IN THE SUPREME COURT OF THE STATE OF OKLAHOMA

TERRY CLINE, et al.,	)	
	)	
Petitioners,	)	
	)	
v.	)	No. 111,939
	)	
OKLAHOMA COALITION FOR REPRODUCTIVE JUSTICE,	)	
	)	
	)	
Respondents.	)	

AMICUS CURIAE BRIEF OF 83 OKLAHOMA LEGISLATORS AND AMERICANS UNITED FOR LIFE ACTION IN SUPPORT OF THE DEFENDANTS/APPELLANTS, FILED ON MOTION FOR LEAVE TO FILE BRIEF

Randy Grau, OBA #19109
Cheek & Falcone, PLLC
6301 Waterford Boulevard, Suite 320
Oklahoma City, Oklahoma 73118
Telephone (405) 286-9191
Facsimile (405) 286-9670
Counsel for Amici Curiae

TABLE OF CONTENTS AND AUTHORITIES

STATEMENT OF INTEREST OF *AMICI CURIAE* 1

Statutes

63 OKLA. STAT. § 1-729a. 1

ARGUMENT AND AUTHORITY 4

Cases

Blevins v. W.A. Graham Co., 72 Okla. 308, 309, 182 P. 247 (Okla. 1919). 4, 8

Planned Parenthood Southwest Ohio Region v. DeWine, 696 F.3d 490 (6th Cir. 2012). 7

State v. Haworth, 2012 OK CR 12, 283 P.3d 311 (Okla. 2012). 4, 8

Other Authorities

American College of Obstetricians and Gynecologists (ACOG), *ACOG Practice Bulletin 67 Medical Management of Abortion* (Oct. 2005). 5

FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11* (July 2011). 6

Guttmacher Institute, *Facts on Induced Abortion in the United States* (Aug. 2011). 5

Mifeprex Final Printed Labeling. 5

PROPOSITION 1:

THE LEGISLATURE INTENDED FOR HB 1970 TO ALLOW THE USE OF MISOPROSTOL FOR CHEMICAL ABORTIONS SO LONG AS MISOPROSTOL IS ADMINISTERED AS DIRECTED IN THE MIFEPREX (RU-486) FPL. 9

A. The Legislature intended the use of the Mifeprex (RU-486) regimen to follow the FDA-approved protocol. 9

Statutes

21 C.F.R. § 314.520. 9

63 OKLA. STAT. § 1-729(a)(3). 14

Other Authorities

FDA, *Feb. 2000 Approvable Letter*. 10

FDA, *CDER Drug and Biologic Accelerated Approvals as of September 30, 2011*. 9

FDA*, Sept. 2000 Approval Letter.* 10, 11

FDA, *Summary of NDA Approvals & Receipts, 1938 to the present* (2011). 9

Memorandum of Department of Health and Human Services to "NDA 20-687 MIFEPREX (mifepristone) Population Counsel" (Sept. 28, 2000). 13, 14

Mifeprex Final Printed Labeling. 12, 13

"Patient Agreement" in *Mifeprex Final Printed Labeling.* 12

U.S. Government Accountability Office, *GAO Report*. 10

B. The Legislature intended to protect women from the potentially harmful effects associated with the misuse of the Mifeprex (RU-486) regimen. 15

Other Authorities

American College of Obstetricians and Gynecologists (ACOG), *ACOG Practice Bulletin 67 Medical Management of Abortion* (Oct. 2005). 16, 18

FDA*, Mifeprex (mifepristone) Information* (July 19, 2011). 18

FDA, *Mifeprex Questions and Answers* (Feb. 24, 2012). 18

FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11* (July 2011). 17

FDA, *Public Health Advisory: Sepsis and Medical Abortion* (Mar. 17, 2006). 18, 19

M. Fjerstad et al., *Rates of Serious Infection after Changes in Regimens for Medical Abortion*, N.E.J.M. 361:145 (2009). 18

Mifeprex Final Printed Labeling. 15, 16

U.S. Government Accountability Office, *GAO Report*. 17

C. The Legislature intended to use its "wide discretion" to regulate a method of abortion. 19

Cases

Gonzales v. Carhart, 550 U.S. 124 (2007). 19, 20, 21

Planned Parenthood v. Casey, 505 U.S. 833 (1992). 19, 21

Roe v. Wade, 410 U.S. 113 (1973). 21

Other Authorities

J.T. Jenson et al., *Outcomes of Suction Curettage and Mifepristone Abortion in the United States: A Prospective Comparison Study*, CONTRACEPTION 59:153-59 (1999). 21

M. Niinimaki et al., *Immediate Complications after Medical compared with Surgical Termination of Pregnancy*, OBSTET. GYNECOL. 114:795 (Oct. 2009). 20

PROPOSITION 2:

THE LEGISLATURE INTENDED TO REGULATE A POTENTIALLY DANGEROUS "ABORTION" PRACTICE—NOT TREATMENT FOR ECTOPIC PREGNANCY. 21

Cases

Blevins v. W.A. Graham Co., 72 Okla. 308, 309, 182 P. 247 (Okla. 1919). 21

State v. Haworth, 2012 OK CR 12, 283 P.3d 311 (Okla. 2012). 21

Statutes

63 OKLA. STAT. § 1-729a. 22

63 OKLA. STAT. § 1-729a(A)(1). 22

63 OKLA. STAT. § 1-730. 22

63 OKLA. STAT. § 1-730(A)(1). 22

CONCLUSION 24

CERTIFICATE OF SERVICE 25

STATEMENT OF INTEREST OF *AMICI CURIAE*[1]

The Majority of the Oklahoma Legislature

Amici Curiae include 27 Senators and 56 Representatives in the State of Oklahoma who voted for[2] and/or support House Bill (HB) 1970, codified at 63 OKLA. STAT. § 1-729a. As such, *Amici* represent the majority of both Chambers of the Oklahoma Legislature and present to this Court the intent of the Legislature in passing HB 1970.

