

SAFE AND EFFECTIVE FOR HUMAN
EXECUTIONS?
GLOSSIP V. GROSS AND THE EIGHTH
AMENDMENT BAR AGAINST OFF-LABEL
DRUG LETHAL INJECTION

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INTRODUCTION

In June¹ the U.S. Supreme Court will decide *Glossip v. Gross*, a challenge to Oklahoma's lethal-injection protocol brought by three death row inmates.² The inmates argue that the protocol's first drug, midazolam, violates the Eighth Amendment's prohibition against cruel and unusual punishment because it does not reliably induce unconsciousness. Midazolam's inadequacy, they claim, could result in "severe pain" during the protocol's death-inducing phase.³ Most relevantly midazolam is not FDA approved as a stand-alone anesthetic,⁴ meaning its use in lethal injections is "off-label." I argue that off-label drug use in lethal injections raises significant Eighth Amendment questions and that the Court should invalidate the protocol at issue in *Glossip* because of its lack of FDA approval. Although courts are increasingly recognizing the constitutional

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1. See Description of Death Penalty Cases Heard by the Supreme Court in the 2014-2015 Term, DEATH PENALTY INFO. CTR., <http://www.deathpenaltyinfo.org/united-states-supreme-court-decisions-2014-2015-term> (last visited Mar. 17, 2015) ("*Glossip* will be argued in April and likely decided by the end of June.>").

2. *Glossip v. Gross*, No. 14-7955 (U.S. argued Apr. 29, 2015).

3. *Warner v. Gross*, 776 F.3d 721, 727 (10th Cir. 2015) (quoting Record, Vol. 1, at 963) (internal quotation mark omitted), *cert. granted*, 135 S. Ct. 1173 (2015).

4. See Roche Pharm., Package Insert for Versed (dated 1999), available at http://www.fda.gov/ohrms/dockets/dailys/01/Mar01/032101/cp000001_exhibit_02.pdf (listing midazolam's FDA-approved use as "induction of general anesthesia, before administration of other anesthetic agents"). Midazolam, trade name Versed, is the only anesthetic in the lethal injection protocol in *Glossip*.

significance of off-label use in landmark cases like *United States v. Caronia*,⁵ they have yet to analyze off-label use in the Eighth Amendment context. Instead, courts traditionally review the use of off-label execution drugs under statutory standards.⁶

Although the *Glossip* petitioners highlight the lack of FDA approval,⁷ it is a superficial component of their claim. They focus on midazolam's pharmacology⁸ and the medical consensus surrounding its use,⁹ and they do not directly discuss the constitutional implications of off-label use. I elaborate this underdeveloped but consequential facet of their claim in three parts. In Part I, I will examine the medical context of midazolam's off-label use. In Part II, I will situate *Glossip* in the Court's Eighth Amendment lethal injection jurisprudence. Finally, I will conclude that midazolam's lack of FDA approval should carry great weight in the Court's ruling on the constitutionality of Oklahoma's protocol, and in the fate of lethal injection across the nation.

I. THE MEDICAL LANDSCAPE

Oklahoma turned to midazolam for its executions in April 2014 after manufacturers of the anesthetics it had previously employed cut off access because of objections to its use in this context.¹⁰ Midazolam is FDA approved for use as an anesthetic only in combination with other anesthetic agents.¹¹ When it is the only drug administered to induce anesthesia, such as in *Glossip*, it is being used for a non-FDA-approved purpose, a practice known as "off-label" use.¹² Although off-label use of prescription drugs is legal¹³ and

5. 703 F.3d 149, 168-69 (2d Cir. 2012) (holding that a ban on marketing of off-label uses of drugs violated the First Amendment).

6. See, e.g., *Cook v. FDA*, 733 F.3d 1, 7-11 (D.C. Cir. 2013) (reviewing importation of drugs for off-label use in executions under the Food, Drug, and Cosmetic Act and the Administrative Procedure Act).

7. Brief for Petitioners at 13, *Glossip v. Gross*, No. 14-7955 (U.S. argued Apr. 29, 2015), 2015 WL 1045426 ("[M]idazolam is neither approved by FDA for use as, nor used as, the sole drug to maintain general anesthesia . . .").

