[PUBLISH]

IN THE UNITED STATES COURT OF APPEALS

FOR THE ELEVENTH CIRCUIT

No. 19-13276

D.C. Docket No. 0:18-cv-61047-UU

UNITED STATES OF AMERICA,

Plaintiff - Appellee,

versus

US STEM CELL CLINIC, LLC,
a Florida limited liability company,
US STEM CELL, INC.,
a Florida profit corporation,
KRISTIN C. COMELLA,
individually,

Defendants - Appellants.

Appeal from the United States District Court
for the Southern District of Florida

(June 2, 2021)

Before JORDAN, MARCUS, and GINSBURG,* Circuit Judges.

GINSBURG, Circuit Judge:

US Stem Cell Clinic, LLC, its parent company, and its chief scientific officer (collectively, the Clinic) offer a procedure in which they remove fat tissue from a patient, isolate the portion containing stem cells, and inject that portion back into the patient. This procedure purportedly treats all manner of chronic conditions, from pain to Parkinson's disease.

The United States Food and Drug Administration is skeptical of the Clinic's claims. It sued the Clinic, alleging the stem cell procedure violates the Federal Food, Drug, and Cosmetics Act (codified at 21 U.S.C. §§ 301 et seq.). The district court granted summary judgment for the FDA and enjoined the Clinic from offering its procedure until it can demonstrate to the FDA that its stem cell therapy is safe and effective. The Clinic appeals, arguing it is exempt from regulation because the procedure falls into either the "same surgical procedure" exception or the "361 HCT/P" exception to regulation under the FDCA. *See* 21 C.F.R. § 1271.15(b); *id.* § 1271.10. We disagree: The procedure does not fall within the first exception because the biological material implanted into the patient is not the same as that removed and the procedure does not fall within the second exception

* Honorable Douglas H. Ginsburg, United States Court of Appeals for the District of Columbia Circuit, sitting by designation.

because the Clinic intends the stem cells to perform functions after the procedure beyond the basic functions the stem cells performed prior to the procedure. We therefore affirm the judgment of the district court.

I. Background

Since 2001 the FDA has regulated human cells, tissues, and cellular and tissue-based products or "HCT/Ps," which the FDA defines as "articles containing or consisting of human cells or tissues that are intended for implantation, transplantation, infusion, or transfer into a human recipient," 21 C.F.R. § 1271.3(d), under both the FDCA and the Public Health Service Act (codified at 42 U.S.C. §§ 201 et seq.). *See* Human Cells, Tissues, and Cellular and Tissue-Based Products, Establishment Registration and Listing, 66 Fed. Reg. 5447, 5447-69 (Jan. 19, 2001) (codified at 21 C.F.R. § 1271) [hereinafter Final Rule]. The FDA has three goals in regulating HCT/Ps:

> 1) preventing unwitting use of contaminated tissues with the potential for transmitting infectious diseases such as AIDS and hepatitis; 2) preventing improper handling or processing that might contaminate or damage tissues; [and] 3) ensuring that clinical safety and effectiveness is demonstrated for tissues that are highly processed, are used for other than their normal function, are combined with non-tissue components, or are used for metabolic purposes.

Food & Drug Admin., *Proposed Approach to Regulation of Cellular and Tissue-based Products* 6 (Feb. 28, 1997), https://www.fda.gov/media/70704/download

[hereinafter *Proposed Approach*]. Recognizing "different HCT/Ps may present different concerns," the FDA adopted a "tiered, risk-based approach" to regulating them. Final Rule, 66 Fed. Reg. at 5450. The two provisions at issue here are aspects of this tiered approach.

The first is the "same surgical procedure" exception, which applies where an establishment "removes HCT/Ps from an individual and implants such HCT/Ps into the same individual during the same surgical procedure." 21 C.F.R. § 1271.15(b). HCT/Ps in this category are not regulated by the FDA at all – under neither the FDCA nor the PHSA – because "[t]he communicable disease risks, as well as safety and effectiveness risks, would generally be no different from those typically associated with surgery." *Proposed Approach* at 12.

