VI. Metrology: Concepts of qualification and calibration

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Learning objectives:

By the end of the lesson, students will be able to:

1. Explain core principles of metrology
2. Evaluate measurement quality
3. Navigate the world of metrological practices

Content

- Introduction

1. Definition of metrology
    - 1.1. Meter Convention
    - 1.2. International System of Units (SI)
    - 1.3. WHO International Units
    - 1.4. SI prefixes
    - 1.5. Terminology
2. Qualification of measures
    - 2.1. Measurement of accuracy
    - 2.2. Measurement of trueness
    - 2.3. Measurement of precision
3. Metrological vocabulary
4. Organizations linked to metrology
    - 4.1. At an international level
    - 4.3. In Algeria
5. Calibration
    - 5.1. Calibration hierarchy
    - 5.2. Metrological traceability chain
    - 5.3. ISO/IEC 17025
6. Reference standards in the European Pharmacopoeia
    - 6.1. Terminology
    - 6.2. Use of reference standards
6. Declaration of conformity
7. Measures in the field of health

- Conclusion

Introduction

Population growth, longer life expectancies, increased international travel and trade, and innovations in modern medicine are placing ever-increasing demands on health care systems. As a result, these systems face new challenges, for example the increased complexity of the measurements involved.

Each health-related measurement follows a predefined method; measurements can be simple (such as body temperature, heart rate and blood pressure or the amount of API in a tablet) or much more complex (such as determining doses of x-rays or scanner radiation).

It is essential that measuring and testing equipment conforms to agreed standards or specifications, producing the same results regardless of where the measurements are made. Guidelines and regulations that cover medical equipment and methods can only be applied if the measurements used to verify their compliance are accurate, traceable to internationally recognized reference measurement standards, and carried out using approved and properly calibrated instruments.

1. Definition of metrology

Science of measurement and its application

NOTE Metrology includes all theoretical and practical aspects of measurement, whatever the measurement uncertainty and field of application.

$$Y = y \pm U$$

Coverage factor: $k = 2$

Where y is the measurement value

U is the uncertainty value

k is the coverage factor which indicates the confidence interval

1.1. Metre Convention

The Meter Convention is the international treaty signed on May 20, 1875 in Paris (France) by 17 States with the aim of establishing a world authority in the field of metrology. It thus succeeds the international commission of the meter set up in 1870.

To do this, three structures were created.

- General Conference on Weights and Measures (CGPM),
- International Committee for Weights and Measures (CIPM)
- International Bureau of Weights and Measures (BIPM) the authority to act in the field of metrology, ensuring harmonization of the definitions of the different units of physical quantities.

This work ultimately led to the creation of the International System of Units (SI).

1.2. International System of Units (SI)

1.2.1. Unit of quantity: The value of a quantity is generally expressed as the product of a number and a unit. Ex: v = 25 m/s or v = 90 km/h, where metre per second and kilometre per hour are alternative units for the same value of the quantity speed.

1.2.2. The 7 defining constants:

The seven constants are chosen in such a way that any unit of the SI can be written either through a defining constant itself or through products or quotients of defining constants.

Starting from 2019, the International System of Units, the SI, is the system of units in which the defining constants are as follows:

- the unperturbed ground state hyperfine transition frequency of the caesium 133 atom, Δv_{Cs}, is 9 192 631 770 Hz,
- the speed of light in vacuum, c, is 299 792 458 m/s,
- the Planck constant, h, is 6.626 070 15 × 10−34 J s,
- the elementary charge, e, is 1.602 176 634 × 10−19 C,
- the Boltzmann constant, k, is 1.380 649 × 10^{-23} J/K,
- the Avogadro constant, N_A, is 6.022 140 76 × 10^{23} mol^{-1} ,
- the luminous efficacy of monochromatic radiation of frequency 540 × 10^{12} Hz, K_{cd}, is 683 lm/W,

where the hertz, joule, coulomb, lumen, and watt, with unit symbols Hz, J, C, lm, and W, respectively, are related to the units second, metre, kilogram, ampere, kelvin, mole, and candela, with unit symbols s, m, kg, A, K, mol, and cd, respectively, according to Hz = s^{-1} , J = kg m^2 s^{-2} , C = A s, lm = cd m^2 m^{-2} = cd sr, and W = kg m^2 s^{-3} .