8. *Id.* at 26 ("Midazolam's pharmacological properties . . . mean that it cannot create deep comalike unconsciousness.").

9. *Id.* ("The medical consensus is that midazolam cannot generate deep, comalike unconsciousness.").

10. See Brady Dennis & Lena H. Sun, *For More States, Execution Means Improvisation as Drug Supplies Dwindle*, WASH. POST (Apr. 30, 2014), <http://wapo.st/1rH897r>.

11. See Roche Pharm., *supra* note 4.

12. See "Off-Label" and Investigational Use of Marketed Drugs, Biologics, and Medical Devices—Information Sheet, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/RegulatoryInformation/Guidances/ucm126486.htm> (last updated June 25, 2014).

13. See Jerry Avorn & Aaron Kesselheim, Editorial, *A Hemorrhage of Off-Label Use*, 154 ANNALS INTERNAL MED. 566, 567 (2011) ("[O]ff-label prescribing by physicians is not illegal . . .").

frequent,¹⁴ it lacks critical safeguards. For one, a drug's prescribing information only contains instructions for FDA-approved uses. These instructions are based on rigorous clinical trials, but by definition these investigations do not cover off-label uses.¹⁵ Moreover, off-label use is often not supported by evidence.¹⁶ Although a few organizations analyze off-label uses,¹⁷ these reviews can be inferior to the FDA's approval process because studies of off-label uses of drugs often involve far fewer clinical participants and less detailed outcome analyses.¹⁸ This lack of evidence is consequential because it raises the risk of harm.¹⁹ Physicians who prescribe off-label cannot consistently rely on FDA guidance or prior investigations to proactively identify and avoid negative outcomes.

The risks that attach to off-label use apply with particular force in the lethal injection context. The limited data on the off-label use of midazolam in that context suggest that it is associated with a grave risk—botched executions.²⁰ The broader data on midazolam support this negative assessment. Studies have found that it is not an effective surgical anesthetic.²¹ In fact, research has

14. See, e.g., U.S. GOV'T ACCOUNTABILITY OFFICE, GAO-08-835, PRESCRIPTION DRUGS: FDA'S OVERSIGHT OF THE PROMOTION OF DRUGS FOR OFF-LABEL USES 2 (2008), available at <http://www.gao.gov/assets/280/278832.pdf>.

15. See *Unapproved Prescription Drugs: Drugs Marketed in the United States That Do Not Have Required FDA Approval*, U.S. FOOD & DRUG ADMIN., <http://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/enforcementactivitiesbyfda/selectedenforcementactionsonunapproveddrugs/default.htm> (last updated Dec. 3, 2014) (explaining that FDA's process ensures that physicians have enough information to understand a drug's risks and how to use it properly).

16. See, e.g., Nicole Ansani et al., *United States Medical Practice Summary: Innovative Off-Label Medication Use*, 21 AM. J. MED. QUALITY 246, 250 (2006) (finding that off-label use often occurs with "limited data support" and "potentially unfavorable risk-to-benefit ratios").

17. One example of such an organization is Truven Health Analytics. See Truven Health Analytics, *Micromedex Drugdex* (2013), available at http://micromedex.com/Portals/1/Assets/Brochures/International/INTL_12342_0613_INTL%20Drugdex_Web1.pdf.

18. See, e.g., Rebecca Dresser & Joel Frader, *Off-Label Prescribing: A Call for Heightened Professional and Government Oversight*, 37 J.L. MED. & ETHICS 476, 479 (2009) (referring to such reviews as "not as rigorous as FDA review").

19. See *id.* at 476 ("The potential for harm is greatest when an off-label use lacks a solid evidentiary basis.").

20. See, e.g., Adam Liptak & Erik Eckholm, *Justices to Hear Case over Drugs Used in Executions*, N.Y. TIMES (Jan. 23, 2015), <http://www.nytimes.com/2015/01/24/us/justices-to-hear-case-on-execution-drugs.html> ("Oklahoma botched the execution of Clayton D. Lockett . . . Midazolam was also involved in prolonged, possibly painful executions last year in Ohio and Arizona.").

