Supplementary Training Modules on Good Manufacturing Practice

Validation

WHO Technical Report Series, No. 937, 2006. Annex 4.

Validation

- Part 1. General overview on qualification and validation
- Part 2. Qualification of HVAC and water systems
- Part 3. Cleaning validation
- Part 4. Analytical method validation
- **Part 5. Computerized system validation**
- Part 6. Qualification of systems and equipment
- Part 7. Non sterile product process validation

Computerized systems validation

Part 5

WHO Technical Report Series,
No. 937, 2006. Annex 4. Appendix 5

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Validation

Objectives

To discuss validation of computerized systems including:

- System specifications
- Functional specifications
- Security
- Back-ups
- Validation:
  - *Hardware*
  - *Software*

Validation

General

- Validated - level appropriate
  - *or their use and application.*
- Production and quality control.
- Computer systems used in planning, specification, programming, testing, commissioning, document operation, monitoring and modifying.
- Validation: Evidence and confidence
  - *intended use, accuracy, consistency and reliability.*

1.1 – 1.3

Validation

General (2)

- Both the system specifications and functional specifications should be validated.
- Periodic (or continuous) evaluation should be performed after the initial validation.

1.4 – 1.5

Validation

- Written procedures for:
  - *performance monitoring, change control, programme and data security, calibration and maintenance, personnel training, emergency recovery and periodic re-evaluation*
- During validation, consider:
  - *networks*
  - *manual back-ups*
  - *input/output checks*
  - *process documentation, monitoring*
  - *alarms, and*
  - *shutdown recovery*

1.6 – 1.7

Validation

System specification (Control document)

- In place, stating:
  - *objectives of a proposed computer system*
  - *the data to be entered and stored*
  - *the flow of data*
  - *how it interacts with other systems and procedures*
  - *the information to be produced*
  - *the limits of any variable*
  - *the operating programme and test programme*

(Examples of each document produced by the programme should be included)

2.1

Validation

System specification (Control document) (2)

- System elements that need to be considered in computer validation include:
  - *hardware (equipment)*
  - *software (procedures)*
  - *people (users)*

2.2

Validation

Functional specification (Performance specification)

- Provide instructions for:
  - *testing, operating, and maintaining the system*
  - *names of the person(s) (development and operation)*
- When using computer systems, consideration:
  - *location*
  - *power supply*

  (Fluctuations in the electrical supply can influence computer systems and power supply failure can result in loss of memory).
  - *temperature*
  - *magnetic disturbances*

3.1 – 3.2

Validation

Functional specification (Performance specification) (2)

GMP requirements for computer systems:

- **Verification and revalidation**
  - *After a suitable period of running a new system*
  - *Independently reviewed and compared with the system specification and functional specification*
- **Change control**
  - *Alterations made in accordance with a defined procedure*
  - *Provision for checking, approving and implementing the change*
- **Checks**
  - *Data checked periodically*
  - *Confirm accurate and reliable transfer*

3.2 – 3.3

Validation

Security

- Production as well as in quality control
- Data entered or amended - authorized persons
- Security systems to prevent unauthorized entry or manipulation of data
- SOPs for entering data, changing or amending incorrect entries and creating back-ups
- Security procedures in writing

4.1 – 4.3

Validation

(continued)

- Traceability is of particular importance
- Audit trail:
  - *identify the persons who made entries*
  - *identify the persons who made changes*
  - *identify the persons who released material*
  - *identify the persons who performed other critical steps in production or control*

4.4

Validation

(continued)

- Entry of critical data by an authorized person
- Independent verification and release for use by a second authorized person
  - *e.g. for entry of a master processing formula.*
- SOPs for certain systems or processes validated
  - *e.g. action in case of system failure or breakdown including disaster recovery procedure in the event of a breakdown*

4.5 – 4.6

Validation

Back-ups

- Regular back-ups of all files and data
  - *Secure storage (prevent intentional or accidental damage)*

Validation

- Validation process should include:
  - *Planning*
  - *Validation policy*
  - *Project plan and SOPs*