1.2.3. The base units: The names and symbols of the base units of the SI are given in the following table.

Base quantity Grandeur de base	Base unit Unité de base	
Name Nom	Name Nom	Symbol Symbole
length longueur	metre mètre	m
mass masse	kilogram kilogramme	kg
time temps	second seconde	s
electric current courant électrique	ampere ampère	A
thermodynamic temperature température thermodynamique	kelvin kelvin	K
amount of substance quantité de matière	mole mole	mol
luminous intensity intensité lumineuse	candela candela	cd

1.3. WHO International Units:

There is a class of units for quantifying the biological activity of certain substances used in medical diagnosis and therapy that cannot yet be defined in terms of the units of the SI. This lack of definition is because the mechanism of the specific biological effect of these substances is not yet sufficiently well understood for it to be quantifiable in terms of physico-chemical parameters. In view of their importance for human health and safety, in 1965, the World Health Organization (WHO) has taken responsibility for defining WHO International Units (IU) for the biological activity of such substances.

Ex: Insulin (Fourth Standard) = 0.04167 mg

Vitamin D 3 (Second Standard) = 0.000025 mg

1.4. SI prefixes

The SI prefixes for multiples and submultiples of units are:

Factor Facteur	Prefix Préfixe	
	Name Nom	Symbol Symbole
10^{24}	yotta yotta	Y
10^{21}	zetta zetta	Z
10^{18}	exa exa	E
10^{15}	peta péta	P
10^{12}	tera téra	T
10^{9}	giga giga	G
10^{6}	mega méga	M
10^{3}	kilo kilo	k
10^{2}	hecto hecto	h
10^{1}	deca déca	da
10^{-1}	deci déci	d
10^{-2}	centi centi	c
10^{-3}	milli milli	m
10^{-6}	micro micro	μ
10^{-9}	nano nano	n
10^{-12}	pico pico	p
10^{-15}	femto femto	f
10^{-18}	atto atto	a
10^{-21}	zepto zepto	z
10^{-24}	yocto yocto	y

Multiplying factor	Name	Symbol
10^{27}	ronna	R
10^{-27}	ronto	r
10^{30}	quetta	Q
10^{-30}	quecto	q

Measure carefully to decide correctly!

A measurement or test result is a technical information that is communicated to another person. This information serves as a basis for making a decision: acceptance or rejection of a product, conformity of an environment, etc.

1.5. Terminology

- **A measurement** is a process which makes it possible to obtain one or more values which can reasonably be attributed to **a measurand**. A measurement begins with an appropriate definition of the measurand, and the measurement process.
- **A measurand**: is the quantity intended to be measured.
- **Result of a measurement**: Set of quantity values being attributed to a measurand together with any other available relevant information. It is generally expressed as a single measured quantity value and a measurement uncertainty.
- **Measurement uncertainty**: non-negative parameter characterizing the dispersion of the quantity values being attributed to a measurand, based on the information used
  Ex.: (51.4 ± 0.5) °C

2. Qualification of measures

To compare measurements of the same reference by different measurement processes, we may have to use qualifying terms. These terms are accuracy, trueness and precision of measurement

2.1. Measurement accuracy

“closeness of agreement between a measured quantity value and a true quantity value of a measurand"
True value (of a quantity): Value compatible with the definition of a given particular quantity. This is a value that would be obtained by perfect measurement. Any true value is by nature indeterminate.

2.2. Measurement trueness

Closeness of agreement between the average of an infinite number of replicate measured quantity values and a reference quantity value

2.3. Measurement precision

closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions.
The specified conditions may be, for example, **repeatability conditions**, of the **intermediate precision conditions** or some **reproducibility conditions**

2.3.1. Repeatability condition

Measurement condition in a set of conditions which include:

- ✓ the same measurement procedure,
- ✓ the same operators,
- ✓ the same measuring system,
- ✓ the same operating conditions
- ✓ the same location,
- ✓ as well as replicate measurements on the same or similar objects over a short period of time.

