



The Johns Hopkins Clinic for Public Health Law and Policy

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State Departments of Corrections Are Violating FDA's Investigational New Drug Regulations By Experimenting With Lethal Injection Drugs

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I. Introduction

Recently the Departments of Correction (DoCs) in those States that use lethal injection to carry out capital punishment have exhausted their supplies of one or more of the three drug combination that the U.S. Supreme Court affirmed under an Eighth Amendment analysis in *Baze v. Rees*.¹ The drug shortage has forced the DoCs to deviate from the lethal injection protocol approved in *Baze*. This situation has led the DoCs to experiment on humans with various drugs, at various doses, in an attempt to carry out executions by lethal injection in compliance with the Eight Amendment.²

In January 2014, the federal district court in *In re Ohio Execution Protocol Litigation (McGuire)* was required to resolve a classic ‘Battle-of-the-Experts’ over the possible effects of the Ohio DoC’s experimental protocol. The court in *McGuire* held that:

There is *absolutely no question* that Ohio's current [lethal injection] protocol presents an *experiment* in lethal injection processes. The science involved, the *new mix of drugs* employed at doses based on theory but understandably lacking actual application in studies, and the unpredictable nature of human response make today’s inquiry at best a contest of probabilities.³

These DoCs’ experiments constitute ‘clinical investigations’ that are regulated by the U.S. Food and Drug Administration (FDA). In 1962, as a result of the thalidomide

¹ 553 U.S. 35 (2008).

² See Seema Shah, *How Lethal Injection Reform Constitutes Impermissible Research on Prisoners*, 45 Am. Crim. L. Rev. 1 (2008); Koniaris LG, Goodman KW, Sugarman J, Ozomaro U, Sheldon J, Zimmers TA. Ethical Implications of Modifying Lethal Injection Protocols. PLoS Med 2008;5(6):e126 (arguing that systematic modifications of lethal injection protocols require clarity in the applicable ethical framework).

³ 2014 WL 130609 at *6 (S.D. Ohio Jan. 13, 2014) (emphasis added).

birth defect tragedy,⁴ Congress granted FDA comprehensive authority over the investigational use of drugs. FDA regulations adopted pursuant to this statutory authority require the submission to FDA of an ‘Investigational New Drug’ application (IND) when such a clinical investigation is undertaken.

In its IND regulations, FDA has defined ‘clinical investigation’ to mean “any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects,” and it further defines ‘experiment’ in this context to mean “any use of a drug except for the use of a marketed drug in the course of medical practice.”⁵ This regulatory definition fits perfectly the experiments some DoCs have been conducting, especially in light of the recent holding in the Southern District of Ohio (as quoted above).

Significantly, FDA regulations do not require prior FDA approval for the DoCs’ clinical investigations. But these regulations—promulgated in wake of the tragic experience with thalidomide—*do* require the DoCs to submit their protocols for lethal injections to FDA *before* using those protocols to execute condemned prisoners. FDA’s regulations apply to the DoCs’ clinical investigations even when the DoCs’ protocols rely on drugs lawfully marketed in the United States.

The IND process—fortified by FDA’s unmatched expertise with drug protocols—would ensure that the DoCs’ protocols are effective in reducing the risk that lethal injection will subject a condemned prisoner to pain that would violate the Eighth Amendment. It would also remove the federal courts from their unwanted role in

⁴ Note, *Regulation of Investigational New Drugs: “Giant Step for the Sick and Dying”?*, 77 Geo. L. J. 463, 469 and n. 47 (1988) (citing legislative history of 1962 Drug Amendments).

⁵ 21 C.F.R. § 312.3(b).

evaluating those protocols.⁶ While it is true that FDA’s regulations on clinical investigations would be technically challenging for many DoCs, such a safeguard is completely appropriate to ensure their protocols comply with federal law.

