic zones is not easy



Depending on the type of product, the grade of the zone and the risks, different biocides can be used



DISINFECTANTS

A. HOW TO SELECT THE ADEQUATE BIOCIDE TO DISINFECT

GENERAL BIOCIDAL ACTIVITY

- bactericide
- fungicide
- sporicide
- virucide

DISINFECTANTS

B. EFFECT OF THE MOST COMMON BIOCIDES (ORIENTATIVE)

ALCOHOL (IPA y etanol al 70%)	BACTERICIDE	FUNGICIDE	VIRUCIDE	
QUATERNARY AMMONIUM	BACTERICIDE	FUNGICIDE	VIRUCIDE	
HYDROGEN PEROXIDE 3%	BACTERICIDE	FUNGICIDE	VIRUCIDE	
HYDROGEN PEROXIDE 6%	BACTERICIDE	FUNGICIDE	VIRUCIDE	SPORICIDE (in some cases)
SODIUM HYPOCHLORITE	BACTERICIDE	FUNGICIDE	VIRUCIDE (depending on concentration)	SPORICIDE
HYPOCHLOROUS ACID	BACTERICIDE	FUNGICIDE	VIRUCIDE (depending on concentration)	SPORICIDE
HYDROGEN PEROXIDE + PERACETIC ACID	BACTERICIDE	FUNGICIDE	VIRUCIDE	SPORICIDE

DISINFECTANTS

B. EFFECT OF THE MOST COMMON BIOCIDES (ORIENTATIVE)

ALCOHOL	BACTERICIDE	FUNGICIDE	VIRUCIDE	
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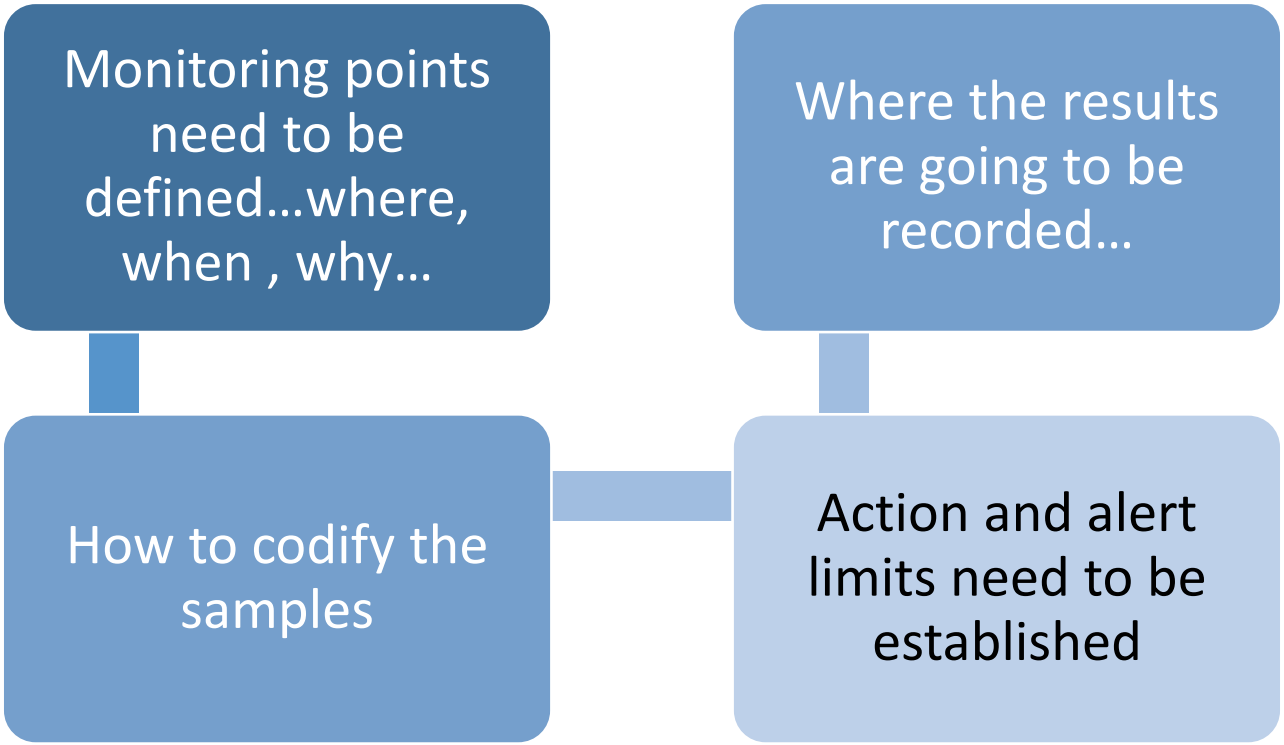
SODIUM HYPOCHLORITE				
HYPOCHLOROUS ACID				
HYDROGEN PEROXIDE + PERACETIC ACID	BACTERICIDE	FUNGICIDE	VIRUCIDE	SPORICIDE

Depending on the microorganism identified in your facility…the specific zone, grade….