In chemistry, the term "intra-serial precision condition of measurement" is sometimes used to designate this concept.

2.3.2. Intermediate precision condition

Measurement condition in a set of conditions which include:

- ✓ same measurement procedure,
- ✓ same operators
- ✓ same measuring system
- ✓ same operating conditions
- ✓ same location
- ✓ as well as replicate measurements on the same or similar objects over an extended period of time.

In chemistry, we sometimes use the term ""inter-serial precision condition of measurement" to designate this concept.

2.3.3. Reproducibility condition

Measurement condition in a set of conditions which include:

- ✓ different locations,
- ✓ different operators and
- ✓ different measuring systems,
- ✓ as well as replicate measurements on the same or similar objects

Different measurement systems may use different measurement procedures.

3. Metrological vocabulary

The VIM,*International metrology vocabulary, fundamental and general concepts and associated terms* includes 06 main chapters in the latest 4th edition-Committee Draft (VIM4 CD) of 2021:

* Chapter 1, “Quantities and units” introduces the key entities of metrology: quantities, units, values, and scales.
* Chapter 2, “Measurement” focuses on measurement as both an experimental and mathematical process, by also including the entries related to measurement models.
* Chapter 3, “Measurement quality”, is about what characterizes the quality of measurement processes and procedures, measurement instruments and systems, and of course measurement results, thus first of all measurement uncertainty but also measurement error, accuracy, and so on.
* Chapter 4, “Measuring devices and their properties” is about measuring instruments and systems, their components and their properties.
* Chapter 5, “Measurement standards (etalons) and metrological traceability” expands the context by dealing with metrological systems, including measurement standards and calibration: what is required for guaranteeing the metrological traceability of measurement results.
* Chapter 6, “Nominal properties and examinations”, devoted to nominal properties and their examination.

4. Organizations linked to metrology

4.1. At an international level

We can cite :

- the International Bureau of Weights and Measures (BIPM) located at the Pavillon de Breteuil in Sèvres, created by the diplomatic treaty of the Meter Convention. There are 55 Member States of the BIPM and 41 associated with the CGPM (as of 1 January 2015);
- the International Committee of Weights and Measures (CIPM);
- the General Conference on Weights and Measures (CGPM), the highest global authority on metrology;
- l'International Laboratory Accreditation Co-operation (ILAC) ;
- the European cooperation for accreditation (EA);
- the International Organization of Legal Metrology (OIML);
- the Committee on Data for Science and Technology (CODATA);
- l'International Measurement Confederation (IMEKO) ;
- l'International Accreditation Forum (IAF).

4.3. In Algeria

The National Office of Legal Metrology (ONML)

The ONML is a public administrative establishment (EPA), reporting to the Ministry of Industry, Small and Medium Enterprises and Investment Promotion with financial autonomy and created in 1986 by decree no. 86-250 of September 30, 1986.

Its main mission is to ensure the reliability of the measurement of instruments requiring legal qualification and having a direct impact on:

- Fairness in trade
- Health
- Security
- The environment
- The quality of industrial production

Its objectives are the safeguarding of the public guarantee, the protection of the national economy in terms of national and international trade and the protection of the consumer.

The ONML is headed by a director appointed by decree and assisted by:

- 02 technical departments and an administrative department at management level
- 04 regional annexes (Center – East – West – South)
- 36 wilaya branches

To date, the ONML workforce is 211 agents, of which technical staff represents 71%.

