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New Developments
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Cook v. FDA and the importation and release of lethal injection drugs

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In Cook v. FDA,[1] the US Court of Appeals for the District of Columbia Circuit unanimously affirmed a March 2012 decision by the DC District Court permanently enjoining the Food and Drug Administration (FDA) from permitting the entry of foreign manufactured sodium thiopental (thiopental) into interstate commerce. The decision is a serious setback for the FDA's use of its enforcement discretion. *Cook* may also limit the FDA's ability to import unapproved drugs to alleviate shortages, and could affect lethal injection litigation in dozens of states.

ANALYSIS OF *COOK*

Cook is the result of a lawsuit brought in the US District Court for the District of Columbia by a group of death row inmates in three states against the FDA, the Department of Health and Human Services, and the officials in charge of each agency for allowing state correctional departments to import thiopental—a misbranded, adulterated, and unapproved new drug used in lethal injection protocols—in violation of the Food, Drug, and Cosmetic Act (FDC Act) and the Administrative Procedure Act (APA).[2]

Thiopental had been manufactured in the USA until 2009, at which time Hospira Inc., the sole US manufacturer, stopped production due to difficulties procuring its active ingredient. Hospira intended to resume production of the drug in Italy, but Italian authorities threatened legal action if Hospira could not prevent the drug from being used in executions. Due to this threat, in January 2011, Hospira stopped all manufacturing of thiopental.[3] As a result, states using it for lethal injections began importing it

1 Cook v. Food and Drug Administration, 733 F.3d 1 (D.C. Cir. 2013).
2 Beaty v. Food and Drug Administration, 853 F. Supp. 2d 30 (D.D.C. 2012) (The case was restyled Cook v. FDA following execution of the named plaintiff).
3 *See* Deborah W. Denno, *Lethal Injection Chaos Post-Baze*, 102 Geo. L.J. 35 (2014).

from Europe,[4] and the FDA exercised its enforcement discretion to allow such importation without the product proceeding through the usual approval process.[5]

In *Cook*, Plaintiffs alleged that the FDA actions violated § 706(2)(A) of the APA[6] by improperly allowing shipments of a misbranded and unapproved new drug to enter the USA contrary to the FDC Act, thereby 'departing from longstanding the FDA policies and undermining the purpose of the FDCA.'[7] Imported thiopental was misbranded, Plaintiffs alleged, because it failed to include adequate warnings and certain required information on the label, and because it was manufactured in a facility not registered with the FDA.[8] Moreover, Plaintiffs alleged that imported thiopental was adulterated because it was not manufactured in accordance with the FDA's Good Manufacturing Practices (GMP) regulations and did not conform to the standard formulation established in the US Pharmacopeia.[9]

Central to *Cook* was the meaning of language in FDC Act § 801(a)[10] concerning imported drugs. That statute states, in relevant part, that if it appears 'from the examination of such samples or otherwise' that a drug violates the FDC Act's misbranding or new drug approval requirements, 'then such article *shall* be refused admission' (emphasis added).[11] Although the FDA contended that FDC Act § 801(a) does not impose a *mandatory* duty to refuse admission of a drug, the District Court declared that the statute was clear: 'Congress' intent was for 'shall' to impose a mandatory obligation…to refuse to admit the misbranded and unapproved drug…into the United States.'[12] The District Court also ruled that the FDA's determination not to pursue enforcement action was arbitrary and capricious under the APA.[13] As a result, the Court permanently enjoined the FDA from permitting the entry of foreign manufactured thiopental that is misbranded or in violation of FDC Act § 505.[14]

The FDA had long taken the position that it may exercise enforcement discretion and defer to law enforcement on matters involving pharmaceuticals for lethal injection. In 1985, the US Supreme Court held in Heckler v. Chaney that the FDA has discretion not to investigate or commence proceedings for certain violations of FDC Act § 331, the provision that prohibits the introduction of an adulterated or misbranded drug into interstate commerce.[15] However, the District Court distinguished *Heckler* from *Cook* on the grounds that the former did not address the FDA's obligations under FDC Act § 801, which mandates the FDA to refuse the admission of a drug into the USA that appears to be adulterated or misbranded.[16] The District Court also agreed with Plaintiffs that *Heckler* had addressed the unapproved use of approved drugs, whereas *Cook* concerned the importation of foreign unapproved, adulterated, and misbranded

