

## Response to ACS Nano Editorial “Standardizing Nanomaterials”

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The November 2016 ACS Nano editorial entitled “Standardizing Nanomaterials” highlighted the need for standardization and called for minimum material characterization requirements in nanotechnology-related research.<sup>1</sup> We strongly support this call as it is aligned with existing efforts to develop documentary standards in nanotechnology. International documentary standards are essential not only for academia as highlighted,<sup>1</sup> but also for industry, regulators, governments, and non-governmental organizations. We encourage all researchers to contribute to standardization efforts. The use of standards provides validation and increased confidence in an academic publication or a commercial innovation, enabling comparability between laboratories and ensuring that data are defensible.

The fact that the editorial did not reference the substantial body of work produced by international, consensus-based, standards development organizations was a wake-up call for us. It is clear that we, and the standardization organizations we represent, have to invest more time and energy into disseminating our activities and outputs especially to academia, and this is the main reason for this response that was submitted back in 2017 and is published now.

The table below shows the approximate participation and the numbers of standards<sup>2</sup> developed to date by expert groups in some technical committees of international standardization bodies.

<b>Committee</b>	<b>When Founded</b>	<b>Membership</b>	<b>Developed Standards</b>	<b>Standards under development</b>
<b>ISO/TC 229 Nanotechnologies</b>	2005	37 Participating countries 18 Observing countries	81 (including 6 joint documents led by IEC)	51 (including 16 proposals and 3 joint documents led by IEC)
<b>CEN/TC 352 Nanotechnologies</b>	2005	34 Countries	24	19
<b>IEC TC 113 Nanotechnology for electrotechnical products and systems</b>	2006	16 Participating countries 19 Observer countries	45 (including 14 joint documents led by ISO)	56 (including 15 proposals and 7 joint documents led by ISO)
<b>ASTM International TC E56 Nanotechnology</b>	2005	174 members, 48 of whom are international	25	16

Table 1 International Standardization Committees. ISO, International Organization for Standardization; CEN, The European Committee for Standardization; IEC, International Electrotechnical Commission. The term “standard” used here includes technical reports, technical specifications and standard test methods.

In addition to committees mentioned in Table 1, a large number of other standardization bodies and organizations develop standards<sup>2</sup> for the characterization of nanomaterials. These groups include the technical committees ISO/TC 24 and ASTM E29, ISO/TC 201 and ASTM E42, and ISO/TC 202 and ASTM D11, which cover particle characterization and surface chemical analysis, including scanning probe microscopy and electron microscopy, respectively. In addition, the Organization for Economic Cooperation and Development (OECD) publishes test guidelines based on the extensive testing program of its Working Party on Manufactured Nanomaterials.

The editorial compared the development of standard measurement methods for nanomaterials to those for organic compounds.<sup>1</sup> The standard measurement toolbox for organic molecular characterization did not appear overnight; a process taking decades of innovative developments and validation studies was required. A similar process is occurring in the nanomaterial characterization field today, where instrumentation and protocols are evolving to improve measurement performance, reproducibility, and reliability. However, nanomaterials are often more complex and pose many characterization challenges that can be substantially different from well-defined organic compounds. Nanomaterials need to be described by physical and chemical characteristics that go beyond basic chemical composition and structure.<sup>6,7</sup> These characteristics and the resulting properties can, and often do, change over time and may depend on manufacturing processes and the medium in which the nanomaterial is present.

Although the work in characterizing organic compounds is indeed more mature and more widely adopted than that for nanomaterials, nanotechnology standardization is progressing in developing agreed-upon terminology, reproducible characterization, and widely accepted safety methodologies. Unfortunately, academic research has been slow to adopt uniform terminology and validated measurement techniques. The editorial seems to suggest that most researchers are unaware of existing measurement standards, standardized terminology, and the need to verify vendor-provided

material data independently.<sup>1</sup> There are already great numbers of standards,<sup>2</sup> including internationally accepted terminology in nanotechnology published by our organizations. Of note, ISO offers free access to all its terms and definitions through the Online Browsing Platform,<sup>8</sup> and standards are often accessible free of charge through university subscriptions. More substantial involvement by experts in academia, industry, and government agencies would ultimately lead to timelier, technically relevant, and useful standards.

To ensure that documentary standards, and especially measurement standards, are developed with high levels of quality, *i.e.*, relevance and reliability, the standardization communities rely on published peer-reviewed research that details the scientific evidence supporting method validation. Relevance, reproducibility, and reliability of methods, including pre-treatment and preparation of samples, have to be carefully demonstrated. Such publications may include reports of international inter-laboratory tests, which investigate the degree of agreement between results from independent laboratories for example, from the international VAMAS organization<sup>9</sup> or ASTM International's Interlaboratory Study Program.<sup>10</sup> Papers describing evaluation and validation, including uncertainty analysis, not only for new techniques and methods but also for existing ones, are very welcome and needed.

We commend the editorial because it supports incorporating standard measurement techniques into published research. Declaring the use of well-established standardized techniques and methods will benefit researchers, because the measured data and results will be accepted with higher confidence. This inclusion would also simplify editorial acceptance of articles. However, the reality is that the application of these techniques to different nanomaterials, nano-enabled products, and specific applications is not always trivial.<sup>11,12</sup> The discussion, as presented in the last paragraph of the editorial, in our opinion, understates both the breadth and the difficulty of nanotechnology standardization, a principal theme of recent Global Summits on Regulatory Science held at the U. S. National Institutes of Health<sup>13</sup> and the European Commission's Joint Research Centre regulatory event.<sup>14</sup> Information on the applicability of measurement techniques and methods as well as sample preparation for different nanomaterials should be compiled and good practices shared by academic, government, and industrial communities. We believe that providing researchers and engineers with such useful information is an important role of the standardization community.

The editorial also states that "It is appropriate to consider creating a prescribed or expected set of characterization requirements for publication." The MINChar Initiative<sup>15</sup> and others tried to establish this set a few years ago, but unfortunately, at the time, were not successful. The reasons were varied, but we support the launch of a new, coordinated effort to achieve this objective as invited by the editorial. The growing pressure from regulatory agencies<sup>16</sup> and legislation<sup>17</sup> to distinguish and to classify different forms of nanomaterials may well play decisive roles in this matter.

The editorial calls for increased effort and rigor with respect to the standardization of nanomaterial measurements and reporting. We believe this aspiration requires a cooperative approach involving peer-reviewed journals, standards development organizations, and leaders in the field from academia, industry, and government. After all, the ultimate goal is to advance reproducible science leading to the safe and sustainable development of innovative nanotechnology. Reproducibility and comparability of scientific results not only make great publications, but yield faster and more cost-

effective research often funded by national and international programs, and in the era of pandemics, this action may mean lives saved.

**Note from the editors:** An earlier version of this Comment was received in 2017. Our Reply was published in our September 2020 editorial “Tutorials and Articles on Best Practices” DOI: 10.1021/acsnano.0c07588.<sup>18</sup> We apologize to the authors of the original comment for the long delay. As a result of these conversations, in part, we are looking forward to publishing a series of articles on standards in nanomaterials.

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