5.1 – 6.1

Validation (2)

- Define computer-related systems and vendors
- Vendor and product evaluated
- System designed and constructed
  - *Consider types, testing and quality assurance of the software*
- Extent of qualification depends on complexity of the system

6.2

Validation (3)

Qualification includes:

- Installation
- Evaluation of the system
- Performance
- Change control, maintenance and calibration, security, contingency planning, SOPs, training, performance monitoring and periodic re-evaluation

6.3

Validation

Validation of hardware

- Appropriate tests and challenges to the hardware
- No influence of static, dust, power-feed voltage fluctuations and electromagnetic interference
- Hardware is considered to be equipment
  - *focus on location, maintenance and calibration as part of the qualification*

7.1.1 – 7.1.2

Validation

Validation of hardware (2)

It should prove:

- Appropriate capacity
- Operational limits
  - *e.g. memory, connector ports, input ports*
- Performance under worst-case conditions
  - *e.g. long hours, temperature extremes*
- Reproducibility/consistency
  - *e.g. by performing at least three runs under different conditions*

7.1.3

Validation

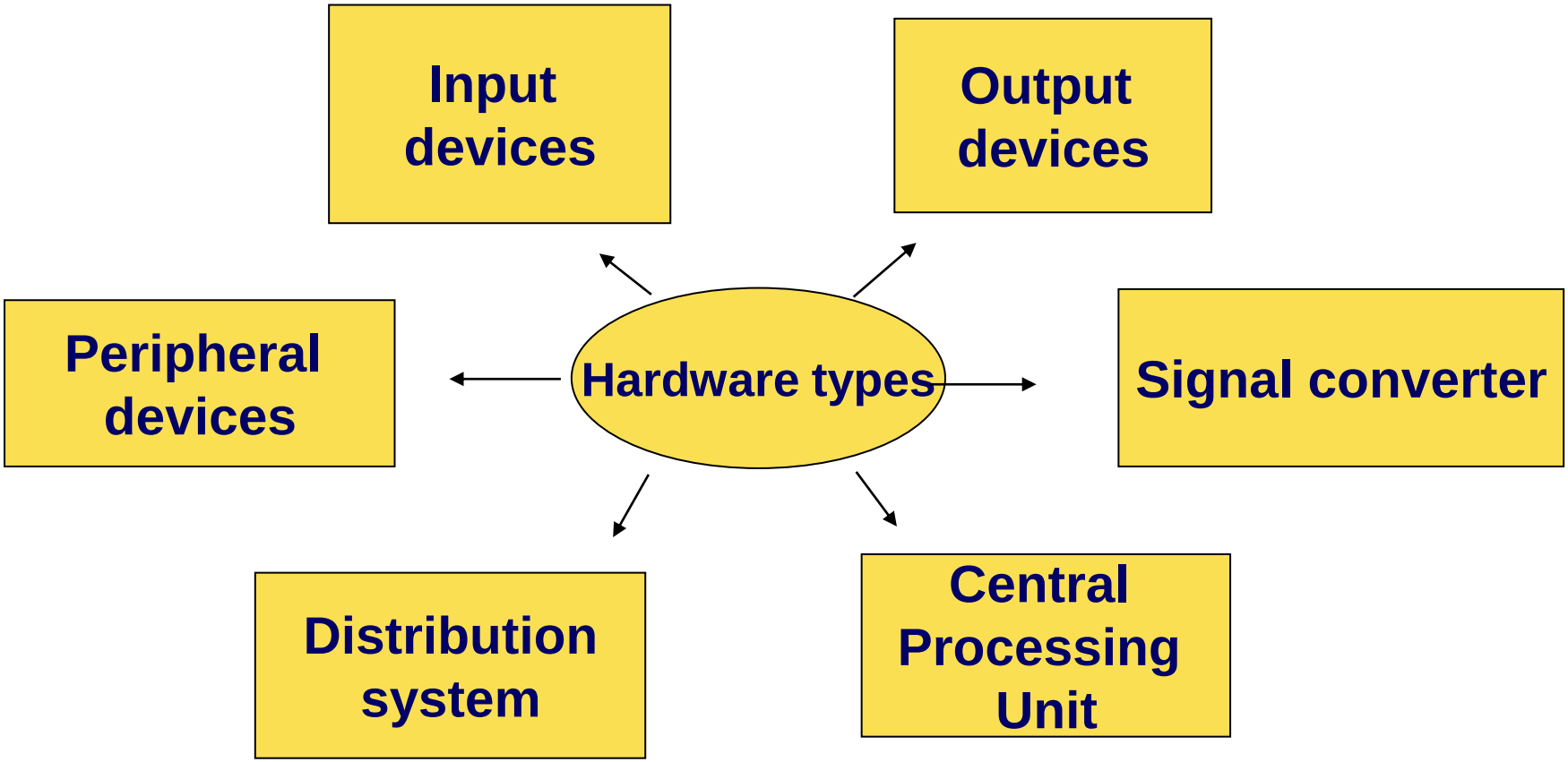
Validation of hardware (3)