II. Jurisdictional Challenges

There are important jurisdictional challenges to prevail on a claim against a DoC based on its failure to comply with FDA’s IND requirements, especially because the Federal Food Drug & Cosmetic Act (FDCA) explicitly provides that actions to restrain violations of the FDCA must be brought in the name of the United States.⁷ Most of the claims raised under the FDCA in the context of lethal injection have been based either on §1983 or have been declaratory judgment actions.⁸ In general, those challenges have not fared well.⁹

Only one reported federal circuit court decision specifically addressed a prisoner’s claim that a DoC violated FDA’s IND regulations.¹⁰ In that case, the prisoner filed a §1983 claim asserting that the drugs used had not been shown to be safe and effective for their intended use in violation of the FDCA. The court noted the IND issue was

⁶ *In re Ohio Execution Protocol Litigation (Lorraine)*, 840 F.Supp.2d 1044, 1046 (S.D. Ohio 2012) (“[N]o judge is a micro-manager of executions and no judge wants to find himself mired in ongoing litigation in which he must continually babysit the parties”).

⁷ FDCA § 310(a); 21 U.S.C. § 337(a) (“[A]ll such proceedings for the enforcement, or to restrain violations, of this chapter shall be by and in the name of the United States”).

⁸ 42 U.S.C. § 1983; 28 U.S.C. § 2201; Fed. R. Civ. P. 57.

⁹ *E.g., Jones v. Hobbs*, 745 F.Supp.2d 886, 889 (E.D. Ark. 2010) (rejecting §1983 claim that the drugs for use in lethal injections “have not been approved by the FDA for that use”).

¹⁰ *O’Bryan v. McKaskle*, 729 F.2d 991 (5th Cir. 1984).

not argued by the parties at the hearing and explained that it was “unable to identify the legal footing of [petitioner’s] effort to enforce this detailed federal administrative scheme....” The court then denied the condemned prisoner’s claim, based in part on the FDCA’s provision excluding private enforcement.

While it is beyond the scope of this paper to offer any litigation strategy, there may be two bases for asserting the DoCs’ failure to comply with the IND regulations: the Fourteenth Amendment and preemption.

Fourteenth Amendment

The jurisdictional challenge of §337 for death row inmates to enforce the IND regulations might be avoided on Fourteenth Amendment grounds. A condemned prisoner might have a cognizable due process right to be assured that the DoC has complied with federal IND regulations with respect to the method and choice of drug to be used in his execution.¹¹

The FDA has not reviewed pursuant to an IND the lethal injection protocol of any State. As discussed *infra* §III, the use of drugs under revised lethal injection protocols constitute clinical investigations, as that term is defined in 21 C.F.R. §312.3(b), and require the submission of an IND. Moreover, the FDCA does not provide an exception to the IND application process for any drug on the basis that it is used in an execution.

¹¹ The Fourteenth Amendment to the United States Constitution provides, in relevant part: “[N]or shall any State deprive any person of life, liberty, or property, without due process of law...” U.S. Const. amend. XIV. *See also Spaziano v. Florida*, 468 U.S. 447, 468 (1984) (Stevens, J., concurring in part and dissenting in part)(“[A] State’s deprivation of a person’s life is...qualitatively different from any lesser intrusion on liberty”).

Under the Eighth Amendment, a State has an obligation to ensure that an execution be conducted in a manner that avoids a “substantial risk of serious harm.”¹² This constitutional mandate is supported by the Fourteenth Amendment’s requirement that prisoners receive due process in the deprivation of their life. Subsumed within these constitutional obligations is the DoC’s duty to comply with the federal regulatory safeguards designed to ensure the rights and welfare of human subjects of experimentation and clinical investigation.¹³

In the context of establishing sound lethal injection protocols, the condemned prisoner *is* the human subject of the clinical investigation. In all other circumstances, great care is taken to afford protection and to ensure minimal risk to the human subjects of clinical investigation.¹⁴ A condemned inmate, by contrast, is an involuntary and coerced participant in the State’s efforts to reformulate its execution procedures. The DoCs’ failure to comply with FDA’s IND regulations work a deprivation of life without due process of law in violation of the Fourteenth Amendment.¹⁵

¹² *Baze v. Rees*, 553 U.S. 35, 52 (2008) (plurality opinion of Roberts, C.J.).