This Court is presented with two certified questions from the United States Supreme Court arising out of the petition for certiorari filed with that Court in the above-captioned matter. The answers to those questions hinge on this Court's interpretation of House Bill (HB) 1970 pursuant to Oklahoma state law. HB 1970 requires that physicians who provide mifepristone (RU-486) or any other abortion-inducing drug to provide the drugs in the way approved by the FDA as explained in the drug label for RU-486 or the other abortion-inducing drug. As Legislators who voted for HB 1970, *Amici* have a vested interest in ensuring that this Court interprets HB 1970 in accordance with the intent of the Legislature and the plain meaning of the statute.

The first certified question asks whether HB 1970 prohibits the use of misoprostol to induce abortions, including the use of misoprostol in conjunction with mifepristone according to a protocol approved by the Food and Drug Administration. *Amici* urge this Court to answer that question in the negative in accordance with the intent of the Legislature and the reasonable interpretation of HB 1970 which allows the use of misoprostol for

---

[1] Per Okla. Sup. Ct. R. 1.12, *Amici* file this brief with consent of the parties.

[2] *Amici* include 21 Senators and 47 Representatives who were in office and voted in favor of HB 1970.

chemical abortions so long as misoprostol is administered as directed in the Mifeprex FPL, and prohibits the use of misoprostol in a manner not approved by the FDA.

The second certified question asks whether HB 1970 prohibits the use of methotrexate to treat ectopic pregnancies. Again, *Amici* urge the Court to answer this question in the negative in accordance with the intent of the Legislature and the reasonable interpretation of HB 1970, which allows the use of methotrexate to treat ectopic pregnancies because treatment of ectopic pregnancy is not "abortion."

Amici include Senators Greg Treat (sponsor of HB 1970 in the Senate), Cliff Aldridge, Mark Allen, Don Barrington, Brian Bingman (President Pro Tempore of the Senate), Josh Brecheen, Rick Brinkley, Corey Brooks, Bill Brown, Brian Crain, Nathan Dahm, Kim David, Eddie Fields, John Ford, AJ Griffin, Jim Halligan, Rob Johnson, Clark Jolley, Kyle Loveless, Mike Mazzei, Dan Newberry, Mike Schulz (Majority Floor Leader of the Senate), Wayne Shaw, Ralph Shortey, Frank Simpson, Rob Standridge, and Gary Stanislawski and Representatives Randy Grau (sponsor of HB 1970 in the House), Gary Banz, John Bennett, Scott Biggs, Lisa Billy, Gus Blackwell, David Brumbaugh, Dennis Casey, Mike Christian, Bobby Cleveland, Josh Cockroft, Donnie Condit, Marian Cooksey, David Dank, Lee Denney, David Derby, Jon Echols, John Enns, Dan Fisher, Elise Hall, Tommy Hardin, Arthur Hulbert, Mike Jackson (Speaker Pro Tempore of the House of Representatives), Dennis Johnson, Charlie Joyner, Sally Kern, James Lockhart, Scott Martin, Mark McBride, Mark McCullough, Randy McDaniel, Skye McNiel, Lewis Moore, Glen Mulready, Jason Murphey, Jason Nelson, Tom Newell, Jadine Nollan, Charles Ortega, Leslie Osborn, Pat Ownbey, Pam Peterson, Marty Quinn, Dustin Roberts, Sean Roberts, Mike Sanders, T.W. Shannon (Speaker of the House of Representatives), Jason Smalley, Todd

Thomsen, Mike Turner, Steve Vaughan, Ken Walker, Weldon Watson, Paul Wesselhoft, Justin Wood, and Harold Wright.

Americans United for Life Action

Amicus Americans United for Life Action (AULA) is the legislative action arm of Americans United for Life, a nonprofit, public-interest law and policy organization founded in 1971. Among other things, AULA provides expert legislative consultation to state legislators on issues involving abortion and its maternal health implications. AULA seeks to protect women from the harms inherent in abortion through the enactment and enforcement of commonsense abortion regulations. In this regard, AULA assisted the Oklahoma Legislature in drafting and enacting HB 1970 and has a particular interest in assuring that HB 1970 is upheld.

ARGUMENT[3]

As noted above, two questions have been certified to this Court from the United States Supreme Court which requires this Court to interpret HB 1970 pursuant to Oklahoma state law. Under general rules of statutory construction, courts look to the clear meaning of a statute, and *Amici* adopt the arguments presented in the State's brief on this point.

But this Court has also said that the "ultimate goal of statutory construction is to ascertain the intention of the Legislature." *See*, *e.g.*, *State v. Haworth*, 2012 OK CR 12, 283 P.3d 311, 315 (Okla. 2012). It is the longstanding practice of this Court to "look to each part of the statute in question, to other statutes on the same or related subjects, to the evils and mischiefs to be remedied by these provisions, and to the natural or absurd consequences of any particular interpretation." *Id*.; *see also Blevins v. W.A. Graham Co*., 72 Okla. 308, 309, 182 P. 247, 248 (Okla. 1919). To that end, *Amici* present to this Court the Legislature's intent in passing HB 1970. Through HB 1970, the Legislature [hereinafter "*Amici*"] sought to "remedy" or limit the serious risks women may face when abortion providers fail to abide by restrictions imposed by the U.S. Food and Drug Administration (FDA) on abortion-inducing drugs.

