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The use of reference materials in internal quality control

Marina Patriarca

Laboratory Accreditation

A TWO-DAY TRAINING COURSE - CRITICAL ISSUES OF THE ACCREDITATION STANDARDS - ISO/IEC 17025:2017 AND ISO 15189:2012

Nicosia (Cyprus), 21st - 22nd February 2019

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Aim of the training

To give you an overview of

- IQC and why we need it
- Key-elements for IQC planning
- Guidance available
- Reference and Quality Control Materials for IQC
- Control Charts and how to build them
- Decisions based on IQC evidences
- QMCs production

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ISO/IEC 17025:2017
7.7 Ensuring the validity of results

- Have a procedure for monitoring the validity of results
- Record the resulting data so that:
  - trends are detectable
  - (where practicable), statistical techniques can be applied to review the results.
- Plan and review the monitoring activities

Internal Quality Control

Planning IQC

Define:

- What to measure (parameter)
- With respect to what (target value)
- Control limits (fitness-for-purpose)
- How to measure it (method, replicates, stats)
- How often to measure it (frequency)
- How to record data
- How to evaluate trends
- How to deal with problems

Useful tools: control charts

7.7 Ensuring the validity of results

Using:

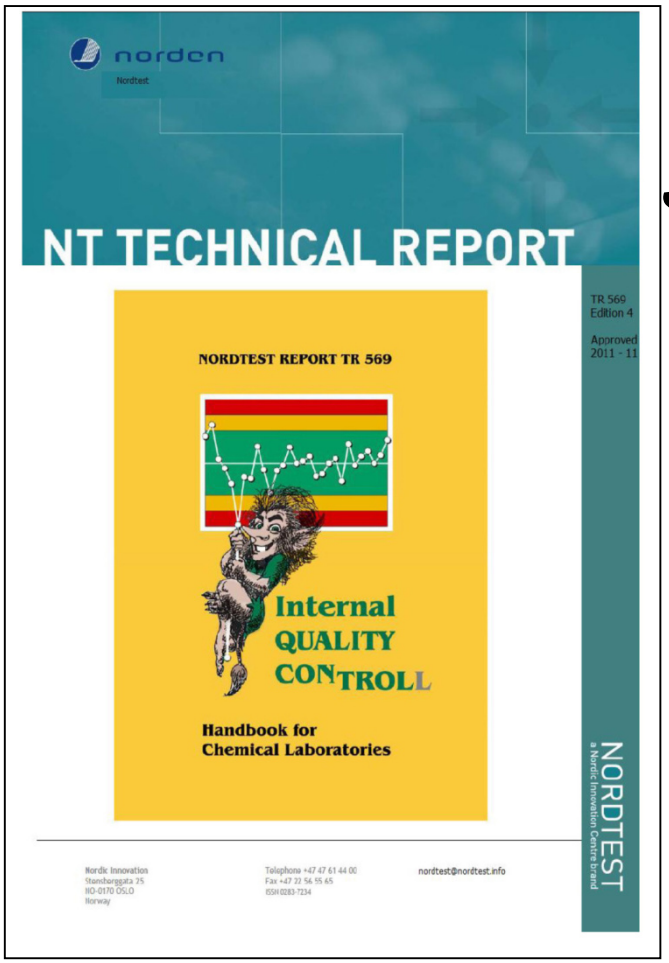
- reference materials or quality control materials;
- results obtained with alternative instrumentation;
- functional check(s) of measuring and testing equipment;
- check/working standards;
- intermediate checks on measuring equipment;
- replicate tests using the same or different methods;
- retesting of retained items;
- correlation of results for different characteristics of an item;
- review of reported results;
- intralaboratory comparisons;
- testing of blind sample(s).

