NATIONAL PHYSICIANS ALLIANCE

November 13, 2014

Rep. Diana DeGette (D-CO)
Rayburn House Office Building, Room: 2368
Independence and S. Capitol St., S.W.
Washington, DC 20515

Rep. Fred Upton (R-MI)
Rayburn House Office Building, Room: 2183
Independence and S. Capitol St., S.W.
Washington, DC 20515

Rep. Joe Pitts (R-PA)
Cannon House Office Building, Room: 420
1st and Independence Ave., S.E.
Washington, DC 20515

Dear Chairman Upton, Chairman Pitts, and Congresswoman DeGette:

As practicing physicians and members of the National Physicians Alliance FDA Taskforce, we are writing to express concern about recent efforts regarding the promotion of drugs for off-label uses—particularly proposed changes to FDA procedures. The National Physicians Alliance (NPA) serves as a professional home to physicians across more than 40 medical specialties who share a commitment to patient-centered health care and evidence-based health policy. Our Taskforce supports the organization's work in defense of a strong, scientifically rigorous FDA that maximizes meaningful clinical outcomes for our patients. Proposals to loosen regulation around off-label promotion pose serious threats to patients in this country.

Physicians depend on the FDA to determine whether scientific research has shown the benefits of a drug to outweigh its risks *for well-defined medical conditions or patient populations* (for example, adults with type 2 diabetes or patients with stage 4 prostate cancer). A drug with serious side effects may be considered "safe enough," for metastatic prostate cancer because it could help those men survive for more months or years, but we cannot generalize that the drug will work for metastatic breast cancer without an adequate clinical trial in that population.

Because physicians caring for patients with less common diseases—and the patients themselves—often wish to try drugs not approved for their condition, we support the FDA's existing "expanded access" program to make experimental interventions available for patients who do not qualify for ongoing drug trials. However it is imperative that we conduct randomized trials to understand which agents are genuinely effective and which are harmful. This is how we advanced knowledge and developed effective drug protocols against HIV.

Under current law, physicians can prescribe any FDA-approved drug for any purpose. However, drug companies are not allowed to promote off-label uses for the drugs, and insurance companies may choose not to reimburse for the costs of such uses. This provides strong and vitally important incentives for pharmaceutical companies to conduct well-designed studies to submit to the FDA for expanded approval.

It is our understanding that you heard testimony that "off-label" research information is "locked up" and unavailable to physicians. On the contrary, companies are quick to publish articles regarding the safety and effectiveness of their products for off-label uses, and will do so even before they submit an application to the FDA. They are already allowed to distribute peer-reviewed information on off-label uses. Because of this, many drugs are widely used off-label, and in many cases insurance will pay for that use if there is solid evidence for such use.

Regarding information in scientific journals, scientists studying clinical trials have found that reporting biases, a sort of cherry-picking of results, "appear to be more likely in studies funded by the pharmaceutical industry than in studies funded by other sponsors." (Vedula 2009; Rising K et al 2008). As the former authors state: "This practice threatens the validity of evidence for the effectiveness of off-label interventions." Companies also pay medical education and communication companies to develop articles for publication in journals that highlight data advantageous to the marketing of their drug. (Fugh-Berman).

In another study, scientists examined how closely the information submitted to the FDA corresponded to information published in journals. They found that results which didn't favor the drug were often omitted from the journal papers. In a few cases, the statistical significance of results and study conclusions actually changed, and results that had been unfavorable to the drug in the FDA submission were reported as favorable. (Rising)

In the Food and Drug Administration Modernization Act, Congress wisely recognized the careful balance that must be made between ensuring providers have information on new uses and limiting the promotion of such uses prior to further study, by requiring that distributed new-use information be peer-reviewed. Further, the numerous drug settlements for off-label promotion initiated by complaints under the False Claims Act are a testament to the recognized public interest in protecting patient safety from non-FDA approved drug uses and from drug-company promotion of such use. Allowing the distribution of drug-company-collected, non-scientifically-peer-reviewed data would establish a dangerous precedent and would render irrelevant the very scientific method we have fought so hard to uphold as a standard for FDA approval and patient safety.

The 21st Century Cures campaign is designed to consider innovative ways of providing new medical treatments in a more timely manner. Such an effort will only save lives and improve the quality of patients' lives if the new medical treatments are scientifically evaluated for safety and efficacy and if there is a clear standard—FDA approval—that physicians can rely upon to assess the benefits and risks of a new treatment. Integrity of the label "FDA approved" is critical to us as

physicians. Allowing drugs to be advertised without that approval jeopardizes the entire system of standards we depend upon. Without the backup of FDA approval or at the very least peer review and access to a judicial review process, who will determine what constitutes "truthful information" that should be passed on to the provider?

We would greatly appreciate a conference call with you to discuss our concerns, as well as the opportunity to testify at an Energy and Commerce hearing. Thank you for your consideration.

Sincerely,

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