July 21, 2023

Robert M. Califf, MD
Commissioner of Food and Drugs
Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD, 20993

CC: Cynthia LaCivita, PharmD
Director
Division of Risk Management
Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD, 20993

Via Electronic Submission

RE: FDA-2023-N-0573-0002 Changes to Third-Party Vendors for Risk Evaluation and Mitigation Strategies; Establishment of a Public Docket; Request for Comments

Dear Commissioner Califf,

The undersigned organizations, representing thousands of physicians, pharmacists and other medical professionals who treat patients with life-threatening, complex, chronic conditions writes this letter in response to the Food and Drug Administration (FDA) request for public comment on factors that the FDA should consider when it reviews a proposed risk mitigation and evaluation strategy (REMS) modification that is prompted by or related to a change in a REMS administrator for a REMS with certain elements to assure safe use (ETASU).[1] We greatly appreciate the ongoing dialogue between FDA and the public to ensure patients have access to safe and effective treatments while attempting to improve prescriber experiences and minimize administrative burdens.

Our chief concern is that drug sponsors and REMS administrators do not seek input from physicians, other prescribers, pharmacists, patients and their representatives, and other stakeholders, including wholesalers, health systems, or specialty societies, prior to developing, implementing, or modifying a REMS, which has resulted in significant disruptions in care that exposes patients to serious symptoms and complications. When significant changes are made by drug sponsors, it has been our experience that they do not share any details of planned modifications beforehand in a timely manner to allow for prescribers, their staff, and patients to prepare for the change, nor did they seek prescriber input into how their proposed changes would impact patient access to a drug subject to a REMS with ETASU.

In fact, there have been several cases of delayed patient care because of REMS-related system failures and untimely updates from drug sponsors and their REMS administrator. For example, the iPLEDGE REMS system update in December 2021 led to major disruptions necessitating multiple meetings with the FDA and the iPLEDGE Manufacturers, call center failures, and innumerable difficulties experienced by physicians, patients, and pharmacists, resulting in treatment disruptions for patients across the country.[2] Additionally, when the Clozapine REMS was on hold, community pharmacies were still being audited for adherence to REMS. Even

[1] https://www.regulations.gov/document/FDA-2023-N-0573-0002
[2] https://www.medscape.com/viewarticle/964925

though the FDA was not enforcing the REMS, pharmacies were losing money and they stopped filing scripts for clozapine, leading to unnecessary delays in treatment. Delays in accessing clozapine have led to psychological distress, severe rebound psychosis, mania, prolonged hospitalizations for patients, and in a few instances death.

There is a need for transparent, open dialogue between key stakeholders, including third-party vendors, REMS administrators, drug sponsors, FDA staff, and prescribers. A transparent communication process must include input from multiple stakeholders and beta testing with prescribers, pharmacists, and patients when there are significant changes in the technologic workflows and upgrades. This must include user acceptance beta-testing of new systems as well as demonstrations of planned changes with prescribers of any significant changes to the REMS system prior to full implementation. Infrequent meetings with physicians and other stakeholders have not yielded meaningful conversations with drug sponsors about prescriber and patient experiences. Occasional FDA listening sessions have not been sufficient to ensure that REMS administrators and drug sponsors receive timely feedback on REMS-related system changes. Moreover, failure modes and effects analysis should be included in all REMS. Plans for systems failures should be discussed and everyone should be informed of the same rules.

The undersigned organizations recommend the FDA consider physician or prescriber representation with a REMS administrator tasked with managing and modifying the REMS system. Stakeholder input and physician representation among REMS administrators will alleviate program users' frustration since their concerns would be identified and resolved before implementation of any major changes made by drug sponsors or REMS administrators. Furthermore, prescriber issues, such as system failures or minor clerical errors, can be resolved by having a consistent and responsive point of contact for prescribers' compliance questions or appeals with a REMS administrator. We strongly urge FDA to require continued and transparent communication between physicians, pharmacists, and REMS administrators, including identifying a consistent point of contact for prescriber grievances and compliance issues.

We look forward to working with the FDA to ensure our patients have timely and safe access to life-changing treatments. To discuss this matter further or schedule a meeting, please have your staff contact Stephanie Croney, JD, American Academy of Dermatology Association's Assistant Director of Regulatory Policy at scroney@aad.org or via phone at 202-712-2612 or Brooke Trainum, JD, American Psychiatric Association, Director Practice Policy at btrainum@psych.org or via phone at 757-876-4772.

Sincerely,

American Academy of Dermatology Association

American Psychiatric Association

American Acne & Rosacea Society

American Society for Dermatologic Surgery Association

American Society for Mohs Surgery

Arkansas Dermatological Society

CalDERM

Colorado Dermatological Society

Florida Academy of Dermatology

Illinois Dermatological Society

Maryland Dermatologic Society

Minnesota Dermatological Society

Nevada Society for Dermatology & Dermatologic Surgery

Pennsylvania Academy of Dermatology & Dermatologic Surgery

Society for Pediatric Dermatology

Utah Dermatology Society

Virginia Dermatology Society