Before the Court is Plaintiff's Motion for summary judgment [31], Defendants' Supplemental Brief in Support of Judgment for Defendants [33], and Intervenor-Defendant's Cross-Motion for summary judgment [29]. Upon consideration of Plaintiff's Motion and Memorandum in Support thereof [32], Defendants' Supplemental Brief in Support of Judgment for Defendants, Intervenor-Defendant's Cross-Motion and Opposition [30], the arguments made in open court on April 29 and May 18, 2015, the entire record in this case, and the applicable law, the Court will DENY Plaintiff's Motion [31] for summary judgment and GRANT summary judgment for Defendants and Intervenor-Defendant [29]. The Court will explain its reasoning in the following analysis.

I. BACKGROUND

A. Statutory and Regulatory Framework

1. Orphan Drug Exclusivity, New Drug Applications, and Abbreviated New Drug Applications

Congress passed the Orphan Drug Act ("ODA") to encourage the development of "orphan drugs," drugs that treat diseases or disorders affecting only a small number of people. Pub. L. No. 97-414, 96 Stat. 2049 (1983). When a company develops a drug that the FDA has designated an "orphan drug," the Act gives that developer seven years of market exclusivity, during which time the FDA may not approve any other entity's application "for such drug for such disease or condition," barring certain exceptional circumstances not applicable here. 21 U.S.C. § 360cc(a).

Under the FDCA, pharmaceutical companies seeking to market "pioneer" or "innovator" drugs must first obtain FDA approval to do so by filing a new drug application ("NDA"). 21 U.S.C. § 355(a)–(b). The NDA must contain extensive scientific data and other information, including investigative reports demonstrating the drug's safety and effectiveness, a statement of

the drug's components, and specimens of proposed labeling for the packaging of the drug. 21 U.S.C. § 355(b)(1).

The Drug Price Competition and Patent Term Restoration Act of 1984 ("Hatch-Waxman Amendments"), codified at 21 U.S.C. § 355 and 35 U.S.C. §§ 156, 271, and 282, lets generic versions of already-NDA-approved drug products bypass the lengthy NDA process and proceed instead via abbreviated new drug applications ("ANDAs"). 21 U.S.C. § 355(j). The Hatch-Waxman Amendments were intended to balance encouraging innovation in drug development with accelerating the availability of lower-cost generic alternatives to innovator drugs. *See* H.R. Rep. No. 98-857 (Part I), 98th Cong., 2d Sess. at 14–15 (1984), *reprinted in* 1984 U.S.C.C.A.N. 2547–48; *see also Tri-Bio Labs., Inc. v. United States*, 836 F.2d 135, 139 (3d Cir. 1987). Though an entity submitting an ANDA must still obtain FDA approval, the ANDA need not include clinical evidence establishing the safety and effectiveness of its proposed generic drug. Instead, the ANDA may point to the already-approved innovator drug that their generic drug mimics, known as the reference listed drug ("RLD"), and rely instead on the FDA's previous finding that the RLD is safe and effective. *See* 21 U.S.C. 355 § (j)(2).

To use this shortcut, the ANDA applicant must show that its proposed drug is the "same as" the RLD in all key respects (including active ingredient, dosage form, strength, route of administration, and, with certain exceptions, labeling), and is bioequivalent to the RLD. 21 U.S.C. § 355(j)(2)(A)(ii)–(v). The statute also requires that an ANDA contain "information to show that the conditions of use prescribed, recommended, or suggested in the labeling proposed for the new drug have been previously approved for a [listed drug]." 21 U.S.C. § 355(j)(2)(A)(i). The FDA must approve an ANDA unless it finds, among other things, that the ANDA has not provided sufficient evidence of the foregoing. 21 U.S.C. § 355(j)(4).

