American Society of Anesthesiologists®

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August 3, 2021

The Honorable Janet Woodcock
Acting Commissioner
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions; Public Workshop; Request for Comments (FDA-2021-N-0275)

Dear Acting Commissioner Woodcock:

On behalf of the American Society for Anesthesiologists (ASA) and our 53,000 members, we are writing in response to the Food and Drug Administration's (FDA) recent request for comments on *Morphine Milligram Equivalents: Current Applications and Knowledge Gaps, Research Opportunities, and Future Directions,* solicited in conjunction with the public workshop held on June 7-8, 2021. We are pleased to see the FDA address this topic as part of the agency's ongoing efforts to address the critically important issue of opioid use and addiction. ASA believes it is important to fully understand the role various analgesic modalities play in patient care. Given that Morphine Milligram Equivalents (MMEs) are increasingly being used to indicate abuse and/or overdose potential and to set thresholds for prescribing, we agree with FDA's sentiment that it is necessary to refine and improve the scientific basis of MME applications.

**Safe, Effective & Individualized Pain Care**

*Role of Physicians*
Physicians play an important role in ensuring the responsible prescribing of opioid medications. The specific role that physician anesthesiologists play in the delivery of care make these specialists uniquely positioned to help curb inappropriate use and abuse of opioids throughout the perioperative period and upon discharge. These specialists not only have extensive experience with the intricacies of short-term (acute) pain management such as following a surgical procedure or minor injury, but they also focus on long-term pain management related to chronic conditions like arthritis or low back pain (chronic pain). While certain pain can be managed very effectively with non-opioid treatments, other types of pain require the use of opioids. It is essential that pain care be properly tailored to the individual patient need and not necessarily limited by misleading strength or dosage restrictions.

With the ongoing and worsening opioid epidemic, physicians have recognized the need to develop and implement best practice guidelines to alleviate the adverse outcomes of opioid over-prescription. Many of these guidelines include recommendations with MME thresholds as a marker for certain quantitative levels that might be considered high-risk for patients. For example, the 2016 Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain included recommendations with a 90 MME threshold, but no detailed guidance was offered to help physicians justify when higher dosing is necessary. The CDC Guideline was then carried out and misapplied in a number of venues with applications to all patients in all circumstances, rather than just primary care physicians treating chronic

pain. The Federation of State Medical Boards (FSMB) and many payers also created policies based upon this guideline. Patient access to pain care was also greatly impacted.

**ASA Feedback on FDA Discussion Questions**

*Scientific Impact of MMEs*
While we understand that the agency is seeking information about the impact of the science of MMEs on patient care, ASA suggests that the misapplication of the CDC Guideline is one of the most egregious unintended consequences of science.

Patients suffered the consequences—some experiencing refusal of treatment by physicians and others have had to undergo a rapid decrease in their medications. Sometimes this has been unmanageable for patients and resulted in depression, illegal substance use, and even suicide. The lesson learned is that any policy that includes MME thresholds must also consider the diagnosis and previous response to treatment for a patient and any clinical nuances that would support such prescribing as falling within standards of good quality patient care. No entity should use MME thresholds as anything more than guidance. Individualized patient care and safety should be the utmost priority when treating patients with pain. The treatment plan and modality should be the decision of the treating physician and the patient after jointly discussing options, weighing benefits and risks, as well as expectations.

The MME scale was originally developed to help physicians with safe and effective opioids prescriptions. MMEs assist physicians with dose conversions when switching or using multiple opioid medications concurrently. Over time, MMEs began to influence opioid prescribing policies and regulations, as well as dispensing and reimbursement. They increasingly tend to be associated with risk of abuse or overdose and have even been weaponized against physicians. Reverse prescription drug monitoring program (PDMP) inquiries have been made in some states to target and even penalize physician prescribing beyond certain MME thresholds. State medical boards have used the Guideline to discipline physicians prescribing outside of the recommendations in the CDC Guideline and many payers used the Guideline to implement strict prescribing policies. These practices do not promote safe, high-quality care for patients.

Again, MMEs are a clinical tool to initiate and guide opioid therapy in acute and chronic pain patients. While the goal is to reduce or eliminate the practice of overprescribing, ASA does not support its use as the sole marker for limiting or tapering drug dosing in patients who have clinically justifiable reasons for using higher opioid doses.

*Knowledge Gaps*
While research supports that the risk of adverse events is correlated with higher MMEs, MMEs, when used alone, cannot accurately predict the risk of abuse. However, this pharmacologic measure can provide some insights into past or current opioid abuse, it has no bearing on a patient's psychiatric history or social determinants of health. ASA strongly believes MMEs should not be used as an absolute threshold without considering the risks and benefits for each patient. Patients should be considered on a case-by-case basis.

*Additional Factors to Inform/Supplement the Use of MMEs*
The ASA believes individualized patient care is critical, and it's important to consider a patient's detailed history, physical examination, review of records, family history, diagnostic testing, and psychologic and social determinants of health. When combined with individual patient assessments and risks vs. benefits optimization, MMEs can better help clinicians decide which patients need increased surveillance for opioid-related adverse outcomes and help guide decisions around when a patient might warrant receiving

naloxone with their opioid prescription. The need for higher dosing should be assessed on an individual basis and the goals of treatment. Physicians should have a candid discussion with their patients about expectations, alternate methods of analgesia, limitations, and side effects of opioids.

*MME Conversion Tables*
ASA strongly believes that the MME calculator provided by the CDC should be utilized as a means of standardization across all platforms, and to keep variability low among physicians using the tool. The lack of consistent application of MME tools can impact interpretation of health disparity data. The Society hopes the FDA would use the ASA as a resource to disseminate information. A venue like ASA's annual meeting might be a good opportunity to share that information.

*Recommended Studies/Research on MMEs*
ASA suggests that new research focus on which medical conditions opioids are most effective for treating patients. Currently, many studies do not include chronic pain patients. There is also value in looking at genetic variability and the nuances around behavioral health. Many studies do not include buprenorphine either and this can lead to selection bias. Another important component around research is exploration of how certain MME data is used. For example, studies that evaluate MMEs should examine impact on patient care and physician practice, rather than just informing prescribing thresholds or regulations, or as a means to discipline or sanction physicians.

ASA would welcome the opportunity to work with the FDA on any guidance or policy document being drafted by the FDA on this topic. Thank you for your leadership in addressing the opioid epidemic in communities across the nation. We appreciate the opportunity to provide our comments to the FDA as the agency continues to address this issue. If we can be of further assistance, please do not hesitate to contact Ashley Walton, ASA's Associate Director of Congressional and Political Affairs, via email at a.walton@asahq.org or by telephone at (202) 289-2222.

Sincerely,

Beverly K. Philip, MD, FASA, FACA
President
American Society of Anesthesiologists