21. See, e.g., T.G. Short et al., *Hypnotic and Anaesthetic Action of Thiopentone and Midazolam Alone and in Combination*, 66 BRIT. J. ANAESTHESIA 13, 17-18 (1991) ("[W]e were unable to demonstrate any anaesthetic action by midazolam . . .").

shown that administering midazolam can have a “paradoxical” effect in certain patients, leading to agitation and restlessness.²²

In addition, use of non-FDA-approved drugs in executions violates the enabling premise of off-label use—deference to the practice of medicine.²³ Off-label use rests on the implicit assumption that medical judgment is sufficiently risk mitigating,²⁴ but this protection is absent in the *Glossip* context. Oklahoma’s death penalty statute only requires that a physician pronounce death, not perform the execution.²⁵ Similarly, the Oklahoma Department of Corrections does not require physician participation.²⁶ Indeed, one of Oklahoma’s botched midazolam executions was believed to be in part the result of inadequate medical expert support.²⁷ Oklahoma would find it difficult to increase medical involvement; the physicians with the expertise most relevant to the administration of midazolam—anesthesiologists—face severe penalties for participation in executions.²⁸ The American Board of Anesthesiologists will revoke the certification of an anesthesiologist who participates in an execution,²⁹ a penalty that can cause physicians to lose hospital practice privileges.³⁰ In addition, the American Medical Association,³¹ American Nurses Association,³² National Association of Emergency Medical Technicians,³³ and American Public Health Association³⁴ have all issued

22. See, e.g., Luciano Santana Cabrera et al., *Paradoxical Reaction to Midazolam Reversed with Flumazenil*, 3 J. EMERGENCIES TRAUMA & SHOCK 307, 307 (2010), available at <http://www.onlinejets.org/text.asp?2010/3/3/307/66551>.

23. See, e.g., Philip M. Rosoff & Doriane Lambelet Coleman, *The Case for Legal Regulation of Physicians’ Off-Label Prescribing*, 86 NOTRE DAME L. REV. 649, 659 (2011).

24. See *id.*

25. See OKLA. STAT. ANN. tit. 22, § 1014(A) (West 2011).

26. See OKLA. DEP’T CORR., OP-040301, EXECUTION OF OFFENDERS SENTENCED TO DEATH 7-8 (2014), available at <http://www.ok.gov/doc/documents/op040301.pdf>.

27. See Tara Culp-Ressler, *Why There Weren’t Any Doctors to Prevent Oklahoma’s Botched Execution*, THINKPROGRESS (Apr. 30, 2014, 9:05 AM), <http://thinkprogress.org/health/2014/04/30/3432495/oklahoma-execution-doctors>.

28. See Rob Stein, *Group to Censure Physicians Who Play Role in Lethal Injections*, WASH. POST (May 2, 2010), <http://www.washingtonpost.com/wp-dyn/content/article/2010/05/01/AR2010050103190.html>.

29. Commentary, J. Jeffrey Andrews, Sec’y, Am. Bd. Anesthesiology, Anesthesiologists and Capital Punishment (May 2014), available at <http://www.theaba.org/pdf/CapitalPunishmentCommentary>.

30. See, e.g., Stein, *supra* note 28 (“The loss of certification would prevent an anesthesiologist from working in most hospitals.”).

31. AM. MED. ASS’N, CODE OF MEDICAL ETHICS, OP. 2.06—CAPITAL PUNISHMENT (2000), available at <http://www.ama-assn.org/ama/pub/physician-resources/medical-ethics/code-medical-ethics/opinion206.page?>

32. AM. NURSES ASS’N, POSITION STATEMENT: NURSES’ ROLE IN CAPITAL PUNISHMENT 1 (2010), available at <http://www.nursingworld.org/MainMenuCategories/EthicsStandards/Ethics-Position-Statements/prtetcptl14447.pdf>.

