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Comments on Deng, et al: The potential for Isotope dilution-LC-MS/MS to improve laboratory measurement of c-peptide; reasons and critical determinants

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To the Editor,

We read with interest the article by Deng, et al [1], "The potential for Isotope Dilution-LC-MS/MS to improve laboratory measurement of C-peptide: reason and critical determinants". We share many of these authors' concerns about the lack of standardization of c-peptide after so many years of effort by several groups [2]. However, we also have a few concerns about some content in the article: The first is that although a C-peptide standardization committee is mentioned, the authors do not say what the committee is and they do not cite the most recent paper describing this committee's work. The committee is actually supported by the US National Institutes of Health. The authors state that there are no secondary reference materials ("secondary calibrators") available to manufacturers. However, in this 2017 article and editorial [2–4] (in part based on the work of this committee), a complete traceability chain for C-peptide measurement is described, including certified primary reference materials, an ID/MS reference method, and commutable secondary reference materials. This traceability chain is also shown on the c-peptide standardization website (http://cpeptide.org/traceability.html). The secondary materials are serum-based and have been available to manufacturers for a few years. Although they have not been certified, these frozen serum samples have been analyzed by most c-peptide manufacturers over the past few years. Deng et al also state that this lack of secondary material is the reason why C-peptide is not yet standardized and this is certainly not the case. After many meetings with manufacturers (supported by this standardization committee), it is clear that c-peptide standardization is a low priority for manufacturers [5], although it is considered medium priority by The International Consortium for Harmonization of Clinical Laboratory Results (ICHCLR, https://www.harmonization.net/measurands/). Interest from manufacturers in moving forward with standardization could come through two approaches. The first could be specific clinical recommendations from clinical organizations (e.g., American Diabetes Association, European Association for Study of Diabetes) that would increase awareness of the clinical utility of c-peptide testing. The second pathway could come from the implementation and enforcement of the In Vitro Diagnostic Regulation (IVDR), which requires that "the traceability of values assigned to calibrators and/or control materials must be assured through available reference measurement procedures and/or available reference materials of a higher order" [6].

Once manufacturers re-calibrate their assays, evaluation of results through proficiency testing can be achieved and fine-tuning of re-calibrated results can begin. Creation of certified serum-based secondary reference materials could then also become available. We welcome further discussion by Deng et al and others about these roadblocks to standardization. This issue may also be addressed at an upcoming JCTLM Members and Stakeholders meeting – Overcoming challenges to global standardization of clinical laboratory testing: reference materials and regulations (https://www.bipm.org/en/committees/jc/jctlm/wg/jctlm/2021–12-06)

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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