FDA regulations allow for a labeling "carve-out," whereby a generic drug's labeling may differ from the RLD's to omit those parts of the RLD's labeling that "are protected by patent, or by exclusivity." 21 C.F.R. § 314.127(a)(7). Such carve-outs are allowed, however, only where the omissions "do not render the proposed drug product less safe or effective than the listed drug for all remaining, non-protected conditions of use." *Id.* When a proposed labeling carve-out renders the generic product less safe than the RLD, the FDA may not approve the ANDA. *Id.* The FDA has acknowledged that this language reflects Congress's intent that the generic drug be safe and effective for each "condition of use" prescribed, recommended, or suggested in the generic drug labeling. *See* FDA Letter to Dexmedetomidine Hydrochloride Injection NDA Holder/ANDA Applicant, Docket No. FDA-2014-N-0087 (Aug. 18, 2014) at 7, *available at* http://www.regulations.gov/#!documentDetail;D=FDA-2014-N-0087-0025.

B. Factual Background

1. FUSILEV®

The name of Spectrum's innovator drug product at issue in this case is FUSILEV®. FUSILEV® contains levoleucovorin, a variant of leucovorin, a drug that has been used to treat the toxic effects of the cancer medicine methotrexate. A.R. 183–84.

a. The Methotrexate Indications

On March 7, 2008 the FDA approved FUSILEV® for injection, in the form of a freeze-dried powder single-use vial containing the equivalent of 50 mg levoleucovorin (the "small vial"), for the following medical uses ("indications"): (1) Rescue after high-dose methotrexate therapy in osteosarcoma, and (2) Diminishing the toxicity and counteracting the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists. A.R. 135–38. These indications are referred to collectively herein as the "Methotrexate Indications." Before the

drug contained in the small vial can be injected intravenously it must first be reconstituted through mixture with another chemical, and once reconstituted becomes unsafe for use after twelve hours. A.R. 65. The typical individual dose for the Methotrexate Indications is roughly 7.5 mg. A.R. 26. The Methotrexate Indications were protected by orphan exclusivity until March 7, 2015. A.R. 2, 1706.

b. The Colorectal Indication

On December 8, 2008, Spectrum submitted a supplemental NDA seeking approval of a new indication for FUSILEV®: The palliative treatment of patients with advanced metastatic colorectal cancer (the "Colorectal Indication"). A.R. 513. The use of leucovorin for the Colorectal Indication had been eligible for orphan exclusivity since 1990. A.R. 1732–34. On December 22, 2010, Spectrum submitted another supplemental NDA seeking approval of two new, larger vials of FUSILEV® in a liquid ready-to-use ("RTU") form (the "large vials") to be used with the Colorectal Indication, which requires larger doses than the previously-approved Methotrexate Indications. Verified Compl. Ex. 3. On April 20, 2011, the FDA approved the large vials proposed in the second of the two supplemental NDAs. A.R. 1181, 1186. Nine days later, on April 29, 2011, FDA approved the Colorectal Indication as a supplemental indication for FUSILEV®. AR 513–16. For the Colorectal Indication, FUSILEV®'s individual dose is either 15 mg or 150 mg.

Spectrum ultimately chose not to market the large vials. A.R. 23. Because Spectrum does not market FUSILEV® in the large vials, oncologists routinely use multiple small vials to achieve the appropriate dose for colorectal cancer patients. *Id.* The Colorectal Indication is protected by orphan exclusivity until April 29, 2018. A.R. 1706.

2. Sandoz's ANDA

On October 26, 2011, Sandoz submitted an ANDA seeking permission to market a

generic version of FUSILEV®. A.R. 1370. At that time, Sandoz sought permission to market its drug solely for the Colorectal Indication, and in the larger vials associated with that indication. A.R. 1714. After the FDA formally granted Spectrum orphan drug exclusivity for the Colorectal Indication on November 7, 2011, Sandoz amended its ANDA on December 14, 2011, to carve out the Colorectal Indication and instead seek approval for the Methotrexate Indications, A.R. 1703, 1706. Sandoz did not, however, change the proposed vial size, and continued to seek approval for the large vials even after amending its ANDA to carve out the Colorectal Indication and include the Methotrexate Indications. A.R. 1370–72. On February 9, 2012, FDA granted Sandoz's ANDA expedited review in order to address a "drug shortage." A.R. 1513, 1650, 1652. One FDA document discussing the expedited review described Sandoz's generic as "indicated for . . . colorectal cancer." A.R. 1513.

