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January 16, 2018

The Honorable Greg Walden
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Frank Pallone
Ranking Member
Committee on Energy and Commerce
U.S. House of Representatives
2322A Rayburn House Office Building
Washington, D.C. 20515

The Honorable Michael Burgess
Chairman, Health Subcommittee
Committee on Energy and Commerce
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Gene Green
Ranking Member, Health Subcommittee
Committee on Energy and Commerce
U.S. House of Representatives
2322A Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Walden, Ranking Member Pallone, Chairman Burgess, and Ranking Member Green:

Public Citizen, a consumer advocacy organization with more than 400,000 members and supporters nationwide, respectfully submits the following comments for the record for the Health Subcommittee's January 17 markup of three bills, including H.R. 2026, the Pharmaceutical Information Exchange Act of 2017.

Public Citizen strongly urges you to oppose H.R. 2026 because the legislation would further erode the restrictions on the promotion of drugs for unapproved (off-label) uses that have been approved by the Food and Drug Administration (FDA) for at least one use. The bill would threaten patient health and safety by undermining the current regulatory regime for ensuring that drugs are safe and effective for each intended use. In particular, the proposed new subparagraph (2) to be inserted in Section 502(a) of the Food, Drug, and Cosmetic Act (21 U.S.C. § 352(a)) would allow pharmaceutical companies to promote unapproved uses to payors, formulary committees, and other similar entities.

As the FDA articulated in 2017, the existing regulatory restrictions on manufacturer communications regarding unapproved uses of approved or cleared medical products are overwhelmingly justified by the substantial government interest in protecting patient health and safety. These restrictions advance health and safety by:

- motivating the development of robust scientific data on safety and effectiveness for each new use of a medical product;
- maintaining the premarket review process for safety and effectiveness of each intended use in order to prevent harm; protect against fraud, misrepresentation, and bias; and prevent the diversion of health care resources to ineffective treatments;

- ensuring that required product labeling is accurate and informative;
- protecting the integrity and reliability of promotional information regarding medical product uses;
- protecting human subjects who are receiving experimental treatments, ensuring informed consent, and maintaining incentives for clinical trial participation;
- protecting innovation incentives, including statutory grants of exclusivity; and
- promoting the development of products for underserved patients.¹

Together, these interests support the FDA's overarching mission of protecting and promoting public health. That interest outweighs any purported public health benefit of expanding manufacturer communications regarding unapproved uses of pharmaceutical products.

Although the FDA approves new drugs before they are marketed, it—and the public—maintains a strong interest in evaluating the products' safety and effectiveness for any additional uses that were not evaluated at the time of initial approval. For example, a drug that poses a serious risk to the patient's immune system may merit approval to treat cancer but not to treat a headache. Thus, the FDA does not evaluate safety in a vacuum: For each proposed use, the agency balances the drug's risk of harm against its potential for benefit. Furthermore, the government has a powerful interest in ensuring that a drug is not only safe for each use for which a manufacturer markets it, but also effective. Marketing for a safe but ineffective use can have detrimental health effects if it diverts patients from effective treatment.²

Moreover, a drug's safety for a second use is not established once a drug has been approved (and thus deemed safe and effective) for a first use. To the contrary, a drug that is safe for one use can be life-threatening for another.

Although prescribing drugs for unapproved uses is common, scientific evidence supporting most such uses often is lacking. For example, a recent study conducted in Canada found that the vast majority of off-label uses—81 percent—lacked strong scientific evidence of effectiveness.³ Patients who received a prescription for an off-label use lacking strong evidence of effectiveness were 54 percent more likely to experience an adverse drug reaction that resulted in stopping use of the drug than were those who were prescribed a drug for an approved use. The increased risk of serious adverse events when drugs are prescribed for off-label uses, combined with the lack of strong evidence of benefit, demonstrates that a favorable risk-benefit relationship has not been established for most off-label uses of drugs and further supports strong restrictions against promotion of unapproved uses.

History shows that after-the-fact enforcement of safety and efficacy standards for marketing of drugs is inadequate to protect patient safety. Rather, when an unproven assertion of safety and

¹ FDA. Memorandum: Public health interests and first amendment considerations related to manufacturer communications regarding unapproved uses of approved or cleared medical products. January 2017. Available at <https://www.regulations.gov/contentStreamer?documentId=FDA-2016-N-1149-0040&attachmentNumber=1&contentType=pdf>. Accessed January 16, 2018. At 3-16.

² *Wash. Legal Found. v. Friedman*, 13 F. Supp. 2d 51, 69 (D.D.C. 1998) (noting evidence that off-label use of calcium channel blockers deprived patients of more effective treatments).

³ Egualé T, Buckeridge DL, Verma A, et al. Association of off-label drug use and adverse drug events in an adult population. *JAMA Intern Med.* 2016;176(1):55-63.

effectiveness is relied on to market a medical product, the resulting harm may be severe—even life-threatening.

We urge you to oppose H.R. 2026 and any similar controversial legislation that is introduced in the future. Thank you for considering our views on this important matter.

Sincerely,

A handwritten signature in black ink, appearing to read "Michael Carome".

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

cc: Members of the Committee on Energy and Commerce, U.S. House of Representatives