Setting Standards for Wearable Biochemical Measurement Devices: Defining Nomenclature and Guidelines

The field of wearable chemical measurement devices has undergone extensive review, with widespread recognition of the need for further development to enhance functionality and broaden applications [1,2]. Key areas for improvement include expanding the range of detectable substances, enabling simultaneous monitoring of multiple analytes and physical parameters (*e.g.,* heart rate, motion, temperature), and increasing data reliability, consistency, stability, and interpretability. As these devices evolve, integration with advancements in data transfer, informatics, and artificial intelligence could enable real-time responses, unlocking applications such as biomarker identification, continuous monitoring of chronic conditions (*e.g.,* diabetes), tracking patient status for critical conditions (*e.g.,* heart disease, epilepsy), and optimizing pharmaceutical drug dosing and compliance. These non-invasive devices, which can draw data from saliva, tears, sweat, and interstitial fluid, have two primary applications: medical use and consumer-focused purposes like fitness and sports tracking. While regulatory frameworks address safety and data management in both areas, stringent requirements govern clinical applications, creating potential overlap and ambiguity between consumer and medical use cases. This highlights the need for clear definitions and standardized terminology. Additionally, the unique characteristics of wearable devices—such as their reliance on variable sample types and continuous data collection—may require reinterpretation or amendment of existing validation and calibration guidelines. Regulations must also account for the fluctuating correlation between biomarker levels in blood or plasma and alternative sample media, which vary with population, environment, and physiological state. Accurate clinical interpretation will therefore depend on multi-parametric data and robust correction mechanisms.

The ongoing IUPAC project titled "Assessing the need for nomenclature, standards and guidelines for wearable devices that provide chemical / biochemical measurement readouts" is mainly focusing on these objectives:

- Assess the requirements for internationally agreed definitions for wearable devices based on different use cases.
- Research and evaluate existing guidelines for validation / critical evaluation of data / traceability for remote and wearable devices.
- Make recommendations on future guidelines to support standardization and metrology.
- Consider the need for training and awareness raising in this important and emerging field of science.

The establishment of internationally agreed definitions for wearable devices is critical to ensuring consistency, clarity, and interoperability across diverse use cases. Wearable devices serve a broad spectrum of applications, from medical diagnostics and continuous patient monitoring to consumer-focused activities such as fitness tracking and wellness management. Each use case presents unique requirements in terms of data accuracy, reliability, and regulatory compliance, necessitating clear and standardized terminology to distinguish between device functionalities, intended uses, and performance expectations. For medical applications, definitions must align with stringent clinical and regulatory standards to ensure patient safety, diagnostic accuracy, and therapeutic efficacy. Conversely, consumer-oriented devices require a focus on usability, non-invasiveness, and data privacy. The lack of unified definitions risks creating ambiguities in regulatory frameworks, complicating device classification, validation, and market approval processes. Therefore, internationally agreed nomenclature should account for the overlap and distinctions between medical and non-medical use cases, providing a framework that accommodates evolving technologies while addressing compliance, data transfer, and user interpretation across global markets. During the past months we assessed several technical definitions, but the first quest should be about a correct definition of wearable devices. According to the International Electrotechnical Commission (IEC) and International Organization for Standardization, a wearable device is defined as "a portable electronic device worn on the body that integrates sensors, electronics, and communication technologies to measure physiological, biochemical, or physical parameters [3]. These devices can be used for medical, fitness, or general wellness applications." Although the definition is very comprehensive (broad definition across several fields), it is not detailed and exhaustive because it does not consider the accuracy and precision of the measurement, which play a key role in the approval from Food and Drug Administration (FDA). For instance, the US FDA approved several guidelines for each medical device like blood glucose monitoring systems (BGMS). In this specific context, there is a net distinction between "Systems

for Prescription Point-of-Care Use" and "Systems for Over-the-Counter Use", and wearable devices might fall in the second category. However, most of the BGMSs, belonging both classes, are validated based on the criteria set by ISO document 15197. FDA considers the criteria outlined in the ISO 15197 standard insufficient to ensure adequate protection for patients relying on BGMSs in professional healthcare environments. For precision, there are two aspects that need to be considered: within-run precision and intermediate precision. Within-run precision studies assess device variability by repeatedly measuring samples across the claimed glucose range using different meters and test strip lots. Intermediate precision studies evaluate variability under simulated use conditions with multiple operators, days, and reagent lots, often using control solutions instead of blood samples. In both cases, FDA recommends specific procedures to perform the measurements, data analysis and presentation within the 510(k) premarket submission [4,5].

