bio-conjugates such as ADCs, and the deployment of immune-related biomolecules as therapeutics, would it be useful to have: (a) A glossary and/or tutorial pertaining to the biological disposition/metabolism of medium and/or large molecule therapeutics, perhaps something like our recently published document pertaining to small molecule therapeutics (Pure Appl. Chem., 2021, 93, 273-403 and then republished in the ACS series Medicinal Chemistry Reviews, 2021, 56, 463-659); and/or (b) A hDMdb something like the one described above but instead dedicated to (focused upon) metabolism data collected only from medium/large molecule (biomolecule) therapeutics?

Any other comments you may want to contribute toward this topic, beyond the questions noted above, are most certainly, additionally welcome. They may also become important for adding to the intended white paper. Please note the level of recognition that you would like to have for whatever additional information you choose to share.

We respectfully request any assistance you can provide for this non-profit undertaking which we hope will be of specific value to the drug metabolism, drug discovery-development, and toxicology fields, as well as to the global pharmaceutical corporate-academic-public enterprise in general. **Please send your response *via* email attachment to paul.erhardt@utoledo.edu by no later than September 30**, so that a summary white paper can be issued in early 2025.

For more information and comment, contact Task Group Chair Paul Erhardt <paul.erhardt@utoledo.edu > | https://iupac.org/project/2000-010-1-700/

JCGM Guides in Metrology—IUPAC working in the field of metrology with others broadly-based international organizations

by Stephen L R Ellison

The Joint Committee for Guides in Metrology (JCGM) is a partnership between eight member organisations, all concerned with measurement and the standardisation of measurement.* The Committee maintains guidance on measurement uncertainty, based around the "Guide to the Expression of Uncertainty in Measurement" (known as the GUM) [1] and guidance on terminology for metrology applications, via the "International Vocabulary of Metrology" (known as the VIM) [2]. The JCGM operates through two working groups: JCGM-WG1, with responsibility for the GUM and related documents, and JCGM-WG2, with responsibility for the VIM. IUPAC takes a close interest in both of the working groups. Guidance on measurement uncertainty is important for working analytical chemistry laboratories; not only because an understanding of the measurement uncertainty associated with results is good practice, but also because laboratories accredited to ISO/IEC17025 are required to evaluate measurement uncertainty and to report it where relevant [3]. Vocabulary for metrology is important because it provides a consistent set of concepts, terms and definitions for use across all fields of measurement. For IUPAC, this is important because chemists, and particularly analytical chemists, need to understand standardised terms as they apply to chemical measurement. In addition, close involvement in the development of generic terminology helps to make sure generic terms can be applied in chemistry and in IUPAC's own terminology guides. For example, the most recent edition of the IUPAC Orange Book [4] adopts many terms from the current version of the VIM.

IUPAC currently has three representatives on JCGM-WG1: Stephen Ellison (LGC, UK) has recently been joined by two very welcome new representatives, Ivo Leito (University of Tartu, Estonia), and Francesca Pennecchi (INRIM, Italy) Ellison has also recently joined JCGM-WG2, supporting established WG2 members Zoltan Mester (NRC, Canada) and Jeremy Frey (University of Southampton, UK).

Work in WG1 has for some time focused on reshaping the series of JCGM guidance documents on measurement uncertainty. Although still a key

*The eight members organizations of JCGM are

- the Bureau international des poids et mesures (BIPM),
- the International Electrotechnical Commission (IEC),
- the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC),
- the International Laboratory Accreditation Cooperation (ILAC),
- the International Organization for Standardization (ISO),
- the International Organization of Legal Metrology (OIML),
- the International Union of Pure and Applied Chemistry (IUPAC), and
- the International Union of Pure and Applied Physics (IUPAP).

document, the GUM has long been supported by documents on the use of Monte Carlo methods for measurement uncertainty evaluation [5], on measurement uncertainty for the multivariate case [6], and on measurement uncertainty in conformity assessment [7]. In 2017, WG1 agreed to restructure the measurement uncertainty documents in its portfolio. The whole suite of documents is now known as the "Guide to the expression of uncertainty in measurement", and as documents are updated or developed, documents will be re-numbered to fit into the new structure. The first of these was the relatively recent guide on developing and using measurement models [8]; this was published in 2020 as JCGM GUM-6.