Relevant Guidance

Reading list (www.eurachem.org)

- M. Thompson, B. Magnusson, Methodology in internal quality control of chemical analysis, Accred. Qual. Assur., 2013, 18, 271-278 (www.link.springer.com)
- M. J. Gardner, Quality control techniques for chemical analysis: some current shortcomings and possible future developments, Accred. Qual. Assur., 2007, 12, 653-657 (www.link.springer.com)
- M. Thompson, R. Wood, Harmonized guidelines for internal quality control in analytical chemistry laboratories, IUPAC Technical Report, Pure Appl. Chem., 1995, 67, 49-56 (www.degruyter.com/pac)
- AMC Technical Briefs, RSC, (www.rsc.org/Membership/Networking/InterestGroups/Analytical/AMC/TechnicalBriefs.asp)

Relevant Guidance



- ISO 7870-1:2014 Control charts – Part 1: General guidelines
- ISO 7870-2:2013 Control charts – Part 2: Shewhart control charts
- ISO 7870-3:2012 Control charts – Part 3: Acceptance control charts
- ISO 7870-4:2011 Control charts – Part 4: Cumulative sum charts
- ISO 7870-5:2014 Control charts – Part 5: Specialized control charts
- ISO 7870-6:2016 Control charts – Part 6: EWMA control charts
- ISO/DIS 7870-7 Control charts – Part 7: Multivariate control charts [Under development]
- ISO 7870-8:2017 Control charts – Part 8: Charting techniques for short runs and small mixed batches

Analytical measurements

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RMs and CRMs

Reference material – RM (VIM3, 5.13)

- sufficiently homogeneous and stable properties
- established to be fit for its intended use

Certified reference material – CRM (VIM3, 5.14)

- Specified property values, uncertainties and traceabilities
- Obtained using valid procedures
- Fully documented
- Issued by an authoritative body

CRMs are special types of measurement standards

Quality Control Materials (QCMs)

- Materials used routinely to assess precision of test procedures
- Other names: “in-house reference materials”, “quality control samples”, “check samples”, “set up samples”….
- QCMs cannot be used to establish metrological traceability or trueness of a measurement result
- Often prepared by a laboratory for its own internal use
- Often characterized only for a limited scope
  - limited number of property values
  - specific laboratory applications.

Some uses of QCMs

- IQC
- method development
- instrument performance checks
- repeatability, reproducibility, robustness studies
- impact of changes to the environmental conditions (e.g. temperature, humidity
- comparisons (degree of equivalence) between methods / instruments / laboratories
- training / qualification of operators

Why choosing/preparing QCMs

- To better represent routine samples
- Suitable day-to-day RM to complement a commercially available CRM
- No suitable CRM exists
- Uses not requiring the characteristics – traceability, uncertainty - and related cost of a CRM
  - Typically studies involving only precision

Requirements for QCMs

- As other RMs, sufficiently homogeneous and stable properties
  - Homogenenity: better than the process variability / the acceptability criteria
  - Stability: at least for the intended period of use
- If prepared by the laboratory for its own use, some requirements can be relaxed
  - E.g. transport stability
- Guidance:
  - ISO Guide 80, ISO 17034, ISO Guide 35