¹³ FDA, Guidance for Clinical Investigators, Sponsors, IRBs: Investigational New Drug Applications (INDs)—Determining Whether Human Research Studies Can Be Conducted Without an IND (Sept. 2013) at 2 (primary objective of an IND is “to assure the safety and rights of subjects in all phases of an investigation”), *available at* <http://www.fda.gov/downloads/Drugs/Guidances/UCM229175.pdf> [hereinafter FDA IND GUIDANCE]; Human Subject Protection; Foreign Clinical Studies Not Conducted Under an Investigational New Drug Application. 73 (82) Fed. Reg. 22800 (April 28, 2008) (IND “helps ensure the protection of human subjects”).

¹⁴ 45 C.F.R. § 46.101 *et seq.* (HHS Policy for Protection of Human Research Subjects, usually known as the ‘Common Rule’).

¹⁵ *Evitts v. Lucey*, 469 U.S. 387, 401 (1985) (holding that “when a State opts to act in a field where its action has significant discretionary elements, it must nonetheless act in accord with the dictates of the Constitution – and, in particular, in accord with the Due Process Clause”). Until the moment of

In addition, the IND regulations establish an administrative framework that provides procedural due process.¹⁶ The submission of revised execution protocols to FDA for review can reduce the “substantial risk of serious harm” to prisoners from the untested combinations and dosing of drugs used in executions. In this way, the DoCs’ compliance with the IND procedures can ensure adherence to the Eighth and Fourteenth Amendment requirements.

Preemption

In 2010, in *Ringo v. Lombardi*, the district court for the Western District of Missouri (Laughrey, J.) held that condemned prisoners had stated a claim that the FDCA preempted Missouri’s protocol for lethal injection.¹⁷ The prisoners in that case sought a declaratory judgment that the protocol violated the FDCA “because the drugs are not prescribed by a licensed practitioner and have not been approved by the FDA for use in lethal injections.”¹⁸ The court reasoned that, “because preemption claims hinge

death, a condemned prisoner maintains a constitutionally protected residual life interest; all facets of the process by which the State seeks to deprive him of that interest, therefore, must comply with the requirements of due process. *See e.g., Ohio Adult Parole Auth. V. Woodard*, 523 U.S. 272, 281 (1998) (plurality opinion).

¹⁶ *Matthews v. Eldridge*, 424 U.S. 319 (1976) (holding that Social Security benefits were a property interest that could be denied only pursuant to due process).

¹⁷ 2010 WL 3310240 at *5 (W.D. Mo. Aug. 19, 2010). The court reached the same holding with respect to preemption by the Controlled Substances Act.

¹⁸ *Id.* at *1. See discussion *infra* at pages 17-18 of this type of FDCA ‘off label use’ argument.

on the supremacy of federal law, rather than individual rights, the absence of a private right of action in . . . the FDCA does not defeat Plaintiffs' preemption claim."¹⁹

It is true that subsequently the *Ringo* court granted summary judgment to defendants on the ground that plaintiffs had failed to "show any perceptible, present harm" and therefore lacked standing to maintain their preemption claim.²⁰ Furthermore, the court stated that, "on further reflection, [the court is] not convinced that Plaintiff's preemption claim is viable."²¹ (The Eighth Circuit reversed and vacated the district court's summary judgment decision on the ground that Missouri could not obtain the necessary drugs and therefore the case was moot.²²

Pharmaceutical companies are routinely permitted to assert preemption defenses to State-law-based pharmaceutical product liability claims, and these defenses sometimes are successful.²³ Thus, the *Ringo* district court is not alone in finding that the limitation in 21 U.S.C. §337(a), which requires actions to enforce the FDCA be in the name of the United States, does not preclude a private claim that State law is preempted by the FDCA.

¹⁹ *Id.* at *5. The court's reference to the putative lack of a 'private right of action' under the FDCA was based on 21 U.S.C. § 337(a), which requires actions to enforce the FDCA be brought in the name of the United States.

²⁰ *Ringo v. Lombardi*, 2011 WL 3584476 at *8 (W.D. Mo. Aug. 15, 2011).

²¹ *Id.* at *10.

²² *Ringo v. Lombardi*, 677 F.3d 793 (8th Cir. 2012).

²³ *Pliva, Inc. v. Mensing*, ___ U.S. ___, 131 S.Ct. 2567 (2011) (holding that it would be impossible for generic drug manufacturer to comply with FDCA and State product liability law and therefore the State law was preempted).

