



Re: Docket No. FDA – 2014 – D – 0758: Draft guidance for industry on distributing scientific and medical publications on risk information for approved prescription drugs and biologic products – recommended practices.

Comments Submitted August 25, 2014 on behalf of the National Physicians Alliance (NPA) FDA Task Force. The NPA is a multispecialty physician organization advocating foremost for the interests of our patients and the public health; we are dedicated to promoting conflict-of-interest free medicine.

In its present form, the FDA draft guidance referenced above undermines the FDA’s primary mandate to protect patient safety and our country’s public health. We urge the FDA either to revise these guidelines substantially or to abandon entirely the concept of disseminating off-label risk reduction.

We view the proposed guidance from the perspective of practitioners who would be receiving journal articles selected and interpreted by pharmaceutical representatives across the country. Such detailing presents a clear conflict of interest, as the information distributed would be prepared by companies with an obligation to increase profit for their shareholders. As clinicians, we depend on FDA approvals and drug labeling to be scientifically accurate. Why should we heed drug labels at all if the FDA knowingly allows companies to advertise off-label to us about possible risk reductions? Our concerns around the draft guidance include:

- (1) The guidance allows companies to discuss risk reduction before such data are presented to the FDA. At the very least, if companies present such information to providers, they should also be required to point out to providers any risks in approved labeling that are new, or if not new, more serious than as presented on the label. Presumably such information was not included in this guidance since it is already a legal requirement for companies to present such data to the FDA. We strongly believe that at the same time drug representatives would present new information on lowered risks, they should also be required to present any data reflecting *increased* risk—data which they would have already submitted to the FDA by law but which might not yet be included on the label.
- (2) Evidence has shown that pharmaceutical sales representatives omit or misreport information, including serious adverse events, in order to increase sales.¹
- (3) To rebut a prior determination, companies may present data from new controlled trials, but they may also use non-clinical, pharmacoepidemiologic studies or meta-analyses. Such studies do not have the same degree of rigor used in the original determination of safety by the FDA. The guidance requires companies to discuss the limitations of studies on a cover sheet, but it is vague in stating that the studies should be “at least as persuasive as the data sources that underlie the existing risk assessment.” What are the criteria for determining the meaning of “at least as

¹ B Mintzes, et al., “Pharmaceutical Sales Representatives and Patient Safety: A Comparative Prospective Study of Information Quality in Canada, France and the United States,” *Journal of General Internal Medicine* 10: 1368-75, doi:10.1007/s11606-013-2411-7.

persuasive”? If the material presented is from drug-company sponsored studies, the bias is more apparent. A study that examined more than 500 clinical trials for 5 major classes of drugs showed that 85% of industry-funded studies showed positive results, whereas only 50% of government-funded studies had positive outcomes for the products.²

- (4) Suggesting that articles selected should be published in “independent, peer-reviewed journals” does not mean the studies are rigorous. Journals vary significantly in their data requirements and review standards for publication. One study that examined every trial of psychiatric drugs in four academic journals over 10 years found that pharmaceutical company sponsors received positive outcomes for their drugs 78% of the time, whereas independently-funded trials received favorable results 48% of the time.³ Thus, it would be preferable for the guidance to state that articles should be from studies that are independently funded in peer-reviewed journals.
- (5) We know that a single study, even independently funded and in a reputable journal, may later be refuted or even found fraudulent.
- (6) Finally, it should not be assumed that doctors in busy practices will critically read cover sheets where disclosures by companies regarding lack of FDA review are likely to be included and perhaps buried.

We find it frankly confusing that the FDA would sanction companies presenting data the agency has not reviewed and that companies interpret as refuting the FDA. The draft guidance undermines the integrity of the risk information provided to us as prescribers and decreases the usefulness of labels on drugs and biologics. We would appreciate learning of examples in which data implying a reduction of side effects were so important and time-sensitive that it justified rushing this information to doctors without a thorough FDA review.

To protect our patients and public health, we urge the FDA to revise these draft guidelines for industry on distributing publications to providers and health agencies. When evidence supports reduced risk associated with use of a prescription drug or biologic product, companies should present new data stating their case directly to the FDA so that labeling may be changed appropriately after careful consideration in a non-conflicted way.

Thank you for inviting and reading our comments on this draft guidance. Please contact us directly for any questions.



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² Burgeois FT, Murthy S, Mandl KD. Outcome Reporting Among Drug Trials Registered in ClinicalTrials.gov. *Annals of Internal Medicine*. 2010;153(3): 158-66.

³ Kelly RE Jr., Cohen LJ, Semple RJ, Bailer P, Lau A, Bodenheimer A, et al. Relationship between drug company funding and outcomes of clinical psychiatric research. *Psychol Med* 2006 Nov;36(11):1647-56.