In Reply My Viewpoint called attention to a determination by the FDA that relabeled a class III device as accurate for use in dosing insulin, without the previously required need for a confirmatory blood glucose measurement. The decision was made despite more than 25 000 reports to the FDA of potentially harmful device inaccuracies. These reports were not mentioned to an advisory panel or directly addressed in the summary of safety and effectiveness data for the decision.

Dr Beck mentions that current CGMs can, in some instances, be more accurate than some currently marketed blood glucose meters. Typically, though, they are not.[1] But the comparative average accuracy of different devices is not directly relevant to the issue of whether it is safe to dose insulin solely using a device potentially susceptible to large intermittent inaccuracies. Inaccuracies in blood glucose meters can lead to insulin-dosing errors,[2] and large inaccuracies in CGMs raise the same risks.

The risks from severe hypoglycemia or hyperglycemia resulting from an erroneous glucose measurement were illustrated in the Supplement to my article, which presented 100 illustrative cases of reported device inaccuracy including 37 cases of loss of consciousness, 8 accompanied by seizures, 4 car crashes, and 4 hospitalizations for diabetic ketoacidosis. Many others were near misses. Almost all of these incidents occurred during the time when device labeling was still advising users to confirm CGM readings; however, there is no reason to believe that there will now be fewer occurrences with the safety check removed.

Two of the studies mentioned by Beck deal with a device and FDA decision other than the one discussed in the Viewpoint. The third study[3] is said to demonstrate no increased risk, on average, from nonadjunctive use of CGMs in adults, but the study did not examine the importance of blood glucose confirmation in cases of inaccurate CGM values. Beck states that further studies are needed to assess the safety of nonadjunctive CGM use in children and adolescents. However, even before this study was published, the FDA had determined that nonadjunctive use of the Dexcom G5 CGM was safe and effective for patients 2 years or older.

Beck concludes that "any added potential risk in dosing insulin based on use of a CGM alone seems acceptable compared with the potential benefit of more widespread CGM use." However, this conclusion might not be acceptable to the individuals who experienced stays in an intensive care unit, car crashes, seizures, and loss of consciousness, particularly if such serious outcomes could have been avoided with simple precautions.

Most persons living with diabetes who take insulin look forward to the availability of devices that can lift some of the burden of vigilance needed to avoid the hazards of hypoglycemia and hyperglycemia. Many such devices are currently being developed.[4] The promise of relief from the strain of this constant vigilance would not be met if it were replaced with a need for constant vigilance for rare device malfunctions. The FDA has the opportunity to ensure that the sense of freedom promised by these devices is delivered.

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Conflict of Interest Disclosures: The author has completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest and none were reported.

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Glyphosate Levels in Older Adults

To the Editor The study on excretion of glyphosate in older adults[1] was analyzed inappropriately. First, Table 1 reported levels above the limit of detection (LOD). To report quantifiable values, a limit of quantification (LOQ) is required. Only values greater than the LOQ are reliably quantifiable. Levels greater than the LOD and less than the LOQ can only be interpreted as "presence," whereas levels less than the LOD can only be interpreted as "absence."[2]

Second, samples with nondetectable levels were handled in an atypical manner that may bias the differences over time toward higher values.[3]

Third, no information on the validation of their assay was reported.

Glyphosate has been in use since 1974, and the most recent human health risk assessment continues to support the conclusion that it is safe for all intended uses.[4] Contrary to the authors' assertion, just measuring glyphosate in urine is not informative of safety. Even if the data were valid, the reported maximum concentration in urine is at least 1 million times less than the no-adverse-effect level. We also disagree with the claim that glyphosate exposure causes liver disease in animals. This claim was based on a publication by Mesnage et al[5] that drew from a now-retracted controversial study[4] and does not provide clinical evidence of fatty liver.

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being employees of Monsanto, the manufacturer of glyphosate, and having stock options in Monsanto.

1. Mills PJ, Kania-Korwel I, Fagan J, McEvoy LK, Laughlin GA, Barrett-Connor E. Excretion of the herbicide glyphosate in older adults between 1993 and 2016. *JAMA*. 2017;318(16):1610-1611.