The original 1962 enactment of the authority for FDA to regulate clinical investigations contains an explicit provision preempting State law where there exists a “direct and positive conflict” with that enactment.²⁴ This shows that Congress recognized that the 1962 Drug Amendments might in fact preempt some State laws where those laws were in “direct and positive conflict” with those amendments—including the authorization for FDA to require submission of an IND.²⁵

It may be that consideration should be given to asserting claims on behalf of condemned prisoners that the IND regulations preempt any State laws that authorize DoCs to conduct lethal injections pursuant to protocols that have not first been submitted to FDA for review as part of an IND.

²⁴ The section of the FDCA that required FDA to adopt its IND regulations was added by the 1962 Drug Amendments, which provides:

Nothing in the amendments made by this Act to the [FDCA] shall be construed as invalidating any provision of State law which would be valid in the absence of such amendments unless there is a *direct and positive conflict* between such amendments and such provision of State law.

1962 Drug Amendments, Pub. L. 87-781, 76 Stat. 780, 793, § 202 (emphasis added). (The IND provisions are contained in § 103(b), 76 Stat. at 783.)

²⁵ In *Wyeth v. Levine*, 555 U.S. 555, 567 (2009), the Court characterized § 202 as a ‘savings clause’ intended to limit preemption of State law. Section 202, by its terms, contemplated that in some circumstances State law could be preempted. *Wyeth* was a pharmaceutical product liability case that turned on FDA’s authority over drug labeling—which has been extensively amended since 1962. In contrast, the IND authorization in the 1962 Drug Amendments remains relatively unchanged and thus should be subject to § 202.

III. FDA's IND Regulations

The FDCA prohibits any “new drug” from being marketed and distributed in interstate commerce unless FDA has received and approved a “new drug application” (NDA) that demonstrates the drug is safe and effective for a specific use or uses.²⁶

The phrase ‘new drug’ is a statutory term of art. Even a drug that has been marketed for many years can be deemed a new drug for purposes of the FDCA.²⁷

Moreover, if the sponsor of a new drug (who is usually the manufacturer) wishes to market the drug for additional uses not previously approved by FDA—including for example different combinations or doses—the sponsor is required to submit a separate NDA to FDA. The drugs used by the States for their lethal injections may be, or have been, the subjects of approved NDAs for some uses, but certainly not in combinations used in lethal injections and not at the doses administered by DoCs.

The FDCA provides an exception to the requirement of an approved NDA for clinical investigations of a new drug (including a new use of a previously approved drug).²⁸ Without such an exception, it would be illegal to move the drug in interstate commerce for purposes of a clinical investigation. The statute provides FDA with

²⁶ FDCA § 505(a); 21 U.S.C. § 355(a). The interstate commerce requirement was addressed in *United States v. Sullivan*, 332 U.S. 689 (1948) (Black, J.) (holding that a retail pharmacy violated the FDCA in interstate commerce by selling sulfathiazole it had repackaged without including FDA-required warnings on the label). See FDCA § 709; 21 U.S.C. § 379a (in an action to enforce FDCA’s requirements for drugs, “the connection with interstate commerce required for jurisdiction shall be presumed to exist”).

²⁷ *United States v. 50 Boxes More or Less*, 909 F.2d 24 (1st Cir. 1990)(a drug that had been sold for 35 years was nevertheless deemed a “new drug” because it was not generally recognized among experts as safe and effective).

²⁸ FDCA § 505(i); 21 U.S.C. § 355(i).

explicit authority to promulgate regulations for the conditions and procedures for this investigational drug use, which are incorporated in 21 C.F.R. Part 312.

FDA's regulations state that Part 312 applies to all "clinical investigations" of new drugs.²⁹ Section 312.3(b) then defines a "clinical investigation" as follows:

Clinical investigation means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.³⁰

This is an extremely broad definition. Stripped to its essentials, this definition means that using a drug outside of medical practice constitutes a 'clinical investigation,' and that even 'medical practice' is limited to "marketed drugs."

