Letter to the Editor

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Misleading nomenclature of units of WHO materials used for standardization of SARS COv-2 serology

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To the Editor,

The mission of the Committee of Nomenclature for Properties and Units (C-NPU), a joint commission of International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and International Union of Pure Applied Chemists (IUPAC), is to recommend an standardized laboratory terminology for reporting laboratory results that include proper kinds-of-properties (e.g. category, mass concentration) and measurement units. In this letter, we express our deep concerns of a new unit concept recently introduced by WHO.

The necessary, and prompt work by WHO to establish an international standard (IS) labelled 20/136, as a Certified Reference Material (CRM) for measurement of the activity of SARS CoV-2 antibodies, is acknowledged. However, in the correspondence “WHO International Standard for anti-SARS CoV-2 immunoglobulin,” we were puzzled by the new metrological unit concept, referred as “Binding Antibody Unit” (BAU) [1].

In version 1.0 of the certificate for IS 20/136, the value “250 IU/ampoule” was assigned for both calibration of measurements of neutralizing antibodies and for (“binding”) antibodies [2]. In the second version, BAU was introduced as a unit concept for harmonization (n.b. not calibration) of results from binding antibody assays [3]. The reason was recently developed: “For example, it is inappropriate to assign a protective titre for vaccine efficacy in IU/mL when using an assay that is not measuring an antigen associated with protection. Such cases have arisen for measles and rubella, and have led to a misplaced lack of confidence in the use of the International Standard” [4]. Hence, the reason to introduce separate units for results from “neutralising antibody” assays and results from “binding antibody” assays, was the lack of confidence to CRM when users had not clearly distinguished two different measurands. The use of separate unit names for the same kind-of-quantity (e.g. mass concentration), instead of separate names for the components (analytes), is a deviation from international nomenclature conventions used by WHO to assign International Units to CRM [5]. It is a concern that should cause alarms in scientific societies, standardisation bodies and health care organisations.

Before the SI unit system, literally numerous different units for the same kind-of-quantity existed [6, 7]. This non-transparent practice created confusion in trade (exchanging goods with measurements) across geographically borders, even between close-by-cities. Same confusion can and will happen in health care with potentially mistreatment of patients if multiple international units are introduced for results of the same kind-of-quantity.

Thus, a limited number of internationally recognized units (preferable SI units or international recognized non-SI units) has been recommended in laboratory medicine since 1966 [8]. However, it is acknowledged that it may not be possible to assign an SI unit to a measurand of a CRM, e.g. CRM for a biological activity. In these cases, WHO assigns an arbitrary value of the amount of a biological substance in a CRM expressed as multiples of International Units (IU). As example, CRMs for Hepatitis Virus
B s-antigen antibody are IRP W1042 and IS 07/164, both with assigned values expressing the antibodies' functional effects or potency as IU [9].

No doubt, it is essential to distinguish between results for different measurands, but the distinction should not be made at a unit level. Instead it should be held at the expression of either the kind-of-quantity (e.g. mass concentration or substance concentration) or of the component (analyte). In the case of two types of SARS CoV-2 antibodies, the same kind of amount-of-substance for two different components (analytes) are measured. Thus, the kinds-of-quantity being measured are the same. The component differs and distinguishes therefore what is being measured, e.g. “SARS CoV-2 neutralising antibody”, “SARS CoV-2 Spike glycoprotein antibody (IgG)”, and “SARS CoV-2 nucleoprotein antibody (IgG)”. The result together with a reference to the specific CRM which defines the size of the unit and the traceability of the result, should be fully understandable. This approach has been described previously [10].

C-NPU proposes following descriptions of the intended measurands and the use of the common term “IU” for the unit as long as a common CRM is referred to:

- Plasma—SARS CoV-2 neutralising antibody; arbitrary substance concentration (IS 20/136, procedure) = ? IU/L.
- Plasma—SARS CoV-2 spike glycoprotein antibody (IgG); arbitrary substance concentration (IS 20/136, procedure) = ? IU/L.
- Plasma—SARS CoV-2 nucleoprotein antibody (IgG); arbitrary substance concentration (IS 20/136, procedure) = ? IU/L.

An alternative to use a common unit is to use a unique unit specified by the procedure, if for example the intended measurand is unknown. Even in this case, the term “binding antibody unit” is inappropriate.

We appeal to scientists and WHO to follow the international unit nomenclature conventions, so a precedent will not cause an overflow of units in health care sectors with potential confusion for clinicians and patients and risk of patient mistreatment. Furthermore, with the advent of results going directly electronically to patients, as a laboratory community, we need to take more efforts into standardised nomenclature and units of tests carefully.

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**References**