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Peter Pitts explains exactly why this matters

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communicating “non-compliant” off-label claims that, in many
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Drug Administration, always concerned about protecting the free
and fair dissemination of scientific information, remained mostly
silent. That silence of the regulatoryGetX4X4X
was the misleading headline.
And it wasn’t a case of an off-target headline written by an uninterested
editor. Here’s how the article began: “The Food and Drug Admin-
istration is proposing to allow pharmaceutical companies to under-
mine official safety warnings in sales presentations to customers.”
That’s not true. What the draft guidance addresses is the ability of
pharmaceutical companies to present research published in peer-
reviewed journals that goes beyond the information provided in the
FDA label. That undermines nothing. In fact, it leads to the convey-
ance of scientifically acceptable, often cutting-edge information.
Under the proposal, the FDA would not “object to the distribu-
tion of new risk information that rebuts, mitigates or refines risk
information in the approved labeling.” The studies must be “well
designed” and “at least as informative as the data sources” that the
FDA used in generating the official warning. In sum, it’s the FDA
recognizing that knowledge is power in pursuit of the public health.
Furthermore, this language makes it clear that the FDA retains the
right to object when such information does not meet this standard.
And since there is no definite “standard,” the FDA’s actions will be
carefully watched. The Center for Drug Evaluation and Research’s
office of medical policy currently lacks a permanent director. When
that slot is filled, this is a key issue that person will need to prioritize.
Public Citizen offered the expected broadside that the proposal
proposes to let drug companies undermine official safety warnings.
Unfortunately, it was interesting for the wrong reasons, because the
headline was misleading.

Circa 2015 Communication
The first thing to point out is that this agency action preempt
approves logical safety warnings. According to the House
Energy and Commerce Committee’s “21st Century Cures” initia-
tive white paper, “Communication about how certain treatments are
working in patients is happening through a multitude of media
around the globe. These conversations between and among
doctors, patients, researchers, and scientists in academia and industry
should be facilitated and encouraged.
As PSRMA has pointed out in the past, some of the FDA regula-
tions and guidance have a more direct impact on patient care than
others. The FDA’s restrictions on biopharmaceutical companies’
ability to share authoritative, regulated data about prescription
medicines limits healthcare professionals’ access to information that
can help them make informed decisions based on the healthcare
needs and preferences of their patients. The new FDA draft guidance opens a door for companies to
share truthful, scientifically accurate and data-driven information
with healthcare professionals to inform treatment decisions. Some
examples of this kind of information include:
• Observational data and “real world evidence”: information on
the safety and effectiveness of medicines taken from medical
records based on actual use of approved medicines.
• Subpopulation data: information on the safety and effective-
ness of medicines in subpopulations, including gender and
race, which can help HCP’s tailor treatment regimens.
• Observational and comparative data: information from the use
of a medicine outside of randomized clinical trials, especially
comparisons between two or more therapies.
• Economic information: healthcare economic data and infor-
mation on the economic value of medicines can improve
the efficiency of patient care.
• Information on medically accepted alternative uses of medi-
cines. Patients being prescribed medicines off-label deserve to
know that their HCP’s have the latest information.
There is a distinction between “off-label communications” and
“off-label marketing,” and it is a distinction with a difference. “Off-
label marketing” means sharing information with the intent to impact
sales—“ofﬁcial communications within the context of the
FDA’s views of off-label promotion within the context of the
free-and-fair dissemination of scientiﬁc data.” The new FDA action clearly is directed at off-label
communications. Another way to look at it is that “communications = education” and “marketing = sales.”

Patients Join the Fray
Patient groups have had their say so well. The National Organization
for Rare Disorders noted that “Congress should seek new policies
that permit drug companies to share appropriate information without
fear of enforcement.” The World Health Organization has ex-
pressed its worries that proposed changes might “chill off-label use of drugs and the dissemination of scientifi-
cation about non-approved uses.”
There’s much food for thought here, but two things in particular
should be mentioned: This is not an out-of-the-blue action by the
FDA and it’s not about communications with physicians—payer
formulary committees are another audience. Let’s look at the record.

To address concerns that FDA regulations were limiting the dissemination of outcomes research, Congress added Section 114 (in 1997) to set a new, less stringent standard applicable to promo-
tional dissemination of healthcare economic information to MCO
formulary committees: “competent and reliable scientific evidence.”
Still, as deputy center director for clinical science and acting deputy
director of the Office of Drug Evaluation, Bob Temple, noted, FDA
114 “is an interesting section, and it’s not entirely simple
to figure out what’s included and what’s not included.” No kidding.
One of the phrases in Section 114 that defies easy interpretation
is that promotion must involve a claim that “directly relates to an
advertisement approved” by the FDA. In the draft guidance, PhRMA
proposed that extrapolation from data included on labeling would
be appropriate at least under the following circumstances: from
duration of use in labeling to actual duration of use found in phar-
macy databases, from dosages included in labeling to actual dosages
found in pharmacy databases and from controlled trial settings to
actual practice settings.

PSRMA recommended that FDA allow the competent and reli-
able standard to be satisfied with data obtained through a number of
different methods, including observational study designs, database
reviews and other economic modeling techniques. “There should be
no pre-specified number or type of study required to substantiate
a claim,” the organization wrote in a 2012 white paper. “A claim
that a drug is more cost-effective than a competing drug may be
proved where the cost savings are due to reduced resource utilization
resulting from improved efficacy outcomes, decreased administra-
ton or monitoring costs, or where the difference in cost is due to
the drug causing fewer adverse events... these differences are
supported by competent and reliable evidence.”

Risks/Benefits
For industry, the new FDA guidance opens up tremendous potential
for enhanced (but restrained and responsible) sharing of important
scientific data. The key question is this: Do the opportunities out-
weigh the risks? There are a few ways to answer this.
There’s the First Amendment angle. Did the Caronia Pharr
decision—which, in December 2012, held that the federal
government could not prosecute a sales representative for speech
promoting the legal off-label use of an FDA-approved drug—impact
the way the FDA views off-label communication within the context of
the free-and-fair dissemination of scientific data?
An extreme way to look at it is that in a post-Caronia world, some
pharmaceutical companies may no longer feel obligated to seek FDA
approval for new indications, since they can open up “promote” them
without fear of prosecution. This is a flawed argument. Indications
of the on-label variety have many benefits, not least among which
is reimbursement. But such unintended consequences are important.
Any company that chooses this route would be acting in a highly
irresponsible manner, putting promotion before the public health.
The recent FDA action makes this a relatively implausible option.
In other words, the FDA’s action advances the public health by
accelerating the free and fair dissemination of scientific data while
maintaining appropriate regulatory oversight of communications.
That’s the FDA doing its job both protecting and advanc-
ing the public health. Bravo!

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