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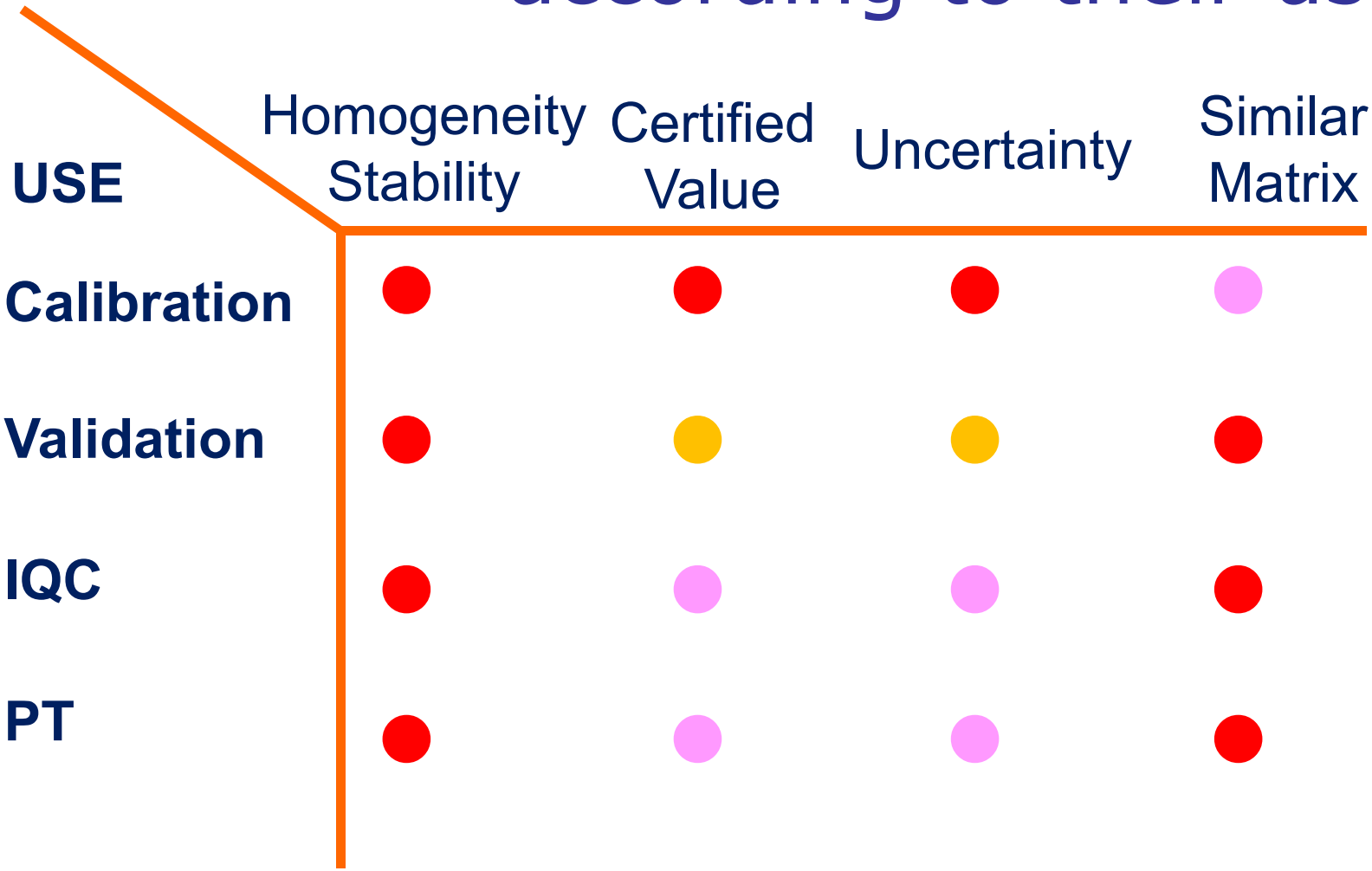
Requirements of RMs according to their use