The instruments subject to metrological controls by ONML are:

- Weighing instruments
- Dimensional measuring instruments
- Electric energy meters
- Gas meters
- Water meters
- Turbine counters
- Taximeters
- Vehicle Exhaust Gas Analyzers
- Fuel dispensers
- Tanks intended for the transport and storage of fuel
- Chromatographs
- Radar speed meters
- All measuring instruments included in the dynamic counting system (temperature probe, temperature transmitters, pressure transmitters, etc.)
- Miscellaneous in accordance with OIML regulations

5. Calibration

It is the operation that, under specified conditions, in a first step, establishes a relation between the **quantity values** with **measurement uncertainties** provided by measurement standards and corresponding indications with associated measurement uncertainties and, in a second step, uses this information to establish a relation for obtaining a **measurement result** from an indication

5.1. Calibration hierarchy

Sequence of calibrations from a reference to the final measuring system, where the outcome of each calibration depends on the outcome of the previous calibration.

5.2. Metrological traceability chain

Sequence of measurement standards and calibrations that is used to relate a measurement result to a reference . Metrological traceability requires an established calibration hierarchy.

The organizations that participate in the calibration chain are laboratories located at different levels of precision compared to the primary laboratories which constitute the top of the measurement hierarchy. Depending on the country, the calibration chain system is a two or three-tier system, most countries adopt the three-tier system using three types of laboratories:

– primary laboratory (level 1),

– secondary laboratory (level 2),

– working laboratory (level 3).

Calibration is the basis of metrology, it ensures the consistency of measurement results.

– It is therefore essential that the company has reference standards and has them compared to national (or international) references, through accredited calibration laboratories.

– The correct choice of calibration frequency is essential since an error made on a standard can have much greater consequences than that made on a measuring instrument.

5.3. ISO/IEC 17025

ISO/IEC 17025 is the international standard for testing and calibration laboratories. It sets out requirements for the competence, impartiality, and consistent operation of laboratories, ensuring the accuracy and reliability of their testing and calibration results.

Importance of ISO/IEC 17025

This standard is vital for laboratories as it enhances the credibility of their testing and calibration work, fostering trust among clients and regulatory authorities. Compliance with ISO/IEC 17025 demonstrates a laboratory's commitment to quality, technical proficiency, and scientific rigor.

Benefits of ISO/IEC 17025

- Establishes a global benchmark for laboratory quality and reliability
- Enhances confidence in test and calibration results, both domestically and internationally
- Facilitates cooperation between laboratories and other bodies by generating wider acceptance of results
- Reduces the need for retesting, saving time and resources

6. Reference standards in the European Pharmacopoeia

6.1. Terminology

Chapter 5.12 of Eur.Ph states the following:

- *Primary standard*. A standard shown to have suitable properties for the intended use, the demonstration of suitability being made without comparison to an existing standard.
  Secondary standard. A standard established by comparison with a primary standard.
- *International standard.* An international standard is a primary standard that defines an International Unit.
- *European Pharmacopoeia reference standard*. A reference standard established under the aegis of and approved by the European Pharmacopoeia Commission.
- *European Pharmacopoeia Chemical Reference Substance (CRS).* A substance or mixture of substances intended for use as stated in a monograph or general chapter of the European Pharmacopoeia. European Pharmacopoeia CRS are primary standards, except for those (notably antibiotics) that are calibrated in International Units. The latter are secondary standards traceable to the international standard.
- *European Pharmacopoeia Biological Reference Preparation (BRP).* A substance or mixture of substances intended for use as stated in a monograph or general chapter of the European Pharmacopoeia. European Pharmacopoeia BRP are either secondary standards calibrated in International Units or primary standards, which may be used to define a European Pharmacopoeia Unit. Other assigned values may also be used, for example, virus titre, or number of bacteria.
- *Reference Material (RM).* A material or substance, one or more of whose property values are sufficiently homogeneous and well established to be used for the calibration of an apparatus, the assessment of a measurement method, or for assigning values to materials.
- *Certified Reference Material (CRM).* A reference material, accompanied by a certificate, one or more of whose property values are certified by a procedure that establishes its traceability to an accurate realisation of the unit in which the property values are expressed, and for which each certified value is accompanied by an uncertainty at a stated level of confidence.