As to the first question—whether HB 1970 prohibits the use of misoprostol to induce abortions—as demonstrated herein, *Amici* did intend for HB 1970 to allow the use of misoprostol as long as it is administered as approved by the FDA and directed in the Mifeprex (RU-486) drug label. The Legislature intended to prohibit uses of misoprostol that are not approved by the FDA. As to the second question—whether HB 1970 prohibits the

[3] References to the specific exhibits in the record below are documented in the footnotes the first time a particular document or source is cited, where Respondents appeared as "Plaintiffs" and Petitioners appeared as "Defendants."

use of methotrexate to treat ectopic pregnancies—HB 1970 does not regulate any treatment for ectopic pregnancies. Specifically, *Amici* intended to regulate a potentially dangerous *abortion* practice—not the treatment for other medical circumstances such as ectopic pregnancies.

By way of background, there are two general categories of abortion: surgical and chemical (or medical). Surgical abortion involves the use of instruments to empty the uterus. Examples include aspiration as well as dilation and evacuation (D&E). According to the Guttmacher Institute, the majority of first trimester abortions are surgical abortions. *See* Guttmacher Institute, *Facts on Induced Abortion in the United States* (Aug. 2011).[4]

Chemical abortion, on the other hand, involves the use of abortion-inducing drugs. The recommended method of chemical abortion in the United States is commonly referred to as RU-486, but it is actually the combined use of two drugs: mifepristone (or RU-486) followed by a second drug, misoprostol. American College of Obstetricians and Gynecologists (ACOG), *ACOG Practice Bulletin 67 Medical Management of Abortion* (Oct. 2005).[5] In the United States, mifepristone is marketed under the brand name "Mifeprex," meaning that the terms "Mifeprex," "mifepristone," and "RU-486" are routinely used interchangeably when referring to the first drug in the regimen. *Mifeprex Final Printed Labeling* [hereinafter *Mifeprex FPL*].[6] Together, the administration of mifepristone and the

[4] Available at http://www.guttmacher.org/pubs/fb_induced_abortion.html.

[5] Appendix 4, Exhibit B to Plaintiffs' Motion for Summary Judgment.

[6] Appendix 6, Exhibit A to Plaintiffs' Motion for Summary Judgment; Exhibit V to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Also available at http://www.accessdata.fda.gov/drugsatfda_docs/label/2005/020687s013lbl.pdf (last visited Sept. 28, 2012).

second drug, misoprostol—the only method of chemical abortion approved by the FDA—is known as the "Mifeprex regimen" or the RU-486 regimen.

Despite the fact that the FDA approved a specific administration protocol for the use of mifepristone and misoprostol in the Mifeprex (RU-486) regimen, abortion providers routinely follow an unapproved protocol. This unapproved protocol has been associated with severe complications in some women.

According to the FDA, there have been more than 2,200 reported complications, or "adverse events," related to use of the RU-486 regimen, including 14 deaths. Eight deaths were the result of bacterial infection, and each death followed an unapproved use of the Mifeprex (RU-486) regimen. FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11* (July 2011).[7] Specifically, the women administered misoprostol either vaginally or bucally, as opposed to the FDA-approved oral use. *Id*. On the other hand, the FDA has not received a single report of a woman dying from bacterial infection following the FDA-approved oral use of misoprostol.

Concerned about the serious risks and the complications reported following misuse of the Mifeprex (RU 486) regimen, many state legislatures around the country sought to protect maternal health by requiring the administration of the regimen to follow the protocol approved by the FDA. In 2004, Ohio became the first state to enact such a law, and the Sixth Circuit Court of Appeals has determined that it does not pose an "undue burden." *See*

---

[7] Exhibit P to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Also available at http://www.fda.gov/downloads/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/UCM263353.pdf (last visited Sept. 28, 2012).

Planned Parenthood Southwest Ohio Region v. DeWine, 696 F.3d 490 (6th Cir. 2012) (one issue remains before the trial court).[8]

Then in 2011, *Amici* enacted House Bill (HB) 1970—a law *Amici* designed to protect women from the dangerous unapproved use of abortion-inducing drugs—to further its important and legitimate state interests in protecting maternal health. Specifically, HB 1970 requires that the Mifeprex (RU-486) regimen be administered in the way approved by the FDA. It does not ban the use of the Mifeprex (RU-486) regimen, nor does it ban the use of misoprostol when used as approved by the FDA. HB 1970 simply requires that the regimen—which the FDA approved to include both mifepristone and misoprostol—be administered in the way deemed safest by the FDA.

In October 2011, Respondents filed this facial attack in state court, seeking to deviate from the FDA approved use of the Mifeprex regimen. A preliminary injunction was issued shortly thereafter; a hearing on summary judgment was held on April 26, 2012; the trial court permanently enjoined the law on May 11, 2012; and appeal to this Court followed.

After this Court affirmed the trial court's decision on December 4, 2013, the State filed a petition for certiorari in the United States Supreme Court. On June 27, 2013, the U.S. Supreme Court granted partial certiorari, directing this Court to answer the following two questions: 1) whether HB 1970 prohibits the use of misoprostol to induce abortions, including the use of misoprostol in conjunction with mifepristone according to a protocol approved by the Food and Drug Administration, and 2) whether HB 1970 prohibits the use of methotrexate to treat ectopic pregnancies. Based upon the following, the answers to both of those questions must be "no."

[8] Similar laws have been enacted in Arizona and North Dakota. The law Arizona has not been challenged and is currently in effect; the law in North Dakota is in litigation.