The second provision is 21 C.F.R. § 1271.10, which subjects HCT/Ps meeting each of several criteria to a lighter regulatory burden. HCT/Ps meeting the specified criteria are called "361 HCT/Ps," and they are regulated under § 361 of the PHSA (codified at 42 U.S.C. § 264) only to prevent the spread of infectious disease. An HCT/P that fails to satisfy one or more criteria may be regulated as a biological product under the PHSA or as a drug or device under the FDCA. 21 C.F.R. § 1271.20. The only criterion at issue here is that the HCT/P must be "intended for homologous use only." 21 C.F.R. § 1271.10(a)(2). "Homologous

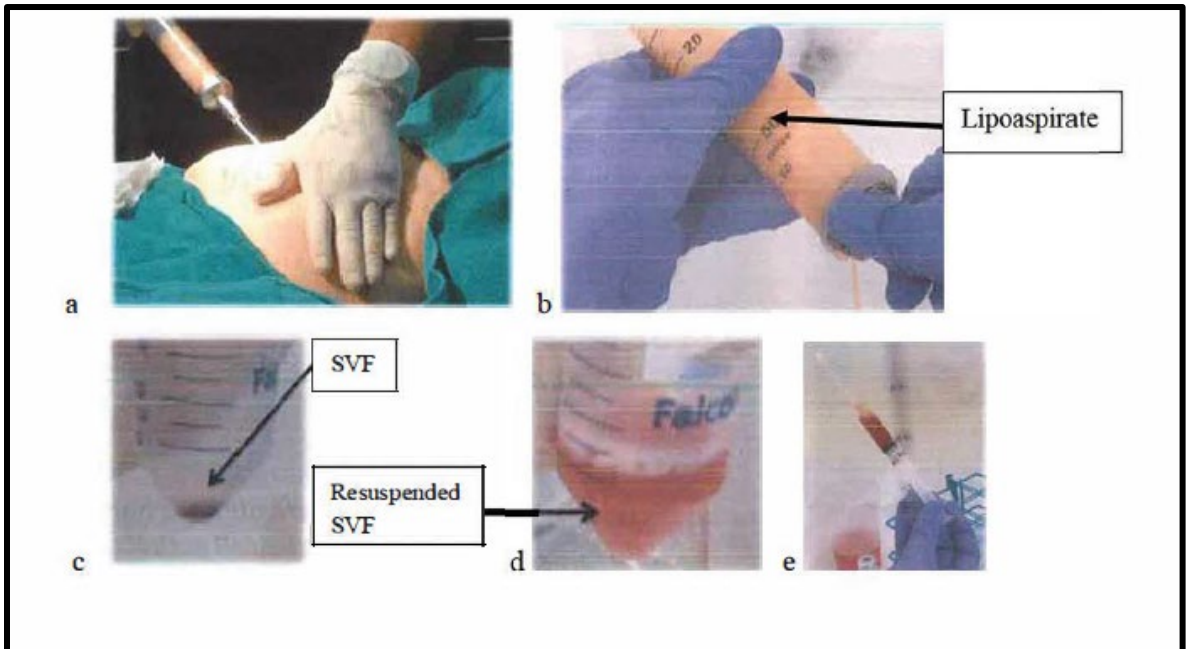
use" is "the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P that performs the same basic function or functions in the recipient as in the donor." *Id.* § 1271.3(c). Grafting skin from an arm to replace lost skin on a face would be a homologous use, for example, but "use of amniotic membrane in the eye" would not be. Final Rule, 66 Fed. Reg. at 5458; *see also* Proposed Rule on Establishment Registration and Listing for Manufacturers of Human Cellular and Tissue-Based Products, 63 Fed. Reg. 26744, 26749 (May 14, 1998). In essence, the party offering the procedure must intend that the HCT/P do the same basic job before and after it is transplanted. To divine the company's intent, the FDA looks to "the labeling, advertising, or other indications of the manufacturer's objective intent." 21 C.F.R. § 1271.10(a)(2).

* * *

The Clinic marketed its body-fat-derived stem cell therapy for the treatment of a plethora of autoimmune, neurological, and degenerative conditions, including ALS, Parkinson's disease, kidney disease, brain and spinal cord injuries, COPD, diabetes, rheumatoid arthritis, osteoarthritis, stroke, liver disease, congestive heart failure, and others.