3. Spectrum's Citizen Petition and Sandoz's ANDA Approval

On September 30, 2014, Spectrum submitted a Citizen Petition asking the FDA to (1) not approve any ANDAs carving out the CRC Indication and requesting approval for the large vial sizes, and (2) not approve any proposed generic levoleucovorin products in the large vial sizes before the expiration Spectrum's orphan protection for the Colorectal Indication on April 29, 2018. A.R. 16–17. On February 24, 2015, the FDA denied Spectrum's Citizen Petition and tentatively approved Sandoz's ANDA. A.R. 1–15. On March 9, 2015, the FDA gave Sandoz final approval to distribute its generic drug in the single-use large vials for the Methotrexate Indications. A.R. 1370–72.

II. STANDARD OF REVIEW

The Court reviews the FDA's decision under the Administrative Procedure Act ("APA"). 5 U.S.C. §§ 701 *et seq.* Under the APA, a court may set aside final agency action that is "arbitrary,

capricious, an abuse of discretion, or otherwise not in accordance with law" or "unsupported by substantial evidence." 5 U.S.C. § 706(2)(A), (2)(E). When a litigant moves for summary judgment under Rule 56(c) in a challenge to final agency action brought under the APA, "the standard set forth in Rule 56(c) does not apply because of the limited role of a court in reviewing the administrative record." *ViroPharma, Inc. v. Hamburg*, 916 F. Supp. 2d 76, 79 (D.D.C. 2013) (citing *Sierra Club v. Mainella*, 459 F. Supp. 2d 76, 89 (D.D.C. 2006)). Instead, the district court must "review the administrative record to determine whether the agency's decision was arbitrary and capricious, and whether its findings were based on substantial evidence." *See Forsyth Mem'l Hosp., Inc. v. Sebelius*, 639 F.3d 534, 537 (D.C. Cir. 2011) (citing *Troy Corp. v. Browner,* 120 F.3d 277, 281 (D.C. Cir. 1997)).

A court reviews "an agency's construction of the statute which it administers" under the two-step process of *Chevron, U.S.A., Inc. v. Natural Resources Defense Council, Inc.*, 467 U.S. 837, 842 (1984). Under *Chevron,* the court must determine first "whether Congress has directly spoken to the precise question at issue." *Id.* If Congress's intent is clear, "that is the end of the matter; for the court, as well as the agency, must give effect to the unambiguously expressed intent of Congress." *Chevron*, 467 U.S. at 842–43. "[I]f the statute is silent or ambiguous" on that question, the court must defer to the agency's interpretation so long as it is "based on a permissible construction of the statute." *Alabama Educ. Ass'n v. Chao*, 455 F.3d 386, 392 (D.C. Cir. 2006) (quoting *Chevron,* 467 U.S. at 843).

An agency's interpretation of its own regulations, on the other hand, has "controlling weight unless it is plainly erroneous or inconsistent with the regulation." *Thomas Jefferson Univ. v. Shalala,* 512 U.S. 504, 512 (1994) (internal quotations omitted). Therefore, the court "must defer to [that] . . . interpretation unless an 'alternative reading is compelled by the regulation's plain

language or by other indications of the Secretary's intent at the time of the regulation's promulgation.'" *Id.* (quoting *Gardebring v. Jenkins*, 485 U.S. 415, 430 (1988)).

III. ANALYSIS

A. Spectrum's Arguments

Spectrum argues that it is entitled to summary judgment vacating the FDA's approval of Sandoz's generic drug for four reasons: (1) the FDA's approval of Sandoz's generic drug violated the ODA; (2) the FDA's expedited review of Sandoz's generic drug on the grounds of drug shortage violated the FDCA provisions governing drug shortages and the FDA's own regulations regarding the same; (3) the FDA's approval of Sandoz's generic drug in the large vials for the Methotrexate Indications was an arbitrary and capricious reversal of an earlier FDA position on the permissible uses of the large vials; and (4) the FDA's approval of a labeling carve-out of the Colorectal Indication for Sandoz's generic drug violated FDA regulations governing labeling carve-outs by making the generic drug less safe for its remaining on-label uses.

