UNITED STATES COURT OF APPEALS
FOR THE DISTRICT OF COLUMBIA CIRCUIT

No. 20-5026

ORAL ARGUMENT HAS NOT YET BEEN SCHEDULED

GENUS MEDICAL TECHNOLOGIES LLC,

Plaintiff-Appellee,

v.

U.S. FOOD AND DRUG ADMINISTRATION,

Defendant-Appellant

On Appeal from the United States District for the District of Columbia
Case No. 1:19-cv-0544
The Honorable James E. Boasberg, District Court Judge

BRIEF OF *AMICUS CURIAE* GISKIT B.V. IN SUPPORT OF DEFENDANT-APPELLANT U.S. FOOD AND DRUG ADMINISTRATION

James A. Boiani, Esq.
EPSTEIN BECKER & GREEN, P.C.
1227 25th Street, N.W., 7th Fl.
Washington, D.C. 20037
(202) 861-1891
JBoiani@ebglaw.com

Counsel for *Amicus Curiae* Giskit B.V.

Of Counsel:

James P. Flynn, Esq.
Yael Spiewak, Esq.

CERTIFICATE AS TO PARTIES, RULINGS, AND RELATED CASES

A. Parties and Amici

Except for the following, all parties, intervenors, and amici appearing before this Court are listed in the brief for Defendant-Appellant FDA:

Giskit B.V.

B. Rulings Under Review

All rulings under review are listed in the brief for Defendant-Appellant FDA.

C. Related Cases

All related cases are listed in the brief for Defendant-Appellant FDA.

RULE 26.1 CORPORATE DISCLOSURE STATEMENT

Pursuant to Rule 26.1 of the Federal Rules of Appellate Procedure and D.C. Circuit Rule 26.1, Giskit B.V. ("Giskit") makes the following disclosures:

The following are parent companies, subsidiaries, or affiliates of Giskit that have issued shares or debt securities to the public: None.

Publicly Held Company that Owns 10% or More of Giskit's Stock: None.

Giskit's General Nature and Purpose: Giskit B.V. is a corporation which develops innovative new medical products for patients, including the FDA-approved contrast agent drug, ExEm Foam (air polymer-type A) intrauterine foam.

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Fed.R.App. P. 29(a)(4)(D) Statement
Of *Amicus Curiae's* Identity And Interest

Amicus Curiae Giskit B.V. ("Giskit") holds a new drug application ("NDA") approval to market a contrast agent regulated by the U.S. Food & Drug Administration ("FDA").[1] Giskit's approval is consistent with long-standing practice, confirmed since *Bracco Diagnostics v. Shalala*, 963 F.Supp. 20, 28 (D.D.C. 1997), to regulate a contrast agent as a "drug" under the Federal Food, Drug, and Cosmetic Act ("FDCA"). As stated in the accompanying motion, Giskit seeks leave to file this brief as *amicus curiae. See* Fed.R.App.P. 29; D.C. Cir. Rule 29.

Giskit's separate participation as *amicus* benefits the Court by bringing it the perspective of a market participant that, like two decades of other market participants, has accepted and abided by FDA's expert agency determination to regulate contrast agents as drugs in furtherance of public health, safety, and the statutory schema Congress created. *Nat'l Ass'n. of Home Builders v. U.S. Army Corps of Engineers*, 519 F. Supp. 2d 89, 93 (D.D.C. 2007) ("[T]he court has broad discretion to permit NRDC's participation in this suit as an *amicus curiae*...Because NRDC seeks to support the government's arguments in favor of the validity of its action and its interpretation of the scope of the CWA, the court may benefit from

[1] NDA. No. 212279 (ExEm Foam (polymer-type A) intrauterine foam).

NRDC's input."); *Cobell v. Norton*, 246 F. Supp. 2d 59, 62 (D.D.C. 2003) (*amicus* "has unique information or perspective that can help the court beyond the help that the lawyers for the parties are able to provide").

The Court's decision here will reach beyond the fate of barium sulfate – it will either affirm or throw into chaos a regulatory regime built over 23 years, affecting Giskit and many other manufacturers of contrast agents. Most, if not all, contrast agents create their primary intended effect (improving visualization of anatomical features) fundamentally the same way – they are administered into the body, providing a substance that will absorb or scatter energy – which might be in the form of X-rays (X-ray contrast imaging), magnetic pulses (magnetic resonance imaging), sound waves (ultrasound imaging) – differently than surrounding tissues. This creates "contrast" with those tissues, allowing anatomical features to be seen. Though chemical action and metabolism often play no role in the intended effect, these products are chemicals ingested, injected, or otherwise administered into the body, are manufactured like other drugs, and raise similar safety concerns (e.g., potential adverse reactions to ingredients and degradation products).