At the first step of the therapy, the Clinic uses a syringe to remove two ounces of the patient's adipose tissue (that is, body fat). The adipose tissue is

made up primarily of fat cells and a network of collagen fibers, but it also contains various stromal and vascular cells. These stromal and vascular cells are known collectively as the "stromal-vascular fraction" of the adipose tissue; among them are the titular stem cells.



a) "mini-liposuction" procedure. 60 ml of adipose tissue are recovered from the patient. b) 60 ml syringe filled with aspirated adipose tissue (lipoaspirate). c) Isolated non-adipocytic cellular component of adipose tissue (SVF) after digestion of structural (non-cellular) components of 60 ml of lipoaspirate. d) SVF resuspended in approximately [redacted] ml of solution (USSCC SVF Product). e) Final USSCC SVF Product in [redacted] ml syringe for patient administration.

After removing adipose tissue from the patient, the Clinic uses a five-step process to isolate the stromal-vascular fraction (i.e., to turn the syringe of body fat in picture (b) into the tube of stromal and vascular cells in picture (c)). First, the adipose tissue is rinsed with a cell wash solution to remove blood cells. Second, the Clinic uses an enzyme to digest the collagen fibers. Third, the solution is

centrifuged to separate the stromal-vascular fraction from the fat cells. Fourth, the Clinic uses a cell extractor and cell strainer to strip away everything except the stromal-vascular fraction. Finally, the stromal-vascular fraction is centrifuged a second time. The isolated stromal-vascular fraction is then suspended in saline solution or in platelet-rich plasma and injected back into the patient.

The FDA inspected the Clinic in 2015 and 2017. The inspectors found fault with several of the Clinic's practices, including its failure to keep a sterile environment and to prevent contamination; test stromal-vascular fraction samples for contamination; and label the stromal-vascular fraction solution as a drug. The Clinic responded to the FDA's adverse findings by asserting it was exempt from regulation.

* * *

In 2018 the FDA sued the Clinic, alleging the stromal-vascular fraction solution is an adulterated and misbranded drug. While the lay person may not think of stem cells as a "drug," the FDCA's definition of that word is expansive; any "article[] intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease" is a drug for purposes of the statute. 21 U.S.C. § 321(g)(1)(B). In keeping with its "core objective[]" of ensuring drugs sold in the United States are safe and effective, *FDA v. Brown & Williamson Tobacco Corp.*,

529 U.S. 120, 133 (2000) (citing 21 U.S.C. § 393(b)(2)), the FDCA forbids the adulteration or misbranding of drugs, *see* 21 U.S.C. § 331(k). The FDA alleged the Clinic's solution was "adulterated" because it was not manufactured, processed, or stored in conformity with its regulation establishing "good manufacturing practice." 21 U.S.C. § 351(a)(2)(B); *see* 21 C.F.R. §§ 210-11. It further alleged the solution was "misbranded" because it did not bear a label providing "adequate directions for use." 21 U.S.C. § 352(f)(1); *see* 21 C.F.R. § 201.5. In fact, the FDA argued, the Clinic could not label the stromal-vascular fraction solution in compliance with the FDCA because "there is no scientifically valid evidence to show that it is safe or effective for *any* indication."

The Clinic did not claim to have complied with the FDA's good manufacturing practice or labeling requirements. Instead, opposing the FDA's motion for summary judgment, the Clinic argued either the same surgical procedure or the 361 HCT/P exception applied. The district court rejected those arguments and granted the FDA's motion. *United States v. US Stem Cell Clinic, LLC*, 403 F. Supp. 3d 1279, 1287-98 (S.D. Fla. 2019).

Regarding the same surgical procedure exception, the district court first held the HCT/Ps implanted into the patient must be the same HCT/Ps, in their original form, as the ones removed from the patient. *Id.* at 1288-89. The court based this

holding on the text of the regulation, which exempts only an establishment that removes HCT/Ps from a patient and reimplants "such HCT/Ps" into the same patient. *Id.* The Clinic had argued the stromal-vascular fraction was an HCT/P removed from the patient and reimplanted in its original form, so the procedure was exempt. According to the FDA, however, the HCT/P removed was adipose tissue and the stromal-vascular fraction solution was obtained only after substantial processing; therefore, the Clinic was not exempt. *See* Food & Drug Admin., *Same Surgical Procedure Exception Under 21 CFR 1271.15(b): Questions & Answers Regarding the Scope of the Exception: Guidance for Industry* (Nov. 2017), https://www.fda.gov/media/89920/download [hereinafter *Guidance Document*] (announcing the FDA's view of how this exception applies in regard to adipose stem cell therapies). The district court deferred to the FDA's interpretation of its regulation and held the same surgical procedure exception did not apply. 403 F. Supp. 3d at 1289-94.

