American Society of Anesthesiologists®

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September 1, 2015

Stephen Ostroff, M.D.
Acting Commissioner
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

Re: Docket No. FDA-2015-N-2734; Physiological Closed-Loop Controlled Devices; Public Workshop; Request for Comments

Dear Acting Commissioner Ostroff:

The American Society of Anesthesiologists (ASA), on behalf of over 52,000 members, is pleased to comment in advance of the public workshop on physiological closed-loop controlled (PCLC) devices. We thank the Food and Drug Administration (FDA) for recognizing that current regulatory pathways inhibit innovation in drug delivery medical devices that are safely used outside of the United States and for seeking more progressive paths to regulatory approval. ASA is guardedly supportive of PCLC technologies, and below offers recommendations to enhance the safety of these devices.

ASA believes there are many promising applications of PCLC devices that could improve patient safety in operating rooms and intensive care units by closely regulating certain physiologic variables. PCLC devices are expected to decrease the rate of over-dose and under-dose events, as well as decrease clinician workload by allowing the clinician to take on a supervisory role.

PCLC medical devices will change the nature of clinician work, and this will create opportunities and challenges. For example, in high workload situations, PCLC devices could improve a clinician's ability to maintain high-level situation awareness. However, in low workload situations, the opposite may be true and these devices could decrease vigilance and situation awareness if safety features are not provided. First and foremost, patient safety should always be considered in implementing the use of any medical device.

ASA strongly encourages the FDA and manufacturers to involve physician anesthesiologists in all levels of development and testing of these devices. In addition, those health care professionals involved in development and testing should represent the breadth of expected use and users (e.g., physician, nurse, pharmacist; operating rooms, various ICUs). Operating

rooms are safe environments to introduce PCLC devices, and even safer than intensive care units, because of the continuous presence and supervision by physicians.

Critical clinical events from PCLC devices are more likely to arise from user errors and sensor problems, than from the control algorithms. The FDA and manufacturers should pay special attention to user-interface design to decrease the chance of user errors. Usability tests should be performed early in the design cycle, and should be repeated in simulated and real clinical settings to demonstrate safety. It is especially important to test clinicians' ability to safely use PCLC devices alongside other clinical devices during demanding situations in real work environments. The FDA and manufacturers should also pay special attention to the prevention and detection of sensor problems, and should consider requiring redundant, independent sensors of the feedback signal(s).

In aviation, flight crews can become confused about the state of advanced automation, such as the autopilot and flight management computer. This condition is often referred to as decreased mode awareness. Therefore, closed-loop systems should prominently display whether control is on or off and the controller mode. It is also important that users be able to monitor how the device is performing its control functions. Therefore, closed-loop systems should display a graphic trend of all relevant variables and parameters. Controller output is an especially important variable to display, because the feedback signal only monitors the state of the controller, and not the state of the underlying system (i.e., the patient). It is important that clinicians are able to monitor and track the input signal(s) and the controller output as an indication of the state of the system. Auditory alarms with descriptive text messages should notify the user if the device automatically changes mode, if relevant variables and parameters reach specified limits for alerts and alarms, or if user input is required for safe operation. The user should always be able to determine what the controller is doing, why it is doing it, and what it will do next.

There is a higher potential for artifact in physiologic sensors (e.g., invasive blood pressure, electroencephalogram, cardiac output, respiratory gases) than there is in sensors of mechanical systems (e.g., flows, pressures, and gas concentrations internal to machines). The FDA already allows feedback control of mechanical systems signals (e.g., delivered tidal volume during pressure control ventilation), and it is encouraging to see a move toward allowing feedback control of physiologic signals. Feedback of a direct indicator of the controlled process (e.g., arterial pressure, pulse oximeter saturation, muscle response to electrical neuro-stimulation) is generally more reliable than feedback of signals that are either indirect to the controlled process (e.g., exhaled carbon dioxide as a surrogate of arterial carbon dioxide), or extrapolated to estimate the controlled process (e.g., pulse contour analysis to estimate cardiac output, or processed EEG to estimate level of hypnosis).

ASA urges the FDA to consider approving closed loop controllers of inhaled anesthetics that feedback on anesthetic agent concentrations, prior to considering anesthetic controllers that feedback on processed EEG. Commercial devices that control end-tidal anesthetic concentration have been safely used outside of the United States for over 10 years. Anesthesia practitioners universally accept end-tidal anesthetic concentration as the variable to control. They recognize that end-tidal anesthetic concentration is a surrogate for plasma level now, and for brain concentration in the near (2 – 5 minutes) future.

ASA is pleased to have the opportunity to comment on this important issue and looks forward to working with the FDA and manufacturers to develop criteria for approval of safe PCLC medical devices. If you have any questions, please feel free to contact Lisa Pearlstein, J.D., at l.pearlstein@asahq.org or 202-289-2222.

Sincerely,

J.P. Abenstein, M.S.E.E., M.D.
President
American Society of Anesthesiologists