6.2. Use of reference standards

Reference standards are used for:

- Identification,
- Purity testing
- Assay of substances for pharmaceutical use and pharmaceutical preparations.
- Determination of the content of components of herbal drugs and herbal drug preparations.

If a reference standard is to be used for purposes other than those for which it was established, its suitability for the new use must be fully demonstrated.

A European Pharmacopoeia reference standard with an assigned content/potency for use in the assay of a substance for pharmaceutical use may be suitable to **determine the content of that substance in a pharmaceutical preparation** where all the following conditions are fulfilled:

– the chromatographic assay method described in the active substance monograph is employed;

– the user verifies the applicability of the method to the particular pharmaceutical preparation (absence of interference);

– any pre-treatment of the sample (e.g. extraction) is validated for the particular pharmaceutical preparation;

– the use is approved by the competent authority.

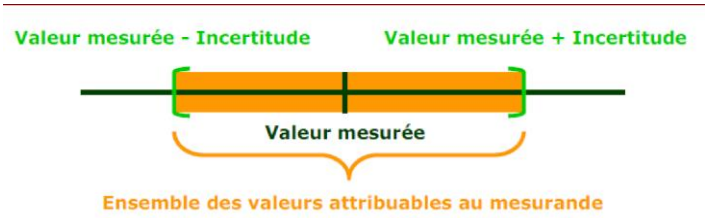
A secondary standard may be used for routine quality control purposes for any of the uses described above for primary standards, provided that it is established by reference to the primary standard.

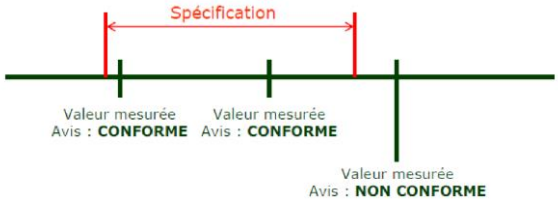
A secondary standard is established and used to reduce the use of the primary standard.

