



Schweizerische Eidgenossenschaft
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Federal Institute of Metrology METAS



Correct choice and application of certified reference materials in method validation in food analysis

Gisela Umbricht

Agenda

1. Introduction - Food safety at METAS
2. Certified reference materials
3. Use of certified reference materials

Agenda

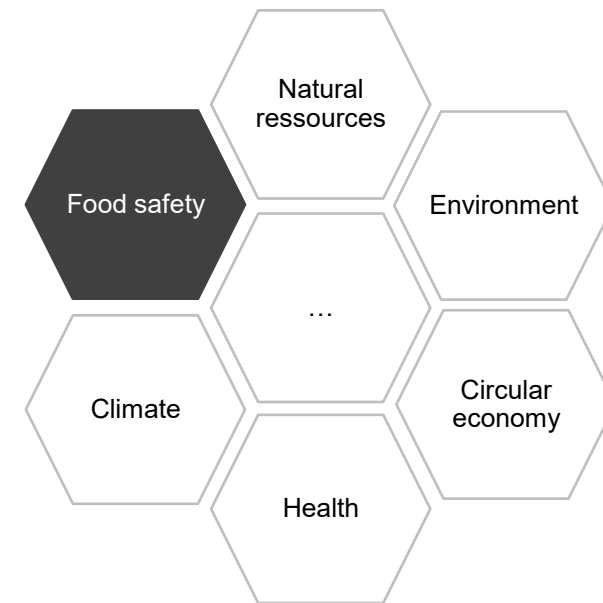
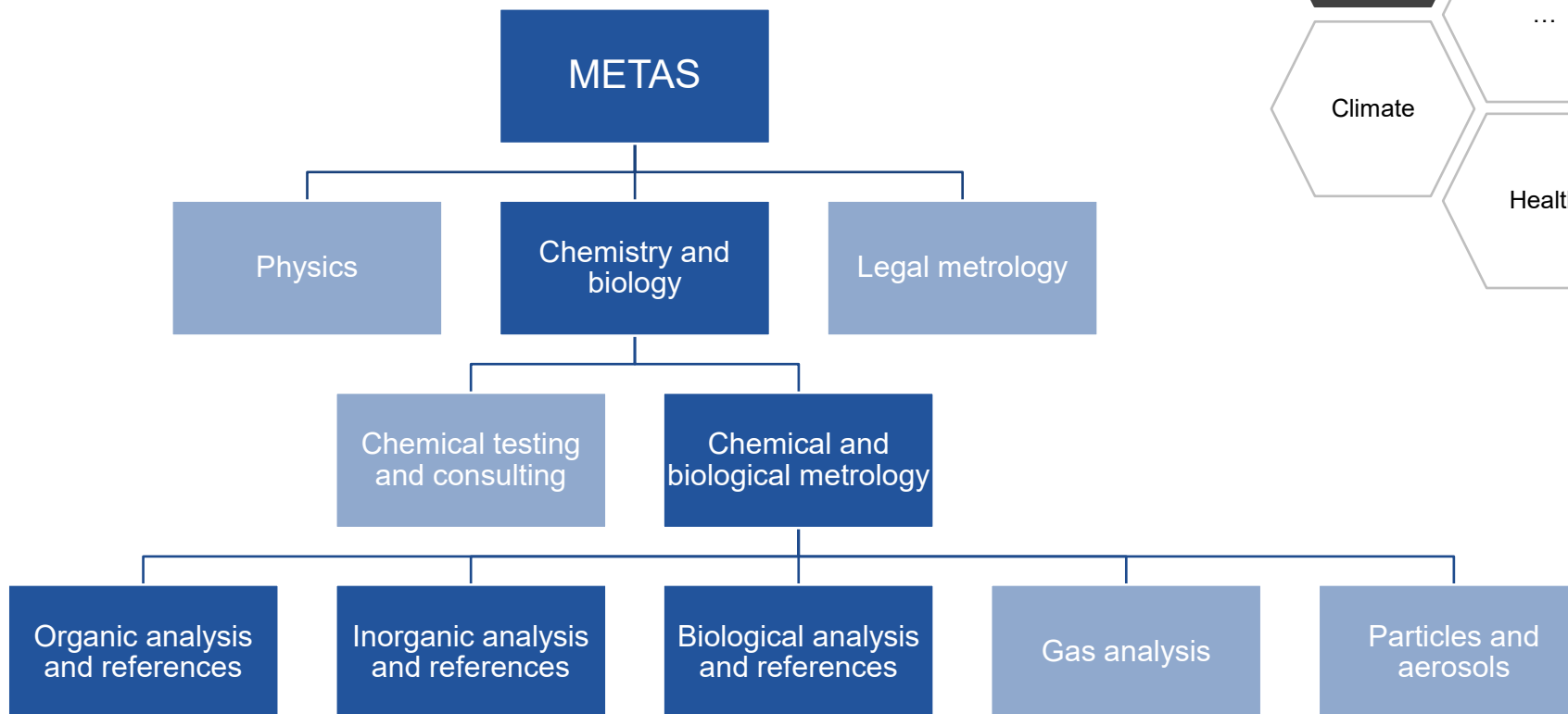
1. Introduction - Food safety at METAS
2. Certified reference materials
3. Use of certified reference materials