Next, the court held the 361 HCT/P exception inapplicable because the stromal-vascular fraction solution was not intended solely for homologous use. *Id.* at 1297-98. The Clinic had protested that it "intend[ed] the [stromal-vascular fraction] to perform the same basic regenerative function before and after the procedure." *Id.* at 1298. Looking to the Clinic's marketing materials, however,

the district court found the Clinic intended that the stromal-vascular fraction treat a "litany of illnesses in the recipient," which is not the "same basic function" the stromal-vascular fraction performed before the procedure. *Id.*

The district court went on to hold the Clinic violated the FDCA based upon the FDA's undisputed contentions that the stromal-vascular fraction solution was a drug, that it was adulterated, and that it was misbranded. *Id.* at 1298-1300. In a separate order, the district court permanently enjoined the Clinic from offering its adipose stem cell therapy unless and until several conditions were met, including FDA approval of a new drug application or biologics license application for the stromal-vascular fraction solution.

II. Analysis

On appeal, the Clinic again argues it is exempt from regulation under the FDCA because either the same surgical procedure exception or 361 HCT/Ps exception applies.

A. Same surgical procedure exception

Recall the applicable regulation provides: "You are not required to comply [with the FDA's rules regarding HCT/Ps] if you are an establishment that removes HCT/Ps from an individual and implants such HCT/Ps into the same individual during the same surgical procedure." 21 C.F.R. § 1271.15(b). The Clinic's view is

straightforward: The stromal-vascular fraction is removed from the patient and then reinjected; therefore, the Clinic removes HCT/Ps from the patient and then implants "such HCT/Ps" into the same patient; therefore, the Clinic is exempt from regulation under the same surgical procedure exception. The FDA counters that, due to the substantial processing necessary to isolate the stromal-vascular fraction, the solution injected into the patient does not contain the same HCT/P as was removed, and therefore is not "such HCT/P[]" as that term is used in the regulation. That is, the HCT/P removed was adipose tissue, whereas the HCT/P implanted is the stromal-vascular fraction, so the exception does not apply.

At first glance, both readings seem plausible. There was a time when a court faced with a regulation that seemed "impenetrable on first read" might simply "wave the ambiguity flag" and defer to the agency's interpretation. *Kisor v. Wilkie*, 139 S. Ct. 2400, 2415 (2019). No longer. The Supreme Court recently clarified that judicial deference is appropriate only if a regulation is "genuinely ambiguous." *Id.* Before declaring a regulation genuinely ambiguous, we must "exhaust all the traditional tools of construction," which entails "carefully consider[ing] the text, structure, history, and purpose of [the] regulation." *Id.* (internal quotation marks omitted). We will consider the parties' textual arguments, giving the agency's view no special weight "except to the extent it has

the 'power to persuade.'" *Id.* at 2414 (quoting *Skidmore v. Swift & Co.*, 323 U.S. 134, 140 (1944) ("The weight of [an agency's interpretation] will depend upon the thoroughness evident in its consideration, the validity of its reasoning, [and] its consistency with earlier and later pronouncements")). In this case, our tools of construction resolve the apparent ambiguity in the FDA's favor, so we need not decide whether to defer to the interpretation expressed in the *Guidance Document*.

Each side argues its interpretation is textually required. The Clinic first argues the relevant HCT/P must be the stromal-vascular fraction because adipose tissue does not fall within the definition of an HCT/P. Specifically, the Clinic says cells or tissues can be HCT/Ps only if they are "intended for implantation" into a patient. Appellants' Br. 13 (quoting 21 C.F.R. § 1271.3(d)). This is not correct. HCT/Ps are "articles *containing* or *consisting of* human cells or tissues that are intended for implantation" into a patient. 21 C.F.R. § 1271.3(d) (emphasis added). The adipose tissue *contains* the stromal-vascular fraction, which *consists of* cells intended for implantation into a patient. Therefore, both adipose tissue and stromal-vascular fraction are HCT/Ps.

