United States Senate
WASHINGTON, DC 20510

June 29, 2017

The Honorable Scott Gottlieb, M.D.
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Anne Schuchat, M.D.
Acting Director
Centers for Disease Control and Prevention
1600 Clifton Road
Atlanta, GA 30329

Dear Commissioner Gottlieb and Acting Director Schuchat:

We write regarding a recent announcement from the U.S. Food and Drug Administration (FDA) and Centers for Disease Control and Prevention (CDC) that calls into question the accuracy of certain lead detection tests. According to the joint press release, certain tests manufactured by Magellan Diagnostics provide artificially-low results of blood lead levels, when the sample used was drawn from a vein. Reports indicate that Magellan was aware of problems with the accuracy of their tests as early as 2014, yet for three years, parents, children, and providers continued to base healthcare decisions on these inaccurate test results. We write to better understand the reasons for this significant delay, whether other tests may be similarly impacted, and what steps the FDA has taken to address this problem.

According to the CDC, there is no safe level of lead in the blood. Lead can affect nearly every system in the body and is particularly dangerous to infants and young children, in whom it can significantly and irreversibly affect brain development. Because there are no immediate and obvious symptoms of lead exposure, it can go unrecognized and untreated, leading to serious health issues. Therefore, accurate blood tests are the only definitive way to determine lead exposure and intervene with treatment as needed. The American Academy of Pediatrics recommends a lead risk assessment and, if warranted, a blood lead test to be performed nine times between the ages of six months and six years.[1] Many state Medicaid programs require a universal blood lead level test twice in the first two years of life. Testing may also occur in adults and pregnant women who are at risk for lead exposure in the home or workplace.

It is alarming whenever a diagnostic test is found to be inaccurate, but even more so when children are the predominant population for whom the test is used. It is imperative that any inaccuracies in these sorts of tests are promptly identified and reported by the manufacturer to the FDA for further action. In this case, the issue with Magellan's tests dates back to 2014, however, the company did not alert FDA of any issues with the tests until the following year. Magellan's reporting to the FDA in 2015 and 2016 significantly downplayed the seriousness of the issue. It was not until May 17, 2017, that the FDA issued a public warning regarding LeadCare Testing Systems, a series of blood lead level tests manufactured by Magellan Diagnostics. The FDA accompanied these warnings with a recall of the LeadCare Plus and LeadCare Ultra Blood Lead Testing Systems, and further expanded that recall in June to include two other devices known as the LeadCare and LeadCare II Blood Lead Testing Systems.

[1] https://www.aap.org/en-us/advocacy-and-policy/aap-health-initiatives/lead-exposure/Pages/Detection-of-Lead-Poisoning.aspx

As of May 17, the FDA estimated that around eight million blood lead level tests were run though the Magellan Testing Systems in question since 2014, though the majority were not performed using blood from the vein, the only sampling method in question. Nonetheless, the CDC has recommended retesting for any child under the age of six, as well as women who are pregnant or breastfeeding, if they previously used this diagnostic system and had a venous blood sample result that was low (below 10 μg/dL).

While we acknowledge the FDA's recent attention to this issue, it is troubling that signs of inaccurate blood lead level readings first appeared nearly three years ago. According to reports[2], Magellan knew it had a problem with its LeadCare tests as far back as August 2014, when the company received complaints that samples tested more than once yielded higher results on repeat tests. The company was then notified in October 2014 that its validation tests comparing LeadCare results with other blood lead analyzer systems had failed. However, the company did not notify the FDA of any issue with its system until April 2015, and at that time did not accurately report the problem, describing the safety risk as "low," which did not trigger action from the FDA.

Since 2014, when Magellan was first made aware of the issue with its diagnostic system, the lead exposure crisis in Flint, Michigan brought national attention to the issue of lead in the water system that resulted in significantly high blood levels in local children. A similar crisis occurred in Sebring, Ohio in early 2016. And children across the country in regions where older homes and schools common are more likely to have lead paint or lead-lined pipes that increase the risk of lead poisoning. In all of these areas, children have potentially been misdiagnosed given the inaccuracies of Magellan's systems. The underestimated blood lead levels produced by these systems affects personal and public health decisions.

It is also alarming that, in the nearly three years since problems with the testing first appeared, Magellan Diagnostics has not yet identified the origin of the inaccuracies, and continued to troubleshoot potential solutions to no avail. It is further concerning that much of the data used by Magellan Diagnostics regarding the prevalence of these inaccuracies was unreliable. In fact, the FDA may not have known about the seriousness of this issue had it not been for the company's request to change the labeling on a product, which triggered an agency review ultimately leading to the recent recall.

To better understand the FDA's role in oversight of these testing systems, we ask for your prompt reply to the following questions:

1. Magellan Diagnostics submitted a malfunction report about LeadCare Testing Systems to the FDA in 2015.
    a. Is this the first instance FDA learned about the inaccurate venous blood lead level readings by LeadCare Testing Systems?
    b. What steps did the agency take to respond to this notice?