The FDA's approach to contrast agent regulation is supported in law, fair to manufacturers, considers patient safety, and should be upheld by this Court.

Fed.R.App. P. 29(a)(4)(E) and 29(d) Statement
As To Brief Of *Amicus Curiae* Giskit B.V.

The below signing counsel of Giskit, along with firm colleagues and in consultation with Giskit, is sole author of this brief. Giskit alone paid, or will pay, counsel's fees associated with same. Giskit certifies that a separate brief is necessary to bring its unique perspective on the appealed issue before this Court.

Pertinent Statutory Provisions

Pertinent statutory provisions are reproduced in the addendum to this brief.

LEGAL ARGUMENT

Summary

The court below incorrectly interpreted the FDCA to require contrast agents (like Genus Medical Technologies' Vanilla SilQ barium sulfate contrast agents) be deemed devices. The court below incorrectly held that the FDA had no discretion to require such contrast agents be regulated as "drugs." The FDA's discretion to regulate these contrast agents in a like manner (namely as drugs) was confirmed in *Bracco*, 963 F. Supp. at 28, a decision: (i) in which Congress has long acquiesced despite changing the FDCA in other ways; (ii) that is consistent with the very structure of the FDCA, which provides overlapping definitions of "drug" and "device" (in 21 U.S.C. § 321(g) and (h)) and a mechanism to request that the FDA determine (under 21 U.S.C. § 360bbb-2(a)) the class (drug/device) in which a product will be regulated; and (iii) that the FDA and many courts have invoked to

confirm the FDCA's meaning and the discretion afforded the FDA. As these support the FDA's position here, such position is a reasonable one that compels reversal, whether or not given deference under *Chevron U.S.A., Inc. v. Natural Res. Def. Council, Inc.*, 467 U.S. 837 (1984), or *Skidmore v. Swift & Co.*, 323 U.S. 134 (1944).

The lower court adhered unflinchingly (and erroneously) to the "old and familiar rule" that "the specific governs the general." *Genus Medical Technologies, LLC v. FDA*, 427 F. Supp. 3d 74, 83 (D.D.C. 2019), invalidating regulation of contrast agents as drugs because the specific and misleadingly referenced "exclusionary" clauses defining a device could apply to these barium sulfate contrast agents. In doing so, the district court ignored the customary interpretative tools it had earlier acknowledged that it "must use:--'text, structure, purpose, and legislative history…'" *Genus*, 427 F. Supp. 3d at 82 (citation omitted). The lower court's analysis instead erroneously assigned like provisions differing labels, and applied a rule used to resolve conflicts of statutory definitions that were, in fact, complementary.

Since 1997, the FDA has exercised its court-acknowledged discretion to regulate contrast agents (such as barium sulfate) as drugs rather than devices. The decision below refused to defer to the expert agency's long-standing approach, finding that the FDA had no such discretion, and was required to treat Genus's

Vanilla SilQ barium sulfate contrast agents as devices. Such a reading, however, contravenes *Chevron*, ignores material canons of statutory construction in favor of undue reliance on a single canon, and contradicts Congressional intent imbued in the statutory structure and confirmed through decades' long legislative acquiescence to the FDA's regulation of contrast agents as drugs. In adopting such a reading, the district court erred, upset the FDA's reasoned and reasonable approach to regulating contrast agents ingested by patients just like other drugs in liquid forms, neutered important FDA policy determinations, and frustrated reasonable reliance that regulated parties like Giskit and the market have placed on the FDA's regulating contrast agents as drugs. The ruling below should not stand.

Standard Of Review

This Court reviews *de novo* appeals from a district court's grant of summary judgment in an action under the Administrative Procedures Act, only allowing a court "to set aside agency action that is arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law." *Grunewald v. Jarvis*, 776 F.3d 893, 898 (D.C. Cir. 2015).

Giskit notes, however, that in conducting such review, deference to the FDA's decision and interpretations here is appropriate under the *Chevron* standard and, independently, under the *Skidmore* standard. *See Chevron*, 467 U.S. at 844;

Shays v. FEC, 414 F.3d 76, 96 (D.C. Cir. 2005) (outlining *Chevron* framework);[2] *see also Skidmore*, 323 U.S. at 140; *Orton Motor, Inc. v. HHS*, 884 F.3d 1205, 1211 (D.C. Cir. 2018) (deferring to an FDA interpretation under *Skidmore*).[3] Though Giskit asserts deference under each standard as appropriate here, reversal of the district court is appropriate even in the absence of such deference.