The Clinic next draws our attention to the opinion of a district court in California that, in a similar suit against a clinic offering a similar procedure, rejected the FDA's interpretation under the canon against surplusage – the idea that

a reading of a statute or regulation which gives each word independent meaning is generally to be preferred over a reading that makes some words superfluous. *United States v. Cal. Stem Cell Treatment Ctr., Inc.*, No. 5:18-cv-01005, 2020 WL 1289543 (C.D. Cal. Jan 27, 2020); *see also Rimini Street, Inc. v. Oracle USA, Inc.*, 139 S. Ct. 873, 881 (2019) (explaining the canon against surplusage and its limitations). That court reasoned that through its use of the word "HCT/Ps," § 1271.15(b) refers to the removal and reimplantation of both cells and tissues: "Because cells make up tissues and organs, cells can only be removed from a patient along with those larger systems." *Cal. Stem Cell*, 2020 WL 1289543 at *8; *but see id.* at *8 n.12 ("[T]he Government attorney asserted that technology to remove only cells did exist. However, no evidence was submitted on this point."). Therefore, the court concluded, the FDA's characterization would "eliminate[] the possibility of a cell removal and implantation," and thus fail to give "full effect to all words" in the regulation. *Id.* at *8.

For its part, the FDA focuses upon the word "such." The regulation exempts only establishments that remove HCT/Ps from a patient and implant "such HCT/Ps" back into the same patient. As the district court in this case correctly explained, the word "such" in legal documents is typically used to refer back to an antecedent. *See* 403 F. Supp. 3d at 1288-89. Here, this means the HCT/Ps

implanted must be the same as the antecedent HCT/Ps – that is, the HCT/Ps that were removed. If significant processing steps expose the HCT/Ps to foreign substances and alter their form prior to reimplantation, then the HCT/Ps cease to be the same as they were at the time of removal. This interpretation seems, at the outset, to be the more natural of the two readings.

The FDA's view is all the more persuasive because it is consistent with its early (as well as its recent) pronouncements, *see Skidmore*, 323 U.S. at 140, and consonant with the history and purpose of the regulation, *Kisor*, 139 S. Ct. at 2415. In 2001, when the FDA first proposed the rule that would become § 1271, it received just one comment on the same surgical procedure exception. Final Rule, 66 Fed. Reg. at 5460. Responding to that comment, the FDA noted that certain ways of processing an HCT/P could render the exception inapplicable, giving the example of cell or tissue expansion. *Id.* Specifically, the FDA was asked whether the exception covered "hospitals retaining [a patient's own] tissue ... to be used in a subsequent application on the same patient." *Id.* The FDA indicated the exception would apply in that scenario "so long as the hospital does not engage in any other activity encompassed within the definition of 'manufacture'.... For example, if the hospital expanded the cells or tissues, it would not meet the terms of the exception." *Id.* "Manufacture" encompasses "the recovery, processing, storage,

labeling, packaging, or distribution of any human cell or tissue." 21 C.F.R. § 1271.3(e). The FDA's response therefore implied that more than ordinary processing would make the exception inapplicable. Thus, from the start, the FDA treated "such HCT/Ps" as meaning HCT/Ps in their original form, not subjected to significant processing, and informed the public of this understanding. *Cf. Bostock v. Clayton Cty.*, 140 S. Ct. 1731, 1738 (2020) (instructing courts to interpret a law "in accord with the ordinary public meaning of its terms at the time of its enactment").

After establishments such as the Clinic began offering adipose-derived stem cell therapies, the FDA issued a *Guidance Document* expounding on the application of the same surgical procedure exception to these therapies. The agency was of the view that when a procedure involves "intervening processing steps beyond rinsing, cleansing, sizing, or shaping," the same surgical procedure exception usually will not apply. *Guidance Document* at 3. This is because while "limited handling, such as rinsing and cleansing ... solely to remove debris (e.g., lipids, blood, bone particles)" presents no special risks, "processing steps ... for cell isolation, cell expansion, cell activation, or enzymatic digestion" raise "safety concerns, such as contamination and cross-contamination, beyond those typically

associated with surgery."[1] *Id.* at 7. Therefore, an establishment that merely removes and reinjects adipose tissue into a patient would generally qualify for the exception, but an establishment that uses enzymatic digestion to isolate the stem cells from the tissue before reinjection would not. *Id.* at 7-8. The *Guidance Document* is well-reasoned, explaining how its conclusion follows from the FDA's original understanding of the same surgical procedure exception.