Part 312 requires that an IND application be submitted to FDA before a clinical investigation of a new drug is undertaken: "A sponsor *shall* submit an IND to FDA if the sponsor intends to conduct a clinical investigation with an investigational new drug that is subject to 312.2(a)."³¹ An "investigational new drug" is defined as a "new drug" used in a "clinical investigation."³² The "sponsor" is "a person who takes responsibility for and initiates a clinical investigation."³³ Under this definition, a DoC

²⁹ 21 C.F.R. § 312.1(a).

³⁰ *Id.* at § 312.3(b) (emphasis in original).

³¹ *Id.* at § 312.20(a) (emphasis added).

³² *Id.* at § 312.2(a).

³³ *Id.* at § 312.3(b); *Leo Winter Associates, Inc. v. HHS*, 497 F. Supp. 429 (D.D.C. 1980)(contract research organization assumed technical responsibility placed upon manufacturers and sponsors and therefore was a 'sponsor' of the clinical investigation).

is a “sponsor” of a “clinical investigation” for the drugs’ lethal injection use and is required to submit an IND to FDA for this investigational use.

Subpart B of Part 312 specifies the IND requirements, including the requirement that a protocol be submitted to FDA as part of the IND application.³⁴ Many DoCs have adopted protocols for their new uses of drugs in lethal injections, so they would need to include these protocols in the IND submissions to FDA and ensure the protocols comply with the detailed regulatory requirements.

FDA does provide an explicit exception from the requirement of an IND application for clinical investigations of drugs that are “lawfully marketed” in the United States.³⁵ A DoC, however, cannot take advantage of this exception *unless* it satisfies *all* of the five criteria set out in the regulation. At least two of those criteria do not appear to be satisfied by the DoCs’ experiments with lethal injections:

- The DoCs have neither sought nor received approval from an Institutional Review Board (IRB);³⁶
- The routes of administration, doses and other factors in lethal injections “significantly increase the risks” and decrease the “acceptability of the risks” associated with the drugs used by the DoCs.³⁷ The ‘risk’ in this context is that the condemned prisoner

³⁴ 21 C.F.R. § 312.23(a)(6).

³⁵ *Id.* at § 312.2(b).

³⁶ *Id.* at § 312.2(b)(iv) (requiring compliance with requirement for IRB approval).

³⁷ *Id.* at § 312.2(b)(iii).

will be subjected to a degree of pain that violates the Eighth Amendment.

Moreover, the exception is available only for “lawfully marketed” drugs. To the extent a DoC uses drugs compounded by a pharmacy,³⁸ the drugs are *not* “lawfully marketed.” FDA recently made this point clear in the IND context:

Studies that use a drug product that is prepared from *raw materials in place of the approved, finished product marketed by the manufacturer must be conducted under an IND* (21 C.F.R. part 312). These studies cannot meet the criteria for an exemption from the IND requirements for marketed drugs (§312.2(b)) because the drug product manufactured by the investigator or research pharmacy *is not considered to be the lawfully marketed drug.*³⁹

There are two other aspects of FDA’s IND regulations that are worth noting:

- First, a DoC would not require FDA approval of its protocol prior to using the protocol in a lethal injection.⁴⁰ The only requirement is that the DoC submit a sufficient, appropriate protocol as specified in the IND regulations and satisfy the other IND requirements 30 days before putting the protocol into effect in a lethal injection. Unless FDA objects by imposing a ‘clinical hold’ on the protocol, the DoC is legally permitted to follow the submitted protocol—provided the protocol is consistent with the detailed regulatory requirements.

³⁸ Traditional compounding pharmacies prepare a medication for an individual patient, pursuant to a specific prescription from the treating physician, in a form, or in a dose, not commercially available. Non-traditional compounding pharmacies engage in large-scale manufacturing of drugs that are distributed in interstate commerce. *See generally Thompson v. Western States Med. Ctr.*, 535 U.S. 357, 360-61 (2002).

³⁹ FDA IND GUIDANCE, *supra* note 13, at 17 (emphasis added).

⁴⁰ FDCA § 505(i)(2); 21 U.S.C. § 355(i)(2).