I. BECAUSE CONGRESS HAS ACQUIESCED FOR OVER TWO DECADES TO FDA REGULATION OF CONTRAST AGENTS AS "DRUGS" AMIDST POST-DECISION AMENDMENTS TO STATUTORY STRUCTURE, THE DISTRICT COURT ERRED IN CONCLUDING THAT THE FDCA REQUIRES THE FDA TO NOW REGULATE CONTRAST AGENTS AS "DEVICES."

Where, as here, courts and agencies have long construed a statute in a particular manner, it must be understood in that manner:

> If a statute uses words or phrases that have already received … uniform construction by inferior courts or a responsible administrative agency, they are to be understood according to that construction.
>
> [Antonin Scalia & Bryan A. Garner, *Reading Law* 322 (2012) (hereafter "*Reading Law*")]

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[2] *Mylan Laboratories, Inc. v. Thompson*, 389 F.3d 1272, 1280 (D.C. Cir. 2004) (applying *Chevron*); *see also, e.g.*, *Purepac Pharm. Co. v. Thompson*, 354 F.3d 877, 883 (D.C. Cir. 2004) ("FDA interpretations of the FDCA receive deference"). *Chevron*, requires a court to defer to an agency's position that "rests on a permissible construction of the statute" if Congress has not "unambiguously expressed intent" contrary to the agency position. *Mylan*, 389 F.3d at 1280.

[3] "Under *Skidmore*, '[t]he weight [accorded to an administrative judgment] in a particular case will depend upon the thoroughness evident in its consideration, the validity of its reasoning, its consistency with earlier and later pronouncements, and all those factors which give it power to persuade, if lacking power to control.'" *Creekstone Farms Premium Beef, L.L.C. v. Dep't of Agric.*, 539 F.3d 492, 499 (D.C. Cir. 2008).

This general principle of statutory construction has wide recognition,[4] and the construction of the FDCA allowing agency discretion to regulate contrast agents uniformly as drugs since the 1997 decision in *Bracco* has been applied consistently by the FDA and the courts.[5]

Unlike a myopic focus on one rule of construction such as "the specific governs the general," the just quoted "prior construction" canon blends the FDA's argument (and Giskit's presentation here) with other canons of construction that lead to a more consistent approach to statutory construction. That construction liberates both the text and structure of the statute to allow the FDA to carry out the job that Congress intended, and has seen fit to allow remaining with, the FDA.

Finally, the lower court did not consider all elements of the definition of a "device," which provides the FDA with discretion regarding regulation of products

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[4] *See, e.g.*, *Owens v. Republic of Sudan*, 174 F. Supp. 3d 242, 261 (D.D.C. 2016), *aff'd*, 864 F.3d 751 (D.C. Cir. 2017), *certified question answered*, 194 A.3d 38 (D.C. 2018), *and vacated and remanded sub nom. on other issues Opati v. Republic of Sudan*, No. 17-1268, 2020 WL 2515440 (U.S. May 18, 2020), *and aff'd*, 924 F.3d 1256 (D.C. Cir. 2019); *see also United States v. Burkholder*, 816 F.3d 607, 617-618 (10th Cir. 2016); *Sachs v. Republic of Austria*, 737 F.3d 584, 598 n.13 (9th Cir. 2013), *rev'd sub nom. on other issues OBB Personenverkehr AG v. Sachs*, 136 S. Ct. 390 (2015); *and see Silver v. Pueblo Del Sol Water Co.*, 423 P. 3d 348, 355 (Ariz. 2018); *Estate of Miller v. Storey*, 903 N.W.2d 759, 771 (Wisc. 2017); *Furtula v. University Of Kentucky*, 438 S.W.3d 303, 320 (Ky. 2014).

[5] *See* Section I.A.1 below.

like contrast agents that might "appear" to meet the definition of a device on the surface, but on closer examination are better regulated as drugs.

Thus, this Court should reverse the decision below.

A. For Over Twenty-Three Years, Courts Have Relied On *Bracco*, The FDA Has Adhered To It In Considering Contrast Agents Drugs, Industry Has Relied On Consistent FDA Conduct In Coming To Settled Expectations And Making Investment-Based Decisions, And Congress Made No Effort To Overrule *Bracco* Or Change The Statute In Any Way To Limit FDA Discretion.

