Drug developers caution against US mifepristone ban

A lawsuit against the FDA embroils pharmaceutical companies in debates over access to abortion. Susan Jaffe reports from Washington, DC.

Less than 1 year after the US Supreme Court ended its 1973 constitutional guarantee to an abortion and told state lawmakers that they could decide whether a person ends their pregnancy, abortion is now back before the court. But this fresh legal challenge has dragged the nation's entire drug approval system along with it, rousing a powerful lobbying group and economic force that has mostly managed to avoid the fray—the pharmaceutical industry.

A preliminary ruling by federal court Judge Matthew Kacsmaryk on April 7, 2023, removed US Food and Drug Administration (FDA) approval of mifepristone—a drug commonly used to end pregnancy—in a lawsuit filed by the Alliance for Hippocratic Medicine, a coalition of anti-abortion groups, three other organisations, and three doctors. This is the first time that a federal court has overturned the FDA's approval of a drug. As *The Lancet* goes to press, his ruling was being appealed. If it takes effect, his decision would ban mifepristone across the USA, including in so-called abortion haven states.

Kacsmaryk, appointed by former President Donald Trump and known for his anti-abortion views, supported claims that mifepristone was unsafe and that the FDA should not have approved it 23 years ago. The lawsuit was filed just 10 months after the Supreme Court's, June, 2022, decision in Dobbs *v* Jackson Women's Health Organization eliminated abortion rights at the federal level established under Roe *v* Wade.

"It's no accident that this case ended up before a judge who was willing to follow wherever abortion opponents led him", Jennifer Dalven, Director of the American Civil Liberties Union Reproductive Freedom Project, told reporters. "The group that brought this case had no connection to Amarillo, Texas, where the case was filed", she said, adding that Texas prohibits abortion, including the use of mifepristone.

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"This lawsuit was manufactured by anti-abortion advocates and based on biased anecdotes and junk science", said Jenny Ma, Senior Counsel at the Center for Reproductive Rights, which represented the abortion clinic at the centre of the Dobbs decision. "This is another step in taking away the bodily autonomy of pregnant people and an attempt to end abortion in every single state."

Almost 53% of the abortions provided in the USA in 2020 were drug-induced abortions, according to the Guttmacher Institute. Mifepristone is used for drug-induced abortions in approximately 80 countries, including the UK, Sweden, and France.

Nevertheless, the Alliance for Hippocratic Medicine claims "mifepristone is a dangerous drug and it's hurting women", according to Donna Harrison, an obstetrician–gynaecologist and the group's chairperson. "We believe that the safest thing for women is to get this drug off the market."

Kacsmaryk also agreed with the plaintiffs' arguments that sending mifepristone to people was prohibited by the 1873 Comstock Act, a largely ignored federal anti-obscenity law that bans mailing drugs or other products or materials used for an abortion.

The Biden Administration quickly appealed Kacsmaryk's decision to the 5th Circuit Court of Appeals. A panel of three judges temporarily restored FDA approval, but rolled back conditions expanding access that the FDA has added since 2016 in response to new scientific studies. Without these conditions, mifepristone can be prescribed for up to 7 weeks of pregnancy instead of 10 weeks and requires three in-person doctor visits. The drug can not be mailed to patients.

Mifepristone is usually part of a two-drug regimen and is prescribed to end a pregnancy. The second drug, misoprostol, makes the uterus expel the products of conception. Misoprostol alone can also be used safely, although the process is completed in less time when combined with mifepristone. Kacsmaryk's decision does not apply to misoprostol, which is also used to manage miscarriages, induce labour, treat post-partum haemorrhage, and prevent stomach ulcers.

"The FDA did not follow its own regulations and governing rules when it allowed mifepristone on the market in 2000", Denise Harle, one of the Alliance for Hippocratic Medicine attorneys, told *The Lancet*. She said the FDA approved mifepristone under a programme used for life-saving medications and, to use this process, it "categorised pregnancy as an illness and claimed that the abortion drug provides a therapeutic benefit".

Harrison added that as many as 5% of people who take mifepristone require an "additional [surgical] procedure to remove remaining tissue or terminate a pregnancy". Surgical intervention at that rate is "by definition, a severe complication". However, Harrison and Harle did not know if any people or their families had sued the drug's manufacturer or the FDA for damages.

The FDA has estimated that as of June, 2022, 5·6 million people had taken mifepristone for an abortion since 2000. Of 4213 adverse events among people who took the drug, only 28 deaths occurred during

that time. Other complications included hospitalisation, blood loss requiring transfusion, and infections. However, the FDA could not establish if mifepristone caused these complications due to a lack of information about people's health status and other factors.