Food safety at METAS (I)

Departments

Sections

Laboratories



Food safety at METAS (II)

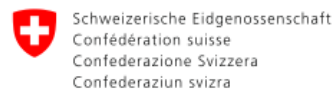
Organic analysis and references

Inorganic analysis and references

Biological analysis and references

- Production of certified reference materials (CRMs)
- Food monitoring studies*
- Population biomonitoring studies*
- National reference laboratories (NRLs)*

Laboratories



Federal Food Safety and Veterinary
Office



* Integration by 01.01.2023

Food monitoring studies

Organic analysis and references

Inorganic analysis and references

Biological analysis and references

Contaminant	Matrix
Per- and polyfluoroalkyl substances (PFAS)	Fish
Endocrine disruptors (BPA, BPS)	Thermal paper
Fern toxins	Surface and groundwater
Extension of the Swiss food composition database with additional elements (Ca, Fe, K, Mg, Na, P, Se, Zn, I) and food products	Milk and meat substitutes
Prevalence of pathogenic vibrio species (<i>Vibrio parahaemolyticus</i> , <i>Vibrio vulnificus</i> , <i>Vibrio cholerae</i>)	Seafood (fresh oysters, tuna, salmon, shrimps)
Alimentary transmission of tick-borne encephalitis virus (TBEV)	Raw goat milk and cream cheese
...	...

Population biomonitoring studies

Organic analysis and references

Inorganic analysis and references

Biological analysis and references

Contaminant	Matrix
Per- and polyfluoroalkyl substances (PFAS)	Serum
National survey on nutritional situation of 6 to 17 years old children and teenagers (As, Se, Zn, Pb, iodine, PFAS, ochratoxin A, bisphenols, phthalates)	Serum
Iodine and endocrine disrupter status of the Swiss population (iodine, phthalates, bisphenols)	Serum and urine
...	...

National reference laboratories (NRLs)