1. *Bracco Has Been Cited And Followed By Courts In This Circuit And Elsewhere: The FDA Has Adhered To Bracco Consistently.*

The approach endorsed in *Bracco* has wide and consistent acceptance fostered and adopted by the courts. For instance, a district court in this Circuit relied on *Bracco's* holding requiring uniform regulation of functionally indistinguishable products as drugs in a matter affirmed by this Court. *See El Rio Santa Cruz Neighborhood Health Ctr., Inc. v. Dep't of Health & Human Servs.*, 300 F. Supp. 2d 32, 42–43 (D.D.C. 2004), *aff'd*, 396 F.3d 1265 (D.C. Cir. 2005).[6] Courts in this Circuit and elsewhere have also followed *Bracco* on the appropriateness of the FDA regulating these contrast agents in a uniform manner. *See, e.g., Doe v. United States Citizenship & Immigration Servs.*, 239 F. Supp. 3d

[6] This Court has also affirmed reliance on *Bracco* on other issues. *Ass'n of Am. Physicians & Surgeons, Inc. v. Food & Drug Admin.*, 539 F. Supp. 2d 4, 23–24 (D.D.C. 2008), *aff'd sub nom. Ass'n of Am. Physicians v. FDA*, 358 F. App'x 179 (D.C. Cir. 2009). The 10th Circuit has also cited *Bracco* on other issues as well. *See Cody Laboratories, Inc. v. Sebelius*, 446 F. App'x 964, 970 (10th Cir. 2011).

297, 307–08 (D.D.C. 2017); *PREVOR v. Food & Drug Admin.*, 895 F. Supp. 2d 90, 99 (D.D.C. 2012); *see also Wyoming v. United States Dep't of the Interior*, 136 F. Supp. 3d 1317, 1344 (D. Wyo. 2015), *vacated and remanded sub nom. on other issues Wyoming v. Sierra Club*, 2016 WL 3853806 (10th Cir. 2016).

The FDA has consistently applied this rationale. For instance, following *Bracco*, the FDA issued a 63-page analysis of why it was appropriate to regulate uniformly all contrast agents as drugs, noting that this approach concentrated "the review of these products in one agency Center, under one statutory scheme, [would] promote administrative efficiency, make better use of agency resources, and minimize the burden on industry and practitioners that a dual regulatory scheme [might] impose." *See* FDA Appeal Brief at 10-11. More recently, the FDA has issued guidance noting that, though a product satisfying both the device and drug definitions will "[g]enerally ... be classified as a device," and would be regulated as a drug when "it falls within a special category." *Classification of Products as Drugs and Devices and Additional Product Classification Issues: Guidance for Industry and FDA Staff* 12 (Sept. 2017), https://go.usa.gov/xdYun. As the FDA's brief notes at page 11, the FDA's consistent approach to all contrast agents of various kinds for over two decades has been to regulate this special category of products as drugs.

This is not some small sample of aberrant precedents; it is, rather, the decision below that is aberrant of judicial endorsements and agency practice. Allowing the

FDA to regulate contrast agents consistently under *Bracco* instead has "the uniform weight of authority…significant enough that the bar can justifiably regard the point as settled law." *Reading Law* 325. In the face of such long-standing acquiescence, *Bracco* reflects a correct understanding of how Congress envisioned the FDCA would work as to these contrast agents. That being the case, this Court should reject the lower court's refusal to reach a result consistent with *Bracco*.

2. Regulated Entities Have Relied On Contrast Agents Being Regulated as Drugs.

Adhering to prior consistent construction brings predictability and fairness to the marketplace, where contrast agent manufacturers, such as Giskit, operate in and wish as *amicus curiae* to reference for the Court. Genus availed itself of this certainty, in fact, when (according to the National Drug Code ("NDC") directory) it registered as a ***drug*** manufacturer, and listed its product as an "unapproved new ***drug***" (along with other manufacturers of barium sulfate products), as early as 2014,[7] apparently to enjoy enforcement discretion FDA offered at the time allowing marketing unapproved barium sulfate drugs.

As *Bracco* recognized, "[r]equiring the FDA to test similar products with the same scrutiny is consistent with the FDA's mission and is in the public interest," 963

[7] *e.g.*, NDC No. 69307-1024-2 (Vanilla SilQ, First Marketed Oct. 27, 2014) *available at,* https://www.accessdata.fda.gov/scripts/cder/ndc/index.cfm (last accessed June 1, 2020).

F. Supp. at 30, and "disparate treatment of functionally indistinguishable products is the essence of the meaning of arbitrary and capricious." *Id*. at 28.[8] Yet, such will be the result unless this Court vacates the lower court here, as that decision will leave Genus' products regulated very differently than all others have been for 23 years. Whether that differential treatment is a head start that leaves a competitor behind those that had begun together, or unfairly allows a newcomer to leap frog time and treasure constraints a predecessor has already sunk, it is inconsistent with both fair competition and good health results to allow competitive products into the market through disparate regulatory pathways. *Bracco*, 963 F. Supp. at 29.

