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Testimony of Vikas Saini, MD
Part 15 Public Hearing, FDA
Manufacturer Communications Regarding Unapproved Uses of Approved or Cleared Medical Products

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My name is Vikas Saini, and I'm a clinical cardiologist who trained and was on the faculty at Harvard, with 20 years of private practice experience. I was also the scientific co-founder of a successful medical device company whose products are used currently around the world, and I'm currently the president of the Lown Institute in Boston.

The Lown Institute is a think tank dedicated to exposing the scope, causes and consequences of poor healthcare and to advocating for a transformed health system.

I want to make several points today.

Overuse, or inappropriate medical care, is a big national problem.

Off-label use is already a big driver of overuse even without loosened restrictions.

The vast majority of information justifying off-label use outside the FDA approval process appears routinely in the medical literature, is not of high scientific quality and drives unjustified indication creep.

Companies routinely seek to expand off-label usage despite the fact that promoting it is not legal.

If companies are to promote such usage legally to medical practitioners and the public, they should be held to the highest evidentiary standards by the FDA in order to protect patients.

In fact, to loosen the regulations now would be in direct conflict with the mission of the FDA, primarily, if we are honest about it, in the interest of expanding corporate sales.

The FDA has to be a bulwark against bad science or patients will get harmed and huge sums of money will be wasted.

I want to make clear that I'm not arguing that physicians should not be allowed to prescribe off-label. I've done it myself. Indeed using nitro for heart failure or antibiotics in children, or insulin, is routinely an off-label usage.

One of the core areas of our work and expertise at the Lown Institute is understanding the epidemic of over-diagnosis and overtreatment in the US health care system. We happen to have a series of five papers in press right now at the Lancet that reviews these issues in much more detail than I have time for today.

Estimates of the amount of unnecessary testing and treatments in the US run into the hundreds of billions of dollars. Most experienced clinicians would agree that a large fraction of what we do in medical practice doesn't improve the health of our patients.

One of the central pillars of this ecosystem of overuse is a culture of more is better. That is true for patients, and also true of most doctors.

Because of this, off-label use is a central driver of overuse.

How? There are many ways.

I'm not a lawyer, but I know that truthful non-misleading information is not the same as scientifically valid knowledge. And I also know that publication in the peer-reviewed literature, the most plausible location for meaningful off-label information, is not necessarily valid scientific information. That peer-reviewed literature is woefully inadequate.

It's inadequate firstly, because rigorous studies are consistently behind practice. The cases of stenting for stable angina and the overuse of pulmonary artery catheters are two examples. And once practice patterns become entrenched, it is very difficult to change them – that waste becomes embedded and perpetuated through training programs, medical meetings, and cultural assumptions.

The literature is also inadequate because it is of extremely poor quality.

For example, in a study of over a thousand systematic reviews in the Cochrane database, only 14% had a high level of quality of evidence for the primary outcome.

Moreover, when 96% of the biomedical literature finds significant results, it is not that useful as a guide to practice.

But perhaps the major way off-label use promotes overuse is through so-called indication creep.

Manufacturers routinely seek to enter a product into commerce for a very narrowly defined indication for a very small number of patients and then expand usage to a vastly larger population with a very different safety profile. This inevitably will expose far larger numbers to the risk of harm.

Such indication creep happens in many ways.

It happens by moving the goal posts of clinical trials. In the CURE trial the study group was switched. Even then it only showed benefit because heart attacks were defined less stringently than in previous trials while bleeding harms increased.

It happens through lousy reporting and wild extrapolations. For example, one important metric is how many patients have to be screened in order to find one patient eligible for the trial. Some studies report it – but many do not. But you need to know it to understand which patients will truly benefit.

For example, in a study of a device for strokes to be used inside arteries in the brain, they found only 1% of screened patients could actually be enrolled in the study; yet an editorial in a major journal calculated, without much evidence, that up to 13% of stroke patients could be eligible.

Indication creep happens because there is a huge amount of embedded bias in the literature. For example, in 2011 in industry sponsored non-inferiority trials the success rate was 96.5%.

It also happens, as you may know, because different information and statistical analyses are registered at clinicaltrials.gov for journal publication than with the FDA. And the journal editors have no way to detect these discrepancies.

Now I realize that the FDA has no control of what appears in the journals – but this is one of the most important ways that practice patterns are set – and how off-label usage drives care that's unproven and could easily cause harm.

In this environment, why would we take out the last bastion of protection from patients by loosening standards even more?

When the courts find that companies have a First Amendment right to state the facts about their product, we need to ask a simple question: How much certainty do we have that we actually know what we know?

In a recent review of 363 consecutive studies, testing an accepted practice that was standard of care 40% of the time, the accepted practice was completely reversed.

I mean, look at the VIOXX story. Applying the FDA's current standards of evidence, we thought we knew. What seemed to be science, what seemed to be true, turned out to be wrong. Even with our best efforts to be careful, we fail regularly.

So if companies were permitted to use their vast sums of money to promote those less certain messages out into the market place, our concerns should skyrocket.

The culture of 'more is better' in America is associated with a celebration of innovation and novelty. But a recent review found that the incremental benefit of new treatments compared to old is on average nearly zero. In other words, patients rarely benefit significantly from the adoption of a new drug or treatment.

For all these reasons, an abundance of caution is always warranted.

We are particularly concerned about communications to health care practitioners and the public that do not meet rigorous standards of scientific evidence. That can only be determined by an independent arbiter. To allow the promotion of products into commerce without that would be tantamount to approving human experimentation on the American public with the harms becoming apparent only after it is far too late.

There is no substitute for creating a group of disinterested experts to examine the evidence carefully. The FDA exists to safeguard people from the harms of weak or of plainly false science. Otherwise we risk of an explosion of 21st Century Snake Oil.