Throughout this litigation, data has been presented outlining the risks associated with the Mifeprex (RU-486) regimen and the State's interest in protecting maternal health. That data, along with *Amici's* stated intent today, confirm that it was not the intention of *Amici* to prohibit all uses of misoprostol in the Mifeprex regimen, but only to prohibit a use of misoprostol that has not been approved expressly by the FDA and is not enumerated in the Mifeprex label. *Amici* sought to "remedy" a situation in which abortion providers were administering drugs in a potentially dangerous way and contrary to FDA restrictions. *See Haworth*, 2012 OK CR 12; *Blevins*, 72 Okla. 308. Likewise, it was not the intent of *Amici* to regulate the uses of any drugs (either as approved or off-label) for the treatment of ectopic pregnancy, because such treatment does not constitute an "abortion" under Oklahoma law. Any other interpretation would result in "absurd consequences." *See Haworth*, 2012 OK CR 12; *Blevins*, 72 Okla. 308.

Instead, it was the intent of *Amici* to restrict the use of the Mifeprex (RU-486) regimen like the FDA intended to restrict the use of the Mifeprex (RU-486) regimen. *See* Proposition 1.A., *infra*. It was also the intent of *Amici* to protect women from the potentially harmful effects linked to the misuse of the Mifeprex (RU-486) regimen. *See* Proposition 1.B, *infra*. Further, it was the intent of *Amici* to use their "wide discretion" to regulate an abortion method in accordance with their interest in protecting maternal health from the outset of pregnancy consistent with the prior decisions of the U.S. Supreme Court. *See* Proposition 1.C, *infra*. Finally, it was the intent of *Amici* to regulate a potentially dangerous "abortion" practice—not a treatment for ectopic pregnancy. *See* Proposition 2, *infra*.

PROPOSITION 1:

THE LEGISLATURE INTENDED FOR HB 1970 TO ALLOW THE USE OF MISOPROSTOL FOR CHEMICAL ABORTIONS SO LONG AS MISOPROSTOL IS ADMINISTERED AS DIRECTED IN THE MIFEPREX (RU-486) FPL.

A. The Legislature intended the use of the Mifeprex (RU-486) regimen to follow the FDA-approved protocol.

The FDA has established a protocol for the use of the Mifeprex (RU-486) regimen. As documented in the record, the FDA approved the Mifeprex regimen under "Subpart H," a special provision in the Code of Federal Regulations for drugs that "can be safely used ***only if*** distribution or use is ***restricted***." 21 C.F.R. § 314.520 (emphasis added).[9] Under Subpart H, the FDA can "require such postmarketing restrictions as are needed to assure safe use" of the drug approved. *Id*. To put this in perspective, out of almost 1,800 New Drug Applications (NDAs) approved between 1992 and 2011, only 70 were approved under Subpart H.[10] Subpart H approvals are rare, and unlike drugs approved under the normal

[9] Exhibit Q to Defendants' Response to Plaintiffs' Motion for Summary Judgment.

[10] *See* FDA, *CDER Drug and Biologic Accelerated Approvals as of September 30, 2011*, available at http://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/DrugandBiologicApprovalReports/UCM278506.pdf (last visited July 30, 2013); FDA, *Summary of NDA Approvals & Receipts, 1938 to the present* (2011), available at http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SummaryofNDAApprovalsReceipts1938tothepresent/default.htm (last visited July 30, 2013). While it is unclear from the FDA's documentation whether Subpart H drugs are excluded from its table of NDAs, *Amici* estimate conservatively that the NDAs listed in the table include any approved Subpart H drugs.

approval process, the use and distribution of Subpart H drugs is intended to be restricted by the FDA.[11]

Prior to approving the Mifeprex (RU-486) regimen, the FDA informed the drug sponsor (the applicant for FDA approval) that restrictions "on the distribution and use of mifepristone are needed to assure safe use" of the Mifeprex (RU-486) regimen. FDA, *Feb. 2000 Approvable Letter*.[12]

Prior to approval, the FDA also instructed the sponsor that it was "necessary" to use certain FDA-recommended language for the product's "final printed labeling" ("FPL"). *Id*. The FDA concluded that available data did not support the safety of home use of misoprostol and ***rejected*** the sponsor's suggestion that the FPL include information on self-administering misoprostol at home. U.S. Government Accountability Office ("GAO"), *GAO Report*, at 23.[13] In its September 2000 Approval Letter, the FDA reiterated that Subpart H restrictions apply when it concludes that a drug can be safely used only if its distribution or use is controlled to protect the safety of its users. FDA*, Sept. 2000 Approval Letter*.[14]

The FDA's Approval Letter clearly and unequivocally sets forth its Subpart H restrictions to assure safe use of the Mifeprex (RU-486) regimen. First, the Approval Letter requires the distribution and use of the Mifeprex (RU-486) regimen be under the supervision of a physician who has the ability to assess the duration of pregnancy, diagnose ectopic

---

[11] While the FDA lacks an enforcement role once it restricts Subpart H drugs, it undisputedly is the states' role to regulate the practice of medicine.

[12] Exhibit R to Defendants' Response to Plaintiffs' Motion for Summary Judgment.

[13] Appendix 3 to Plaintiffs' Motion for Summary Judgment. Also available at http://www.gao.gov/new.items/d08751.pdf (last visited Sept. 28, 2012).

[14] Exhibit S to Defendants' Response to Plaintiffs' Motion for Summary Judgment.

pregnancies, and provide surgical intervention (or have made plans to provide surgical intervention through other qualified physicians). *Id*.

Second, the FDA restricts the distribution and use of the Mifeprex (RU-486) regimen only after the physician signs a "Prescriber's Agreement," requiring the physician to follow certain guidelines, such as having the ability to assess the duration of pregnancy or diagnose ectopic pregnancies. *Id*. It also requires the physician to sign a "Patient Agreement." This is significant, because the physician and patient must attest that they are following certain provisions of the FPL.