Three of Spectrum's four arguments rely on the conclusion that Sandoz's generic drug was, as approved by the FDA, appropriate only for the orphan-protected Colorectal Indication. The Court finds that conclusion, and all four of Spectrum's arguments, unpersuasive.

1. Orphan Exclusivity

The ODA states that during an approved applicant's exclusivity period for an orphan-designated drug and indication, the FDA may not approve any other entity's application "for such drug for such disease or condition." 21 U.S.C. § 360cc(a). Spectrum argues that the FDA violated the ODA's exclusivity provisions by approving Sandoz's generic drug for the Methotrexate Indications even though (1) the FDA knew and intended that the generic drug would be bought and used by healthcare providers for the carved-out and orphan-protected Colorectal Indication,

and (2) the generic drug was approved in a form that was only "appropriate" for the orphan-protected indication. The FDA responds that its approval of Sandoz's generic drug did not violate Spectrum's orphan exclusivity for the Colorectal Indication because (1) Sandoz's approved label carved out the Colorectal indication, and (2) Sandoz's generic drug was, as approved and labeled, safe and effective for the Methotrexate indication.

The Court agrees with the Fourth Circuit's conclusion that the plain language of the ODA's exclusivity provisions is unambiguous: Section 360cc(a), which provides simply that the FDA "may not approve" generics for a protected indication, "is clearly directed at FDA approved-use, not generic competitor intended-use." *Sigma-Tau Pharms., Inc. v. Schwetz*, 288 F.3d 141, 145 (4th Cir. 2002). Congress's use of the words "such drug for such disease or condition" makes plain that § 360cc(a) was to meant to be disease-specific, not drug-specific, and "in view of this textual emphasis on approved-use, the evidentiary basis for the agency's approvals must be the use for which the approvals are sought—that is, *the use for which the generics are labeled*." *Id.* (emphasis added).

Here, as in *Sigma-Tau*, the FDA properly granted labeling approval for the non-orphan-protected indication of a drug that also has a carved-out and orphan-protected off-label use. *See Bristol-Myers Squibb Co. v. Shalala*, 91 F.3d 1493, 1500 (D.C. Cir. 1996) ("[T]he statute expresses the legislature's concern that the new generic be safe and effective for each indication that will appear on its label; whether the label for the new generic lists every indication approved for use of the pioneer [drug] is a matter of indifference"); Mem. Op. at 13, *Otsuka Pharm. Co., Ltd. v. Burwell*, No. 15-cv-0852 (D. Md. Apr. 29, 2015) (stating, in denying a request for Preliminary Injunction to reverse ANDA approval, that the FDA "has broad authority to approve ANDAs carving out exclusivities under the FDCA, including orphan drug exclusivity"). That the FDA

may have known or even intended that Sandoz's generic would be commonly used by healthcare providers for the carved-out, orphan-protected, and off-label Colorectal Indication does not rise to the level of violating Spectrum's exclusivity right: Spectrum's right extends as far as preventing the FDA from approving any other entity's application to market levoleucovorin for the Colorectal Indication, but no further.

Spectrum attempts to distinguish *Sigma-Tau* by arguing that one of the Fourth Circuit's concerns in that case—that requiring the FDA to examine a generic manufacturer's "intended use" of a drug with a carved-out orphan-protected indication would ultimately lead to a difficult and overly anticompetitive "foreseeable-use" test that would hamper the development of generic drugs—is not relevant here where, Spectrum claims, it is not merely possible but in fact certain that Sandoz's generic will be used for the Colorectal Indication and that the FDA intended for it to be so.

An intended- or foreseeable-use test is not the appropriate test. Even setting that aside, the fact that such a test might be easily satisfied here is cold comfort. Such tests must be used consistently, not just when expedient, and there are endless possible fact patterns from which a court would have to glean knowledge, intent, or even the relative strength of multiple simultaneously-held intents. But more importantly, inconvenience was not the *Sigma-Tau* court's only objection to an intended- or foreseeable-use test, as such a regulatory regime would also "be one in which relatively few generics are approved," resulting "in extensions of exclusivity periods that Congress never intended" and "frustrat[ing] the longstanding practice of Congress, the FDA, and the courts not to interfere with physicians' judgments and their prescription of drugs for off-label uses." *Sigma-Tau Pharm., Inc.*, 288 F.3d at 147 (citing *Bristol–Myers Squibb Co.*, 91 F.3d at 1496, and *Rhone–Poulenc Rorer Pharm., Inc. v. Marion Merrell Dow, Inc.*, 93 F.3d 511, 514