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Internal Quality Control

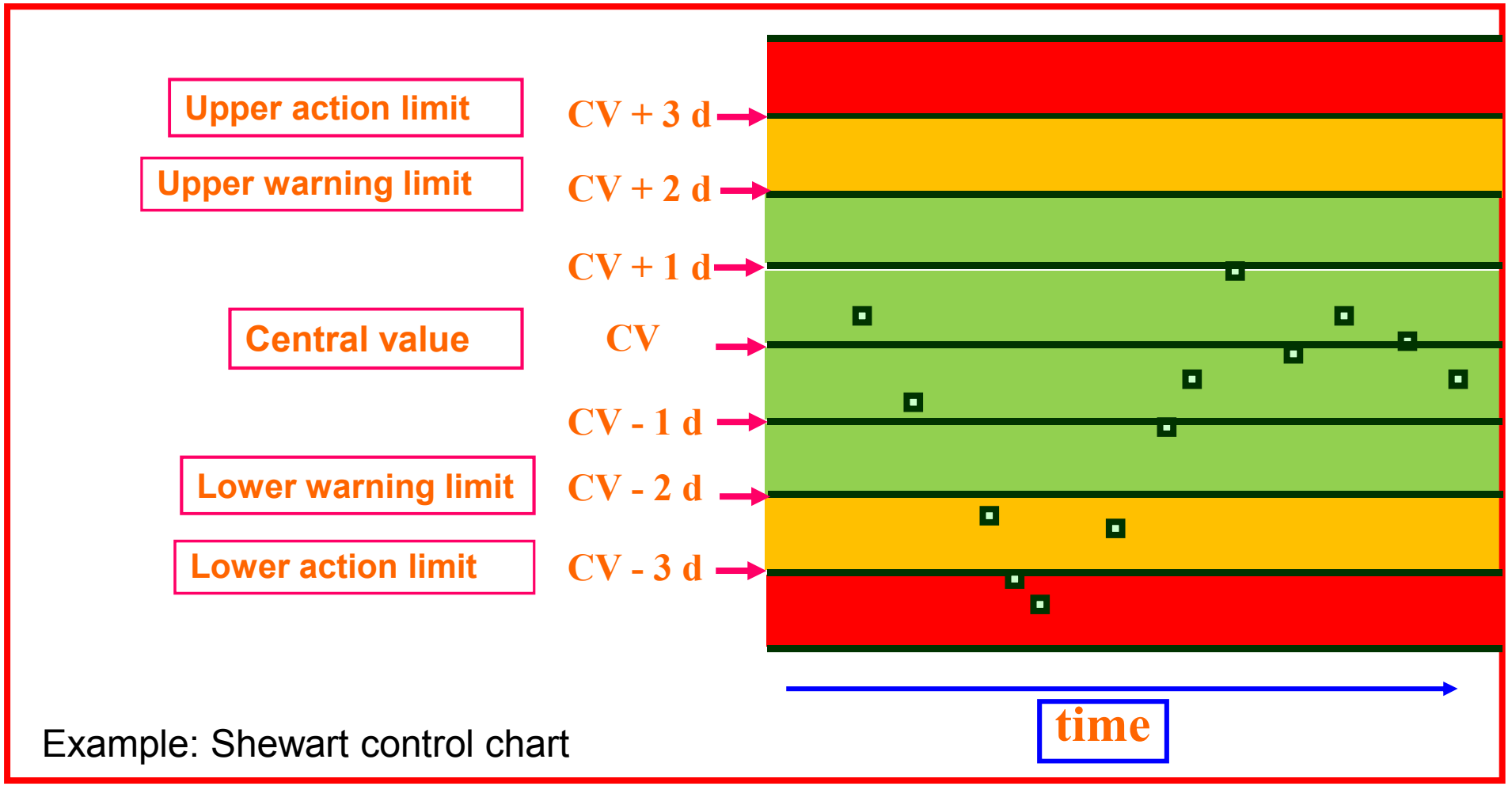
Parameter

- Blank correction
- Drift
- Calibration
- Precision
- Bias
- Overall process

Type of RM

- Matrix CRMs
- Working standards
- Procedural blanks
- Matrix RMs
- Test samples
- Matrix QCMs

Control charts



Example: Shewart control chart

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Central value

- CRMs
  - Certified value
- RMs with an assigned value
  - Assigned value
- QCMs
  - Value needs to be assigned
  - Planned activity
  - Typically based on a series (>20) of data
  - May have to be reassessed over a period of time

