Q&A: Lawyer John Conley Counters Lab Industry Arguments against FDA Regulatory Authority over LDTs

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NEW YORK (GenomeWeb) – Lawyers for the American Clinical Laboratory Association last week issued a white paper laying out their legal arguments against regulation of lab-developed tests (LDTs) by the US Food and Drug Administration.

The 25-page white paper follows FDA's release in October of a draft guidance outlining a nine-year framework for regulating LDTs. In an interview with GenomeWeb this week, lawyers Paul Clement and Laurence Tribe discussed, among other items, how Congress never intended FDA to have statutory authority over lab testing services.

Of course, the FDA has maintained otherwise. According to the agency, it has had the authority to regulate LDTs since the Medical Device Amendments were enacted in 1976. However, while labs performed these tests in limited fashion, the FDA opted not to exercise that enforcement power, or they chose to practice "enforcement discretion." Now, as the FDA sees it, LDTs involve complex technologies and algorithms and are broadly marketed. The agency has even cited examples of public harm from unregulated LDTs. This, the FDA says, has compelled it to lift its practice of enforcement discretion.

In an interview with GenomeWeb, John Conley, an intellectual property and civil litigation expert at Robinson Bradshaw & Hinson, played devil's advocate to the arguments laid out by Clement and Tribe in their white paper, and took a stab at how FDA's lawyers might defend the agency's oversight authority over LDTs. Conley co-authored a paper in 2003 that became the basis for the Association for Molecular Pathology's case against patenting isolated gene sequences, which the US Supreme Court found patent ineligible in 2013. Conley is also editor of *Genomics Law Report*, a blog about legal issues impacting the field of genomics and personalized medicine.

The interview is an intellectual exercise, aimed at exploring different sides of a multi-faceted issue. Conley's statements don't necessarily reflect his personal legal take on this topic or the FDA's for that matter; he's not speaking for the FDA. Below is a transcript of the discussion that has been

edited for clarity.


John Conley

How can the FDA claim to have the authority to regulate LDTs from the 1976 Medical Device Amendments, if Congress specifically created the Clinical Laboratory Improvement Act in 1967 to address lab regulation and then amended it again in 1988 to improve the framework? Doesn't the timing of the CLIA statutes suggest that the MDA doesn't address labs, because if it did then that means Congress would have advanced redundant regulations?

The counterargument there is that we're really talking about apples and oranges. Congress enacted CLIA back in the 60s to regulate labs in a general way — to make sure they met standards as labs, to make sure the tests they were using had analytical validity; that is, that the tests found what they purported to find. That was all about laboratory procedure. Neither that nor the 1988 amendments were about any specific testing that a lab was doing. It was really about laboratory procedures. That remains in place and continues to do what it was set out do.

The 1976 amendments, in bringing medical devices under the FDA regime, was really addressed to a different problem. It was not about whether the labs were functioning appropriately as labs but about whether specific devices were safe and effective. So, if I were arguing for the FDA here, I'd say that we are talking about two different things. CLIA doesn't answer the question of whether any particular test has clinical validity or whether it is safe and effective. The MDA does that, whereas CLIA is … supervising labs in a general procedural way. So, the coexistence of those two regulatory regimes is really neither here nor there with respect to FDA authority over LDTs. [*Editor's note: A test is clinically valid when it detects the disease or phenotype it's designed to detect. A test is analytically valid when it accurately measures the marker or analyte of interest.]*

Let's stay on your point about regulation of specific lab tests. ACLA's argument against FDA regulation is centered on this idea that LDTs are part of the practice of medicine and are not devices. In the white paper, there is an example about a radiologist making use of a regulated device — an x-ray machine — but the radiologist's reading of an x-ray isn't regulated by the FDA. How would you legally counter this example if you were FDA's lawyers?

I would ask what that example proves. A radiologist uses a device, and on the basis of information provided by the device, exercises judgment. So, we can't, at the federal level, encroach on the radiologist's exercise of judgment, even though it involves a device. I think the analog here would be the doctor back in the clinic exercising judgment relying in part on the results of a test. We all agree that the federal government shouldn't encroach on the doctor's exercise of judgment in the clinic, because that's a matter traditionally, if not constitutionally, reserved to the states. But I'm not sure what that says about the ability of the federal government to regulate the test, the x-ray machine, or any other thing like that as a device. I'm not sure what the radiologist example proves.

A lot of the stakeholders who spoke during FDA's two-day workshop last week on the regulation of LDTs repeatedly referred to LDTs as being part of the practice of medicine. They

said that the involvement of lab professionals in developing and performing tests, how they tweaked the tests and continually improved the tests, is part of the practice of medicine and so can't be regulated by the FDA. That's the parallel they're trying to draw.