The FPL[15] prescribes the following protocol:

- "Treatment with ***Mifeprex and misoprostol*** for the termination of pregnancy ***requires*** three office visits by the patient."

- "Mifeprex should be prescribed only in a clinic, medical office, or hospital, by or under the supervision of a physician, able to assess the gestational age of an embryo and to diagnose ectopic pregnancies."

- "Physicians must also be able to provide surgical intervention in cases of incomplete abortion or severe bleeding, or have made plans to provide such care through others, and be able to assure patient access to medical facilities equipped to provide blood transfusions and resuscitation, if necessary."

- On Day 1, the patient must read the Medication Guide, read and sign the Patient Agreement, and take three 200 mg tablets (600 mg) of mifepristone in a single dose.

- On Day 3, the patient ***is to return*** to the healthcare provider. "Unless abortion has occurred and has been confirmed by clinical examination or ultrasonographic scan," ***the patient is to take*** two 200 µg tables (400 µg) of ***misoprostol orally***.

[15] The September 2000 Approval Letter explained that the Mifeprex (RU-486) FPL includes the package insert, the Medication Guide, the Prescriber's Agreement, and the Patient Agreement. Each document is a part of the FPL. Sept. 2000 Approval Letter, *supra*.

- The patient is to return for a follow-up visit approximately 14 days after ingesting mifepristone in order to "confirm by clinical examination or ultrasonographic scan that a complete termination of pregnancy has occurred."

See Mifeprex FPL, *supra*, at 13-14 (emphasis added). Further, the FPL provides that the regimen is indicated only for the medical termination of intrauterine pregnancy through 49 days' pregnancy. It has no other approved indication for use during pregnancy. It "is not approved for ending later pregnancies." *Id*. at 5, 9, 10, 16, 19. Women should not use the regimen if "it has been more than 49 days (7 weeks) since" her last menstrual period began. *Id*. at 17.

Then in the "Patient Agreement," the patient and the physician must attest to the following:

- "I believe I am no more than 49 days (7 weeks) pregnant."
- "I understand that ***I will take misoprostol*** in my provider's office two days after I take Mifeprex (Day 3)."
- "I will do the following… return to my provider's office in 2 days (Day 3) to check if my pregnancy has ended. ***My provider will give me misoprostol*** if I am still pregnant."

"Patient Agreement" in *Mifeprex FPL*, *supra*, at 19.

Thus, the FDA requires that the patient and the physician sign an agreement to follow the FDA-approved protocol for the Mifeprex (RU-486) regimen. If the FDA did not intend for the patient to follow its approved regimen, it would make no sense for the patient and physician to sign such a document. And if physicians are signing the agreement and then providing the drugs to women past 49 days gestation and/or sending them home to self-

administer misoprostol, those physicians are breaching the agreement and causing their patients to do so as well.

Based upon the Subpart H approval and the FDA's restrictions, it is clear that the FDA intended to control the distribution and use of the Mifeprex regimen. Importantly, not only did the FDA mandate certain procedural requirements—including the "Patient Agreement" that outlines portions of the FDA-approved protocol for the Mifeprex regimen—but it also clearly *required* the use of misoprostol as the second drug in the Mifeprex regimen. Throughout the FPL, the FDA connects the use of mifepristone (or Mifeprex or RU-486) and misoprostol; the FDA did not approve the use of one without the other, and the protocol for using both is clearly outlined in the Mifeprex FPL and set forth in the "Patient Agreement." *See Mifeprex* FPL, *supra*, at 5, 11, 13-14, 16, 19.

This interpretation—that the FDA intended to restrict the use of the Mifeprex (RU-486) regimen to the protocol it outlined in the FPL—is affirmed by a memorandum published by the U.S. Department of Health and Human Services upon the approval of the Mifeprex (RU-486) regimen. Memorandum of Department of Health and Human Services to "NDA 20-687 MIFEPREX (mifepristone) Population Counsel" (Sept. 28, 2000).[16] In that memorandum, HHS discussed the necessity of adhering to the FPL, including the Agreements, in ensuring patient safety. For example, HHS stated that "[b]y coupling professional labeling with other educational interventions such as the Medication Guide, Patient Agreement, and Prescriber's Agreement, along with having physician qualification requirements of abilities to date pregnancies accurately and diagnose ectopic pregnancies

[16] Exhibit 10 to Declaration of Donna Harrison, M.D., Exhibit Y to Defendants' Response to Plaintiffs' Motion for Summary Judgment.

(and other requirements), goals of safe and effective use may be achieved." *Id*. at 2. In other words, HHS determined that the "goals of safe and appropriate use" of the regimen can be achieved through the FPL and physician requirements. *Id*.

Likewise, HHS stated that the Medication Guide (part of the FPL) will help "enhance compliance with the regimen for safety and efficacy." *Id*. at 4. The Medication Guide "will encourage patient adherence to directions for use. Patient ***adherence to directions for use and visits is critical to the drug's effectiveness and safety***." *Id*. (emphasis added). Similarly, HHS confirmed the importance of the "Patient Agreement," stating that the "signed agreement form will be given to the patient for her reference." *Id*. at 3. Because the Agreement would be useful as a "reference" only if a woman were using the protocol outlined, commonsense indicates that the FDA intended patients to follow the protocol outlined.

HHS also reported that the drug sponsor and the FDA identified areas that contribute to drug safety and effectiveness, including "***compliance with the regimen*** by physicians and patients through education and monitoring." *Id*. at 8 (emphasis added). Further, HHS stated that returning to the healthcare provider on Day 3 for misoprostol is a "***requirement***" that assures correct administration. *Id*. at 3 (emphasis added).