- Second, a DoC may comply with the IND regulations without having its IND automatically made public. Thus the putative need for secrecy is not a valid argument for avoiding the IND regulations. FDA ordinarily treats IND applications as confidential unless the sponsor (here, a DoC) chooses to make the application public.⁴¹

IV. Medical Practice & Lethal Injections

FDA’s definition of ‘clinical investigation’ *excludes* the use of “a marketed drug . . . in the course of medical practice.”⁴² In other words, a health care professional who is licensed under State law to prescribe a marketed drug may do so “in the course of medical practice” without falling into the definition of “clinical investigation.”⁴³

If the use of a marketed drug is outside the “course of medical practice,” then its use constitutes a ‘clinical investigation’ and—absent an applicable exception in the IND regulations—the requirement that an IND be submitted to FDA applies with full force of federal law.

⁴¹ 21 C.F.R. § 314.430.

⁴² 21 C.F.R. § 312.3(b).

⁴³ FDA GUIDANCE, *supra* note 13, at 4 (The “use of a lawfully marketed drug for an unapproved use in the course of medical practice is not a clinical investigation and does not require an IND because it involves the use in an individual patient where the primary intent is to treat the patient”). *See also id.* at 15 (same).

The use of marketed drugs in lethal injections is not ‘in the course of medical practice.’⁴⁴ As the *New England Journal of Medicine* stated in 2006, “[a]n execution is not a clinical procedure, and capital punishment is not the practice of medicine.”⁴⁵ *Stedman’s* — the leading U.S. medical dictionary — defines ‘medicine’ as: “The art of preventing, diagnosing, and treating disease; the science concerned with disease in all its relations.”⁴⁶ That definition excludes lethal injections, which plainly do not treat disease.

Several States have gone so far as to exclude lethal injections from the practice of medicine by statute. For example, Georgia has provided that:

Notwithstanding any other provision of law, prescription, preparation, compounding, dispensing, or administration of a lethal injection authorized by a sentence of death by a court of competent jurisdiction *shall not constitute the practice of medicine* or any other profession relating to health care which is subject by law to regulation, licensure, or certification.⁴⁷

⁴⁴ *Compare Morales v. Tilton*, 465 F. Supp.2d 972, 983 (N.D. Cal. 2006) (“[A]n execution is not a medical procedure, and its purpose is not to keep the inmate alive but rather to end the inmate’s life”) (note omitted) *with Ringo v. Lombardi*, 2011 WL 3584476 at *3 (W.D. Mo. Aug. 15, 2011) (describing participation in lethal injections by board-certified anesthesiologist, who testified that he “considers himself the condemned prisoner’s doctor”).

⁴⁵ Steinbrook R. New Technology, Old Dilemma—Monitoring EEG Activity During Executions. *New Engl J Med* 2006;354(24):2525-2527, at 2526.

⁴⁶ Dirckx JH, ed. *Stedman’s Concise Medical Dictionary for the Medical Professions*. Baltimore, MD: Williams & Wilkins;1997 (at 522).

⁴⁷ Ga. Code Ann. § 17-10-38(c) (emphasis added).

Other States have adopted similar provisions.⁴⁸ These States, in seeking to avoid their own State law restrictions on prescribing and administering drugs, appear to have fully satisfied the regulatory definition of ‘clinical investigation.’

The American Medical Association (AMA) has adopted an ethics opinion that, “[a] physician, as a member of a profession dedicated to preserving life when there is a hope of doing so, should not be a participant in a legally authorized execution.”⁴⁹ In the case of execution by lethal injection, ‘participation’ would include, *inter alia*, prescribing or supervising injection drugs or their doses.⁵⁰ Despite this clear ethical prohibition, some medical doctors do participate in lethal injections, and although it

⁴⁸ Ala. Code § 15-18-82.1(f) (2002) (“For purposes of this section, prescription, preparation, compounding, dispensing, and administration of a lethal injection shall not constitute the practice of medicine, nursing, or pharmacy.”); Fla. Stat. Ann. § 922.105(6) (West 2005) (“Notwithstanding [citing Florida statutes governing medicine], or any other law to the contrary, for purposes of this section, prescription, preparation, compounding, dispensing, and administration of a lethal injection does not constitute the practice of medicine, nursing, or pharmacy.”); S. D. Codified Laws 23A-27A-32 (2008) (“Any infliction of the punishment of death by intravenous injection of a substance or substances in the manner required by this section may not be construed to be the practice of medicine.”) Two states – Delaware and Oregon – have similar statutory provisions. A bill that would repeal the death penalty in Delaware has been carried over from the 2013 legislative session. Oregon currently has in place a moratorium on executions. *See generally*, Del. Code Ann. tit. 11, § 4209(f) (2013); Or. Rev. Stat. Ann. § 137.473(2) (2005). In New Hampshire, legislation that contained a similar provision with respect to the practice of medicine was recently defeated, *see* N. H. Rev. Stat. Ann. § 630:5 (XVI) (2013). In March 2014, New Hampshire’s House of Representatives overwhelmingly passed a bill (HB 1170) to repeal the death penalty for future offenses. The measure is currently under consideration by the Senate Judiciary Committee. If passed, Governor Hassan has promised to sign the bill into law.