I don't find that a particularly persuasive parallel. When we say the practice of medicine is reserved to the states for regulation, that's a very traditional definition of the sphere. It's a physician interacting with a patient, or in the case of a radiologist, [he or she] is interacting with patients and their doctors to examine a particular form of evidence, in order to treat or prescribe for that particular patient. It's a bit of a stretch to construe a scientific professional in a lab and say they're engaged in the same kind of activity.

Clement and Tribe in the white paper challenge that FDA would have exercised enforcement discretion over LDTs for four decades if truly there was a public health problem and doctors and labs were operating unlawfully. They charge FDA with power grabbing. To a court, could FDA's longstanding practice of enforcement discretion actually work against the agency's assertion that LDTs need to be regulated now because the industry has changed its marketing and business practices and the technology has become more complex?

The first thing I'd point out is that it could both be a power grab and legal. Characterizing it as a power grab is good rhetoric but it really doesn't address the legal point. An analogy here is to prosecutorial discretion and law enforcement — for example, broken windows policing. For as far back as I can remember police departments and prosecutors simply ignored all kinds of low-level, non-violent crimes and violations that were on the books. Then, all of a sudden, when the broken windows theory gained popularity, they started arresting people and prosecuting them for the very same offenses that they'd ignored for a long time. The justification was that in the past they didn't think it made sense to use their very limited resources to prosecute these things, but that now, they've changed their minds. [*Editor's note: The broken windows theory, put forth by James Wilson and George Kelling in 1982, holds that serious crimes may be better prevented in cities by creating social order through stopping smaller infractions, such as acts of vandalism or public intoxication.]*

If you apply that kind of logic to the FDA, their position is that they've always had this authority to [regulate LDTs], but in terms of priorities for their limited resources, given the nature of the LDT market, they didn't think it was a good use of those resources. Because LDTs have become a bigger business, they're more important, FDA now thinks LDTs pose a higher level of risk and they've decided to change their view on that.

I think what the authors of the white paper are trying to do is get … an admission by conduct against the FDA. I don't' think [the FDA] changing its position on how it's going to use limited resources is really an admission in any legal sense or indeed in any sense. They say in their draft guidance that in light of changing circumstances, they've changed their minds and that they ought to be more active in exerting oversight.

The FDA has cited a few examples of how the lack of LDT regulation has resulted in harm. The lab community has countered that the FDA has failed to show systematic harm from LDTs. To this, of course, some have pointed out that it is hard to pin down the extent of harm without a system for tracking adverse events from LDTs. The FDA's oversight plan seeks to put such a system in place. How would a court consider and view this question of harm as a reason for FDA lifting enforcement discretion?

If it goes before a court, then I assume initially it would do so on the narrow question of whether the FDA has jurisdiction to regulate LDTs. The present evidence of harm or risk, I don't think bears on that basic legal question. If they have the authority to regulate, then they have the authority to establish standards and determine harm. Whether there is any present demonstrable harm or not, if they don't have the authority, if they simply do not have the legal mandate to regulate LDTs, then even the presence of demonstrable harm doesn't change that. What's at the core here is a question of legal jurisdiction. Are these things medical devices that come within FDA's jurisdiction? I think that's the hardest question for the FDA.

The presence or absence of harm, on a practical level, could influence a court. Put yourself in the shoes of a judge. You probably went to law school because you were bad at science, and if the FDA is telling you there's a big potential for harm here, I think that would incline most people to giving some deference to the FDA. So, on a practical level, a strong or weak showing of harm could influence a court. But that wouldn't be the initial standard on which a court would decide initially.

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Do you think there might be some lessons learned with how things turned out with compounding pharmacies? Congress amended the Federal Food, Drug, and Cosmetic Act in 2013 to limit FDA oversight of traditional pharmacy compounding but required other types of pharmacies to meet FDA regulations. There are some in the lab community that say more complex algorithm-based tests or tests marketed directly to consumers should be overseen by the FDA. Do you think Congress has a role to play in differentiating the LDT space in the way they did for compounding pharmacies?

Congress could resolve this problem tomorrow. They could resolve this question of congressional intent in CLIA versus the MDA. They could say that they did or they didn't intend the FDA to have jurisdiction [over LDTs.] Congress could clarify that FDA does have jurisdiction over these kinds of LDTs but not over others. So, yes, Congress could take a parallel course here and give us a definitive answer. What a court would be doing here is interpreting Congress' intent in these various statutes. They would be interpreting the phrase "medical device" to see if it includes LDTs. A court would be trying to decipher and discern Congress' intent … and Congress could certainly solve this problem by saying, "This is our intent," as they did in the pharmaceutical compounding instance.