An important new edition in the portfolio is the recent release of the Introduction to the series of documents [9]. Formerly JCGM 104, this new edition of the Introduction fulfils two purposes. First, it forms a very basic introduction to measurement uncertainty, giving the rationale for its evaluation and introducing the main processes and approaches now available for measurement uncertainty evaluation, leaving detail for the different parts of the portfolio. Second, it gives an overview of the portfolio of documents, including future planned documents. Accordingly, the new Introduction acts as both a short introduction and a signpost to detailed guidance; an ideal first document when approaching the JCGM measurement uncertainty suite. It is fittingly numbered JCGM GUM-1.

At the most recent metings—most of which have been online since 2020—JCGM has been busy on other documents. Working Group 1 is working on a revised edition of the Monte Carlo document, which will give updated guidance and which will bring some of the procedures more closely in line with best practice in statistics. In particular, the present direction places less emphasis on the 'maximum entropy' basis for some distributions. This will improve the internal consistency of the guide, which currently uses a mixture of Bayes' rule and maximum entropy to justify distributions. Further effort is being put into a new compilation of examples of measurement uncertainty. This will widen the range of application examples, making it easier for different measurement sectors to apply the principles of the GUM. It will also provide illustrations of the different evaluation approaches, to better show the advantages and disadvantages of each in different applications. The compendium will also be extended over time, adding to the applications and illustrating more approaches. The intent is to include applications of Bayesian methods in time, taking advantage of the developments in Bayesian Statistics and increasing availability of supporting software tools for Bayesian analysis.

WG1 is also actively reviewing terminology and definitions associated with measurement uncertainty. In part, this is driven by a need to encompass the wider range of approaches in use. For example, uncertainty intervals in the GUM are formed by multiplying a standard uncertainty by a "coverage factor" to give an "expanded uncertinty", very similarly to the construction of the well-known statistical confidence interval. By contrast, intervals can be taken directly from the quantiles of Monte Carlo output. It is then not sensible to define a coverage interval merely in terms of expanded uncertainty; rather, it is important to seek a definition that applies well to both approaches.

A second reason for renewed interest in terminology is the current activity of JCGM Working Group 2, which has been working for several years to develop a substantial revision of the VIM. The intent is in part to provide more coherent and simpler terminology, and in

part to add terms related to qualitative ("nominal") properties. Determination of properties such as chemical or biological species identity (for example, confirmation of identity of drugs of abuse or of pathological bacterial species) are covered by different accreditations standards, and IUPAC has published a vocabulary relating to nominal properties [10]. The aim of the VIM revision is to adapt this vocabulary to a wider range of measurement fields. Other topics for the VIM revision include changes leading from the most recent edition of the SI Brochure, in particular on units for "dimensionless quantities" (those for which all SI units cancel, like mass fraction or other ratios) and from the recent redefinition of the SI, and revision of concepts related to the idea of physical quantities (length, time, *etc.*) and their values. Some of these changes have proven contentious and generated a considerable volume of comments; WG2 accordingly expect to provide a further consultation draft later in 2024 after addressing the most recent comments.

Finally, it is worth pointing out that for IUPAC to form a clear view of IUPAC members' needs and views on these key documents, and for those views to carry weight in the working groups, it is vital that individual members take time to check the drafts and to lodge comments. Both WG1 and WG2 always issue draft documents to member organisations, including IUPAC, and allow generous timescales for comment. Both JCGM and IUPAC want documents to serve their communities well; that cannot be done unless members participate actively in their development.

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IUPAC and Wikipedia (cont. from page 18)

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5. See, for example: Jan Kaiser, David Brynn Hibbert, and Jürgen Stohner. "Preparation, formatting and review of IUPAC Technical Reports and Recommendations, IUPAC-sponsored books, or other items carrying the IUPAC label" *Pure App. Chem.* 2022, 94(11-12), 1257-1267; https://doi.org/10.1515/pac-2022-1106
6. See https://creativecommons.org/licenses/by-nc-nd/4.0/ (accessed on 25 March 2024).
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