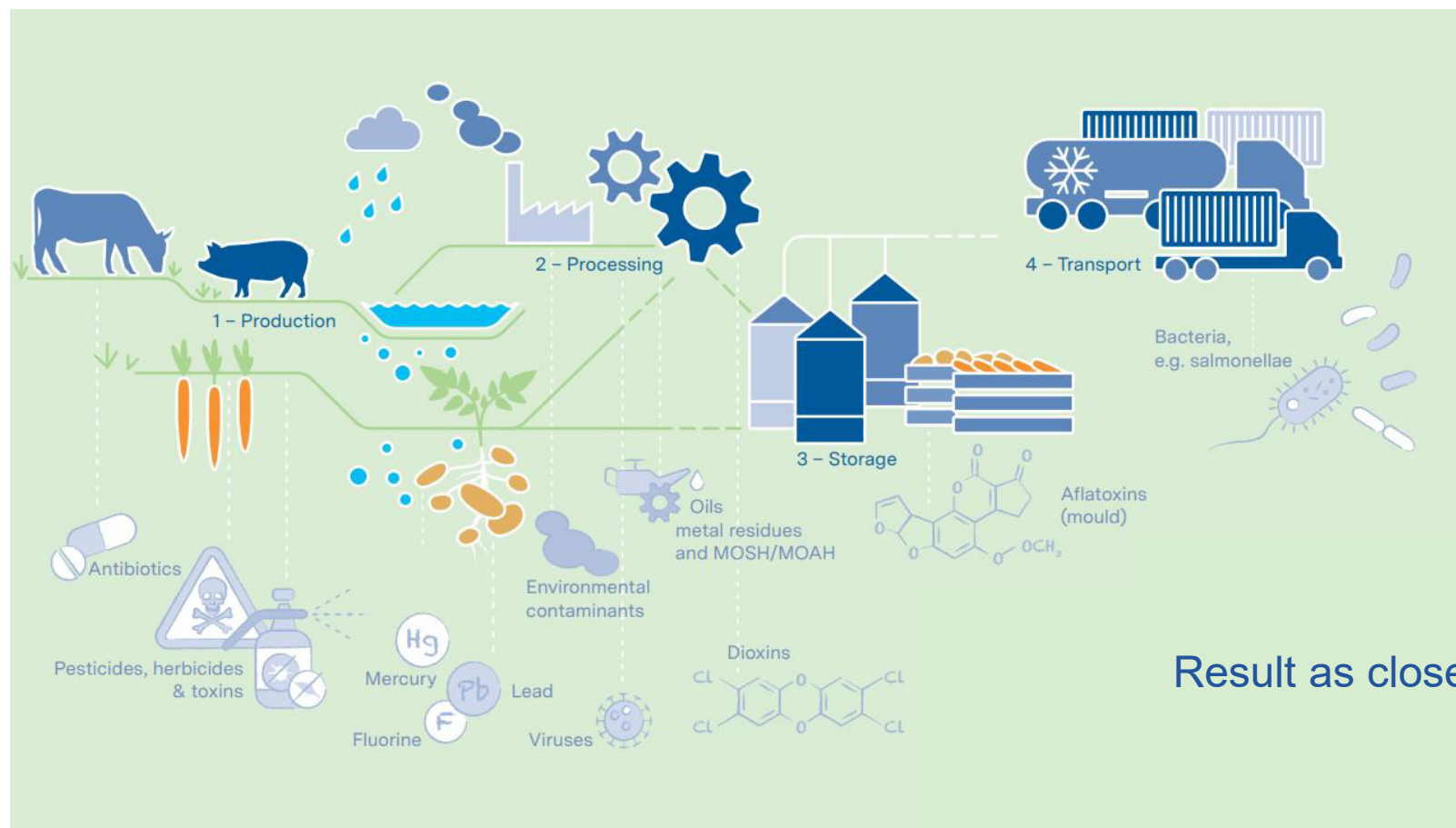
Organic analysis and references

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NRL	Contaminants
Process contaminants	<ul style="list-style-type: none"> - PAHs - MCDPs and GE - Furan and alkylated furans - Acrylamide - ...
Metals and nitrogenous compounds	<ul style="list-style-type: none"> - Pb, As, Cd, Hg - Speciation - Nitrate and nitrite - ...
Foodborne viruses	<ul style="list-style-type: none"> - Hepatitis A and E - Norovirus (genogroup I and II) - Enterovirus and rotavirus - ...
Genetically modified organisms	GMOs

Landscape of food contaminants and matrices



Challenge



Result as close as possible to the «true value»