4 Beaty, *supra* note 2, at 34.
5 *Id.*
6 5 U.S.C. § 706(2)(A).
7 *See* Beaty, *supra* note 2, at 43; *See also*, Baze v. Rees, 553 U.S. 35 (2008) (describing lethal injection protocols).
8 *Id.*
9 *Id.*
10 21 U.S.C. § 381.
11 *Id.*
12 Beaty, *supra* note 2, at 39.
13 *Id.* at 41.
14 *Id.* at 43.
15 *See* Heckler v. Chaney, 470 U.S. 821 (1985).
16 *See* 21 U.S.C. § 381.

drugs.[17] Finally, the Court held that the FDA does not have discretion to allow unapproved new drugs to be shipped or sold in the USA and that the FDA cannot permit marketing of an unapproved new drug.[18] The District Court concluded its opinion stating:

> FDA appears to be simply wrapping itself in the flag of law enforcement discretion to justify its authority and masquerade an otherwise seemingly callous indifference to the health consequences of those imminently facing the executioner's needle. How utterly disappointing![19]

The FDA appealed, emphasizing in its brief, that *Heckler* should be controlling in the case, because under *Heckler* the FDA's decision not to take enforcement action is not subject to judicial review, as 'agency refusals to institute investigative or enforcement proceedings are committed to agency discretion.'[20] The DC Circuit disagreed and affirmed the District Court's ruling, stating:

> The FDCA imposes mandatory duties upon the agency charged with its enforcement. The FDA acted in derogation of those duties by permitting the importation of thiopental, a concededly misbranded and unapproved new drug, and by declaring that it would not in the future sample and examine foreign shipments of the drug despite knowing they may have been prepared in an unregistered establishment.[21]

The mandatory duties, according to the Court, are found in the text of FDC Act § 801(a) concerning imports. Like the Court below, the Circuit Court held the statute was 'unambiguously binding' on the FDA:

> In sum, we hold 21 U.S.C. § 381(a) requires the FDA to (1) sample 'any drugs' that have been 'manufactured, prepared, propagated, compounded, or processed' in an unregistered establishment and (2) examine the samples and determine whether any 'appears' to violate the prohibitions listed in § 381(a)(1)–(4). If, 'from the examination of such samples or otherwise,' the FDA finds an apparent violation of the Act, then it must (3) 'refuse[] admission' to the prohibited drug. Because these are clear statutory guidelines for the agency to follow in exercising its enforcement powers, the FDA's compliance with § 381(a) is subject to judicial review under the standards of the APA.[22]

Therefore, the FDA's policy of admitting foreign manufactured thiopental for use in lethal injection protocols was 'not in accordance with law.'[23] The FDA's individual admissions of thiopental shipments were not in accordance with law because § 381(a) requires the FDA to refuse admission to any drug that appears to violate the substantive

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17 Beaty, *supra* note 2, at 40.

18 *Id.*

19 *Id.* at 43.

20 Cook, *supra* note 1, at 5 ('The FDA's principal contention on appeal is that its "determination whether to invoke [§ 381(a)] and refuse admission to any particular drug offered for import is … not subject to judicial review."').

21 *Id.* at 12.

22 *Id.* at 7 ('The plaintiffs argue each of these directives is unambiguously binding…We agree.').

23 *Id.* at 11.

prohibitions of the FDCA, and because the FDA conceded before the District Court that the thiopental in the shipments 'clearly 'appears' to be an unapproved new drug.'[24]

COOK'S POTENTIAL IMPACT

Cook may have a significant impact on pending lethal injection litigation. As a consequence of the decision and the events leading to it, at least fifteen states have amended their lethal injection protocols to replace thiopental with pentobarbital.[25] This switch has created serious difficulties though, as states' inclusion of the drug in their protocols has engendered a new wave of legal challenges.[26] Much of the litigation involves Eighth Amendment 'cruel and unusual punishment' challenges[27] and is based in part on the sparse data available regarding pentobarbital's effects.[28] This lack of data has spurred litigation by death row inmates and delayed execution dates.[29]