- Written qualification protocols; results in qualification reports kept
- Revalidation – in case of significant changes
- Validation may be performed by the vendor – but ultimate responsibility remains with the company
- If records kept by supplier, manufacturer still has to have sufficient records to allow assessment of the adequacy of the validation
- A mere certification of suitability from the vendor, for example, will be inadequate

7.1.4 – 7.1.7

Validation

Summary: Validation requirements for Hardware (See table 1 in notes)



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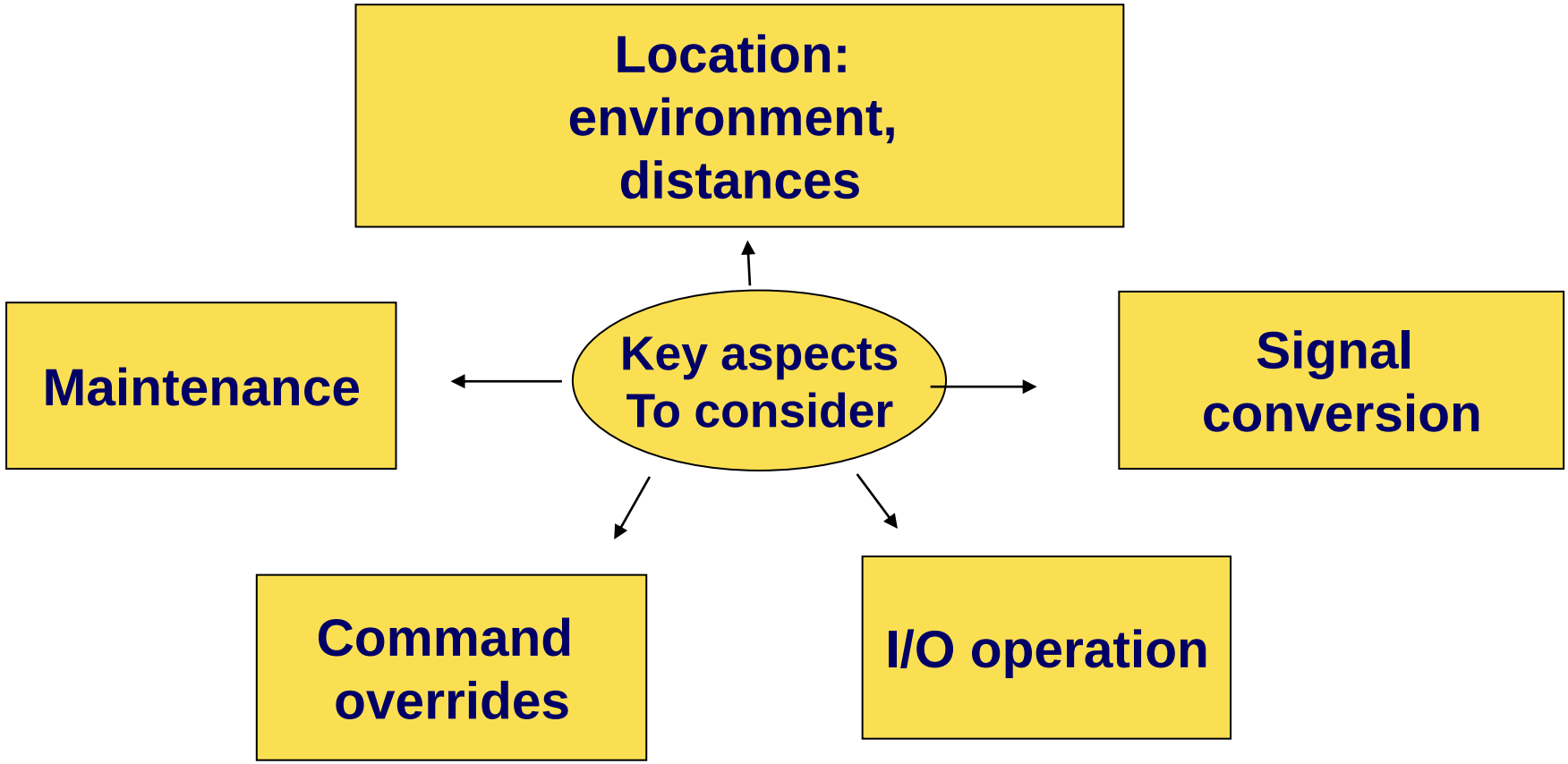