⁴⁹ Council on Judicial & Ethical Affairs, American Medical Ass’n. Opinion 2.06—Capital Punishment, *available at*, <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion206.page>. Other medical societies have adopted similar ethics opinions on participation in lethal injections. *See Baze v. Rees*, 553 U.S. 35, 64-65 (2008) (Alito, J., concurring) (reviewing positions of medical societies).

⁵⁰ AMA Opinion 2.06, *supra* note 48.

appears that no medical doctor has been disciplined by a State licensing authority for such conduct.⁵¹ For example, in 2007, the North Carolina Medical Board issued a ‘Position Statement’ adopting AMA’s ethical position on lethal injection, but the North Carolina Supreme Court held that the Board’s action was invalid because a State statute required that a physician be present at executions.⁵²

V. Chaney & Cook

Almost 30 years ago, the Supreme Court in *Heckler v. Chaney*⁵³ held that FDA had unreviewable enforcement discretion to not take enforcement action against drugs used in lethal injections. The condemned prisoners in that case argued that, “the use of these drugs for human execution was the ‘unapproved use of an approved drug’ and constituted a violation of the [FDCA’s] prohibitions against ‘misbranding.’”⁵⁴ In its decision, the Supreme Court did not address FDA’s IND regulations.

Chaney was an administrative law case against FDA under the federal Administrative Procedure Act (APA), and the Supreme Court’s decision rested on whether FDA’s position was “committed to agency discretion by law” within the meaning of the APA.⁵⁵ The Court did not reach the substantive question of FDA’s jurisdiction over

⁵¹ Ty Alper, *The Truth about Physician Participation in Lethal Injection Executions*, 88 N.C. L. Rev. 11, 26 (2009) (“No doctor has ever been disciplined for participating in an execution in this country”) (note omitted).

⁵² *North Carolina Dep’t of Correction v. North Carolina Med. Bd.*, 363 N.C. 189, 675 S.E.2d 641 (N.C. 2009).

⁵³ 470 U. S. 821 (1985).

⁵⁴ 470 U. S. at 823-24 (note omitted).

⁵⁵ 5 U.S.C. § 701(a)(2).

lethal injection drugs.⁵⁶ Thus, *Chaney* should not be relevant to an action against a DoC challenging its failure to comply with FDA's IND regulations

The FDCA lacks any provision that explicitly prohibits the prescription of a drug for a use that has not been approved by FDA (a so-called 'off label' use), although under current law the sponsor of an approved drug (usually the manufacturer) is prohibited from *promoting* the drug for an unapproved use.⁵⁷

To the contrary, long usage supports the appropriate prescription of approved drugs by State-licensed health-care providers (primarily medical doctors in most States) to treat illnesses or conditions even where FDA has not approved those uses. These off label uses do not violate the FDCA and are an important part of medical treatments for many diseases.

In *Chaney*, the condemned prisoners alleged that, “the drugs used by the States for [lethal injection] although approved by the FDA for the medical purposes stated on their labels, were not approved for use in human executions.”⁵⁸ Thus *Chaney* presented the Supreme Court with the question whether the federal courts could review FDA’s decision not to take enforcement action against the off label use of approved drugs for the unapproved use of executions. (As noted, there is no explicit provision in the

⁵⁶ Annas GJ. *Killing with Kindness: Why the FDA Need Not Certify Drugs Used for Execution Safe and Effective*. Am J Public Health 1985;75(9):1096-1099 (noting that the Supreme Court in *Chaney* declined to address the question of FDA’s jurisdiction over drugs used in lethal injections).

