The kilo, the mole and the commutability of a result to activity

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For all of my scientific life, weight has been traceable to a lump of platinum alloy sitting under a series of glass bell-jars and located in Paris, France. In my early days, amount of substance was expressed as $mg\,L^{-1}$ or ppm, in many labs these units are still commonly found. In 1971 the Mole was made the seventh SI base unit and slowly the idea of molar solutions permeated analytical chemistry.

Now, all that is set to change because on 16 November this year the 26th General Conference on Weights and Measures (CGPM) voted unanimously in favour of revised definitions of the SI base units, a change that the International Committee for Weights and Measures (CIPM) had proposed earlier in the year. The new definitions will come into force on 20 May 2019.

As a direct consequence the kilogram, ampere, kelvin and mole will then be defined by setting exact numerical values for the Planck constant (h), the elementary electric charge (e), the Boltzmann constant (k) and the Avogadro constant (N_A), respectively. This brings them into line with the metre and candela, which are already defined by physical constants, subject to correction to their present definitions and does not change the size of any units, so maintaining continuity with existing measurements.

The changes

The kilogram, symbol kg (lower case) is the unit of mass: the previous definition is that it was equal to the mass of the international prototype of the kilogram.

> 2019 definition: The kilogram is now defined by taking the fixed numerical value of the Planck constant h to be $6.62607015 \times 10^{-34}$ when expressed in the unit J·s, which is equal to $kg{\cdot}m^2{\cdot}s^{-1}$, where the metre and the second are defined in terms of c and $\Delta\nu_{Cs}$.

A consequence of this change is that the new definition of the kilogram is dependent on the definitions of the second and the metre. A second consequence is that a new definition for the mole is required.

The mole, symbol mol, is the SI unit for amount of substance. The previous definition was that it is the amount of substance of a system that contains as many elementary entities as there are atoms in 0.012 kg of carbon-12. When the mole is used, the elementary entities must be specified and may be atoms, molecules, ions, electrons, other particles or specified groups of such particles.

> 2019 definition: One mole contains exactly $6.02214076 \times 10^{23}$ elementary entities. This number is the fixed numerical value of the Avogadro

constant, N_A, when expressed in the unit mol^{-1} and is called the Avogadro number.

A further consequence of these changes is that the current defined relationship between the mass of the ^{12}C atom, the dalton, the kilogram and the Avogadro number will no longer be valid.

As the wording of the ninth SI Brochure[1] implies, the mass of a ^{12}C atom is exactly 12 dalton then the number of daltons in a gram cannot any longer be the numerical value of the Avogadro number: (i.e., $g/Da = N_A \cdot mol$).

These changes are all very interesting at the academic level, but what do they mean to chemical metrology and the use of reference materials? In truth very little, as they are designed to ensure continuity with all existing measurements that in turn underpin the certified values of the CRMs.

A far greater concern is the issue of commutability, a subject I have touched on in the past. It was the laboratory medicine community who first expressed concern about the commutability of data, but with the move to accredit medical diagnostic laboratories to ISO/IEC 17025 the concept has migrated into the world of general analytical chemistry. Why is commutability so important?

Maintaining accurate laboratory measurements over time is crucial to making data comparable. This is generally achieved by the use of an accredited quality system, typically ISO/IEC 17025, and establishing traceability to a reference system, the SI. Reference materials are key components of such reference systems and for establishing traceability this means that commutability of reference materials is a critical property to ensure they are fit for use.

Commutability is defined as the equivalence of the mathematical relationships between the results of different measurement procedures for a reference material and for representative samples taken from the area to be analysed. This material characteristic is of special importance for measurement procedures that are optimised for measuring analytes directly in real-world samples. It becomes even more important when the reference material is certified for some aspect of biological quantity and not an amount of substance.

For example, how do we produce reference materials for use in DNA measurements? The measurement of specific DNA fragments to demonstrate the presence, or absence, of a biological entity has become a key part of food quality measurement and is creeping into microbiology, food, environmental and clinical. Many will recall the 2014 adulteration of beef with horse meat. As a direct consequence, LGC developed new reference materials to underpin the detection of alien species within a defined processed meat. The materials were analysed using three different approaches—DNA sequencing, a PCR-based method and an immunoassay method—to confirm the expected meat species in the samples and the absence of possible species cross-contamination. The limit of detection is below 1 % of one meat species in the presence of another. The Reference Materials were produced by weighing out previously verified pure meat and mixing them in the defined proportion. No subsequent analysis was made. When using Sanger sequencing it is common to use mitochondrial genes, for example MT-RNR1 which encodes RNA 12s and MT-CYB which encodes cytochrome b. Ultimately the identity of the genes is validated against known DNA Sequence Databases.

It seems to me that traceability to a proprietary sequence database is a long way away from traceability to the SI and that the new definitions for amount of substance mean little in this context. The question remains unanswered, just how can traceability and commutability be maintained when an assay of a complex biological material is validated by comparing a sequence with data on a database, most probably supplied by the instrument maker?

Reference

1. *Draft of the Ninth SI Brochure*. BIPM (5 February 2018). https://www.bipm.org/utils/en/pdf/si-revised-brochure/Draft-SI-Brochure-2018.pdf [accessed 22 November 2018]