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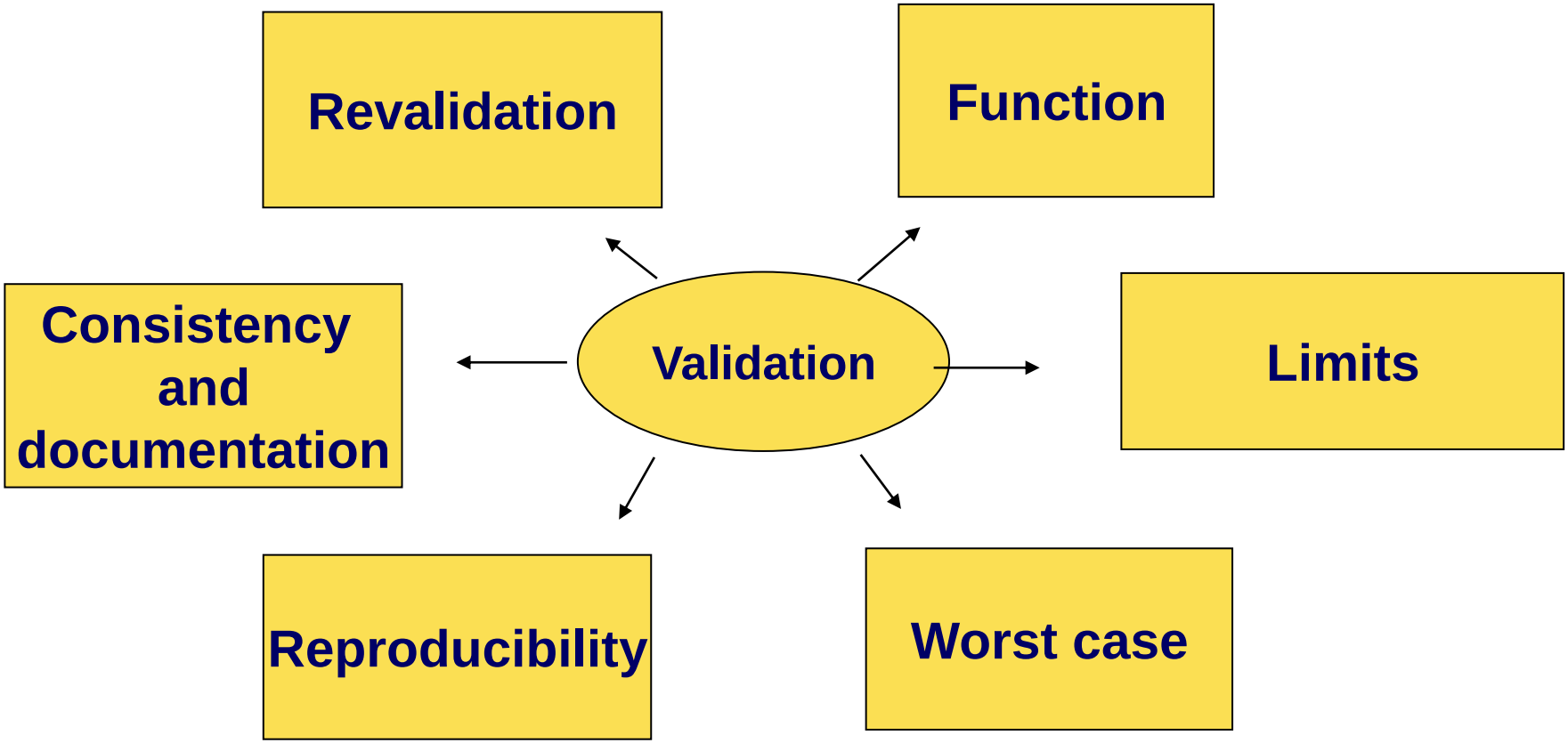