[2] https://www.nytimes.com/2017/05/17/well/family/fda-warns-of-faulty-lead-testing-in-children-and-mothers.html?_r=0

Please provide documentation supporting your response, including any correspondence or other materials prepared or obtained by FDA personnel related to the FDA becoming aware of the extent of the issues concerning the LeadCare Testing Systems.

2. Have there been any adverse reporting related to the use of the LeadCare Testing systems? If so, what were the nature of these reports and did they lead to any subsequent investigations by the FDA?

3. Have any of the LeadCare systems been used as a predicate for a 510k application? If so, and the subsequent 510k substantial equivalency was approved, has the FDA evaluated whether the same inaccuracies and safety concerns exist for the related 510k product?

4. Are there similar blood tests, lead or otherwise, that utilize comparable technologies, reagents or materials to the LeadCare system that may also be impacted? What is FDA's process of evaluating the existence of other impacted products and proactively engaging to mitigate subsequent risk?

5. Generally, capillary tests are the first blood lead level screening administered, and venous test are often sent to a lab to confirm the initial diagnosis. Magellan's LeadCareII test, however, is designed for in-office diagnostics, and can use either a capillary sample or blood from a vein.
    a. What guidelines, if any, does the FDA put in place to ensure that the appropriate test is approved and/or used for the applicable sample type?
    b. What guidance does the FDA provide on the suitable use of in-office lead testing for venous blood samples?

6. When the FDA notices safety, efficacy, accuracy, or reliability issues upon reviewing product malfunction reports or updates to device labels, to what extent has FDA worked with CDC to gain an understanding of the prevalence of malfunctions for high-risk users? Specifically, has the CDC identified how many of these tests were administered in areas with a high-risk of lead poisoning, like Flint, Michigan; Cleveland, Ohio; or Boston, Massachusetts?
    a. Has the FDA or Magellan provided additional assistance or information to product users in high-risk areas?

7. The FDA Safety Communication said the following: *...the FDA found a lack of reliable data identifying the root cause of the problem, the frequency and extent of inaccurate test results for the LeadCare Testing Systems, and a lack of adequate effectiveness to support the mitigating steps taken by Magellan.*
    a. What steps is the FDA taking to help Magellan correct the misinformation cited in the Safety Communication? How will the FDA help Magellan Diagnostics identify the errors that led to this misinformation, and how to prevent such errors for the future?
    b. Does the FDA believe that it was misled by Magellan Diagnostics, and if so, please provide all documents or other records associated with such a belief?

c. If the FDA does believe it was misled by Magellan Diagnostics, what actions could the FDA impose against Magellan Diagnostics?

8. On June 5, 2017, the FDA issued a Class I Recall of LeadCare and LeadCare II Blood Lead Testing Systems, impacting more than seven million devices across the country.
   a. What additional information became available to the FDA, and when did it become available, to necessitate the expanded recall?

9. What additional authorities or resources would help FDA to intervene in these types of situations sooner, or to help rectify such situations as soon as possible to ensure patients receive accurate testing results? Please detail what these resources and authorities would be.

To better understand the CDC's role in oversight of these testing systems, we ask for your prompt reply to the following questions:

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   a. What guidelines, if any, does the CDC put in place to ensure that the appropriate test is approved and/or used for the applicable sample type?
   b. What guidance does the CDC provide on the suitable use of in-office lead testing for venous blood samples?

2. When the FDA notices safety, efficacy, accuracy, or reliability issues upon reviewing product malfunction reports or updates to device labels, to what extent has FDA worked with CDC to gain an understanding of the prevalence of malfunctions for high-risk users? Specifically, has the CDC identified how many of these tests were administered in areas with a high-risk of lead poisoning, like Flint, Michigan; Cleveland, Ohio; or Boston, Massachusetts?
   a. Has the CDC, or Magellan provided additional assistance or information to product users in high-risk areas?

3. What additional authorities or resources would help CDC to intervene in these types of situations sooner, or to help rectify such situations as soon as possible to ensure patients receive accurate testing results? Please detail what these resources and authorities would be.

Thank you for your assistance and cooperation in this matter. We request that you provide a full and complete response within 15 working days or no later than close of business on July 17, 2017. Should you have any questions about this request, please have your staff contact Nikki Hurt of Sen. Markey's staff at (202) 224-2742 or Christa Wagner of Sen. Brown's staff at (202) 224-2315.

Sincerely,

Edward J. Markey
United States Senator

Sherrod Brown
United States Senator

Patty Murray
United States Senator

Elizabeth Warren
United States Senator

Debbie Stabenow
United States Senator

Cory A. Booker
United States Senator

Jack Reed
United States Senator

Robert Menendez
United States Senator

Gary C. Peters
United States Senator

Richard Blumenthal
United States Senator

Tammy Baldwin
United States Senator

Dianne Feinstein
United States Senator