Testimony of R. Alta Charo
before the Subcommittee on Health
Energy & Commerce Committee of the U.S. House of Representatives
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Chairman Burgess, Vice-Chairman Guthrie, Congressman Green, members of the committee, thank you for this opportunity to address you on issues surrounding communication and marketing of medical products for off-label uses. My name is Alta Charo. I am the Warren P. Knowles Professor of Law at the University of Wisconsin, and an elected member of the National Academy of Medicine (formerly known as the IOM), where I have served on a number of committees, including one that examined the system for ensuring drug safety. I also served as an advisor in the Office of the Commissioner at FDA from 2009 to 2011. I would note for the record that I am not here to represent either the National Academies or the FDA, and that the opinions I express here are my own.

There are two possible reasons to expand communication about off-label uses. One is to ensure the law is consistent with the free speech protections of the First Amendment. The other is to promote public health by increasing patient access to safe and effective drugs. I share these goals, but do not find that the two amendments under discussion today are needed. Indeed, the unintended consequence of adopting this language would be to undermine public health, discourage pharmaceutical research, and set pharmaceutical regulation back by more than 100 years.

As noted in an article I co-authored with Josh Sharfstein,[1] formerly the principal deputy commissioner at FDA, our drug regulation system has prohibited false or misleading advertising since 1906. In 1962, when broad marketing for secondary uses of thalidomide caused thousands of severe birth defects worldwide, Congress recognized that a product can be "safe and effective" for one intended use where the benefits exceed the risks, but not "safe and effective" for another. This is why approval of a drug for a labeled indication does not mean it will be safe and effective for off-label uses, and why additional studies are needed to explore them.

This requirement to demonstrate safety and effectiveness for an intended use applies to both the first approval of a new drug and to any approval of a supplemental indication. Despite a handful of cases narrowing constraints on commercial speech regarding unapproved "off-label" uses, courts have consistently upheld commercial speech restriction with respect to the first product approval. If the First Amendment means that off-label promotion must be permitted, then promotion of entirely untested, unapproved drugs should also garner the same

[1] Sharfstein and Charo, "The Promotion of Medical Products in the 21st Century: Off-label Marketing and First Amendment Concerns," JAMA. 2015;314(17):1795-1796.

protection. But this would return us to the 1906 law, where prosecution for false and misleading marketing took place only after people had been harmed.

Scientific journals and conferences are already allowed to present information about off-label uses. Sponsors can answer questions from physicians and provide reprints of peer-reviewed articles, even if related to off-label uses. The proposed amendment of Section 201 muddies these exceptions, and risks eviscerating the general rule against off-label promotion. It also immunizes sponsors from responsibility, even if they know and take advantage of the now blurry line between legitimate scientific exchange and illegal marketing.

The proposed amendment of Section 502 exacerbates this problem, by allowing premature information to be delivered to formularies and payors, with the probable effect of increasing patient use of unproven or unsafe therapies. Studies have repeatedly shown that even products that look promising in early trials will usually be shown to be unsafe or ineffective when larger trials are completed. Indeed, overall only about 1 in 5 compounds successfully move from Phase 2 to Phase 3 trial,[2] with lack of efficacy as the most common reason for failure.[3] And as noted by University of Arizona professor Christopher Robinson, multiple studies show that the majority of off-label uses also turn out to be either unsafe or ineffective,[4] and increasing use without proper research will harm more patients than it helps.

History amply demonstrates that there is compelling public interest in unbiased evaluation of evidence; in clear, accurate communication; and in maintaining incentives for research. The combined effect of these amendments is to expand promotion and payment for unproven uses of drugs. It undercuts the marketing advantages that the law uses as an incentive for sponsors to complete the research needed to see which uses are in fact safe and effective. In turn, it leaves physicians, patients, forumularies and payors without independently verified information. For complex products like drugs, the marketplace of ideas cannot work properly with un-vetted information from a self-interested source. And when using the wrong drug can injure patients or cause them to miss out on effective treatment, it is an invitation to another tragedy when we prevent FDA from doing its job to protect the public.

Thank you for your attention.

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[2] 2015 CMR International Pharmaceutical R&D Executive Summary (http://cmr.clarivate.com/pdf/Executive_Summary_Final.pdf)

[3] Harrison, "Phase II and phase III failures: 2013–2015," NATURE REVIEWS DRUG DISCOVERY 15, 817–818 (2016) [Published online 04 November 2016].

[4] Arizona Legal Studies Discussion Paper No. 16-19, "The Tip of the Iceberg: A First Amendment Right to Promote Drugs Off-Label," by Christopher Robertson June 2017 (citing Tewodros Eguale et al., "Association of Off-Label Drug Use and Adverse Drug Events in an Adult Population," 176 JAMA INTERN MED. 55-63 (Jan. 2016) and David Radley, Stanley Finkelstein, & Randall Stafford, "Off-Label Prescribing Among Office-Based Physicians," 166 ARCH. INT. MED. 1021 (2006).