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Validation of Software

Software:

- is the term used to describe the complete set of programmes used by a computer, and which should be listed in a menu
- Records are considered as software
- Focus should be placed on:
  - *accuracy, security, access, retention of records, review, double checks, documentation and accuracy of reproduction*

7.2.1 – 7.2.2

Validation

- Key computer programmes to be identified:
  - *language, name, function (purpose of the programme)*
  - *input (determine inputs), output (determine outputs)*
  - *fixed set point (process variable that cannot be changed by the operator), variable set point (entered by the operator)*
  - *edits (reject input/output that does not conform to limits and minimize errors, e.g. four- or five-character number entry), input manipulation (and equations) and programme overrides (e.g. to stop a mixer before time)*
- Identification of authorized personnel
  - *to write, alter or have access to programmes*

7.2.3 – 7.2.4

Validation of Software (2)

- **Points to be considered may include:**
  - *Consistency in performance: Within pre-established limits)*
  - *Function: Matching the assigned operational function (e.g. generate batch documentation, different batches of material used in a batch listed)*
  - *Worst case: Validation under different conditions (e.g. speed, data volume, frequency)*
  - *Repeats: Sufficient number of times (e.g. replicate data entries)*
  - *Documentation: Protocols and reports*
  - *Revalidation: In case of significant changes made*