- Measurement accuracy
- Measurement trueness
- Validity and comparability of results

Agenda

1. Food safety at METAS
- 2. Certified reference materials**
3. WP-CBR001 as an example

Definition of (Certified) Reference Material

Definition of a Reference Material (RM) and of a Certified Reference Material (CRM)

- Reference Material: Material, sufficiently homogeneous and stable with respect to one or more specified properties, which has been established to be fit for its intended use in a measurement process.
- Certified Reference Material: Reference material characterized by a metrologically valid procedure for one or more specified properties, accompanied by an RM certificate that provides the value of the specified property, its associated uncertainty, and a statement of metrological traceability.

Definition of (Certified) Reference Material

	Reference material (RM)	Certified reference material (CRM)
Homogeneity	✓	✓
Stability	✓	✓
Specified property value	(✓)	✓
Uncertainty		✓
Metrological traceability		✓
Certificate		✓

Differences between Reference Material (RM) and Certified Reference Material (CRM)

- Metrological traceability – base of confidence and comparability world wide
- Specified property value – as close as possible to the unknown true value
- Estimation of the uncertainty budget
- Certificate

Types of reference material

- **Pure substances** – characterized for chemical purity and/or trace impurities
- **Standard solutions and gas mixtures** – often prepared gravimetrically from pure substances and used for calibration purposes
- **Matrix reference materials** – characterized for the composition of specified major, minor or trace chemical constituents. Such materials may be prepared from matrices containing the components of interest, or by preparing synthetic mixtures
- **Physico-chemical reference materials** – characterized for properties such as melting point, viscosity, density, pour point etc.
- **Reference objects or artefacts** – characterized for functional properties such as taste, odour, etc.
- ...

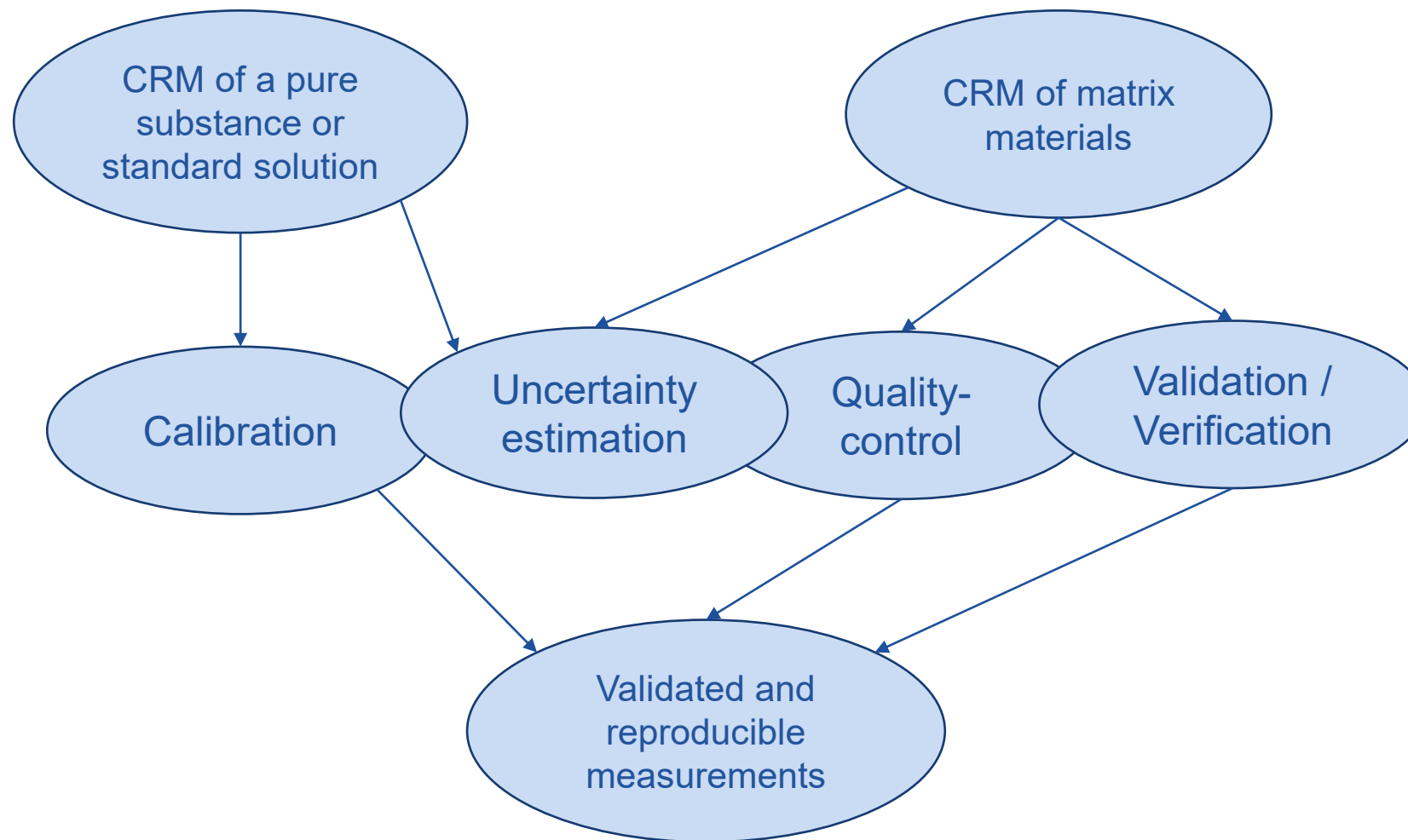
Application of certified reference material in food analysis