Which central value

- Fit-for-the purpose
  - Short range / wide range / decision levels

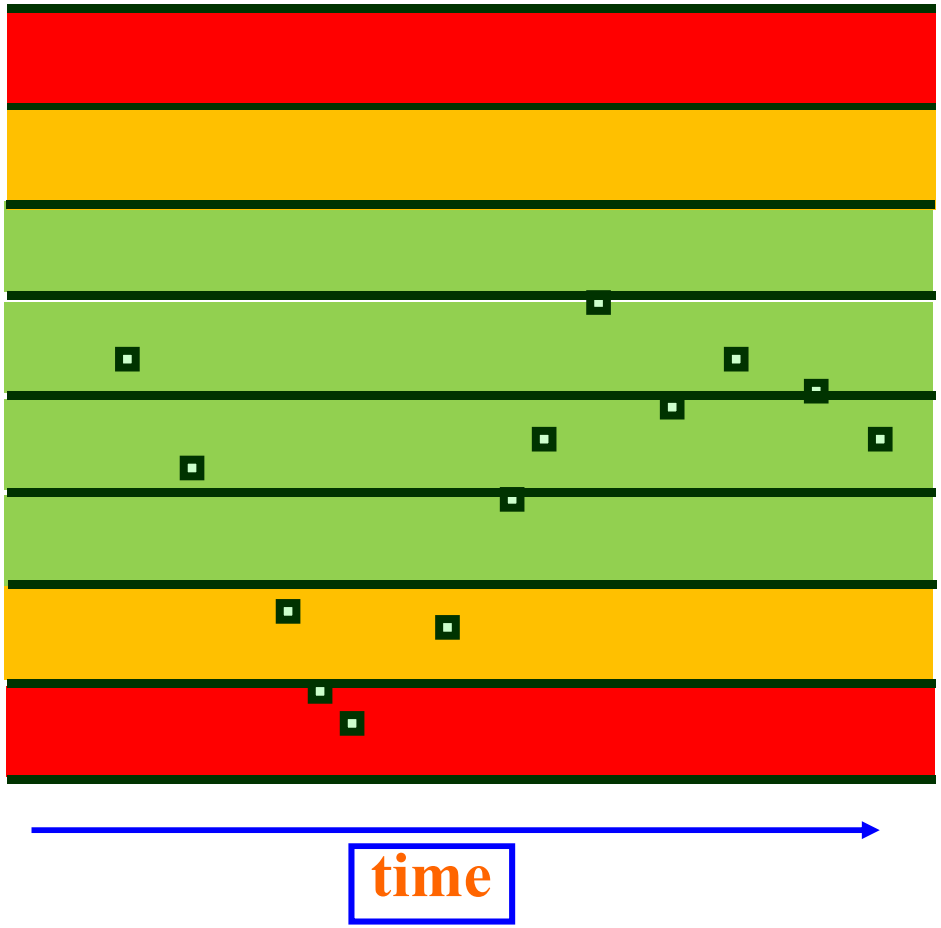
- Uncertainty
  - Ideally negligible in comparison with d
  - A suitable criteria: u <0.3 d

Defining control limits (d)

- Fit-for-the-purpose (target control limits):
  - Legal requirements for the analytical performance?
  - Performance criteria applied in PT schemes?