7.2.5

Validation

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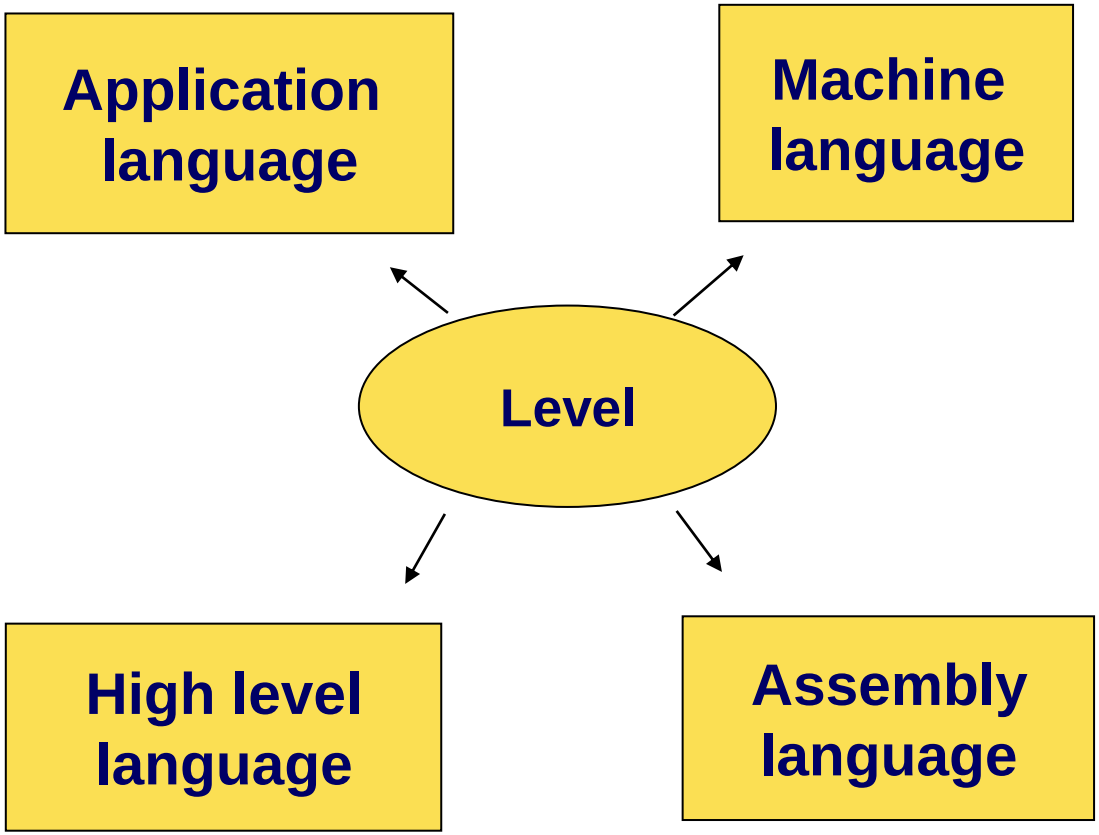

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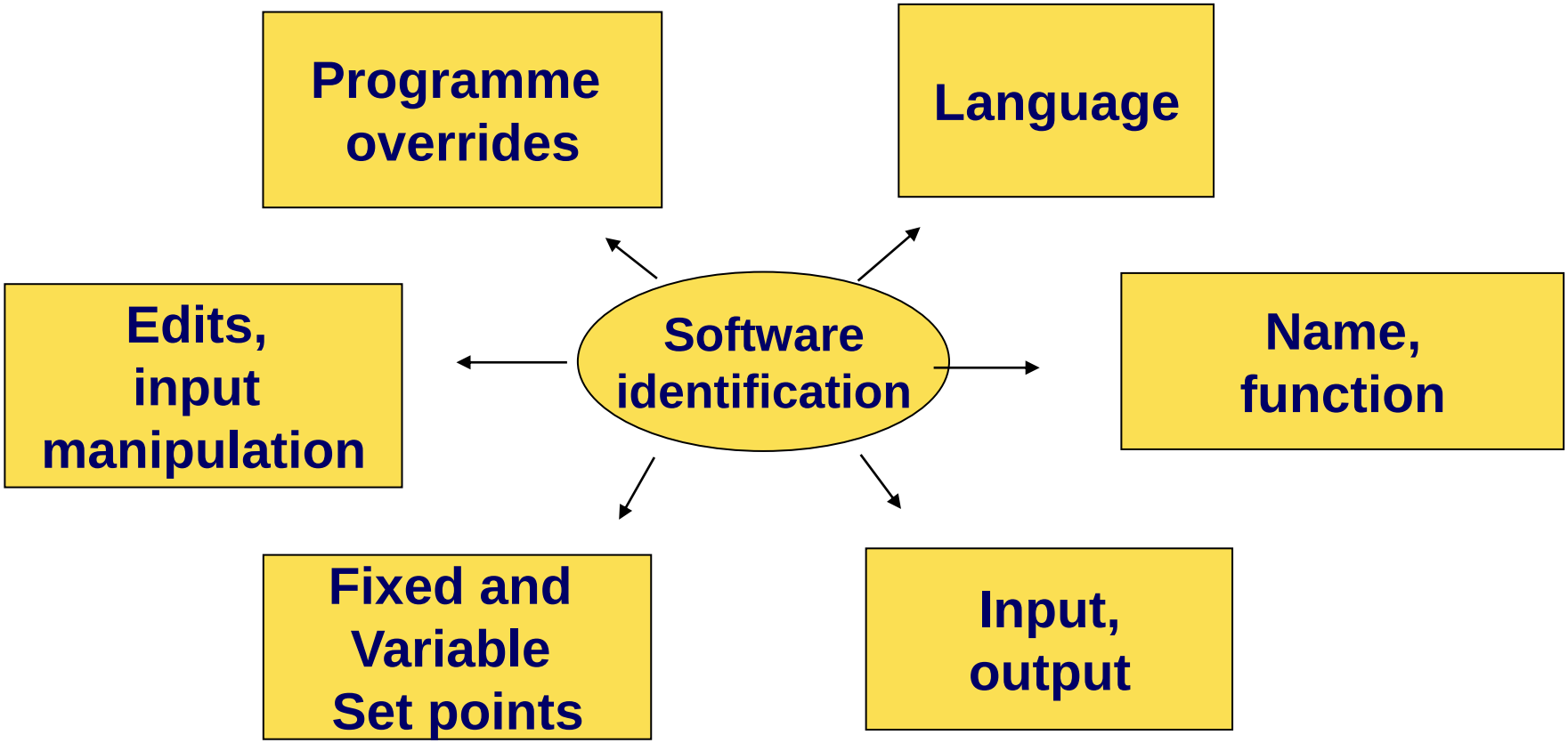