n.3 (8th Cir. 1996)). Much like the *Sigma-Tau* plaintiffs, Spectrum unabashedly discounts the fact that the FDA "must balance the ODA's incentive structure for the development of orphan drugs against . . . the Hatch–Waxman Amendments" and instead "puts all weight on the orphan drug development end of the scale, as if no tension exists between the two statutes that the FDA must negotiate." *Sigma-Tau Pharm., Inc.*, 288 F.3d at 148.

2. FDA Regulations Governing Drug Shortages

Spectrum also argues that the FDA violated the FDCA and its own regulations governing drug shortages when, in February 2012, it expedited Sandoz's ANDA for generic levoleucovorin—a decision that Spectrum argues was intended to undermine Spectrum's orphan exclusivity over the Colorectal indication—without having given Spectrum notice and an opportunity to be heard concerning the shortage of that orphan-protected indication. The FDA responded at a hearing that it expedited Sandoz's ANDA not due to a shortage of any particular indication of the drug, but out of fear that the drug itself, for whatever indication, could become scarce. Hearing Tr. 27:1–9, May 18, 2015. Sandoz likewise argued at that hearing that the shortage was not for any particular indication levoleucovorin, but for levoleucovorin in general, or perhaps for the Methotrexate indications as well, and also argued that the law and regulations Spectrum had cited dealt with decisions to abrogate an entity's exclusivity rights, which Sandoz maintained was not relevant because Spectrum's exclusivity rights had not been breached by any of the FDA's conduct. Hearing Tr. 29:10–30:18, May 18, 2015.

21 U.S.C. § 360cc(b)(1) provides that the HHS Secretary may approve an application for a drug/indication pair protected by orphan exclusivity if she

> finds, after providing the holder notice and opportunity for the submission of views, that in [the exclusivity] period the holder of the approved application or of the license cannot assure the availability of sufficient quantities of the drug to meet the needs of

> persons with the disease or condition for which the drug was designated.

As stated previously, none of the FDA's conduct in this case rises to the level of violating Spectrum's orphan exclusivity over the Colorectal Indication. Given that § 360cc(b)(1) governs only what the FDA must do in order to properly breach orphan exclusivity, that portion of the statute does not apply here.

21 C.F.R. § 316.36, titled "Insufficient quantities of orphan drugs," provides that "whenever the Director has reason to believe that the holder of exclusive approval cannot assure the availability of sufficient quantities of an orphan drug to meet the needs of patients with the disease or condition for which the drug was designated, the Director will so notify" that holder of the possible insufficiency, and will give the holder a chance to either (1) present evidence that the holder can provide enough of the orphan drug to meet the needs of patients requiring the orphan indication, or (2) give the Director consent to approve other applications for the protected drug and indication.

The plain text of the regulation states that the FDA's possession of "reason to believe" that Spectrum could not "assure the availability of sufficient quantities of an orphan drug" was sufficient to oblige the FDA to give Spectrum notice and an opportunity to be heard. The regulation's language is unambiguous, and an agency's interpretation of unambiguous regulatory language merits no *Auer* deference. *Drake v. FAA*, 291 F.3d 59, 68 (D.C. Cir. 2002) (citing *Christensen v. Harris County*, 529 U.S. 576, 588 (2000). Despite Sandoz and the FDA's arguments to the contrary, it does not matter whether the FDA's decision to expedite Sandoz's ANDA related to the Methotrexate Indications, the Colorectal Indication, or the drug generally, because each of these explanations (the only explanations the parties have offered) would have triggered the FDA's duties under § 316.36(a). The Court reaches this conclusion for two reasons.