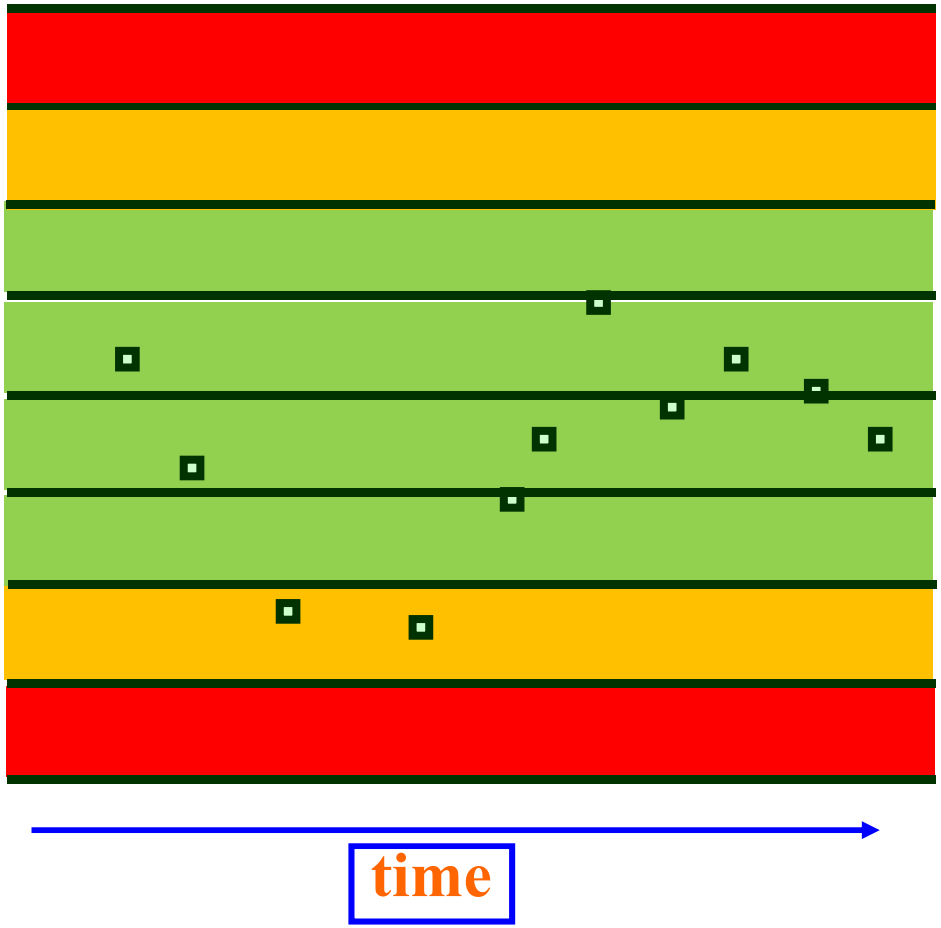
- Representative of the method's performance (Statistical control limits)
  - Experience / precision studies

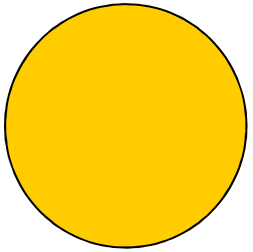
Decisions: control values



- Go ahead
- Pay attention!
- STOP!!!!

Decisions: control values





Stop if:

at least one of the two previous control values is also between the warning and action limits

Nordtest

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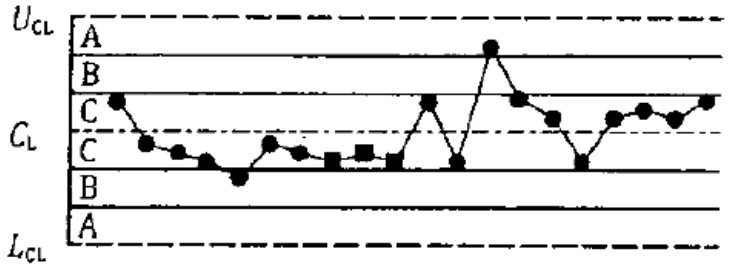
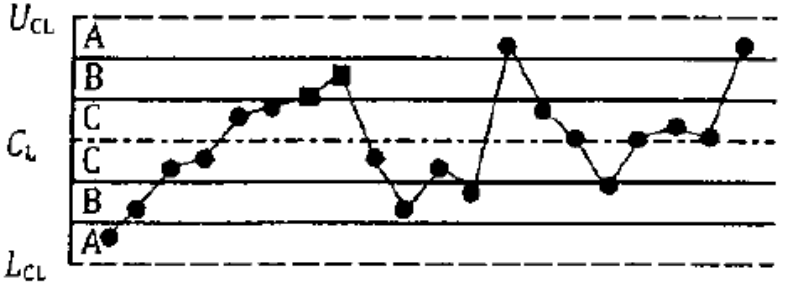
Review: assessing trends