In order to achieve the patient safety intended by the FDA-approved protocol, HB 1970 states that no physician shall fail to provide or prescribe mifepristone or any abortion-inducing drug[17] according to the protocol authorized by the FDA and "as authorized in the drug label for RU-486 (mifepristone) or any abortion-inducing drug." 63 OKLA. STAT. § 1-729(a)(3). Thus, the clear language of the statute calls for physicians to use the regimen

[17] By including "any abortion-inducing drug" in the language, *Amici* were allowing room for the use of other chemical abortion methods that are approved by the FDA in the future.

approved by the FDA that is outlined in the RU-486 (mifepristone) drug label—which is the Mifeprex FPL. As already discussed, the Mifeprex FPL requires the use of misoprostol and outlines the FDA-approved administration of that drug. By referencing the Mifeprex FPL in the statute, the clear intent of *Amici* was for physicians to follow the Mifeprex FPL, including the FDA-approved use of both mifepristone and misoprostol. Based upon *Amici's* intent to restrict the Mifeprex (RU-486) regimen in the same manner in which the FDA restricted the regimen, this Court should conclude that misoprostol for chemical abortions is allowed so long as it is administered as approved by the FDA, but prohibited to terminate a pregnancy in any other manner.

B. The Legislature intended to protect women from the potentially harmful effects associated with the misuse of the Mifeprex (RU-486) regimen.

When the FDA approved the Mifeprex (RU-486) regimen in 2000, certain serious risks associated with the regimen were already known, and the regimen was contraindicated for women without adequate access to emergency care. Since that time, thousands of complications have been reported, and some of the most severe are associated with the use of the Mifeprex (RU-486) regimen contrary to the FDA-approved protocol. Abortion providers readily admit that they do not follow the protocol approved by the FDA. *Amici* intended to help protect women from some of the serious risks of harm by prohibiting any uses of abortion-inducing drugs that are not approved by the FDA.[18]

Even when the FDA-approved protocol is followed, the Mifeprex FPL states that "[n]early all of the women who receive ***Mifeprex and misoprostol*** will report adverse reactions, and many can be expected to report more than one such reaction." *Mifeprex FPL*,

[18] As discussed in Proposition 1.A., *supra*, the use of misoprostol was clearly comprehended and approved—indeed, required—by the FDA.

supra, at 11 (emphasis added). These risks include, but are not limited to, abdominal pain, cramping, vomiting, headache, fatigue, uterine hemorrhage, viral infections, and pelvic inflammatory disease. *Id*. at 5, 12.

Because the Mifeprex (RU-486) approved regimen is associated with serious risks, it is contraindicated for patients who do not have adequate access to medical facilities equipped to provide emergency treatment of incomplete abortion, blood transfusions, and emergency resuscitation during the period from the first visit until discharged by the administering physician. *Id*. at 5. For example, women are instructed that they should not take mifepristone (or Mifeprex or RU-486) if they cannot easily get such emergency help in the two weeks following ingestion of mifepristone, and ACOG admits that women are not good candidates for medical abortion if they cannot return for follow-up visits. *Id*. at 17; AGOG, *supra*, at 6.

Thus, in 2011 *Amici* were faced with a number of facts. The Mifeprex (RU-486) regimen had been approved with restrictions by the FDA, but abortion providers were not following the restrictions. The Mifeprex regimen was contraindicated for women lacking access to facilities that could provide emergency care, but abortion providers were providing the Mifeprex regimen to those very women. Thousands of complications related to use of the Mifeprex regimen had been reported, and the number of deaths from bacterial infection was higher than expected by the FDA. While direct causation had not been established, the deaths triggered the FDA to issue safety warnings and reiterate that there is only one approved protocol. Yet abortion providers continued to administer the Mifeprex (RU-486) regimen in a way that was linked to patient deaths. *Amici* were advancing a legitimate state interest, as well as "remedying" abortion providers' failure to abide by FDA restrictions, in

passing the Act to better ensure that no other women would die or be harmed as a result of the unapproved use of a dangerous abortion-inducing drug. Accordingly, this Court should conclude that HB 1970 does not prohibit misoprostol when used as approved by the FDA.

Following the enactment of HB 1970, in July 2011, the threat of serious complications following the Mifeprex (RU-486) regimen—and specifically the unapproved protocol—was confirmed. The FDA reported 2,207 adverse events in the U.S. after women used mifepristone for the termination of pregnancy. FDA, *Mifepristone U.S. Postmarketing Adverse Events Summary Through 04/30/11* (July 2011), *supra*. Among those were 14 deaths, 612 hospitalizations, 339 blood transfusions, and 256 infections (including 48 "severe infections"). *Id*. Of the 14 deaths, eight women died of severe bacterial infection. *Id*. All eight of those women used misoprostol in an off-label, unapproved manner. *Id*. Seven used the drug vaginally, and one used the drug buccally. *Id*. To the contrary, the FDA has not received a report of women dying from severe bacterial infection following use of the FDA-approved protocol. *Id*.

While *minor* complications arising after use of the Mifeprex regimen have been within the range expected, the U.S. Government Accountability Office has reported that the ***number of women dying from fatal infection is not within the expected range***. GAO, *supra*, at 38.[19] To be clear, the GAO was referring to those deaths from bacterial infection which we now know followed an unapproved use of misoprostol. Those deaths from bacterial infection were not expected by the FDA. Again, it was the misuse of misoprostol (*i.e.*, at-home vaginal or buccal use, as opposed to oral use in a clinic or physician's office)

[19] Appendix 4 to Plaintiffs' Motion for Summary Judgment.

linked to each of those deaths that *Amici* sought to prevent in order to better protect the lives of women in Oklahoma.