First, §316.36(a) does not discuss decisions to expedite ANDAs, but rather requires the FDA to give the holder of an orphan-drug approval notice and the opportunity to be heard once the FDA has reason to expect a shortage of that orphan-protected drug. The relevant inquiry is thus not why the FDA expedited Sandoz's ANDA, but whether the FDA had "reason to believe" Spectrum could not supply sufficient quantities of the orphan drugs it manufactured. Second, when the FDA decided to expedite Sandoz's ANDA in February 2012, both the Methotrexate and Colorectal indications were still orphan-protected, and the defendants have identified no non-orphan-protected uses for the drug. A.R. 1513, 1650, 1652, 1706. Consequently, even if the FDA expedited Sandoz's ANDA not to bolster supplies of the drug for the Colorectal Indication but rather (as it claims) to ensure sufficient quantities of "the drug itself," the FDA had "reason to believe" Spectrum would be unable to "assure the availability of sufficient quantities of an orphan drug," as every FDA-approved use of "the drug itself" was orphan-protected. 21 C.F.R. § 316.36(a). Neither the FDA nor Sandoz have offered arguments to the contrary. The Court therefore concludes that the FDA violated 21 C.F.R. § 316.36 by failing to provide Spectrum with the required notice and opportunity for a hearing

Spectrum has failed, however, to identify any prejudice it suffered from the FDA's violation. The Court's review of the record in the case has revealed none: Spectrum voiced its objections to the FDA's approval of Sandoz's generic in its September 30, 2014 Citizen Petition, A.R. 16–17, and has offered no reason to believe that the arguments raised in its Petition would have been any different, or more persuasive, if made more than two years earlier in the FDA's approval process. Thus, notwithstanding (1) the FDA's February 2012 decision to expedite Sandoz's ANDA and (2) the FDA's failure to give Spectrum notice and an opportunity to be heard with respect to the FDA's then-anticipated levoleucovorin shortage, Spectrum ultimately did have

an unimpaired opportunity to comment on Sandoz's ANDA. Spectrum's request that the Court vacate the FDA's February, 2012 failure to comply with 21 C.F.R. § 316.36 would in practice mean ordering the FDA to reconsider arguments it has already rightly rejected—a pointless exercise. Without reason to believe that the FDA's failure to give Spectrum notice and an opportunity to be heard affected the FDA's approval of Sandoz's generic drug, the Court has no basis to undo that decision.

3. The FDA's Approval of Sandoz's Use of the Large Vials for the Methotrexate Indications

Spectrum asserts that the FDA's approval of Sandoz's ANDA for use in large vials with the Methotrexate indication reversed, without adequate explanation, an earlier FDA position that the large vials were appropriate for only the Colorectal Indication. The Court agrees with the FDA that the FDA never took such a position.

Spectrum makes much of the fact that several documents in the administrative record establish that the FDA has repeatedly discussed the large vials and the Colorectal indication in the same breath. *See* A.R. 1199 (describing the large vials as "support[ing] the new colorectal cancer indication" and the small vial as "support[ing] the high dose methotrexate indication), 1270 (stating that the large vials "support . . . treatment of colorectal cancer"); Verified Compl. Ex. 3 (stating that "[t]he approved [Methotrexate Indications do] not require single use vials larger than 50 mg"). These examples amply prove that the FDA believed the large vials were appropriate for the Colorectal Indication, but say nothing about whether the FDA believed the large vials were not safely usable for anything else. And as the FDA points out, on April 20, 2011, it approved Spectrum's supplement to the FUSILEV® NDA requesting approval of the RTU dosage form in the large vials—the approved labeling included in that letter listed the Methotrexate Indications—

and did not approve the Colorectal Indication as a supplemental indication for FUSILEV® until nine days later. A.R. 1181, 1186, 1732–34.

Though Spectrum protests that it actually applied for the Colorectal Indication first and the large vials second, the FDA nonetheless clearly expressed the view that the large vials could safely and effectively be used in conjunction with the Methotrexate Indication. That Spectrum may have ordered its submissions to avoid this result does not change the fact that it happened, and Spectrum has pointed to no authority stating that it was entitled to have its supplemental NDA applications disposed of in the order in which it submitted them. Furthermore, even if the FDA had responded in Spectrum's desired order, it still reasonably could (and apparently would) have approved the large vials as appropriate for the Methotrexate Indications.