3. Congress Has Not Overruled Bracco, Nor Has It Revised The Statute To Limit FDA Discretion.

The lower court's decision mistakenly ignored multiple canons of statutory construction as guides pointing in the same direction, to wed itself instead to a few, as the Court focused on the so-called "exclusionary" provisions rather than the richness of the statutory structure. *See Reading Law* 59 ("No canon of interpretation is absolute. Each may be overcome by the strength of differing principles that point in other directions." '[C]anons are not mandatory rules. They are guides that 'need not be conclusive.' *Chickasaw Nation v. United States*, 534 U.S. 84, 93 (2001)."); *see also* Point I.A.3 below.

[8] It is also consistent with the reasonable understanding and reliance of the regulated community and its counsel. *See Reading Law* 324.

For example, the lower court here incorrectly suggests that the FDA's interpretation leaves the "device" defining language of 21 U.S.C. § 321(h) superfluous, *Genus*, 427 F. Supp. 3d at 83, ignoring both its own conclusion that the definition of drug and device are overlapping rather than mutually exclusive, *id.* at 85, and that its own construction leaves a significant portion of the statute, namely the Request for Designation provisions at 21 U.S.C. § 360bbb-2(a), without purpose or function. If the overlapping definitions of drug and device in 21 U.S.C. §§ 321(g)(1) and (h) were intended and understood to be fully self-executing and outcome determinative without FDA discretion, 21 U.S.C. § 360bbb-2(a) would be a provision without a purpose – there would be no decision for the Secretary to make as to the request as the outcome would be statutorily compelled. Even more telling, requiring that the FDA "determine the classification of the product" and provide "a written statement" supporting its determination makes little sense unless Congress expected and intended the agency's expertise to applied and exercised. *Id.* § 360bbb-2(b).

Similarly, the lower court's invocation of the specific/general canon of construction is also misplaced, as it is invoked without certain necessary findings and bases. That canon is only appropriately invoked where there are *conflicting* provisions that cannot be reconciled, and one is general and one specific. *Adirondack Med. Ctr. v. Sebelius*, 740 F.3d 692, 698 (D.C. Cir. 2014) (canon "is impotent,

however, unless the compared statutes are 'irreconcilably conflicting'"). As the parties here, and even the court below, have acknowledged, the definitions at issue here are complementary and intentionally overlapping, not conflicting, leaving this canon inapplicable.

Likewise, these provisions – 21 U.S.C. § 321(g)(1) and (h) – are not truly a general one and a specific one, but rather are two complementary, specific provisions defining "drugs" and "devices" respectively. That one's definition encompasses more is not the same thing as saying it is a more general provision. It simply reflects a legislative intent for a more inclusive definition to apply if the expert regulatory agency deems that appropriate.

This is important context to consider as the lower court references what it suggests is legislative silence, or other device liberating amendments. *Genus,* 427 F. Supp. 3d at 82. Rather than it being silence or general liberalization into which one might hesitate to pour meaning, amending the FDCA without touching upon *Bracco* is the sort of two-decades-plus legislative acquiescence that courts regularly accord great weight in interpreting statutes. As noted in *Estate of Miller v. Storey*, 903 N.W2d 759, 771 (Wisc. 2017), "legislative inaction in the wake of judicial construction of a statute indicates legislative acquiescence. [citation omitted] This doctrine of legislative acquiescence applies with equal, if not greater, force where the legislature has acted on the statute, but declines to revise the interpreted

language." Despite the lower court's characterization, this is exactly what happened post-*Bracco*, and it necessarily impacts any understanding of the statute's reach.

Congress has no qualms about expressly overruling the FDA or changing its jurisdiction. For example, the Biologics Price Competition and Innovation Act of 2009 ("BPCI Act") (Pub. L. 111-148) directed that biologically-derived complex drugs approved under the FDCA for decades be "deemed" (*i.e.*, converted to) biological license application ("BLA") approvals under the Public Health Service Act as of March 23, 2020, after which they would subject to a different statutory framework. BPCI Act § 7002(e). Similarly, the 21st Century Cures Act of 2016 (Pub. L. 114-255) included a provision entitled "Clarifying Medical Software Regulation" in which Congress revised the definition of "device" in the FDCA to exclude certain products from its definition. 21st Century Cures Act § 3060. But that has not happened here.