33. NAT’L ASS’N EMERGENCY MED. TECHNICIANS, POSITION STATEMENT: EMT AND PARAMEDIC PARTICIPATION IN CAPITAL PUNISHMENT (2010), available at <http://www.naemt>

admonitions against their members' involvement. This lack of medical expertise heightens the already serious risk of harm associated with Oklahoma's use of an off-label drug in its protocol.

II. THE LEGAL LANDSCAPE

The *Glossip* petitioners are facing substantial legal hurdles. The Supreme Court has never before invalidated a method of execution,³⁵ and courts have not fully addressed the Eighth Amendment implications of off-label drug use in executions. However, the inmates' chances of success will increase if the Court applies the *Baze v. Rees* standard³⁶ and recognizes the centrality of the off-label component of the lethal injection protocol at issue in *Glossip*. In *Baze*, death-row inmates challenged Kentucky's three-drug lethal injection protocol on the ground that the risk of misadministration of the first drug, a different drug than midazolam, constituted cruel and unusual punishment. The inmates claimed that the complexity of the intravenous procedure, in combination with the inadequate qualifications of the administering personnel,³⁷ created a "significant risk that the procedures w[ould] not be properly followed."³⁸ The *Baze* inmates conceded that a properly administered anesthetic and protocol would result in a constitutional and "humane death."³⁹

The Court rejected the *Baze* petitioners' challenge and established a two-part test for assessing the constitutionality of a lethal injection protocol.⁴⁰ The test instructs courts to consider whether a protocol is "objectively intolerable"⁴¹ and involves a "substantial risk of serious harm."⁴² The protocol at issue in

[.org/docs/default-source/Advocacy-Documents/1-26-10_EMT_or_Paramedic_Participation_in_Capital_Punishment.pdf](http://www.apha.org/policies-and-advocacy/public-health-policy-statements/policy-database/2014/07/08/18/10/participation-of-health-professionals-in-capital-punishment).

34. AM. PUB. HEALTH ASS'N, PARTICIPATION OF HEALTH PROFESSIONALS IN CAPITAL PUNISHMENT, Policy No. 8521 (1985), *available at* <https://www.apha.org/policies-and-advocacy/public-health-policy-statements/policy-database/2014/07/08/18/10/participation-of-health-professionals-in-capital-punishment>.

35. *Baze v. Rees*, 553 U.S. 35, 48 (2008).

36. *See id.* at 48, 61-62.

37. *Id.* at 54 ("Petitioners contend that there is a risk of improper administration of thiopental because the doses are difficult to mix into solution form and load into syringes . . . [and] because of inadequate facilities and training . . .").

38. *Id.* at 49.

39. *Id.* at 41.

40. The *Baze* test is widely regarded as ill-defined. *See, e.g.*, Deborah W. Denno, *Lethal Injection Chaos Post-Baze*, 102 GEO. L.J. 1331, 1335 (2014) (referring to the *Baze* standard as "vague and diffuse"). Nonetheless, these two factors form the core of the *Baze* test.

41. *Baze*, 553 U.S. at 53 ("[I]t is difficult to regard a practice as 'objectively intolerable' when it is in fact widely tolerated.").

42. *Id.* ("It is uncontested that, failing a proper dose of sodium thiopental that would render the prisoner unconscious, there is a substantial, constitutionally unacceptable risk of suffocation . . . and pain . . .").

Glossip likely satisfies both prongs. The *Baze* determination of whether the use of a drug in executions is “objectively intolerable” turns on frequency of use; a drug is less likely to be “objectively intolerable” if many states use it in their protocols.⁴³ Only four of the thirty-two death penalty states use midazolam as part of their official execution protocols,⁴⁴ and at least one state has postponed further executions because it does not want to use midazolam.⁴⁵ This widespread distaste paints Oklahoma’s use of midazolam as intolerable, meeting the first prong of the *Baze* test.