Eighth Amendment challenges are not the only issue facing states attempting to replace thiopental. As with thiopental, states that have included pentobarbital in their protocols have had great difficulty obtaining it. For example, the European manufacturer of pentobarbital now requires purchasers to buy the drug through a single wholesaler and to sign forms confirming they are not a prison and do not intend to sell the drug.[30] While it is not entirely clear how much pentobarbital is still available in the USA, it will eventually run out or expire.[31] States will then have to switch to yet different drugs, bringing additional procurement difficulties and further litigation. In fact, recent attempts by states to replace pentobarbital with the drugs propofol and phenobarbital have met with export bans by European nations[32] and stiff resistance from manufacturers.[33] Some states have now turned to local compounding pharmacies—over which the FDA has minimal authority[34]—to produce lethal injection drugs.[35] Moreover, multi-

[24] *Id.*

[25] Death Penalty Information Center, *Executions in 2012, Lethal Injection* (2013), http://www.deathpenaltyinfo.org/execution-list-2012. Denno, *supra* note 3; *Fordham Law Legal Studies Research Paper No.* 2328407, http://ssrn.com/abstract = 2328407 (accessed Feb. 16, 2014).

[26] Arthur v. Thomas, 674 F.3d 1257 (11th Cir. 2012); *See, eg,* Florida v. Valle, 132 S. Ct. 54 (2011); Blankenship v. Owens, 131 S. Ct. 3054 (2011); Jackson v. Danberg, 594 F.3d 210 (3d Cir. 2010); Pavatt v. Jones, 627 F.3d 1336 (10th Cir. 2010); Powell v. Thomas, 643 F.3d 1300 (11th Cir. 2011); DeYoung v. Owens, 646 F.3d 1319 (11th Cir. 2011).

[27] *See, eg,* Thomas, *supra* note 26, at 1259.

[28] *See* Danberg, *supra* note 26, at 213 (arguing that pentobarbital is neither FDA-approved nor used clinically for induction of anesthesia and that no research data exist about its reliability or efficacy).

[29] *See* Denno, *supra* note 25.

[30] Lundbeck, *Lundbeck Overhauls Pentobarbital Distribution Program to Restrict Misuse,* Press Release (1 July 2011), http://investor.lundbeck.com/releasedetail.cfm?ReleaseID = 605775 (accessed Feb. 16, 2014).

[31] *Id.*

[32] *See* Juliette Jowit, *UK to Ban Export of Drug Approved for Use in US Executions,* The Guardian (10 July 2012), http://www.guardian.co.uk/world/2012/jul/10/uk-ban-export-drug-us- executions (accessed Feb. 16, 2014).

[33] *See* Associated Press, *Another Manufacturer Blocks Propofol For Execution Use,* USA Today (28 September 2012), http://www.usatoday.com/story/money/business/2012/09/27/manufacturer-blocks-proprofol-execution-use/1598109/. *See also,* Jeannie Nuss, *Arkansas Turns to Different Lethal Injection Drug,* Associated Press (19 April 2013), http://news.yahoo.com/arkansas-turns-different-lethal-injection-drug-214639034.html (accessed Feb. 16, 2014).

[34] *See* Office of Congressman Edward J. Markey, Compounding Pharmacies Compounding Risk 5 (2012) (addressing current regulatory oversight and gaps in FDA authority over compounding pharmacies).

[35] *See* Death Penalty Information Center, *State by State Lethal Injection,* http://www.deathpenaltyinfo.org/state-lethal-injection (accessed 2 January 2014).

ples states have passed legislation 'enabling the identities of lethal injection suppliers to be shielded from disclosure to the public and the media, and possibly even the judiciary.'[36] This legislation itself is the focus of litigation in multiple states.[37] In sum, *Cook* may not have shut down the administration of the death penalty as activists may have hoped, but it has dramatically increased lethal injection litigation, thereby delaying the executions of dozens of inmates.

