Deconstructing *Genus Medical Technologies, LLC v. FDA:* A Misunderstood Court Decision

April 1, 2022 | Publications

Genus Continues to Sow Confusion and May Prompt Congressional Action

For a court case involving arcane, but important, regulatory issues, *Genus Medical Technologies, LLC v. FDA*, 994 F. 3d 631 (D.C. Cir. 2021), has received a lot of press over the past year.

Unfortunately, much of what has been reported on the internet and in the media is either confused, misleading, or simply incorrect. This *Insight* clarifies what the *Genus* decision stands for and explores steps the U.S. Food and Drug Administration (FDA) and Congress might take to address the issues raised in this case in a manner that does not disrupt a long-standing, stable regulatory regime that produces safe and effective products.

What *Genus* Really Says, and How Congress Could Intervene to Codify Long-Standing Regulation

The *Genus* case has its origins in the decision by a drug manufacturer to launch a drug called barium sulfate without FDA approval on a theory that it fell within a "grandfather clause" of the Food, Drug, and Cosmetic Act (FDCA). Barium sulfate is just one of many "contrast agents," an important class of drugs that are intended to improve the visualization of various structures and functions within the human body when a health care provider performs medical imaging (e.g., X-Ray, CT, Ultrasound, and MRI).

If applicable to the manufacturer's specific barium sulfate drug, the grandfather clause would have exempted the drug from the new drug approval requirement that other barium sulfate manufacturers had fulfilled in bringing their products to market.

People

James A. Boiani
Strategic Advisor
Health Services & Technology
202-861-1891
jboiani@ebglaw.com

Focus Areas

Services

Life Sciences

When FDA rejected the grandfather clause argument in a warning letter, the manufacturer changed tack and argued that its product was a medical device, not a drug. The manufacturer asked FDA, through a process called "request for designation," to formally reclassify the product as a device rather than maintain its status as a drug.

FDA, in its decision on the request for designation, said the barium sulfate product was clearly a drug and "may be a device," and that because contrast agents have for decades been consistently regulated as drugs,[1] the manufacturer's product would be treated as a drug, too. The manufacturer went to court, and ultimately the U.S. Court of Appeals for the District of Columbia Circuit reached the following conclusion of law: a product can be a drug *or* a device, not both. Then the court, rightly, sent the matter back to FDA to evaluate further.

Whatever you may have read elsewhere, ***the court did not say, and could not say, that barium sulfate (or any other contrast agent) was a device***. In fact, the court was quite clear that it was uncertain whether a contrast agent could meet the definition of a device, stating –

We note that ***it is not immediately obvious to us how a contrast agent satisfies the device definition's requirement that the regulated product be "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory...." 21 U.S.C. § 321(h)(1). [The "instrument clause"]*** *Nor is it altogether settled that [the manufacturer's product] satisfies the device definition's mode-of-action clauses. . . Because neither question is part of the administrative decision now under review—the FDA found only that Genus's products "appear to meet" the device definition . . . and both parties continue to agree that they do—we reserve the question whether [the product] satisfies the device definition's instrument and mode-of-action clauses*.[2]

Following the court decision, in an unusual turn of events, FDA initiated an "information request" process to gather feedback from the public at large regarding whether and how to shift the classification of products that have been uniformly regulated as drugs for decades to medical devices.[3] Unlike most actions by FDA, this particular activity was not prompted by public health concerns, and the idea was not embraced by stakeholders—comments made by stakeholders in response to the request raised various legal and policy concerns about why reclassification should not (or could not legally) take place, with many asking FDA to invoke the instrument clause referenced in the quote above to address this matter.

The events precipitated by this case have caused FDA and innovators to spend countless hours trying to reckon with its fallout, and it is likely that even after the request for information process is complete, the *Genus* decision will raise the continued specter of litigation. If FDA proceeds to

reclassify drugs that have been brought through a well-established regulatory framework as medical devices, it is reasonable to expect a wave of litigation from the many affected parties that will need to navigate a host of issues as a result of reclassification. Of course, an FDA decision to maintain consistent drug regulation based on existing authorities—even if well-reasoned—could also prompt litigation.

For that reason, Congress may act soon to clarify that contrast agents and other products that have consistently been regulated as drugs for decades remain drugs. Legislation that would reaffirm the designation of these medical products as drugs would allow FDA to continue pressing work on a host of other important public health issues, rather than divert its attention to a protracted public process and potential litigation for hundreds, if not thousands, of products. Further, if FDA were to reclassify only some drugs as medical devices but not others, it could create a scenario where some manufacturers of a product are regulated by one FDA Center, in its regulatory scheme, and another manufacturer of a similar product is regulated by a different Center under completely different regulations … ironically undoing a conscious decision decades ago by FDA following a 1997 court decision—*Bracco Diagnostics v. Shalala*—to adopt a uniform drug-based regulatory system for contrast agents, consistent with the *Bracco* court's opinion.[4] Not only could inconsistent regulation harm competition, but it could create separate standards for safety, effectiveness, manufacturing, and promotion, and potentially create a variety of challenges across all the interrelated health regulatory regimes where the application of laws and policies turns on whether a product is a drug or device.