Off-label use bears more directly on *Baze*’s second prong, a “substantial risk of serious harm.” The Court divides this standard into two factors: the inevitability and level of pain. According to the Court, accidental pain in an execution is not unconstitutional because missteps are inevitable even in humane procedures.⁴⁶ Yet the Court will find intentionality where missteps and accidents happen repeatedly.⁴⁷ The Court denied the *Baze* petitioners’ claim precisely because it attacked infrequent accidental misadministration rather than recurring problems.⁴⁸ *Glossip*’s off-label use, in contrast, is not one-off or accidental. Midazolam is a sanctioned feature of Oklahoma’s protocol,⁴⁹ implemented intentionally in response to shortages of anesthetic drugs.⁵⁰ Moreover, Oklahoma continues to use midazolam despite recurring problems with its administration in executions; even if an individual incident could be viewed as “accidental,” the pattern of harm raises an inference of intentionality. Thus the *Glossip* petitioners’ challenge should succeed where the *Baze* petitioners failed.

Oklahoma could argue that its use of off-label midazolam is accidental. According to this line of reasoning, Oklahoma did not start using midazolam by intentional design. Forces beyond its control (drug shortages) forced it to substitute its FDA-approved anesthetic of choice for an off-label product. Justice Thomas may find this argument persuasive. In his *Baze* concurrence, he claims that the standard requires a “deliberate[] design[] to inflict pain.”⁵¹

43. *Id.*

44. See *State by State Lethal Injection*, DEATH PENALTY INFO. CTR., <http://www.deathpenaltyinfo.org/state-lethal-injection> (last visited Mar. 21, 2015).

45. See, e.g., Mark Berman, *Ohio Drops Controversial Lethal Injection Drug, Postpones Upcoming Execution*, WASH. POST (Jan. 9, 2015), <http://wapo.st/1Iz6HMV>.

46. *Baze*, 553 U.S. at 50.

47. *Id.* (differentiating an “innocent misadventure” from an “objectively intolerable risk” by example, characterizing a series of failed electrocution attempts as intentional and unconstitutional harm).

48. See *id.* at 41, 50.

49. See Brief for Respondents at 1, *Glossip v. Gross*, No. 14-7955 (U.S. argued Apr. 29, 2015), 2015 WL 1619433.

50. See, e.g., Warren Richey, *Death Penalty Case: Oklahoma Lethal Injection Drug Faces Supreme Court Test*, CHRISTIAN SCI. MONITOR (Apr. 28, 2015), <http://m.csmonitor.com/USA/Justice/2015/0428/Death-penalty-case-Oklahoma-lethal-injection-drug-faces-Supreme-Court-test-video>.

51. *Baze*, 553 U.S. at 94 (Thomas, J., concurring in the judgment).

Although *Baze* provides only limited guidance as to what constitutes an “accident” under the Eighth Amendment, the detail it does provide cuts against Thomas’s reading, which is not precedent. Rather, repeated implementation of lethal injection practices that disregard serious risks and poor outcomes, irrespective of any design to injure, is the authoritative standard. *Glossip* meets this benchmark.

Under the second prong of this part of the *Baze* test, the risk of pain must transcend the suffering inherent in execution in order to generate constitutional concerns.⁵² According to *Baze*, prolonged death is a strong indication that a protocol has breached the constitutionally permissible level of risk.⁵³ Oklahoma’s off-label use of midazolam meets this criterion not only because of documented prolonged deaths in midazolam executions,⁵⁴ but also because of the elevated risk of harm resulting from the inadequate medical evidence⁵⁵ that attends off-label use. Defenders of off-label executions may argue that there is no rigorous evidence that midazolam is inherently harmful, and that a handful of unsightly executions cannot serve as empirically sound data. They might also characterize the evidence that midazolam does not perform well as an anesthetic in the surgical context as inapposite to lethal injection. These arguments, however, ignore the fact that *Baze* does not require scientific certitude; it only requires a *substantial risk*.⁵⁶ This risk is present in *Glossip* because of the absence of medical evidence and guidance.

Another constitutionally relevant consequence of midazolam’s off-label use is the lack of prescribing instructions. The *Baze* Court itself emphasized the Eighth Amendment significance of FDA-approved label instructions, characterizing them as a bulwark against harm.⁵⁷ And although *Baze* upheld a three-drug protocol much like the one at issue in *Glossip*, the *Baze* protocol specified the use of sodium thiopental for anesthesia, which, unlike midazolam, is FDA approved as a self-standing anesthetic and has label instructions for that purpose.⁵⁸ Thus *Glossip* stands apart from *Baze* on the crucial questions of

52. *Id.* at 47 (majority opinion).