⁵⁷ *But see United States v. Caronia*, 703 F.3d 149 (2d Cir. 2012) (vacating misdemeanor conviction under the FDCA of pharmaceutical sales representative for off label promotion on First Amendment grounds). FDA did not seek certiorari in *Caronia*.

⁵⁸ *Chaney*, 470 U. S. at 823.

FDCA that prohibits off label uses of approved drugs.) The Court held that FDA's enforcement decisions in this context were unreviewable under the APA.

Recently the U.S. Court of Appeals for the D.C. Circuit in *Cook v. FDA*⁵⁹ was confronted with an issue different from that in *Chaney*: could FDA be required under the APA to comply with an explicit statutory command in the FDCA that an unapproved drug not be imported into the United States? The court answered this question in the affirmative.

The question in *Cook* was whether the court could review FDA's decision to permit the importation of thiopental into the United States even though the FDCA explicitly required FDA to prohibit the importation of drugs made in foreign facilities not registered with FDA—and the thiopental in question had not been made in a registered facility.

The D.C Circuit may have signaled recently that it does not regard *Cook* as confined to the importation context: in *K-V Pharmaceutical Co. v. FDA*, plaintiffs sued FDA under the APA and alleged that FDA was required to take enforcement action to prevent compounding pharmacies from duplicating plaintiffs' FDA-approved hydroxyprogesterone caproate drug.⁶⁰ The district court dismissed the complaint primarily on *Chaney* grounds, but on January 7, 2014, the D.C. Circuit, in an

⁵⁹ 733 F. 3d 1 (D.C. Cir. 2013).

⁶⁰ 889 F.Supp.2d. 119 (D.D.C. 2012).

unpublished order, vacated the district court decision and remanded for further consideration in light of *Cook*.⁶¹

It appears that *Chaney* is being interpreted, correctly, in the D.C. Circuit, to govern *only* those situations where the FDCA does not contain any explicit statutory requirements for a federal court to enforce. The IND regulations do contain explicit, mandatory requirements.

VI. Conclusion

There is no question that challenging lethal injections on the ground that the DoCs are subject to FDA's IND requirements is an uphill battle. No doubt the statutory provision requiring that enforcement of the FDCA is limited to the United States can be a substantial obstacle.

Nonetheless, there are several considerations that suggest the IND requirements are a stronger ground for such a challenge than other FDA-related arguments that have been made in some cases:

- The IND regulations are concrete, grounded in statutory authority, and phrased as mandatory obligations. (In this respect, an IND claim differs from an 'unapproved use' claim that lacks any basis in the FDCA.)

⁶¹ 2014 WL 68499 (D.C. Cir. Jan. 7, 2014) (unpublished). In that order, the D.C. Circuit also ordered reconsideration in light of the recently enacted Drug Quality & Security Act, Pub. L. 113-54, 127 Stat. 587 (Nov. 27, 2013). That Act clarified the law governing compounding pharmacies and offered a 'safe harbor' for compounding pharmacies that registered voluntarily with FDA. *See generally* Outtersson K. *The Drug Quality and Security Act—Mind the Gaps*. *New Engl J Med*. 2014;370(2):97-99.

- The IND regulations are intended to protect the human subjects of clinical investigations—which should include condemned prisoners.
- The IND regulations would appear to apply squarely to the DoCs’ struggles to cope with the unavailability of the drug combination approved in *Baze*. In particular, FDA’s definition of ‘clinical investigation’ is extremely broad.
- The DoCs’ ‘protocols’ sound just like the central requirement of FDA’s IND regulations, which is the submission of a ‘protocol’ for review.
- The 1962 Drug Amendments contain a provision addressing preemption. Congress plainly anticipated the possibility that the IND regulations might in appropriate circumstances preempt State law.
- Applying the IND regulations to the DoCs’ protocols does not require the DoCs to obtain prior FDA approval and would respect the DoCs’ confidentiality concerns.
- Nonetheless, to comply with the IND regulations would be a substantial and time-consuming technical challenge for those DoCs that lack medical, scientific, and biostatistics expertise.
- Also, the requirement of Institutional Review Board review might be difficult for DoCs to meet.

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