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5. Mesnage R, Renney G, Séralini GE, Ward M, Antoniou MN. Multiomics reveal non-alcoholic fatty liver disease in rats following chronic exposure to an ultra-low dose of Roundup herbicide. *Sci Rep*. 2017;7:39328.

In Reply We are keenly aware that the topic of glyphosate is highly controversial, often acrimonious, and stretches across diverse political and geographical boundaries.

Dr Karberg and colleagues had concerns about our assay. We were not able to include details of our assay methods as we were limited to 6 references. The methodology we used was developed by a research team led by Monsanto scientists.[1] Validation of urine levels included accuracy, precision, specificity, linearity, LOQ (glyphosate and aminomethylphosphonic acid [AMPA] LOQs were set conservatively at 0.25 µg/L), and LOD (glyphosate LOD = 0.03 µg/L; AMPA LOD = 0.04 µg/L). We used accepted and published methods assigning samples as 0 that had values below the LOD. This, together with our conservative LOQ, biased our findings toward underestimating the actual amount of glyphosate in the urine samples.

The authors refuted the claim that glyphosate exposure causes liver disease. In our study, we cited proteomics and metabolomics work by Mesnage et al indicating that animals chronically fed an ultra-low dosage of Roundup (of which glyphosate is the main weed-killing ingredient) showed hepatotoxicity consistent with nonalcoholic fatty liver disease and its progression to steatohepatosis,[2] findings consistent with a prior transcriptome study that predicted such structural and functional effects.[3] The authors mentioned a retracted article, which we had not cited. That study, which was subsequently republished in a peer-reviewed journal,[4] showed liver congestion and necrosis in animals following low-dose glyphosate exposure. Retraction of the original publication was controversial and influenced by Monsanto.[5] A more recent publication by Ford et al showed that glyphosate inhibits liver fatty acid oxidation enzymes and increases levels of triglycerides and cholesteryl esters in mice.[6] Together, these publications provide evidence and potential mechanisms of glyphosate-associated liver damage.

The concept of "safe" levels of glyphosate exposure is controversial and varies markedly by country. Europe, for example, set the acceptable daily intake of glyphosate at 0.3 mg/kg/d, whereas the United States set a level 5.8 times higher at 1.75 mg/kg/d. The research, however, suggests that even ultra-low levels are not safe. In the Mesnage et al study,[2] animals ingesting an ultra-low dosage of 50 ng/L of glyphosate showed hepatotoxicity.

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Conflict of Interest Disclosures: The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Mills reported receiving grant funding for the study discussed from the Solomon Dutka Fund in the New York Community Trust, the Caroline Young Foundation, and the Westreich Foundation; and launching a citizen science crowdfunding site that offers free glyphosate testing with a donation of $130, with tests being run by Health Research Institute Laboratories, which processed the samples for the study, and proceeds going to the University of California, San Diego. Dr McEvoy reported receiving a grant from the National Institutes of Health. No other disclosures were reported.

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Undisclosed Conflicts of Interest

To the Editor In the Research Letter entitled "Excretion of the Herbicide Glyphosate in Older Adults Between 1993 and 2016,"[1] published in the October 24/31, 2017 issue of *JAMA*, the conflict of interest disclosure was incomplete. Dr Mills did not disclose that he established a citizen science crowdfunding site to raise funds for additional research that offers free glyphosate testing with a donation of $130, with tests being run by Health Research Institute (HRI) Laboratories and proceeds going to the University of California, San Diego. Dr Fagan only disclosed an affiliation with the nonprofit 501(c) (3) research organization HRI Laboratories, but not that he is founder, chairman of the board, and senior scientist of HRI Laboratories, which is conducting a citizen science research program in which individuals complete a lifestyle and diet survey, provide a urine sample, and partially cover the cost of testing of the urine sample for glyphosate ($99/sample). The Conflict of Interest Disclosure statement has been corrected online and a correction notice accompanies this letter. We apologize to readers.