Additionally, the Supreme Court has found acquiescence to apply with special strength in the administrative realm, as in *NLRB v. Bell Aerospace*, 416 U.S. 267, 274-275 (1974) ("[A] court may accord great weight to the longstanding interpretation placed on a statute by an agency charged with its administration.") When one notes that such long-standing agency interpretation was left untouched even while other statutory amendments occurred, the case for the interpretation being consistent with legislative intent is a strong one. *See Fed. Deposit Ins. Corp.*

v. Phila. Gear Corp., 476 U.S. 426, 437 (1986) ("congressional failure to revise or repeal the agency's interpretation is persuasive evidence that the interpretation is the one intended by Congress"); *accord Silver v. Pueblo Del Sol Water Co.*, 423 P.3d 348, 355 (Ariz. 2018). For all these reasons, this Court should reverse the lower court here so the FDA can continue regulating these contrast agents as drugs under the FDCA.

B. In Deciding Whether The FDA Has Discretion To Regulate Contrast Agents As Drugs, The Lower Court Failed To Consider The Import Of The FDA Reauthorization Act of 2017, And Congress's Express Adoption Of Language Accepting The FDA's Determination That Contrast Agents Are "Drugs."

In 2017, as part of the FDA Reauthorization Act, Congress defined a "contrast agent" in relevant part as "a drug that ... is intended for use with an applicable medical imaging device." 21 U.S.C. § 360j(p)(4)(B). Though the lower court here read § 360j(p)(4)(B)'s definition of "contrast agent[s]" as "drug[s]" to be irrelevant in light of the statutory reference to that definition applying "[f]or purposes of" § 360j(p), 427 F. Supp. 3d at 85, that misreads the statute, misunderstands the statutory structure, and fails to apply the prior construction canon of statutory interpretation. That canon, as noted above, is applicable where uniform construction by lower

courts or the responsible administrative agency is incorporated into a new statute or related statutes.

That consistent understanding of contrast agents as drugs was thus incorporated into a new statute, and that canon suggests that this has gone beyond legislative silence or acquiescence into Congressional adoption:

> Congress' repetition of a well-established term carries the implication that Congress intended the term to be construed in accordance with pre-existing regulatory interpretations.
>
> [*Bragdon v. Abbott*, 524 U.S. 624, 631 (1998)]

Since *Bracco*, there has existed the same sort of "uniformity of the administrative and judicial precedent construing the definition" of the term "drug" as including these contrast agents. *Bragdon*, 524 U.S. at 643. The Supreme Court has noted that such consistency is "significant." *Id.* Indeed, "[w]hen administrative and judicial interpretations have settled the meaning of an existing statutory provision, repetition of the same language in a new statute indicates, as a general matter, the intent to incorporate its administrative and judicial interpretations as well." *Id*. Repeating here the word "drug" as defining contrast agents illustrates both what that phrase would mean "[f]or purposes of" §360j(p) as well as what it had meant under consistent administrative construction. *Id*.; *and see Reading Law* 322 (noting that prior construction canon "goes beyond" reenactments to apply to the interpretation of related statutes). Consequently, this Court should reverse the lower court's decision.

C. The FDA's Expertise Is Needed To Determine If A Product Is A "Similar Or Related Article" To An "Instrument, Apparatus, Implement, Machine, Contrivance, Implant, [Or] In Vitro Reagent," And Appropriately Regulated As A Device Or Drug.

The lower court observed that a "critical" difference between the definition of "devices" and "drugs" relates to chemical action and metabolism, but ignored a third difference: the definition of "drug" can apply to any "article," whereas a device can only be an "instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article." 21 U.S.C. § 321(h) (emphasis added).

Some history is needed to understand the meaning of these terms. Under the 1938 FDCA, which included a now-removed exclusion of devices from the definition of "drugs," on which the lower court's decision heavily relied, devices were defined to include "instruments, apparatus, and contrivances, including their components, parts, and accessories." 21 U.S.C. § 201(h) (1938). As explained in *United States v. Article of Drug, Bacto-Unidisk*, 394 U.S. 784 (1969), these terms were intended to refer to "electric belts, quack diagnostic scales, and therapeutic lamps, as well as bathroom weight scales, shoulder braces, air conditioning units, and crutches. . . items characterized more by their purely mechanical nature than by the fact that they are composed of complex chemical compounds or biological substances." *Id*. at 799-800. In other words, the concern being addressed was that crutches, not contrast agents, could be viewed as "drugs." The Medical Device

Amendments of 1976, Pub. L. 94-295, revised the definition to add "… implement, machine . . . implant, in vitro reagent, or other similar or related article" to the 1938 definition. 21 U.S.C. §321(m). 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 are generally understood to be mechanical or electromechanical in nature.[9] The term "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." *US v. Williams*, 553 US 285, 294 (2008); *see also Gustafson v. Alloyd Co*., 513 U.S. 561, 575.

