PUBLICCITIZEN
1600 20th Street, NW • Washington, D.C. 20009 • 202/588-1000 • www.citizen.org

March 10, 2015

Jeffrey E. Shuren, M.D., J.D.
Director, Center for Devices and Radiological Health
Food and Drug Administration
Department of Health and Human Services
WO 66, Room 5442
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

RE: Use of experimental Masimo pulse oximeters in the Surfactant Positive Airway Pressure and Pulse Oximetry Trial in Extremely Low Birth Weight Infants (the SUPPORT study)

Dear Dr. Shuren:

As you may recall, on August 2, 2013, Public Citizen, a consumer advocacy organization with more than 350,000 members and supporters nationwide, wrote to you to request that the Food and Drug Administration (FDA) investigate issues related to the use of experimental pulse oximeter devices in the SUPPORT study and the inclusion of one particularly misleading statement in many of the institutional review board (IRB) approved SUPPORT study consent forms regarding these devices (copy of letter enclosed).

At the direction of the SUPPORT study investigators, for the purposes of the clinical trial, the manufacturer of these pulse oximeters — the Masimo Corporation — programmed the study oximeters to include a masking algorithm so that the devices displayed either falsely low or falsely high oxygen saturation levels when the actual oxygen saturation level was between 85 and 95 percent (see enclosed copy of letter from Masimo Corporation). However, nine of the 22 IRB-approved consent forms for the SUPPORT study misleadingly stated that the experimental pulse oximeters used in the research were "FDA-approved."We urged the FDA to address the following key questions in conducting its investigation:

(1) Did the Masimo Corporation or the SUPPORT study investigators contact the FDA and seek approval to use these experimental pulse oximeters in clinical studies? If not, should they have?

(2) Did use of the experimental pulse oximeters in the study require FDA approval of an investigational device exemption?

(3) Did the inclusion of the misleading statement in the IRB-approved consent forms indicating that the pulse oximeters were FDA-approved violate the FDA's human subjects protection regulations?

More than 18 months ago, in a letter dated August 20, 2013, you provided a preliminary response to our inquiry and noted the following:

> The Food and Drug Administration (FDA) is assessing the information you have provided as well as other available information on and surrounding this study. FDA's mandate is to protect and promote public health. We take protection of human subjects very seriously, especially when a vulnerable population such as premature infants is involved. FDA device experts will carefully consider all the information available, and identify an appropriate course of action if we determine that FDA regulations were violated during the conduct of the SUPPORT study.

We have not received any further response from the FDA regarding this important matter. Therefore, we are writing again to request responses to the questions originally posed in our 2013 letter and to the following additional questions:

(1) What was the final outcome of the FDA's review of this matter?

(2) Did the FDA determine that any FDA regulations were violated during the conduct of the SUPPORT study? If yes, please provide a summary of that determination and any actions taken in response.

The public and, more importantly, the parents of infants who were enrolled in the SUPPORT study deserve prompt answers to these important questions. As we stated in our 2013 letter, the SUPPORT study protocol — disturbingly — offered no evidence that it was safe to use the experimental Masimo pulse oximeters, which provided the medical teams caring for the critically ill premature babies enrolled in the study with inaccurate information regarding oxygen saturation levels. Of note, a recently published analysis from another trial using the same type of modified experimental pulse oximeters indicated that "the masking algorithm and its transition from offset to true values may have had an important and unexpected impact on the titration of oxygen therapy."[1]

In separate correspondence, we are requesting all agency documents related to this matter under the Freedom of Information Act. We encourage you to expedite the release of the requested documents.

[1] Schmidt B, Roberts RS, Whyte RK, et al. Impact of study oximeter masking algorithm on titration of oxygen therapy in the Canadian Oxygen Trial. *J Pediatr*. 2014;165(4):666-671.e2

Thank you for your prompt attention to these important human subjects research issues.

Sincerely,

Michael A. Carome, M.D.
Director
Public Citizen's Health Research Group

Sidney M. Wolfe, M.D.
Founder and Senior Adviser
Public Citizen's Health Research Group

Enclosures

cc: Dr. Margaret Hamburg, Commissioner, FDA
Dr. Jerry Menikoff, Director, Office for Human Research Protections (OHRP)
Dr. Kristina Borror, Director, Division of Compliance Oversight, OHRP