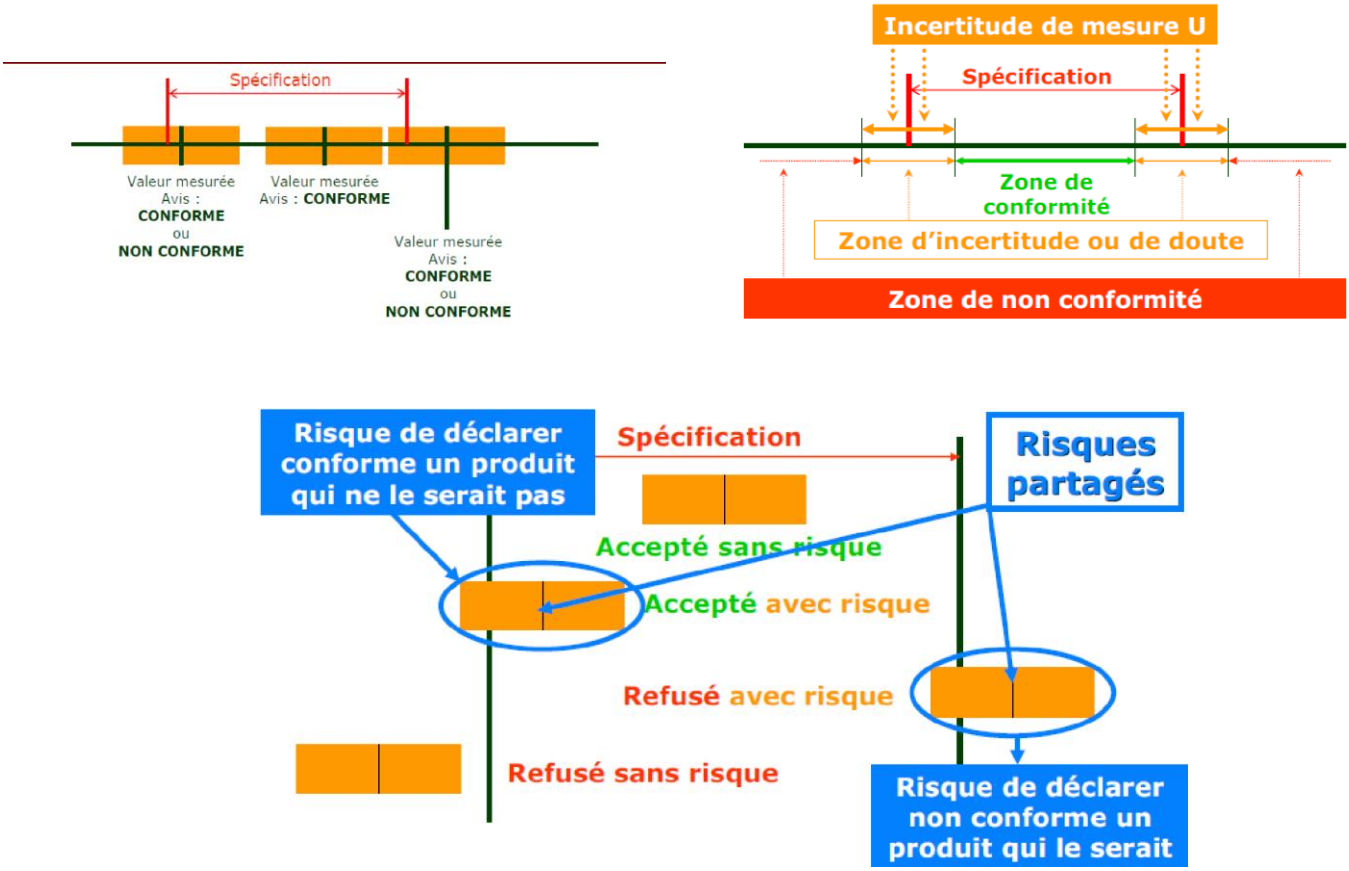
6. Declaration of conformity

Uncertainty is the most important characteristic when making compliance decisions, when the average values and deviations from the specification do not mean that it is compliant. The uncertainty gap will result in the flow of 4 different types of compliance decisions:

- Accepted without risk
- Accepted with risk
- Refused with risk
- Refused without risk







7. Measures in the field of health

Healthcare professionals and risk assessment experts need precise measurements for effective disease identification and treatment.

Precise doses of medications delivered correctly are crucial for successful treatments.

Healthcare plans are now focusing on prevention in addition to treatment to reduce costs and improve health outcomes.

Preventive health plans based on accurate medical measures can significantly reduce healthcare costs and system demands.

International travel increases the risk of disease spread; the WHO's International Health Regulations aim to prevent and respond to global health risks.

A robust measurement system is an essential element in achieving effective health policy. The essential factors for such a system are:

✓ traceability to the International System of Units, or SI (scientific metrology);

- ✓ regulated measurements and measuring instruments (legal metrology); And
- ✓ confidence in test and measurement results through certification, standardization, accreditation and calibration (industrial metrology).

International coordination through organizations like BIPM and OIML ensures compatibility and trust in healthcare measurements and instruments globally.

Conclusion

As demands for precision and quality continue to evolve, the significance of metrology remains paramount. Accurate measurements, traceability to standards, and adherence to regulatory guidelines serve as foundational elements for enhancing trust, confidence, and reliability in critical areas such as healthcare and industrial production.

Metrology and standards play a pivotal role in economic growth and efficiency across countries. In the UK, normalization contributed to approximately 28.4% of GDP growth from 1921 to 2013. Similarly, in Canada, standardization was linked to about 9% of GDP growth between 1981 and 2004. In Germany, the annual economic benefit of standardization is estimated at 0.72% of GDP, which translates to a significant impact given Germany's GDP of 4 trillion dollars in 2022. These figures highlight the tangible economic benefits that result from embracing and implementing standardized practices and metrological principles.

Ultimately, a robust understanding of metrology fosters improved outcomes, efficiency, and excellence across industries, benefiting both consumers and stakeholders alike.

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