The lower court's decision simply ignores all of this language, running contrary to the presumption "that statutory language is not superfluous." *Arlington Central School Dist. Bd. of Ed. v. Murphy*, 548 U.S. 291, 299, n.1 (2006). Is an ingestible liquid solution which adheres to the surface of the gastrointestinal tract to make it radio-opaque of the same character as a machine or the like? The FDA must

[9] *See Implement*. Merriam-Webster.com (last accessed June 1, 2020) (synonymous to "tool," i.e., "a handheld device that aids in accomplishing a task."); *Machine. Id.* ("mechanically, electrically, or electronically operated device for performing a task."); *Implant. Id.* ("something (such as a graft or device) implanted in tissue").

look at the gestalt through its lens of agency expertise and render a determination on this point.

How a product achieves its intended effect is not the only consideration in how to best regulate a product that falls in the gray area between "drug" and "device." For example, are manufacturing controls established for orally ingested pharmaceuticals pursuant to 21 C.F.R. Part 211 more appropriate than those for, e.g., pacemakers, pursuant to 21 C.F.R. Part 820 for devices? Or, with respect to safety, do evaluations of concerns fit more naturally with those performed for drug products or for a crutch? These are considerations that the FDA should be permitted to make in determining the appropriate regulation of products falling within a gray area, and are ones that Congress endorsed through its decades of acceptance of the regulatory regime the FDA has created for contrast agents.

CONCLUSION

For the reasons stated above, this Court should reverse the judgment below.

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Respectfully submitted,

/s/ James A. Boiani
James A. Boiani (D.C.#52489)
Epstein Becker & Green
1227 25th Street, N.W.
7th Floor
Washington, D.C. 20037
Phone (202) 861-1891
Fax (202) 861-3091
JBoiani@ebglaw.com

Of Counsel:

James P. Flynn
Yael Spiewak
Epstein Becker & Green, P.C.
One Gateway Center
13th Floor
Newark, New Jersey 07102-5311
(973) 642-1900

Attorneys for Amicus Curiae Giskit B.V.

CERTIFICATE OF SERVICE

I hereby certify that on June 4, 2020, I electronically filed the foregoing with the Clerk of the Court for the United States Court of Appeals for the District of Columbia Circuit by using the appellate CM/ECF system. Participants in the case who are registered CM/ECF users will be served by the appellate CM/ECF system.

/s/ James A. Boiani
James A. Boiani (D.C. #52489)

CERTIFICATE OF COMPLIANCE

This brief complies with the type-volume limit of Federal Rule of Appellate Procedure 32(a)(7)(B) and Local Rule 29 of the United States Court of Appeal for the District of Columbia Circuit because it contains 4,514 words. This brief also complies with the typeface and type-style requirements of Federal Rule of Appellate Procedure 32(a)(5)-(6) because it was prepared using Microsoft Word 2016 in 14-point Times Roman, a proportionally spaced typeface.

/s/ James A. Boiani_____
James A. Boiani (D.C. # 52489)

ADDENDUM

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21 U.S.C. § 321(g)(1), (h)
§ 321. Definitions; generally
For the purposes of this chapter—
...
(g)(1) The term "drug" means (A) articles recognized in the official United States Pharmacopœia, official Homœopathic Pharmacopœia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clause (A), (B), or (C). ...
(h) The term "device" (except when used in paragraph (n) of this section and in sections 331(i), 343(f), 352(c), and 362(c) of this title) means an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is—

(1) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(2) 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, or

(3) intended to affect the structure or any function of the body of 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. ...

21 U.S.C. § 321(h) (1938)
"The term `device' . . . means instruments, apparatus, and contrivances, including their components, parts, and accessories, intended (1) for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; or (2) to affect the structure or any function of the body of man or other animals."

21 U.S.C. § 355(y)
§ 355. New drugs
...
(y) Contrast agents intended for use with applicable medical imaging devices
(1) In general

The sponsor of a contrast agent for which an application has been approved under this section may submit a supplement to the application seeking approval for a new use
following the authorization of a premarket submission for an applicable medical imaging device for that use with the contrast agent pursuant to section 360j(p)(1) of this title.
(2) Review of supplement
In reviewing a supplement submitted under this subsection, the agency center charged with the premarket review of drugs may—

(A) consult with the center charged with the premarket review of devices; and

(B) review information and data submitted to the Secretary by the sponsor of an applicable medical imaging device pursuant to section 360e, 360(k), or 360c(f)(2) of this title so long as the sponsor of such applicable medical imaging device has provided to the sponsor of the contrast agent a right of reference.