Respondents have claimed that the unapproved use of misoprostol did not cause the deaths from bacterial infection, but that is a mischaracterization of the facts. As early as 2006, after the first four women died from bacterial infection, the FDA issued a safety warning, noting that the deaths "involved the off-label dosing regimen" utilizing vaginal administration of misoprostol.[20] FDA, *Public Health Advisory: Sepsis and Medical Abortion* (Mar. 17, 2006).[21]

Rather than recommend the unapproved use of the Mifeprex regimen, the FDA has stated that "[t]he safety and effectiveness of other Mifeprex dosing regimens, including the use of oral misoprostol tablets intravaginally, has not been established by the FDA." FDA, *Mifeprex (mifepristone) Information* (July 19, 2011);[22] FDA, *Mifeprex Questions and*

---

[20] In response to concerns about these fatal infections, Planned Parenthood—the nation's largest abortion provider—stopped administering misoprostol vaginally. *See* M. Fjerstad et al., *Rates of Serious Infection after Changes in Regimens for Medical Abortion*, N.E.J.M. 361:145-51 (2009). Instead, Planned Parenthood began administering misoprostol buccally, which is also an unapproved use. *See id*. ACOG does not recognize buccal use as an appropriate administration. *See generally* ACOG, *supra*.

[21] Exhibit W to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Also available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/PublicHealthAdvisories/ucm051298.htm (last visited Sept. 28, 2012).

[22] Exhibit N to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Also available at http://www.fda.gov/drugs/drugsafety/postmarketdrugsafetyinformationforpatientsandproviders/ucm111323.htm (last visited Sept. 28, 2012).

Answers (Feb. 24, 2012);[23] FDA, *Public Health Advisory: Sepsis and Medical Abortion*, *supra*. Accordingly, the Legislature acted within its discretion and authority when it passed HB 1970 to protect the health of Oklahoma women by requiring the administration of the Mifeprex (RU-486) regimen to follow the FDA-approved protocol as set forth if the FPL.

C. The Legislature intended to use its "wide discretion" to regulate a method of abortion.

When there is uncertainty over the safety of a regulated abortion procedure, and other procedures that are considered to be safe alternatives are available, an abortion regulation cannot be invalid. *See Gonzales v. Carhart*, 550 U.S. 124 (2007); *Planned Parenthood v. Casey*, 505 U.S. 833 (1992). In fact, the U.S. Supreme Court has stated explicitly that state and federal legislatures are given "wide discretion to pass legislation in areas where there is medical and scientific uncertainty." *Gonzales*, 550 U.S. at 163.

This is exactly what *Amici* intended. There is a degree of medical uncertainty about the safety of the Mifeprex (RU-486) regimen when it is not followed. As already discussed, thousands of complications, including eight deaths from bacterial infection, have followed the unapproved uses of the Mifeprex regimen. There are no reported deaths from bacterial infection following the FDA-approved protocol. With causation not yet established, medical uncertainty over the safety of any off-label regimens persists.

The context in which the U.S. Supreme Court enunciated the "wide discretion" standard is significant here. After recognizing that the government "has an interest in protecting the integrity and ethics of the medical profession" and declaring that the state has

[23] Exhibit O to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Also available at http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm111328.htm (last visited Sept. 28, 2012).

a "significant role to play in regulating the medical profession," the Court stated, "[w]here it has a rational basis to act, and it does not impose an undue burden, the State may use its regulatory power to bar certain procedures and substitute others, all in furtherance of its legitimate interests in regulating the medical profession…." *Id*. at 157, 158.

Importantly, the Court concluded that "[p]hysicians are not entitled to ignore regulations that direct them to use reasonable alternative procedures. The law need not give abortion doctors unfettered choice in the course of their medical practice…." *Id*. at 163. In *Gonzales*, the medical uncertainty over whether the ban's prohibition created a significant health risk provided sufficient basis to conclude (in that facial attack) that the ban did not impose an undue burden. *Id*. at 164.

Simply put, when there is uncertainty over the safety of a regulated procedure and there is availability of other procedures that are considered to be safe alternatives, a law cannot be invalid on its face. *Id*. at 164-65. Here, *Amici* are regulating a procedure fraught with medical uncertainty. What is certain, however, is that nearly all women will experience adverse events following use of the Mifeprex (RU-486) regimen, and eight otherwise healthy women died from bacterial infection after using an unapproved protocol. *Amici* sought not to prohibit FDA-approved uses of misoprostol, but to require that physicians abide by the FDA-approved protocol. This in no way creates an undue burden. Chemical abortion through RU-486 remains an option as long as administered according to the FPL, and surgical abortion—considered "very safe" by the abortion industry—is available.[24]

[24] *Amici* previously documented in this Court that surgical abortion is safer than chemical abortion. For example, one study found that the overall incidence of immediate adverse events is fourfold higher for medical abortions than for surgical abortions. M. Niinimaki et al., *Immediate Complications after Medical compared with Surgical Termination of Pregnancy*, OBSTET. GYNECOL. 114:795 (Oct. 2009), in Exhibit 4 to Declaration of Donna

Moreover, *Amici's* actions comport with the U.S. Supreme Court's clear direction that states have an interest in protecting maternal health from the outset of pregnancy. In both *Gonzales* and *Casey*, the U.S. Supreme Court affirmed *Roe v. Wade*'s "essential" holding, which specifically included "the principle that the State has legitimate interests from the outset of pregnancy in protecting the health of the woman." *Gonzales*, 550 U.S. at 145; *Casey*, 505 U.S. at 846 (both citing *Roe v. Wade*, 410 U.S. 113 (1973)). *Roe* "was express in its recognition of the State's 'important and legitimate interests in preserving and protecting the health of the pregnant woman….'" *Casey*, 505 U.S. at 876-77. This principle must "coexist" with other principles outlined in *Roe*. *Gonzales*, 550 U.S. at 158.