- Makronutritional properties (total fat, protein, etc.) for labelling purposes
- Mikronutritional properties (vitamins, dietary fibers, trace elements, etc.)
- Further examples to support legislation, for instance for natural isotope fractionation used to counter misuse of sugaring to increase alcoholic strength in wine
- Determination of contaminants (PAHs, Dioxines, toxic elements, etc.), residues and natural toxins (aflatoxins, ochratoxin, zearalenone, etc.) in food
- Detection of added growth hormones in meat production
- ...

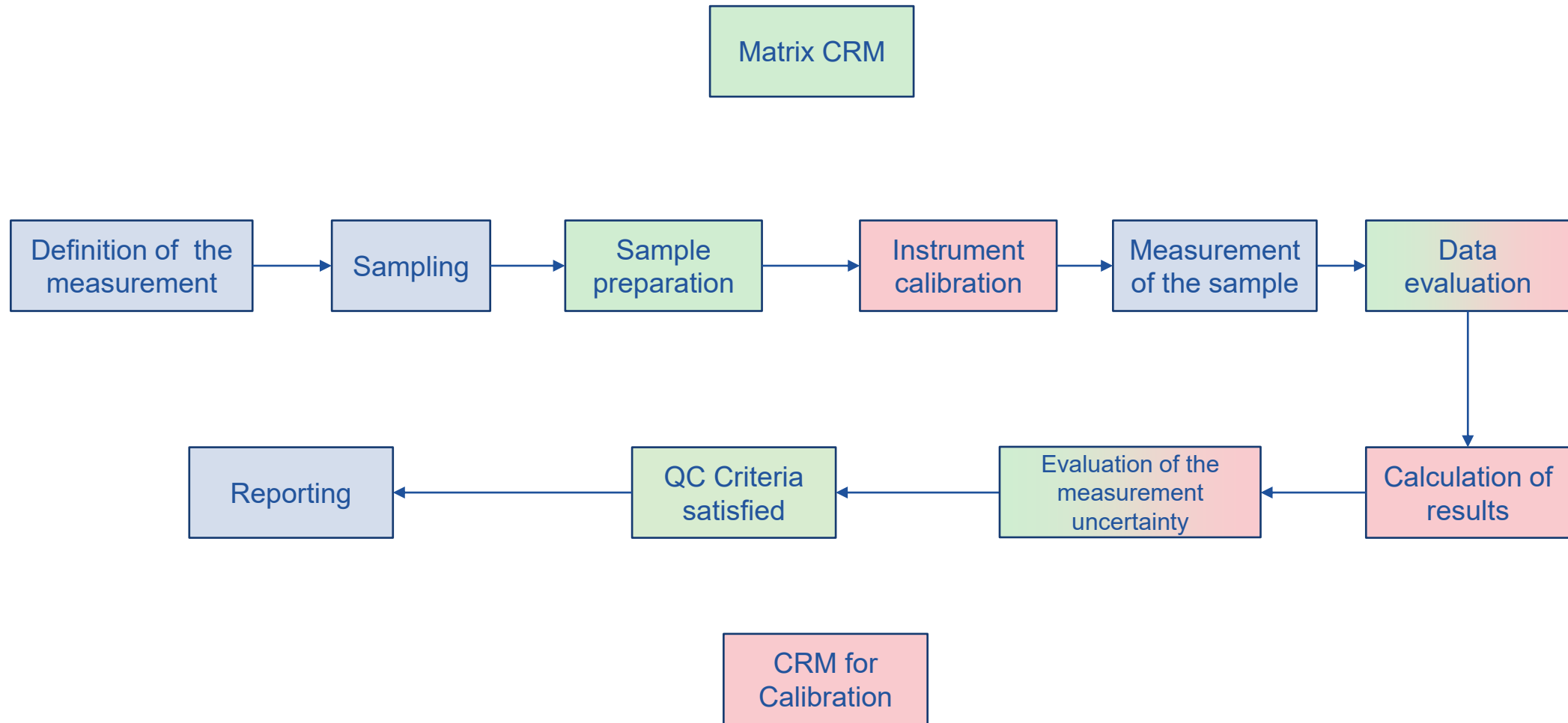
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Usage of certified reference material



Aspects to be considered for choice of certified reference material



Aspects to be considered for choice of certified reference material

- Decision whether to use a qualitative procedure – or – a quantitative method
- Planned usage of the reference material: Calibration (pure material or solution of pure materials), or Validation and/or verification of analytical methods (matrix reference material), or quality control.
- Choice of appropriate matrix (as similar as possible to the matrix to be tested)
- Choice of the appropriate level of the to be tested property (concentration) and of the needed stability of the reference material
- To be aware of the difference between a spiked or “naturally” produced reference material
- The uncertainties at a stated level of confidence given
- If you don't find the appropriate matrix CRM needed, make sure that the second best CRM contains a note in the certificate that it can also be applied to other matrices (commutability)

K.E. Sharpless et al. (NIST), The ABCs of Using Standard Reference Materials in the Analysis of Foods and Dietary Supplements: A Practical Guide, NIST Special Publication 260-181 (<http://dx.doi.org/10.6028/NIST.SP.260-181>)

Choice for matrix CRMs

ORGANIC ANALYSIS WORKING GROUP



(C)RMs inserted in KCDB CMCs

Data extracted on 24/04/2023, covering **last 6 years** (from 01.01.2017)

Measurement service category 11: Food

Measurement service sub-categories:

- Contaminants
- Nutrients
- Other than nutritional constituents, contaminants, and GMOs
- *Matrix* categorised by the AOAC triangle (using the template prepared by HSA)
- Data from 15 NMIs + ad-hoc collected data from JRC, NIST (released CRMs from 01.01.2017-09.06.2022).