Congressional clarification of FDA product jurisdiction is, of course, not unprecedented. Most recently, one could look to the 21st Century Cures Act of 2016, where Congress modified the statutory definition of a "device" to clarify the scope of FDA software regulation.[5] If Congress views the value of maintaining the current drug regulatory system to outweigh the value of upending it, and the associated issues the latter could cause, it may act soon to clarify the law and confirm that barium sulfate and other products that have long been regulated as drugs remain drugs. Such action would be wholly consistent with the *Genus* decision, which, as explained above, did *not* say barium sulfate (or any contrast agent) was a device.

The Instrument Clause That Could Compel FDA to Continue Regulated Contrast Agents and Drugs

One aspect of the *Genus* decision that often goes unreported—but warrants attention—is its application of the "instrument clause" referenced by the court, which provides FDA with clear authority for regulating all contrast agents as drugs, even if they lack chemical action. The reliance on the instrument clause in support of a decision to maintain the classification of contrast agents as drugs is unlikely to obviate the benefit of Congressional action—to provide FDA support, and

thwart continued litigation that could further disrupt long-standing regulation—but FDA may, based on overwhelming feedback it has received in public comments, look to this instrument clause to resolve the issue.

So, what is the "instrument clause"? Under the FDCA's current definitions, a "drug" is an "***article*** intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals,"[6] whereas a "device" is defined as—

"***an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory***, which is . . . intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, . . . and which ***does not achieve its primary intended purposes through chemical action within or on the body of man or other animals*** and which ***is not dependent upon being metabolized for the achievement of its primary intended purposes***."[7]

Thus, whereas drugs cover *all* articles, devices only cover a narrower subset: "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article. . . ." As stated in the concurring opinion in *Genus*, this instrument clause is "a big piece of the device definition," and one would question why "Congress used twenty words in the device definition's instrument clause if it meant nothing more specific than is expressed by the word 'articles' alone in the drug definition."[8]

This instrument clause has its origins in the Federal Food, Drug, and Cosmetic Act of 1938 (which has, through multiple amendments, evolved into the FDCA in effect today), in which "devices" were defined to include "instruments, apparatus, and contrivances, including their components, parts, and accessories."[9] As explained in *United States v. Article of Drug, Bacto-Unidisk,* consistent with their plain meaning, these terms were intended to refer to "items characterized more by their purely mechanical nature than by the fact that they are composed of complex chemical compounds or biological substances."[10] In other words, the concern being addressed by the inclusion of the instrument clause was that crutches (not contrast agents) could be viewed as "drugs" as broadly defined by the FDCA.[11]

The Medical Device Amendments of 1976 revised the definition to add "implement, machine . . . implant, in vitro reagent, or other similar or related article" to the 1938 definition.[12] The addition of "in vitro reagent" is the only reference to a product that is clearly chemical in nature, and directly addressed the subject of *Bacto-Unidisk*. The terms "implement," "machine," and "implant" described items that were then and continue to be generally understood as being mechanical or

electromechanical in nature.[13] The clause "similar or related article" is not defined, but such words "are narrowed by the commonsense canon of *noscitur a sociis* — which counsels that a word is given more precise content by the neighboring words with which it is associated."[14]

The Medical Device Amendments of 1976 also added the mode-of-action criterion to the device definition. The legislative history makes no reference to adding this provision to reclassify contrast agents, which by 1976 were already being approved by FDA as drug products, with several contrast agents having already been approved by the 1950s. If Congress had wanted device determinations to depend solely upon mode-of-action, it likely would have simply removed the instrument clause when it amended the FDCA. If Congress had intended FDA to revoke several FDA new drug approvals for a product class, one would expect that Congress would have at least made a passing reference to that (which it did not). Instead, Congress chose to add to the instrument clause, evidencing that this general limitation on the universe of devices remains in place. FDA, of course, cannot ignore the instrument clause, or its history, in its analysis—and when it considers these points, could reasonably conclude contrast agents are not devices, and thus must continue to be regulated as drugs.