53. *Id.* at 49 (“Punishments are cruel when they involve torture or a lingering death . . .” (quoting *In re Kemmler*, 136 U.S. 436, 447 (1890)) (internal quotation mark omitted)).

54. See, e.g., Michael L. Radelet, *Examples of Post-Furman Botched Executions*, DEATH PENALTY INFO. CTR., <http://www.deathpenaltyinfo.org/some-examples-post-furman-botched-executions> (last updated July 24, 2014) (“Mr. Lockett died 43 minutes after the execution began . . .”).

55. See, e.g., Ansani, *supra* note 16.

56. *Baze*, 553 U.S. at 50.

57. *Id.* at 54 (“[I]f the manufacturers’ instructions . . . are followed, . . . there would be minimal risk . . .” (third alteration in original) (quoting Joint Appendix at 761, *Baze*, 553 U.S. 35 (No. 07-5439)) (internal quotation mark omitted)).

58. *Thiopental Sodium*, DAILYMED, <https://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=48745> (last visited Apr. 28, 2015) (indicating use “as the sole anesthetic agent for brief . . . procedures”).

level of risk as well as inevitability, and these distinctions call for a different outcome in *Glossip*.

CONCLUSION: UNCONSTITUTIONALITY OF OFF-LABEL DRUG EXECUTIONS

Oklahoma was the first state to use lethal injections.⁵⁹ Its off-label use of midazolam is grounds for making it the first state to have its method of execution declared unconstitutional, with other states positioned to fall in its wake. The controversy at the core of *Glossip* is not unique to Oklahoma; other states have turned to off-label drugs because of drug shortages.⁶⁰ The Eighth Amendment prohibits a “substantial risk of serious harm,”⁶¹ and midazolam and other off-label drugs run afoul of this requirement. Off-label use entails increased risks because of inadequate evidentiary bases and the absence of label instructions. In *Glossip*’s death penalty context, with glaring gaps in medical professional involvement and clinical data, these risks reach “substantial” proportions. The FDA’s silence on midazolam’s use as a stand-alone anesthetic speaks volumes, and the Court should listen.

Recognition of the Eighth Amendment implications of off-label use could position *Glossip* as the death knell for lethal injection. And even if the Court upholds Oklahoma’s protocol, the demise of lethal injections may still be on the horizon. Denial of the inmates’ claim would in effect sanction the use of non-FDA-approved drugs. In all likelihood, upholding the Oklahoma protocol would trigger wider off-label use, implementation of executions previously suspended because of a hesitancy to use unapproved drugs,⁶² and more botched executions. This chain of events could culminate in increased awareness of the risk of pain involved in lethal injection using off-label drugs and could foster pressure for abolition.⁶³ Irrespective of the Court’s decision in *Glossip*, drug shortages and increasing reliance on off-label drugs is driving lethal injection into troubled constitutional waters.

59. Vince Beiser, *A Guilty Man*, MOTHER JONES (Sept. 1, 2005, 3:00 AM), <http://www.motherjones.com/politics/2005/09/guilty-man>.

60. See, e.g., *Lacking Lethal Injection Drugs, States Find Untested Backups*, NPR (Oct. 26, 2013, 5:19 PM ET), <http://n.pr/17QrAkE>.

61. *Baze*, 553 U.S. at 50 (quoting *Farmer v. Brennan*, 511 U.S. 825, 842 (1994) (internal quotation marks omitted)).

62. See, e.g., Denno, *supra* note 40, at 1336.

63. See Wade Goodwyn, *Botched Lethal Injection Executions Reignite Death Penalty Debate*, NPR (Jan. 6, 2015, 5:45 PM ET), <http://n.pr/1wSjmDU> (arguing that botched executions increase opposition to lethal injection because “[a] clean and painless death by injection has played a major role in preserving capital punishment”).