«Benefits» by using a certified reference material

- Control of sample preparation (extraction) efficiency
- Calibration of measurement instruments (calibrants)
- Validation and/or verification of analytical methods (single lab and collaborative method validation) as well as «laboratory assistants»
- Uncertainty assessment
- Quality control
- Proficiency tests (PTs) / Interlaboratory comparisons

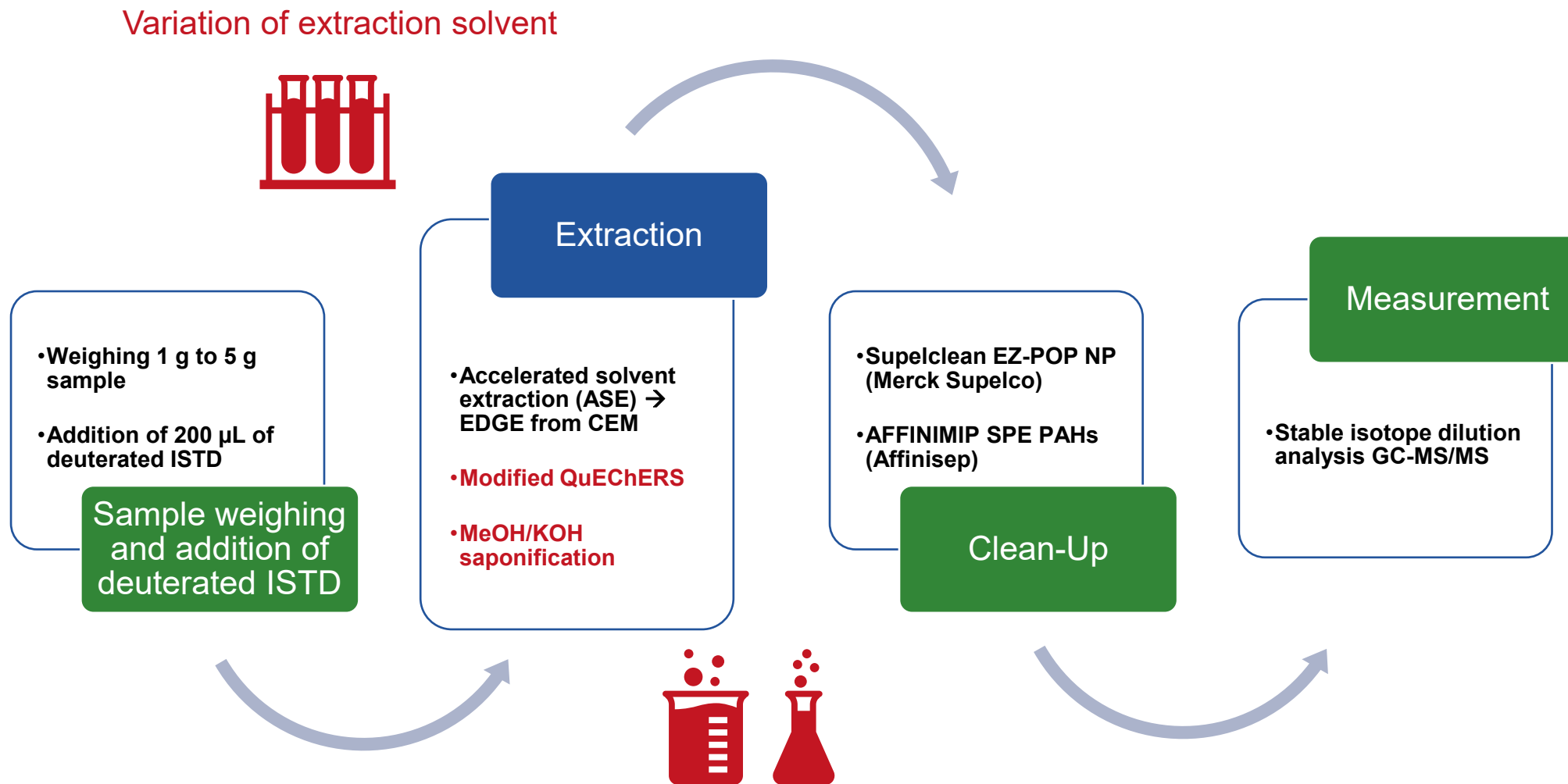
Data evaluation

- Metrological traceability – calibration of measurement system with certified calibration materials (either neat materials or solutions)
- Maximal confidence in measurement process by keeping as low as possible the number of measurement steps (minimizing the measurement uncertainty)
- Validation of the measurement process by using the appropriate matrix CRM under controlled environmental conditions