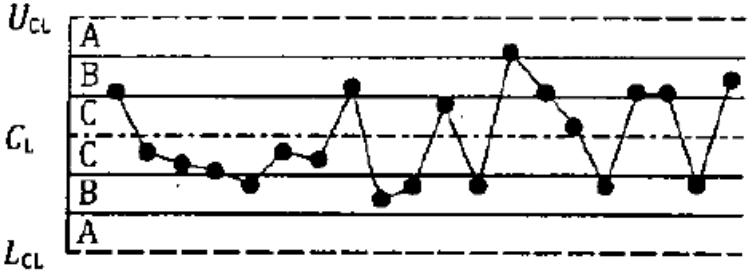
- Aim: to detect potential problems as early as possible
- Some examples from ISO 7870-2
- More rules exist



Test 2: Run – seven or more consecutive points on one side of centre line



Test 3: Trend – seven consecutive points entirely increasing or decreasing



Test 4: Any obvious nonrandom patterns

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Guidance for the in-house preparation of quality control materials (QCMs)

ISO

Reference number
ISO GUIDE 80:2014(E)

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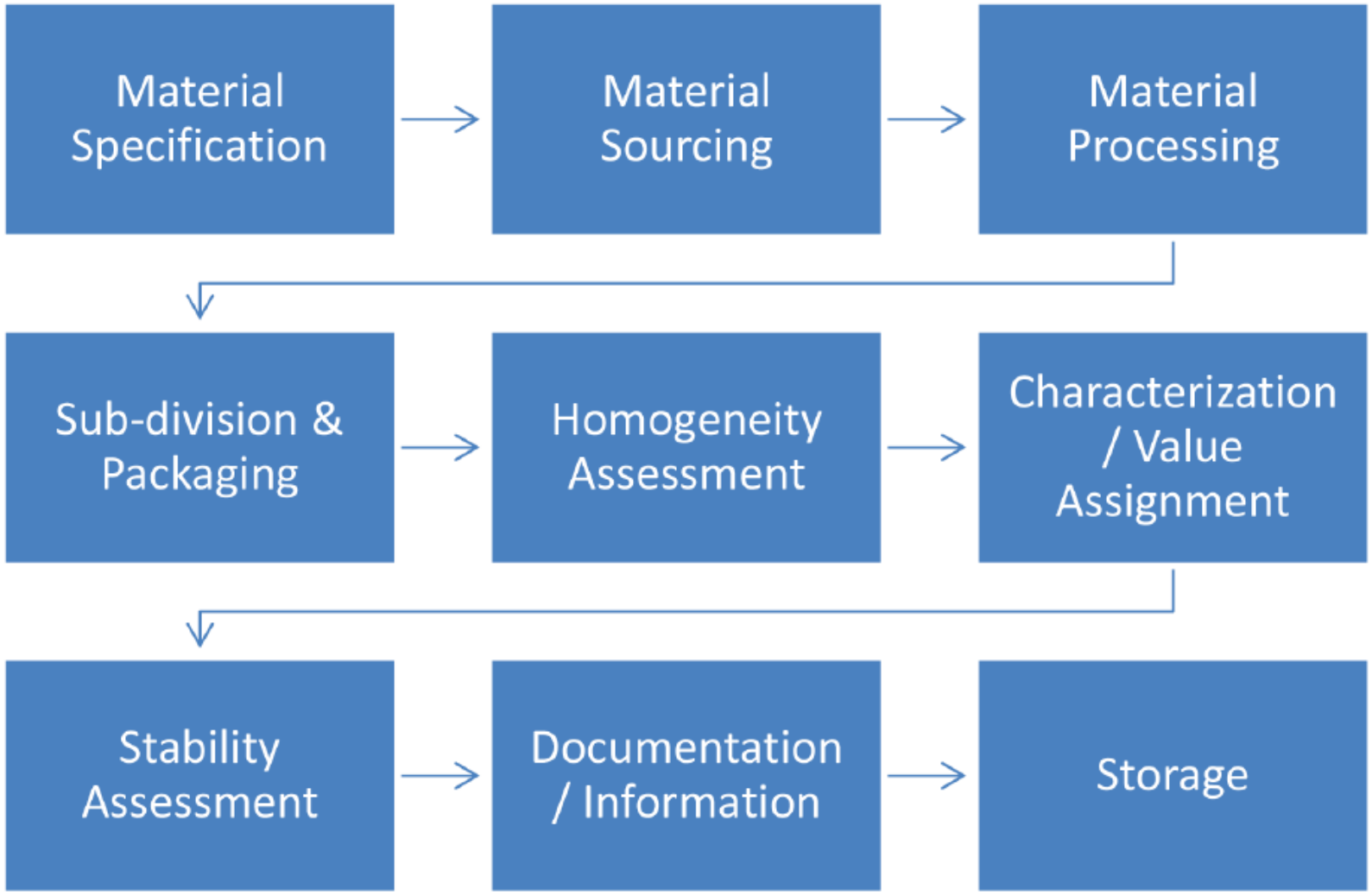
QCMs production