PROPOSITION 2:

THE LEGISLATURE INTENDED TO REGULATE A POTENTIALLY DANGEROUS "ABORTION" PRACTICE—NOT TREATMENT FOR ECTOPIC PREGNANCY

As already stated, it was the intent of *Amici* to regulate a potentially deadly, unapproved abortion practice that has been associated with the deaths of at least eight women. *Amici* were regulating an abortion practice, not treatment of ectopic pregnancy. To interpret HB 1970 otherwise would lead to "absurd consequences" that are not in line with other Oklahoma statutes on "the same or related subjects" of abortion. *See Haworth*, 2012 OK CR 12; *Blevins*, 72 Okla. 308.

Harrison, M.D., Exhibit Y to Defendants' Response to Plaintiffs' Motion for Summary Judgment. Another study found that medical abortion failed in 18.3 percent of patients and that surgical abortion failed in only 4.7 percent of patients. J.T. Jenson et al., *Outcomes of Suction Curettage and Mifepristone Abortion in the United States: A Prospective Comparison Study*, CONTRACEPTION 59:153-59 (1999), in Exhibit 5 to Declaration of Donna Harrison, M.D., Exhibit Y to Defendants' Response to Plaintiffs' Motion for Summary Judgment.

First, HB 1970 was drafted to address the termination of pregnancy through abortion. "Abortion-inducing drugs" is defined to include "a medicine, drug, or any other substance prescribed or dispensed ***with the intent of terminating the clinically diagnosable pregnancy*** of a woman, with knowledge that the termination shall with reasonable likelihood cause the death of the unborn child." 63 OKLA. STAT. § 1-729a(A)(1) (emphasis added). Further, the definition provides that it does not apply to drugs "that may be known to cause an abortion, but which are prescribed for other medical indications…." *Id*. *Amici's* clear focus was on regulating abortion, not on regulating any other obstetrics-related procedures.

Second, Oklahoma law clearly excludes treatment of ectopic pregnancy from the definition of "abortion." HB 1970 was codified at 63 OKLA. STAT. § 1-729a. It is part of Subsection C on "Abortions" in Article 7 on "Hospitals and Related Institutions." In addition to § 1-729a, Subsection C includes a section of applicable definitions, codified at § 1-730. In that section, "abortion" is defined as "the use or prescription of any instrument, medicine, drug, or any other substance or device ***intentionally to terminate the pregnancy*** of a female known to be pregnant with an intention ***other than … to remove an ectopic pregnancy***…." 63 OKLA. STAT. § 1-730(A)(1) (emphasis added). Both "abortion" and "abortion-inducing drugs" require intent to terminate pregnancy. That intent is missing when the purpose is to treat an ectopic pregnancy, and the Oklahoma Statutes make it crystal clear that treatment for ectopic pregnancy is not an abortion.

Amici's clear focus on regulating "abortion" and the Oklahoma Statutes' explicit exclusion of ectopic pregnancy in its definition of "abortion" make clear that HB 1970 does not prohibit the use of methotrexate to treat ectopic pregnancies. Physicians are free to use

any drugs—as approved or off-label—to treat ectopic pregnancies. This Court should answer that HB 1970 does not prohibit methotrexate for the treatment of ectopic pregnancy.

CONCLUSION

Amici intended for HB 1970 to allow the use of misoprostol for chemical abortions so long as misoprostol is administered as directed in the Mifeprex FPL, with only uses of misoprostol not approved by the FDA prohibited. *Amici* intended to regulate abortion, which by definition excludes any treatment for ectopic pregnancy.

In answering whether HB 1970 prohibits the use of misoprostol to induce abortions, including the use of misoprostol in conjunction with mifepristone according to a protocol approved by the Food and Drug Administration, this Court must answer that HB 1970 allows the use of misoprostol for chemical abortions so long as misoprostol is administered as directed in the Mifeprex (RU-486) FPL, but prohibits uses of misoprostol not approved by the FDA.

In answering whether HB 1970 prohibits the use of methotrexate to treat ectopic pregnancies, this Court must answer HB 1970 does not affect treatment for ectopic pregnancy because treatment of ectopic pregnancy is not "abortion."

Respectfully submitted,

Randy Grau, OBA #19109
Cheek & Falcone, PLLC
6301 Waterford Boulevard, Suite 320
Oklahoma City, Oklahoma 73118
Telephone (405) 286-9191
Facsimile (405) 286-9670

Counsel for Amici Curiae

CERTIFICATE OF SERVICE

I hereby certify that on _____, 2013, a true and correct copy of the foregoing instrument was sent by email and U.S. mail, postage prepaid, to the following:

Michelle Movahed*
New York Bar Registration No. 4552063
Illinois Bar No. 62918636
Center for Reproductive Rights
120 Wall St., 14th Floor
New York, NY 10005-3904
Telephone: (917) 637-3600
Facsimile: (917) 637-3666
Email: mmovahed@reprorights.org
* *Admitted pro hac vice*

Patrick R. Wyrick, OBA #21874
Solicitor General
313 NE 21st Street
Oklahoma City, OK 73105
Telephone: (405) 522-4448
Facsimile: (405) 522-0669
Email: patrick.wyrick@oag.ok.gov

_____
Randy Grau, *Counsel for Amici Curiae*