Because the plain text of the regulation suggests that "such HCT/Ps" must be in their original form (rather than subjected to extensive processing), and because this understanding is confirmed by the agency's contemporaneous statements and its later, thoroughly-considered interpretation, we hold the same surgical procedure exception unambiguously does not apply to the Clinic's procedure. The stromal-vascular fraction solution is the product of an intensive cell isolation process involving enzymatic digestion that goes much farther than simple rinsing or sizing. By the time the stromal-vascular fraction is reinjected, it is no longer "such HCT/P" as the adipose tissue removed from the patient.

[1] Recall that the rationale for the same surgical procedure exception was to carve out HCT/Ps that present "communicable disease risks, as well as safety and effectiveness risks," that are "no different from those typically associated with surgery." *Proposed Approach* at 12.

B. 361 HCT/Ps exception

The district court held that the stromal-vascular fraction solution was not a 361 HCT/P because, as a matter of law, the Clinic did not intend the stromal-vascular fraction solely for homologous use. That is, the Clinic intended the stromal-vascular fraction to perform at least some functions in its patients after the procedure that are distinct from the basic functions it performs inside the adipose tissue prior to the procedure. The Clinic claims this was error. It argues there was at least some evidence to the contrary, from which a reasonable fact-finder could arrive at the opposite conclusion, so the district court should not have granted the FDA summary judgment on this issue.

Rather than attempt to refute the Clinic's argument, the FDA urges us not to consider it. According to the FDA, to satisfy the homologous use criterion, the Clinic would need to intend for the stromal-vascular fraction to serve the basic functions of adipose tissue after the procedure (*viz.*, "cushioning and support"). It says the Clinic forfeited any argument to the contrary first by failing to raise it before the district court, and again by failing to raise it on appeal. We see no forfeiture in either court.

In the district court, the FDA raised the homologous use criterion in its motion for summary judgment. It assumed, without analysis, that the relevant

"basic function or functions" were those of adipose tissue. In its response, the Clinic disputed the FDA's assumption: "the regulation ... is silent as to which HCT/P is the appropriate comparative unit ... thus allowing for the [stromal-vascular fraction] cells to serve as the appropriate unit of comparison." The Clinic asserted that it intends the stromal-vascular fraction to "provide a regenerative function" after the procedure, just as it does before the procedure, so the homologous use criterion is satisfied. In its reply, the FDA disagreed and argued in the alternative that the Clinic intended the stromal-vascular fraction to do more than serve a vague regenerative function. This back-and-forth was sufficient for each side to preserve its position in the district court.

On appeal, the Clinic adequately restates its position that the proper benchmark is the basic function of the stromal-vascular fraction in adipose tissue (*viz.*, "regeneration and repair"). We agree. Unlike the same surgical procedure exception, the 361 HCT/P exception and definition of homologous use do not require that an establishment remove an HCT/P from a patient and reimplant "such HCT/P" into the same patient.[2] There is no reason, therefore, the court should not compare stem cells to stem cells.

[2] Throughout its briefs, the FDA attempts to graft the requirements of the 361 HCT/P exception onto the same surgical procedure exception and vice versa. This is a mistake. As the FDA has itself said, "[t]he assessment of whether the [same surgical procedure exception] applies is

Nevertheless, we agree with the district court that the Clinic did not intend the stromal-vascular fraction solely for homologous use.[3] The Clinic has consistently maintained that the stromal-vascular fraction serves a "regenerative function" inside adipose tissue. To determine the Clinic's "objective intent" for the stromal-vascular fraction's function after the procedure, we must look to the Clinic's marketing materials. 21 C.F.R. § 1271.10(a)(2).

The Clinic marketed the stromal-vascular fraction procedure for the treatment of the plethora of conditions we described earlier. The district court was plainly correct that "providing a regenerative function in the donor is [not] the same basic function as restoring cell function, contributing to anti-inflammatory processes, and otherwise treating [a] litany of illnesses in the recipient." 403 F. Supp. 3d at 1298 (citing Final Rule, 66 Fed. Reg. at 5458 (explaining "promotion of an HCT/P for an unproven therapeutic use, such as curing cancer," would be a nonhomologous use)). No reasonable fact-finder could disagree.

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independent from the determination of whether the HCT/P meets the criteria [of the 361 HCT/P exception]." *Guidance Document* at 4.