Material specification

- as close as possible to real samples
- available in appropriate quantities
- properties and property values similar to those of test samples
- unit size based on:
  - the amount of material required for the measurement
  - to be used for single / multiple analysis

Total bulk amount of material

- number of units required per year
- unit size
- preparation yield
- amount of material that can be treated
- how long the QCM should last and the assumed stability
- type and size of the required storage facilities

Matrix selection

- Based on:
  - knowledge of the analytical procedure used on the routine samples
  - Evaluation of the potential effects of variation of the physical/chemical properties of the sample

Example: a freeze-dried food matrix may behave differently during analysis to a similar foodstuff with higher moisture content.

Material processing: common steps

- Drying
- Milling and grinding
- Sieving
- Mixing and blending
- Filtration
- Stabilization
- Sterilization

Sub-division and packaging

- Choice of containers, consider
  - Moisture
  - Oxigen
  - Light
  - Adsorption
  - Leaching
  - Evaporation
- Sub-division procedures
  - Designed so to maintain sample homogeneity

Homogeneity assessment

$$s_{between} \leq 1/3\ s_{intermediate}$$

Table 1 — Homogeneity study of 10 units

Unit number	Result 1 mg·kg^{-1}	Result 2 mg·kg^{-1}	Mean mg·kg^{-1}	Variance mg·kg^{-1}
1	121,3	128,74	125,02	27,68
2	120,87	121,32	121,10	0,10
3	122,4	122,96	122,68	0,16
4	117,60	119,66	118,63	2,12
5	110,65	112,34	111,50	1,43
6	117,29	120,79	119,04	6,12
7	115,27	121,45	118,36	19,10
8	118,96	123,78	121,37	11,62
9	118,67	116,67	117,67	2,00
10	126,24	123,51	124,88	3,73

Characterization and value assignment

- QCM purpose: to detect changes
- Requirement: assess variation in values due to sample heterogeneity
- Indicative value: overall mean, from the homogeneity study
- Uncertainty of the indicative value: $s_{between}$ from the homogeneity study

Stability assessment

- both costly and time-consuming

If QCM is to be used in-house:

- may not be necessary
  - Information / experience on the type of material is available
- assessment of stability not required
- The risk of wrong decisions due to instability of the QCM needs to be evluated

Assigning an expiry date to a QCM

- Based on previous experience and available information
- Not be regarded as absolute, in the event of a QCM giving an unexpected result

Documentation /information

- name and description of the material
- reference number and/or batch number
- date of preparation
- intended use of the material
- instructions for its use
- indicative value(s), if applicable
- minimum amount of material required
- storage instructions
- expected shelf-life
- safety precautions

Storage

- To be stored under conditions that will ensure they remain unchanged
- Storage conditions should be monitored at regular intervals
- The results of the monitoring should be recorded