AMA
AMERICAN MEDICAL ASSOCIATION

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Division of Docket's Management (HFA-305)
U.S. Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products [Docket Number FDA-2016-N-1149]

Dear Sir or Madam:

On behalf of the physician and medical student members of the American Medical Association (AMA), I appreciate the opportunity to respond to the U.S. Food and Drug Administration's (FDA) request for comment on "Manufacturer Communications Regarding Unapproved uses of Approved or Cleared Medical Products," which was the focus of a public hearing on November 9-10, 2016. The AMA strongly supports the need for physicians to have access to accurate and unbiased information about off-label uses of drugs and devices, while ensuring that manufacturer-sponsored initiatives are accomplished in a way that is truthful and not misleading and remain under FDA oversight. Below, we offer some general comments and address some of the questions raised by FDA on this issue. These comments focus primarily on the physician perspective.

Regarding this important issue, AMA policy supports the following views:

The AMA strongly supports the autonomous clinical decision-making authority of a physician and that a physician may lawfully use an FDA cleared or approved drug or medical device for an off-label indication when such use is based upon sound scientific evidence or sound medical opinion. The level of evidence necessary to support off-label use will vary based on the seriousness of the disease, a lack of response to other available therapies, and the consequences of therapeutic failure. Physicians have the responsibility to interpret and put into context information received from any source, including manufacturers, before making clinical decisions, including prescribing a drug or device for an off-label use.

Information to be disseminated by manufacturers about off-label uses should be generally available and efforts should be made to ensure that materials are free of publication bias and are not preliminary findings. Such information should be independently derived, peer-reviewed, scientifically sound, truthful, and not misleading. The information should be provided in its entirety, not be edited or altered by the manufacturer, and be clearly distinguished and not appended to manufacturer-sponsored materials. Such information may comprise journal articles, books, book chapters, or clinical practice guidelines. Books or book chapters should not focus on any particular drug. Dissemination of information by manufacturers to physicians about off-label uses should be accompanied by the approved product labeling and disclosures regarding the lack of FDA approval or clearance for such uses, and disclosure of the source of any financial support or author financial conflicts.

The AMA is aware of existing systems and sources of information that document patterns of prescribing. Notably, the AMA encourages physicians to add a brief notation of purpose on prescriptions. On a larger scale, the AMA promotes efforts to increase data utility and reduce barriers that currently limit access to and use of health care data. Approaches to accomplish this objective should take into account the patient-physician relationship and recognize the autonomy of physicians to determine the best course of action for their patients. The National Prescription

Audit™ (NPA) from QuintilesIMS,™ [1] The National Disease and Therapeutic Index™ (NDTI) from QuintilesIMS,™ [2] and several clinical research registries, such as those listed at the National Institutes of Health,[3] as well as self-contained health care systems (e.g., Kaiser Permanente, Geisinger) are useful for evaluating prescribing patterns. The AMA encourages multi-stakeholder efforts to develop and fund clinical data registries that facilitate improvements in health care, population health, and lower costs and encourages participation in the National Quality Registry Network[4] and in efforts to advance the development and use of clinical data registries to enhance the quality of care.

When the prescription of a drug or use of a device represents safe and effective therapy, third-party payers, including Medicare, should consider the intervention as clinically appropriate medical care, irrespective of labeling, and should fulfill their obligation to their beneficiaries by covering such therapy and be required to cover appropriate off-label uses of drugs on their formulary.

A common theme throughout the questions posed by the FDA in the Federal Register notice was concern about the impact of more widespread dissemination of information regarding off-label uses on the willingness of manufacturers to pursue new indications via supplemental new drug applications. Although a concern, the absolute necessity of off-label prescribing for optimal health, particularly in pediatric patients, and the existing clinical need to offer patients with cancer or other serious life threatening diseases treatment regimens that rely to a certain extent on off-label prescribing, demonstrates an ongoing imperative to evaluate and disseminate existing reliable evidence that can inform those treatment decisions.

The AMA looks forward to continuing to work with the FDA on this important issue and encourages the FDA to work closely with patients and physicians to ensure that patients have access to needed treatment options that are safe and effective. If you have any questions or would like to further discuss these issues, please reach out to Shannon Curtis, Assistant Director, Federal Affairs at shannon.curtis@ama-assn.org or 202-789-8510.

Sincerely,

James L. Madara, MD

[1] Health Services Research Network Data Brief: National Prescription Audit.™ http://www.imshealth.com/files/web/IMSH%20Institute/NPA_Data_Brief-.pdf. Accessed December 10, 2016.
[2] Health Services Research Network Data Brief: National Disease and Therapeutic Index.™ http://www.imshealth.com/files/web/IMSH%20Institute/NDTI_Data_Brief_v17.pdf. Accessed December 10, 2016.
[3] NIH Clinical Research Trials and You: List of Registries. https://www.nih.gov/health-information/nih-clinical-research-trials-you/list-registries. Accessed December 10, 2016.
[4] National Quality Registry Network (NQRN): http://www.ajrr.net/quality-initiatives-tools/collaborations-affiliations-and-other-registries/119-national-quality-registry-network-nqrn, Accessed March 29, 2017.