4. The FDA's Regulations Governing Labeling Carve-Outs

Finally, Spectrum argues that the FDA's approval of Sandoz's ANDA violates FDA regulations prohibiting labeling carve-outs for an ANDA that make the proposed generic drug less safe or effective than its RLD. 21 C.F.R. § 314.127(a)(7). Spectrum argues that Sandoz's generic has two heightened risks: 1) vial contamination and (2) potential overdosing. The large vials, being 175 mg/17.5 ml and 250 mg/25 ml, will contain significant amounts of leftover drug product after a single Methotrexate dose (typically 7.5mg) is withdrawn. Though Spectrum does not dispute that the FDA's approved labeling for Sandoz's generic drug includes instructions to medical providers that the large vials are single-use only, it nevertheless insists that the temptation to economize will spur providers to double-dip. Spectrum also argues that providers could mistake Sandoz's generic drug (stored in liquid RTU form) for levoleucovorin's predecessor leucovorin (also stored in liquid RTU form) because providers treating patients who require the Methotrexate Indication will, being familiar with FUSILEV®, not expect levoleucovorin to come in anything other than the freeze-dried powder form.

To support its premise that the FDA's approval of Sandoz's generic was not only wrong but also an inadequately-explained reversal of an earlier position, Spectrum points to a draft FDA guidance document that warns generally against approving drugs where the appropriate dosage for the drug is far below the size of the injectable vial in which the drug is stored, for the reasons stated above. *See, e.g.*, Verified Compl. Ex. 13 at 4 ("Single-dose vials should not contain a significant volume beyond what would be considered a usual or maximum dose for the expected use of the drug product."). And the draft guidance admittedly recognizes that these risks exist "even when appropriately labeled." *Id.* at 3. But as the FDA points out, this draft guidance concerned drug products generally, and does not analyze the specific risks affiliated with FUSILEV®. The draft guidance was also likewise, if not to the same degree, at odds with the FDA's approval of Spectrum's use of the small vials (containing 50 mg) to administer doses of 7.5 mg. To the extent that the FDA's approval of Sandoz's generic drug was inconsistent with its draft guidance on excess capacity of injectable vials, it was on the basis of the FDA's careful analysis of the specific risks affiliated with the drug under consideration and the extreme rarity of levoleucovorin overdose. *See* A.R. 9–13.

The Court also notes that the FDA's draft guidance, in discussing the risk of single-dose vials containing significantly more drug than required for a single dose, no less strongly warns that "[s]imilarly, the need to combine several single-dose vials for a single patient dose may lead to medication errors and microbial contamination." Verified Compl. Ex. 13 at 3. The fact that Spectrum markets FUSILEV® exclusively in small vials—which, as Spectrum stated in their Citizen Petition, compels oncologists to routinely "use multiple 50 mg vial to achieve the appropriate dose" for patients requiring the Colorectal Indication, A.R. 23, in direct contravention of the draft guidance they now belatedly embrace—supports the Court's conclusion that FDA had

sufficient reasonable basis to disregard that draft guidance with respect to Spectrum's and Sandoz's levoleucovorin products alike.

Spectrum appears to believe that the FDA was obliged to explain not only why it approved Sandoz's ANDA for the Methotrexate Indications in the large vials, but also why it chose not to approve that ANDA for the small vials instead. This view fundamentally misunderstands an agency's obligation to engage in reasoned decisionmaking: Though an agency must have reasons for the options it chooses, it need not pause to justify every option it does not choose. Any other approach would doom agencies to an endless and fruitless cycle of introspection. The FDA's obligation in reviewing Sandoz's ANDA was not to prove why the drug was better suited to one vial or another, but to determine whether Sandoz's generic drug was safe and effective as proposed. *See* 21 U.S.C. § 355(b)(1)(A).

CONCLUSION

For the foregoing reasons, Plaintiff's Motion for summary judgment will be DENIED, and Intervenor-Defendant's Cross-Motion for summary judgment and Defendants' Memorandum in Support of Judgment for Defendants will be GRANTED, in a separate order issued this date.

Signed by Royce C. Lamberth, Judge, on May 27, 2015.