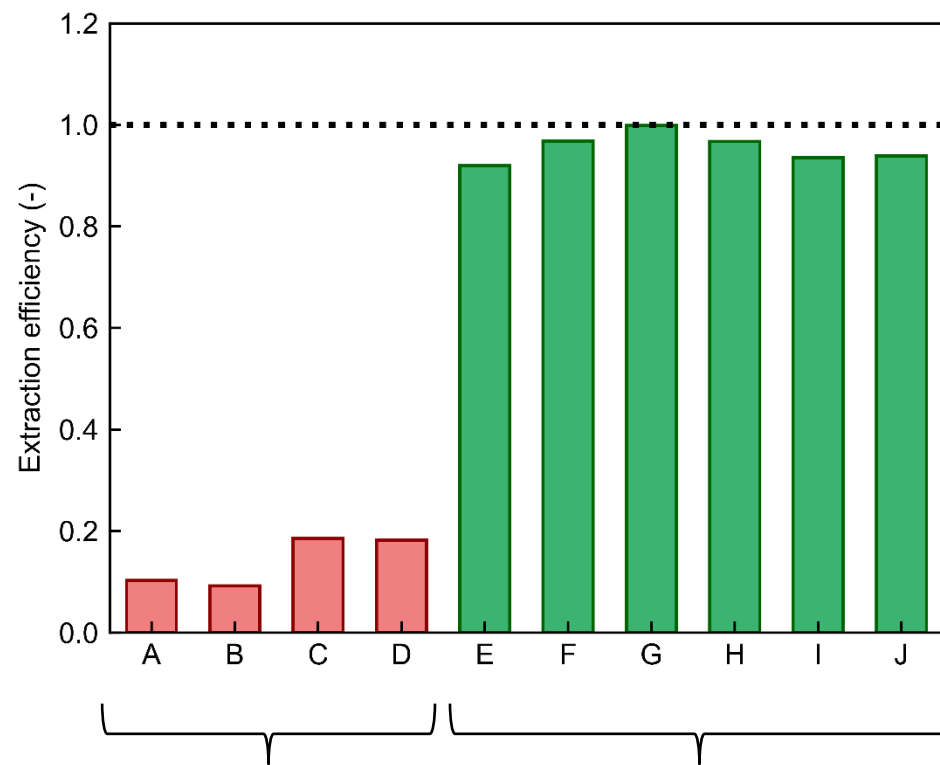
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Example



Variation of extraction method

Example – solvent extraction efficiency



nonpolar /
polar aprotic

polar protic



ASE (EDGE)

- A) n-Hexane
- B) Cyclohexane
- C) Cyclohexane : acetone (1:1)
- D) Cyclohexane : ethyl acetate (1:1)
- E) Methanol : tBME (1:4)
- F) Methanol : tBME (1:1)
- G) Methanol

QuEChERS (aqueous treatment)

- H) n-Hexane:acetone (1:1)
- I) Acetonitrile

KOH/MeOH (saponification)

- J) n-Hexane

Influence of extraction technique: none

Influence of solvent: yes

Summary and key messages

- Matrix CRMs play a key role in ensuring accurate determinations of contaminants in foods
- Matrix CRMs generally provide cautionary validation of the fitness-for-purpose of your measurement procedure for real samples. It is only fit for samples having analyte content and matrix similar to the CRM.
- Always take a look at the entire analytical process (sampling, sample preparation, measurement, evaluation and reporting)
- More matrix CRMs, also for «novel» foods, are needed in all fields of food contaminant analysis

... will develop further CRMs

... can contribute to improve measurement accuracy

... can contribute to food safety

Acknowledgements

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- Dominik Moor



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Thank you very much for your attention