(3) Definitions
For purposes of this subsection—

(A) the term "new use" means a use of a contrast agent that is described in the approved labeling of an applicable medical imaging device described in section 360j(p) of this title, but that is not described in the approved labeling of the contrast agent; and

(B) the terms "applicable medical imaging device" and "contrast agent" have the meanings given such terms in section 360j(p) of this title.

...

21 U.S.C. § 360j(p)
§ 360j. General provisions respecting control of devices intended for human use
...
(p) Diagnostic imaging devices intended for use with contrast agents
(1) In general
The Secretary may, subject to the succeeding provisions of this subsection, approve an application (or a supplement to such an application) submitted under section 360e of this title with respect to an applicable medical imaging device, or, in the case of an applicable medical imaging device for which a notification is submitted under section 360(k) of this title, may make a substantial equivalence determination with respect to an applicable medical imaging device, or may grant a request submitted under section 360c(f)(2) of this title for an applicable medical

imaging device, if such application, notification, or request involves the use of a contrast agent that is not—

(A) in a concentration, rate of administration, or route of administration that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence determination, or grant such request if the Secretary determines that such differences in concentration, rate of administration, or route of administration exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device;

(B) in a region, organ, or system of the body that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence determination, or grant such request if the Secretary determines that such differences in region, organ, or system of the body exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device;

(C) in a patient population that is different from those described in the approved labeling of the contrast agent, except that the Secretary may approve such application, make such substantial equivalence determination, or grant such request if the Secretary determines such differences in patient population exist but do not adversely affect the safety and effectiveness of the contrast agent when used with the device; or

(D) in an imaging modality that is different from those described in the approved labeling of the contrast agent.

(2) Premarket review

The agency center charged with premarket review of devices shall have primary jurisdiction with respect to the review of an application, notification, or request described in paragraph (1). In conducting such review, such agency center may—

(A) consult with the agency center charged with the premarket review of drugs or biological products; and

(B) review information and data provided to the Secretary by the sponsor of a contrast agent in an application submitted under section 355 of this title or section 262 of Title 42, so long as the sponsor of such contrast agent has provided to the sponsor of the applicable medical imaging device that is the subject of such review a right of reference and the application is submitted in accordance with this subsection.

(3) Applicable requirements

An application submitted under section 360e of this title, a notification submitted under section 360(k) of this title, or a request submitted under section 360c(f)(2)

of this title, as described in paragraph (1), with respect to an applicable medical imaging device shall
be subject to the requirements of such respective section. Such application, notification, or request shall only be subject to the requirements of this chapter applicable to devices.

(4) Definitions

For purposes of this subsection—

(A) the term "applicable medical imaging device" means a device intended to be used in conjunction with a contrast agent (or class of contrast agents) for an imaging use that is not described in the approved labeling of such contrast agent (or the approved labeling of any contrast agent in the same class as such contrast agent); and

(B) the term "contrast agent" means a drug that is approved under section 355 of this title or licensed under section 262 of Title 42, is intended for use in conjunction with an applicable medical imaging device, and—

(i) is a diagnostic radiopharmaceutical, as defined in section2 315.2 and 601.31 of title 21, Code of Federal Regulations (or any successor regulations); or

(ii) is a diagnostic agent that improves the visualization of structure or function within the body by increasing the relative difference in signal intensity within the target tissue, structure, or fluid.

...

21 U.S.C. § 360bbb-2

§ 360bbb-2. Classification of products

(a) Request

A person who submits an application or submission (including a petition, notification, and any other similar form of request) under this chapter for a product, may submit a request to the Secretary respecting the classification of the product as a drug, biological product, device, or a combination product subject to section 353(g) of this title or respecting the component of the Food and Drug Administration that will regulate the product. In submitting the request, the person shall recommend a classification for the product, or a component to regulate the product, as appropriate.

(b) Statement

Not later than 60 days after the receipt of the request described in subsection (a), the Secretary shall determine the classification of the product under subsection (a), or the component of the Food and Drug Administration that will regulate the product, and shall provide to the person a written statement that identifies such

classification or such component, and the reasons for such determination. The Secretary may not modify such statement except with the written consent of the person, or for public health reasons based on scientific evidence.

(c) Inaction of Secretary

If the Secretary does not provide the statement within the 60-day period described in subsection (b), the recommendation made by the person under subsection (a) shall be considered to be a final determination by the Secretary of such classification of the product, or the component of the Food and Drug Administration that will regulate the product, as applicable, and may not be modified by the Secretary except with the written consent of the person, or for public health reasons based on scientific evidence.