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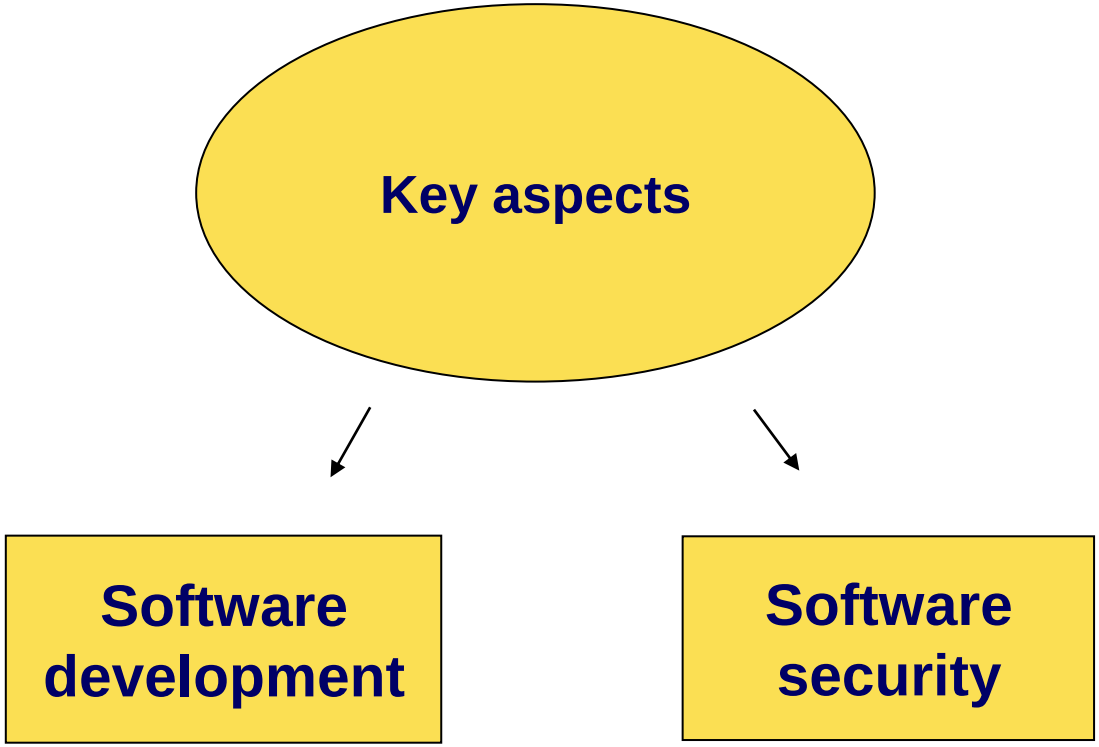