The sporicides have an oxidative and corrosive capacity on aseptic surfaces, so their use needs to be reduced to a minimum

CONTROLS TO BE PERFORMED FOR MONITORING RESULTS

The following aspects need to be described



CONDUCT VALIDATION PROTOCOL

According to the approved validation protocol

Using the records previously defined

By the trained personnel

CLEANING VALIDATION REPORT

A report needs to be prepared including the following aspects:

Summary of the **results**

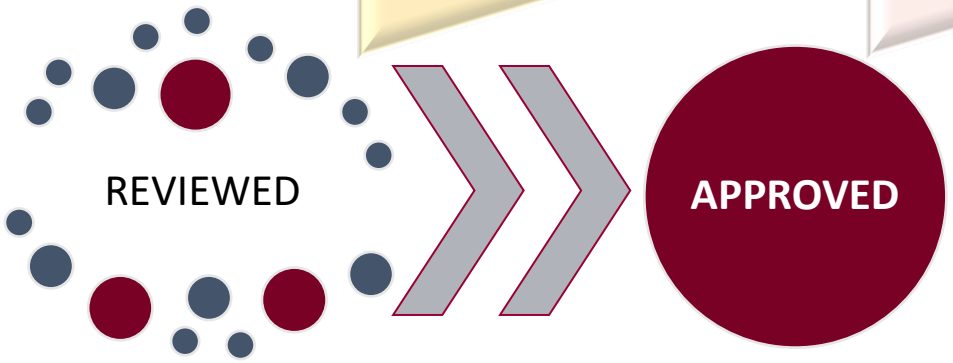
Any **deviation** observed

The **conclusions** reached

Recommended **changes**, if any, to correct deficiencies

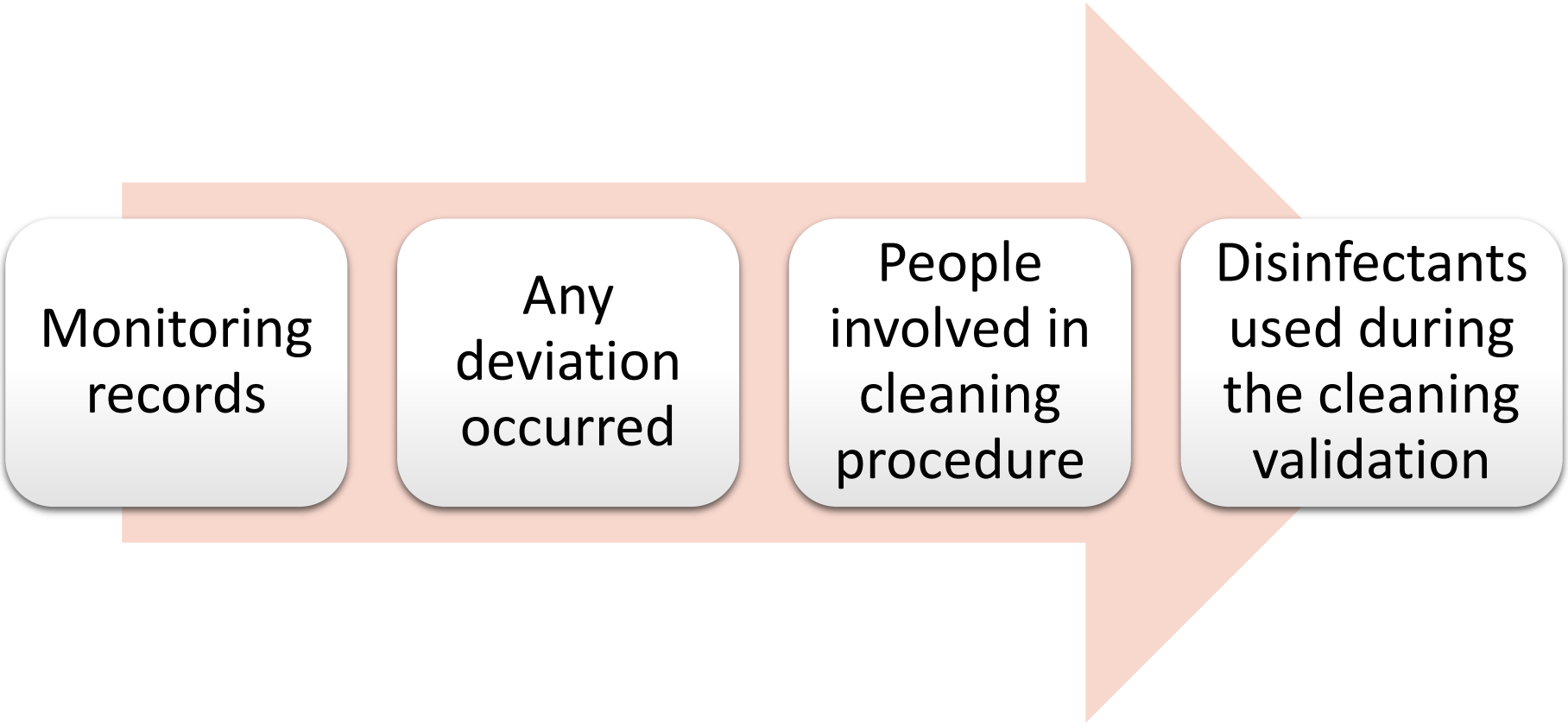
Appropriate **justification** if any changes to the plan need to be done

The established **dirty and clean hold times** after validation



CLEANING VALIDATION REPORT

All primary data need to be stored as part of validation report



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KEYS FOR SUCCESS

CLEANING VALIDATION

To identify the factors that influence the effectiveness of the cleaning process	• Operators • Rinsing times • Cleaning equipment • Cleaning agents used
The worst case scenario should be used	• Number of operators • Number of times operators must enter the facility • Equipment, facilities
Everything needs to be defined prior to start	• Protocol and records • Materials to be used • Cleaning agents to be used and rotation plan • Personnel trained

Have a question? Want to share a suggestion?

The Lab Practices Committee Laboratory Life Line forum is a great way to get in touch with your network for insight, collaboration and help!

https://my.isctglobal.org/forums/Default.aspx

REFERENCES

- Eudralex – Volume 4 Good manufacturing practice (GMP) Guidelines. Part IV – GMP requirements for Advanced Therapy Medicinal Products. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol4/2017_11_22_guidelines_gmp_for_atmps.pdf

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