Another area where *Cook* may have a lasting effect is in the context of drug shortages. Prior to the ruling, the FDA had exercised discretion to release shipments of drugs that were technically in violation of the FDC Act in ways that did not present a threat to public health, usually with the promise that future shipments of the same products would bear appropriate corrections.[38] The FDA has used this authority at least seventeen times since 2010.[39] *Cook* may put an end to this practice, as the Court's analysis of the statute arguably ends the FDA's authority to release a shipment that bears a technical violation and requires refusal of admission. Applying the Court's reasoning in *Cook*, if the FDA finds any evidence related to an imported article that gives rise to the appearance of a violation, then the FDA must either refuse entry or require the importer to recondition and bring the article into compliance, which could create serious adverse health consequences resulting from delayed access.[40]

The Court did address the FDA's concerns that enforcement discretion is needed in this area, but rejected the FDA's arguments, holding that the FDA had sufficient alternatives, such as allowing domestically manufactured unapproved drugs to be sold to alleviate drug shortages:

> By its own account, however, the FDA has ways short of allowing importation of inadmissible drugs to counteract a drug shortage.… The FDA may exercise enforcement discretion to allow the domestic distribution of a misbranded or unapproved new drug, as the Supreme Court recognized in *Chaney*, and in some cases may invoke its express statutory authority to permit the importation of an unapproved new drug. For example, the FDA may designate an unapproved foreign manufactured drug as an investigational new drug (IND), thereby allowing its lawful importation. In any event, even if reading § 381(a) by its terms, as we do, deprives the FDA of one possible response to five percent of all drug shortages, that is hardly an absurd result.[41]

Finally, *Cook*'s greatest impact will likely be felt in litigation involving the FDA's enforcement discretion more generally, and the D.C. Circuit's check on the FDA in *Cook* may foreshadow that Court's decisions in future cases concerning the Agency's enforcement discretion. For example, K-V Pharmaceutical appealed a 2012 decision[42] from the D.C. District Court that halted the company's attempt to restore orphan drug

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[36] Denno, *supra* note 25, at 48.

[37] *Id.* at 49.

[38] For example, *See*, U.S. Food and Drug Administration. *FDA Announces Import of Injectable Nutrition Drugs* (2013), http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm354272.htm (accessed Feb. 16, 2014).

[39] *Id.*

[40] *See* 21 U.S.C. § 381.

[41] Cook, *supra* note 1, at 9 (internal citations omitted).

[42] K-V Pharm. Co. v. U.S. Food and Drug Administration, 889 F. Supp. 2d 119 (D.D.C. 2012) vacated, 12–5349, 2014 WL 68499 (D.C. Cir., 7 January 2014).

exclusivity for the drug Makena, a hydroxyprogesterone caproate injection.[43] K-V Pharmaceutical alleged that the FDA violated 21 U.S.C. § 381 by failing to take enforcement action to stop unlawful competition with Makena by pharmacies compounding hydroxyprogesterone caproate injections.[44] The District Court found K-V Pharmaceutical's claims unreviewable, because the APA 'precludes judicial review of final agency action, including refusals to act, when review is precluded by statute or 'committed to agency discretion by law,' and because *Heckler* was controlling.[45] But, in January of 2014, the D.C. Circuit issued an unpublished judgment vacating the District Court's order and remanded to the District Court for reconsideration in light of *Cook*.[46]

This is a dramatic change. The FDA has long argued that the Supreme Court's decision in *Heckler v. Cheney* gives it exceptionally broad discretion in the use of its enforcement powers. In *Heckler*, the Supreme Court held that 'an agency's decision not to prosecute or enforce, whether through civil or criminal process, is a decision generally committed to an agency's absolute discretion,' and as such, is presumed to be unreviewable under the APA.[47] The decision in *Cook* suggests a serious limitation on the broad enforcement discretion granted to the FDA when statutory language suggests that agency action is mandatory.

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43 *Id.* at 123.

44 *Id.* at 128. K-V Pharmaceutical, like Plaintiffs in *Cook*, argued that the word 'shall' in 21 U.S.C. § 381(a) precludes FDA discretion. *Id.* at 143.

45 *Id.* at 132.

46 K-V Pharm. Co. v. U.S. Food and Drug Administration, *supra* note 42.

47 Heckler, *supra* note 15, at 831.