FDA also has historically relied solely upon the instrument clause in classifying other products as drugs. For example, Lacrisert (Hydroxypropyl Cellulose Ophthalmic Insert) is described in its FDA-approved labeling as a "physiologically inert" substance that is not metabolized by the body, and is intended to treat severe dry eye disease. In considering its regulation relative to other products, FDA stated the following:

Except for implants and *in vitro* reagents, most items in this list are mechanical products that generally are constructed of solid materials such as metal or plastic. *By contrast, a drug is a chemical or a combination of chemicals in liquid, paste, powder, or other drug dosage form that is ingested, injected, or instilled into body orifices, or rubbed or poured onto the body in order to achieve its intended medical purpose. Lacrisert is not an instrument, apparatus, implement, machine, contrivance, implant, or in vitro reagent nor is it similar or related to these products that are listed in the "device" definition; rather, Lacrisert is a combination of chemical entities, intended for in vivo use*.[15]

All contrast agents are combinations of chemicals that are administered to the body, like Lacrisert. Also, like Lacrisert, regardless of whether the product has chemical action or is metabolized, there appears to be a strong basis to conclude contrast agents fail to meet the definition of a "device" because they do not fall within the instrument clause.

What the Future Holds

How Congress and FDA approach the *Genus* decision in the coming weeks and months will be important to determining not just the stability of a long-standing regulatory framework for contrast agents, but also innumerable problems that disrupting the current regulatory framework could cause. From a legal perspective, FDA appears to have the authority (and, perhaps, legal obligation) to maintain consistent drug regulation across all imaging agents. However, the *Genus* case also shows that Congress likely needs to strengthen the law further with a technical clarification that codifies decades of consistent regulation in order to prevent continued litigation, and help FDA maintain its focus on matters that protect and advance the public health.

***

This *Insight* was authored by **James A. Boiani**. For additional information, please contact the author or the Epstein Becker Green attorney who regularly handles your legal matters.

ENDNOTES

[1] Contrast agents have been regulated uniformly as drugs since prior litigation on this topic (*Bracco v. Shalala*, 963 F. Supp. 20 (1997)), and have generally been regulated as drugs since the first iodine-based contrast agents were approved since the early 1950s, so there is an extensive history of drug regulation.

[2] *Genus, at* 634, n. 3.

[3] *FDA, Genus Medical Technologies LLC Versus Food and Drug Administration; Request for Information and Comments*, 86 Fed. Reg. 43553 (Aug. 9, 2021), https://www.govinfo.gov/content/pkg/FR-2021-08-09/pdf/2021-16944.pdf.

[4] 963 F. Supp. 20 (1997). In *Bracco*, the issue was that FDA had chosen to regulate most ultrasound contrast agents as drugs, but one as a medical device. The court, following a long line of court decisions, held that similarly situated parties (and products) must be treated in a similar fashion, and appropriately left it to FDA to decide whether the products would be regulated as drugs or devices. FDA chose uniform drug regulation, which has lasted since that time.

[5] *See* Section 3060(a) of the 21st Century Cures Act (adding FDCA § 520(o)).

[6] 21 U.S.C. § 321 (g)(1) (emphasis added).

[7] 21 U.S.C. § 321(h)(1) (emphasis added).

[8] *Id.* at 648.

[9] Federal Food, Drug, and Cosmetic Act of 1938, P.L. 75-717, Jun. 25, 1938, 52 Stat. 1040; 21 U.S.C. § 321(h) (1938).

[10] *United States v. Article of Drug, Bacto-Unidisk,* 394 U.S. 784 at 799-800 (1969).

[11] The Supreme Court further explained in *Bacto-Unidisk* that when the instrument clause was drafted, Congress intended to define "drug" broadly but exclude items such as "electric belts, quack diagnostic scales, and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units, and crutches" to avoid the "semantic incongruity" of classifying such mechanical items as drugs. *Id.*

[12] Medical Device Amendments of 1976, Pub. L. 94-295, May 28, 1976, 90 Stat. 539; 21 U.S.C. §321 (h).

[13] An "implement" is "a device used in the performance of a task" or that "serves as an instrument or a tool"; a "machine" is "a mechanically, electrically, or electrically operated device for performing a task" or "an instrument (such as a lever) designed to transmit or modify the application of power, force, or motion" or "an assemblage of parts that transmit forces, motion, and energy one to another in a predetermined manner"; and an "implant" is "something (such as a graft or device) implanted in tissue." See, Merriam-Webster.com Dictionary, Merriam-Webster, https://www.merriam-webster.com/dictionary (last visited Mar. 30, 2022).

[14] *United States v. Williams*, 553 U.S. 285, 294 (2008); *See also, Gustafson v. Alloyd Co.,* 513 U.S. 561, 575 (1995).

[15] Food & Drug Admin., Notice, "Merck Sharp & Dohme Research Laboratories; Reclassification of Lacrisert as an Approved New Drug," 47 Fed. Reg. 46,139 (Oct. 15, 1982) (emphasis added). This is hardly the only drug like this; there are in fact many. Another common example are colonoscopy preparation drugs that lack pharmacological action.