The idea that Congress in its present state would get around to sorting out something this complex — don't hold your breath. Congress could certainly do it. I wouldn't bet on Congress actually doing it.

If Congress does nothing … [then,] what do we read into the whole compounding process? If I were arguing for the FDA, I'd say, "Well, when Congress perceived some ambiguity, they fixed it. Apparently, Congress sees no ambiguity here. We have the authority. We'll go ahead and regulate. And Congress isn't taking any steps to remonstrate with us, to discipline us. So, therefore, Congress must think we're acting pursuant to our authority." I'm not sure how powerful an argument like that would be.

So, Congress could solve the problem. If Congress didn't solve the problem, then you have the two sides arguing about what the compounding analogy means for this situation. [*Editor's note: As part of the House of Representatives' 21st Century Cures Initiative, legislators are gathering input on the scientific and policy gaps hindering medical advances, and have asked the life sciences community to provide input on LDT regulation.]*

Many people in the life sciences industry have objected to how FDA promulgated its regulatory plan for LDTs – through guidance instead of rulemaking. Over the years, a lot of legal experts have criticized the agency for making major regulatory overhauls through guidance. How strong is the legal precedence against FDA here? Can FDA's lawyers make a case that the guidance pathway is the right one?

When I go through the Tribe and Clement arguments, the strongest argument against the FDA is the simple, common sense linguistic argument that a test in a lab is not a device. That's a tough one for the FDA and I don't think in the draft guidance when the agency addresses that point, it's all that persuasive.

The Administrative Procedures Act problem you're referring to is also an especially hard one for the FDA. The APA is the basis of the regulatory state. It sets forth a specific rulemaking procedure and the FDA is, from one point of view, circumventing that and shortcutting it by going with this guidance. I think what the FDA would say is, "We don't have to go through the full APA rulemaking procedure because we're not actually issuing a binding rule. All we're saying is we always had this regulatory authority and we're just being transparent about when and how we're going to exercise it." So, from their position, they're saying they're not doing anything new. They're saying, "We're not changing a substantive rule or issuing a new substantive rule that would be covered by the APA. We're doing you a favor. We're just letting you know that from our point of view, given our unquestioned regulatory authority, when and how we're going to exercise it."

Clement and Tribe said they hope their white paper will help FDA's lawyers see the error in their ways, and that this won't have to come to litigation. That's their hope, but it may not turn out that way. You co-authored a paper in 2003 that was very influential for the Association for Molecular Pathology's case against the patent eligibility of isolated gene sequences. At the time that you wrote it, did you have any idea that your arguments in that paper would be used to challenge gene patents in US courts? Did you write that paper with intent toward litigation?

No, I had no tactical goal there. I just thought that nobody had laid out the case against gene patents. We thought we'd do it. I think we recognized that someone might try [to bring suit], but I don't think we envisioned someone would try it in the direct way as was done. That was a little bit different because what we were doing was an academic exercise. We weren't working on behalf of an interested party. We were just saying, "If you want to do it, [challenge gene patents,] here's how to do it."

Tribe and Clement are actually working for a client. They are working for a trade organization with an interest and a point of view. So, whereas we were offering a free roadmap to the world, what they're doing is laying out their client's roadmap. They're saying, "Here's the legal argument we'd make. Our hope is that you, the FDA, will see this and be persuaded and negotiate a proposal that's more acceptable to our client. But if we sue, here are our arguments." So, I think they're previewing litigation but I see no reason not to take them at their word that their first objective here is to try to

get the FDA to change its policy.

But realistically does that happen? Has it happened that after the FDA has issued guidance it has retracted it? I suppose one can point to the 2007 guidance on *in vitro* diagnostic multivariate index assays, but then, the FDA dropped that plan for more comprehensive guidance on LDTs, which it has now issued.

If I had to give a yes or no answer, I'd say no. But if you look at the history of LDTs, the fact that they've exercised enforcement discretion — that is, they've done nothing until now — and the fast track for this is nine years, you can characterize all that as a response to consistent arguments against [FDA regulation]. The consumer genetics industry has attacked FDA's right to regulate LDTs. They've had a chorus of arguments against them for a long time. This is the first time they've done anything, and they're really not doing very much. Even if they do exactly what they say [in guidance,] it's going to take them nine years to get to the end point and much, if not most, of the LDT industry is going to remain untouched. So, one argument for what's happened here is that the FDA has adapted its policy to arguments that have been made against them. And this is just another instance of that happening.

The Q&A with ACLA lawyers Laurence Tribe and Paul Clement that this article references, can be found here.

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