Researching and evaluating existing guidelines for the validation, critical evaluation of data, and traceability of remote and wearable devices necessitates a deep understanding of regulatory frameworks and international standards to ensure that these technologies meet stringent safety, accuracy, and reliability requirements. Regulatory agencies such as the FDA, alongside standards organizations like the International Organization for Standardization (ISO) and the International Electrotechnical Commission (IEC), have established foundational principles to guide manufacturers in ensuring that their devices are fit for purpose. For instance, ISO 15197, which governs glucose monitoring systems, emphasizes the need for validated precision, bias minimization, and total error measurement, serving as a benchmark for similar wearable technologies.

For wearable and remote devices, the continuous and dynamic nature of data collection presents unique challenges. Sensors must operate reliably across a variety of environmental conditions and user interactions, which can introduce variability in measurement outputs. As such, validation guidelines typically require multi-parametric testing under controlled conditions that simulate real-world scenarios, incorporating variables such as temperature fluctuations, motion artifacts, and user variability. These tests ensure that devices can maintain consistent performance across diverse settings and populations.

Critical evaluation of data generated by these devices involves assessing parameters such as precision, accuracy, linearity, stability, and repeatability. Standards like IEC 60601-1 for medical electrical equipment

Image created using OpenAI's DALL·E 3, based on a description provided for the IUPAC project 'Assessing the need for nomenclature, standards and guidelines for wearable devices that provide chemical/biochemical measurement readouts'."

specify requirements for performance testing to ensure data integrity over the device's operational lifespan. Furthermore, advanced data processing technologies such as artificial intelligence (AI) and machine learning algorithms, increasingly used in wearable devices, necessitate new layers of validation to confirm the reliability and interpretability of algorithm-driven outputs [6].

Traceability is another key pillar of existing guidelines. Measurements must be linked to higher-order reference standards or internationally recognized traceability chains to ensure consistency and comparability. For example, in medical applications, wearable devices often require calibration against laboratory-based reference methods, such as those traceable to National Metrology Institutes or certified reference materials. This process is crucial for devices providing critical diagnostic data, as any deviation from traceable standards could result in significant clinical risks.

Emerging regulatory guidance for wearable and remote devices also addresses the integration of connectivity and data transfer technologies. Standards like the IEEE 11073 series focus on the interoperability and secure exchange of medical device data, highlighting the importance of consistent data handling throughout the entire measurement-to-analysis pipeline. Furthermore, the FDA's Digital Health guidelines outline best practices for validating software and ensuring that devices meet cybersecurity and data privacy requirements [7,8].

Recently, we proposed organizing a small symposium on the regulation of wearable devices under the auspices of the Theo Murphy initiative (Royal Society, https://royalsociety.org/science-events-and-lectures/scientific/scientific-meetings/) to bring

together scientists, regulatory authorities, industry representatives, and other key stakeholders. This symposium aims to address critical regulatory challenges associated with wearable devices, including standardization, data validation, traceability, and the integration of emerging technologies such as artificial intelligence. The event will foster interdisciplinary discussions, enabling the identification of gaps in current frameworks and the development of actionable recommendations to improve device safety, efficacy, and interoperability. By engaging diverse stakeholders, the symposium will also explore pathways to harmonize international guidelines, ensuring robust regulatory strategies that support innovation while safeguarding public health. The event will serve as a collaborative platform for knowledge exchange, shaping the future of wearable device regulation in both medical and consumer applications.

Future guidelines for wearable devices should focus on harmonizing international standards, robust validation protocols, and traceability to high-order references. They must address challenges like continuous data collection, algorithm validation, and interoperability. Training and awareness programs are essential to equip stakeholders with skills to navigate this emerging field. Workshops and collaborations should promote best practices, ensuring reliability and widespread adoption of standardized approaches. These initiatives will foster sustainable progress and innovation in wearable device regulation.

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The isotopic composition of VPDB

Update from the IUPAC Commission on Isotopic Abundances and Atomic Weights, ciaaw.org, 20 Dec 2024.

Natural variations of carbon isotope ratios are expressed relative to Vienna PeeDee Belemnite (VPDB) [1]. In 1998, IUPAC recommended [2] the value of the $^{13}C/^{12}C$ isotope ratio in VPDB as reported by Chang and Li [3], and this recommendation was further reaffirmed by IUPAC in 2010 [4]. However, recent measurements of carbon isotope ratios associated with VPDB have led the CIAAW to reexamine the set of reference values describing the isotopic composition of VPDB. The CIAAW now recommends the following value of the $^{13}C/^{12}C$ isotope