Less than 1 h after the April 7, 2023, decision, a federal court judge in Washington state ordered the FDA not to change its mifepristone approval. The ruling came in a lawsuit filed by 17 states and the District of Columbia to ensure that the agency would not restrict access to medications for abortion. The judge, Thomas Rice, issued a second decision 4 days later at the request of the Biden Administration stating that his order prevents the FDA from complying with the Texas court order.

After these two unprecedented and conflicting decisions, the Biden Administration asked the Supreme Court to suspend the Kacsmaryk injunction while it is under appeal. "We will be seeking emergency relief from the Supreme Court to defend the FDA's scientific judgment and protect Americans' access to safe and effective reproductive care", Attorney General Merrick Garland said in a statement.

Justice Samuel Alito, who oversees emergency appeals from the 5th district, responded by restoring full access to the drug and halting Kacsmaryk's order until April 20, 2023. As *The Lancet* goes to press, the Supreme Court has not decided what should happen once that deadline passes.

Should the Supreme Court eventually uphold Kacsmaryk's order, it would do more than overrule those states that allow drug-induced abortion. It would also go a long way towards achieving nationwide abortion restrictions, an option the Supreme Court rejected in the Dobbs decision. Access to abortion varies widely across the USA and, in some places, is still uncertain. According to the Guttmacher Institute, as of April 16, 12 states have full access to abortion, and 12 states ban abortion between 6 weeks and 22 weeks. There are no gestational limits on abortion in six states and the District of Columbia. New York officials bought billboards adverts in Florida, Texas, and Georgia, where abortion is restricted, to remind residents of those states that "Abortion is safe + legal for all in New York City". The message was accompanied by a drawing of the Statue of Liberty.

North Carolina bans abortions after 20 weeks of pregnancy, even though serious complications can develop a few weeks later. When a wanted pregnancy cannot be sustained or endangers the mother's life after 20 weeks, abortion is not an option, said Nicole Teal, a specialist in maternal–fetal medicine in North Carolina. She sees patients in these "heartbreaking situations" every week. People who cannot afford to get an abortion in another state are forced to continue a pregnancy that is dangerous to them. "The increasing restrictions on abortion are tying my hands and that feels unethical", she said. "It's infuriating to have politicians interfering in this way."

Pharmaceutical manufacturers and investment firms vigorously defended the FDA in an amicus curiae brief urging the Supreme Court to block Kacsmaryk's decision. "Congress intended FDA, not the courts, to serve as the expert arbiter of drugs' safety and effectiveness", 272 company executives wrote. "FDA's drug-approval process is the gold standard of scientific review."

The Pharmaceutical Research and Manufacturers of America, which represents drug makers and biotech research companies, also asked the Supreme Court to uphold the FDA's mifepristone approval. Among the arguments in its amicus curiae brief, the group claimed that the plaintiffs had no basis for suing FDA because they have not proven how they were injured by the drug or the FDA's approval process.

Advocates for biomedical research are also concerned about the ramifications of the mifepristone lawsuit. "If we allow legal manoeuvring to supersede the role of the FDA, we risk jeopardising Americans' access to other treatments the FDA has concluded are safe and effective", said Mary Woolley, President and CEO of Research!America, an alliance of research institutes, medical centres, scientific societies, and patient advocacy groups.

If the Alliance for Hippocratic Medicine wins its lawsuit, Harle said that would not inhibit drug development by other companies. "I don't see any reason for them to be concerned, so long as they go through the proper FDA process", she said, and provide sufficient research to support the safety of their product. "Everything should just be fine."

Republicans in Congress have been mostly silent on this latest abortion court battle, even avoiding media requests for comment in stark contrast to their cheers for the Dobbs decision. An amicus curiae brief filed with the 5th Circuit Court of Appeals in support of the Kacsmaryk decision garnered signatures from only 69 Republican members of the Senate and the House of Representatives. By comparison, 253 Democratic Senate and House members filed an amicus curiae brief with the Supreme Court, urging it to support the FDA.

Democratic governors in California, Massachusetts, New York, Washington, and other states are taking emergency steps to stockpile misoprostol in the event that its availability is also jeopardised. New York Governor Kathy Hochul said the state would purchase a 5-year supply of misoprostol, enough to meet the anticipated demand for 150 000 abortions. California has already acquired 250 000 of the 2 million pills it plans to purchase, according to Governor Gavin Newsom. "We will not cave to extremists who are trying to outlaw these critical abortion services", he said.

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