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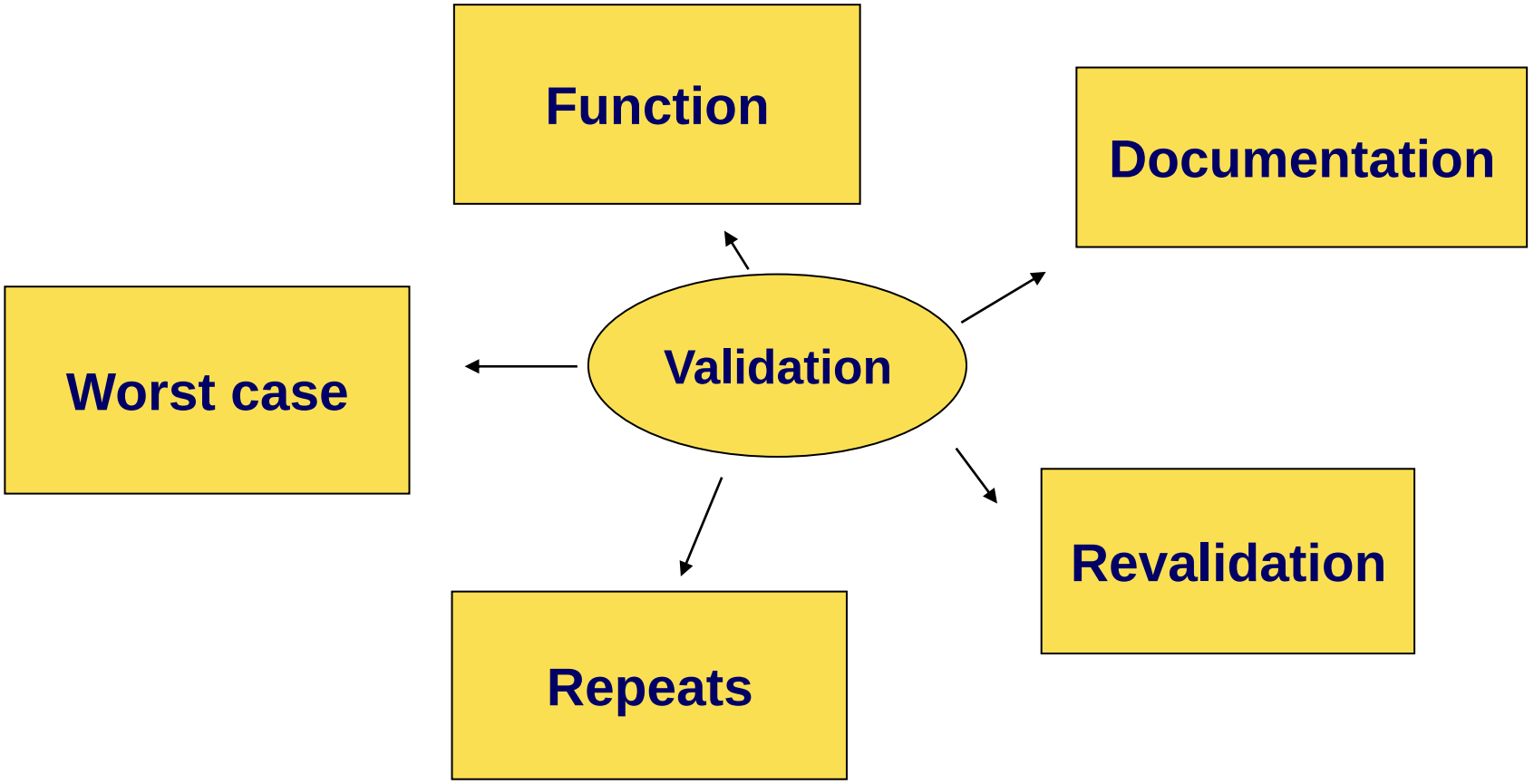

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Validation

- Group session