[3] The Government did not make this argument in its brief on appeal, perhaps out of unwarranted confidence in its forfeiture argument. Still, "[w]hen an issue or claim is properly before the court, the court is not limited to the particular legal theories advanced by the parties." *Kamen v. Kemper Fin. Servs.*, 500 U.S. 90, 99 (1991); *accord Walker v. Prudential Prop. & Cas. Ins. Co.*, 286 F.3d 1270, 1275 n.4 (11th Cir. 2002) ("When addressing the issues in a case, we are not precluded by counsel from applying the law to the record before us").

III. Conclusion

For these reasons, neither the same surgical procedure exception nor the 361 HCT/Ps exception applies to the Clinic's surgical practice. The Clinic did not challenge the district court's judgment upon any other ground. Accordingly, we **AFFIRM** the judgment of the district court.

JORDAN, Circuit Judge, concurring:

I concur in full in Judge Ginsburg's opinion for the court, and write separately concerning footnote 3, which explains that we can address the "homologous use" issue even though the FDA chose not to brief it on appeal.

It is generally true that an appellate court can affirm on any ground supported by the record. *See, e.g., Long v. Comm'r of IRS*, 772 F.3d 670, 674 (11th Cir. 2014). Nevertheless, we have held a number of times that an appellee abandons an alternative ground for affirmance on the merits by not raising it in its answer brief. *See, e.g., Reaves v. Sec'y, Fla. Dept. of Corrections*, 872 F.3d 1137, 1149 n.4 (11th Cir. 2017); *Hamilton v. Southland Christian School, Inc.*, 680 F.3d 1316, 1318-19 (11th Cir. 2012); *La Grasta v. First Union Sec., Inc.*, 358 F.3d 840, 847 n.4 (11th Cir. 2004); *Johnson v. Wainright*, 806 F.2d 1479, 1481 n.2 (11th Cir. 1986); *Pennington v. Spears*, 779 F.2d 1505, 1506 (11th Cir. 1986).

There are good reasons for this default rule of abandonment. First, our adversarial system operates on the premise that parties represented by competent counsel "know what is best for them, and are responsible for advancing the facts and argument[s] entitling them to relief." *United States v. Sineneng-Smith*, 140 S.Ct. 1575, 1579 (2020) (discussing and applying the party-presentation principle). Second, if we address and decide an issue not raised by the parties, we do so without

the critical assistance that focused briefing can provide, and risk depriving the losing side of the opportunity to be heard, which is the essence of due process. *See Brinkerhoff-Faris Trust & Sav. Co. v. Hill*, 281 U.S. 673, 681 (1930).

Having said this, I recognize that the abandonment rule (sometimes called the waiver rule) is prudential in nature. *See Herrera v. Wyoming*, 553 U.S. 851, 861 (2008); *Day v. McDonough*, 547 U.S. 198, 209 (2006). But the Supreme Court has recently told us that deviation from the party-presentation principle is reserved for "extraordinary" circumstances. *See Sinengeng-Smith*, 140 S.Ct. at 1579. I doubt that such circumstances exist here given that the FDA is the quintessential sophisticated litigant—a specialized government agency represented by experienced counsel. But the "homologous use" issue was briefed below, and decided by the district court, *see United States v. US Stem Cell Clinic*, 403 F.Supp. 3d 1279, 1296-98 (S.D. Fla. 2019), so it seems that there is at least a somewhat stronger claim for us reaching the issue sua sponte on appeal.

Despite my hesitation about the propriety of sua sponte consideration of merits issues, I do not dissent or concur on different grounds. That is because we have precedent that permits the sua sponte consideration of the "homologous use" issue in the circumstances before us. *See Olson v. Superior Pontiac-GMC, Inc.*, 776 F.2d 265, 266-67 (11th Cir. 1985) (on rehearing).

Later this month we are going to hear an en banc case which provides an opportunity to set out definitive guidance as to when it is appropriate for us to consider and decide a merits issue on our own. *See United States v. Campbell*, 970 F.3d 1342 (11th Cir. 2020), *vacated and rehearing en banc granted*, 981 F.3d 1014 (11th Cir. 2020). I hope we conclude that sua sponte consideration and resolution of such an issue should be the rare exception, justified only by truly extraordinary circumstances.