

News in focus

or predict how proteins fold. Whereas symbolic AI is inherently rigorous, neural networks can only make statistical guesses, and their operations are often mysterious.

De Moura helped symbolic AI to score some early mathematical successes by creating a system called Lean. This interactive software tool forces researchers to write out each logical step of a problem, down to the most basic details, and ensures that the maths is correct. Two years ago, a team of mathematicians succeeded in translating an important but impenetrable proof – one so complicated that even its author was unsure of it – into Lean, thereby confirming that it was correct.

The researchers say the process helped them to understand the proof, and even to find ways to simplify it. “I think this is even more exciting than checking the correctness,” de Moura says.

As well as making solitary work easier, this sort of ‘proof assistant’ could change how mathematicians work together by eliminating what de Moura calls a “trust bottleneck”. “When we are collaborating, I may not trust what you are doing. But a proof assistant shows your collaborators that they can trust your part of the work.”

Sophisticated autocomplete

At the other extreme are chatbot-esque, neural-network-based large language models. At Google in Mountain View, California, former physicist Ethan Dyer and his team have developed a chatbot called Minerva, which specializes in solving maths problems. At heart, Minerva is a very sophisticated version of the autocomplete function on messaging apps: by training on maths papers in the arXiv repository, it has learnt to write down step-by-step solutions to problems in the same way that some apps can predict words and phrases. Unlike Lean, which communicates using something similar to computer code, Minerva takes questions and writes answers in conversational English. “It is an achievement to solve some of these problems automatically,” says de Moura.

Minerva shows both the power and the possible limitations of this approach. For example, it can accurately factor integer numbers into primes – numbers that can’t be divided evenly into smaller ones. But it starts making mistakes once the numbers exceed a certain size, showing that it has not ‘understood’ the general procedure.

Still, Minerva’s neural network seems to be able to acquire some general techniques, as opposed to just statistical patterns, and the Google team is trying to understand how it does that. “Ultimately, we’d like a model that you can brainstorm with,” Dyer says. He says it could also be useful for non-mathematicians who need to extract information from the specialized literature. Further extensions

will expand Minerva’s skills by studying textbooks and interfacing with dedicated maths software.

Dyer says the motivation behind the Minerva project was to see how far the machine-learning approach could be pushed; a powerful automated tool to help mathematicians might end up combining symbolic AI techniques with neural networks.

Maths v. machines

In the longer term, will programs remain part of the supporting cast, or will they be able to conduct mathematical research independently? AI might get better at producing correct mathematical statements and proofs, but some researchers worry that most of those would be uninteresting or impossible to understand. At the October symposium, Gowers said that there might be ways of teaching a computer some objective criteria for mathematical relevance, such as whether a small statement can embody many special

cases or even form a bridge between different subfields of maths. “In order to get good at proving theorems, computers will have to judge what is interesting and worth proving,” he said. If they can do that, the future of humans in the field looks uncertain.

Computer scientist Erika Abraham at RWTH Aachen University in Germany is more sanguine about the future of mathematicians. “An AI system is only as smart as we program it to be,” she says. “The intelligence is not in the computer; the intelligence is in the programmer or trainer.”

Melanie Mitchell, a computer scientist and cognitive scientist at the Santa Fe Institute in New Mexico, says that mathematicians’ jobs will be safe until a major shortcoming of AI is fixed – its inability to extract abstract concepts from concrete information. “While AI systems might be able to prove theorems, it’s much harder to come up with interesting mathematical abstractions that give rise to the theorems in the first place.”

US LAWSUIT THREATENS ACCESS TO ABORTION DRUG

Nature explains the science behind the case, which could weaken the FDA’s regulatory authority.

By Mariana Lenharo

A lawsuit in Texas not only has the potential to ban a popular abortion drug across the United States – but could also set a dangerous precedent by overturning the approval of a medication by the US Food and Drug Administration (FDA).

Following the reversal of *Roe v. Wade* last year, some US states have banned abortions, driving more pregnant people to seek medication abortions. The lawsuit against the FDA, brought by anti-abortion groups and physicians, seeks to overturn the agency’s approval of the abortion drug mifepristone, which happened in 2000. The plaintiffs allege that mifepristone, which is used in combination with another drug, misoprostol, is not safe – a claim that is not corroborated by the scientific evidence, say researchers who spoke to *Nature*. Legal specialists think there is a good chance that the judge deciding the case, Matthew Kacsmaryk in the US District Court for the Northern District of Texas, will rule in favour of the plaintiffs. Appointed by former US president Donald Trump, who promised to

help overturn *Roe*, Kacsmaryk “has deep ties to the religious right, and he has issued rulings that are based on very, very conservative ideologies”, says Amanda Allen, an attorney and director of The Lawyering Project, an organization based in New York City that works to improve abortion access.

The effects of this case might reverberate across the country, further affecting health care for pregnant people. “If the plaintiffs get what they’re asking for, mifepristone will be banned in all states – it doesn’t matter if the state has a law in place that protects access to abortion,” Allen says.

Here, *Nature* explains the evidence in the case, what’s on the line and what abortion options will be available to people in the United States if the FDA loses.

Is mifepristone safe?

All the evidence suggests that the answer is yes, contrary to what the plaintiffs argue. A 2013 systematic review published in the journal *Contraception*, for example, found that failure to terminate a pregnancy occurred in fewer than 5% of pregnant people who had taken mifepristone combined with misoprostol, and



Mifepristone and misoprostol are usually used in combination to terminate a pregnancy.

only 0.3% of people were hospitalized after the treatment (E. G. Raymond *et al. Contraception* **87**, 26–37; 2013). The World Health Organization (WHO) lists the regimen as safe, and so does the American College of Obstetricians and Gynecologists (ACOG).

The plaintiffs also allege that the FDA made a mistake when it approved the drug in 2000, and a generic version in 2019. They say that the agency approved the drug using an accelerated process that required it to consider pregnancy an ‘illness’, for which the abortion drug would provide a ‘meaningful therapeutic benefit’. “But pregnancy is not an illness,” the plaintiffs state in their complaint.

In response to the lawsuit, the FDA’s attorneys have written that mifepristone’s approval did not involve an accelerated review (the approval process took four years). They also said that the plaintiffs do not provide any concrete example of a patient who might have suffered serious adverse events associated with mifepristone. “That omission is particularly telling, given the more than two decades that mifepristone has been in use,” the court filing says.

If the FDA loses, can people seeking abortion still use misoprostol?

Although the combination of mifepristone and misoprostol is the most commonly prescribed regimen for medication abortion in the United States, both the ACOG and the WHO say that using misoprostol by itself is a safe and effective alternative.

“Mifepristone gets so much attention because it was approved as an abortion drug,” says Cari Sietstra, a specialist in reproductive health and justice and principal consultant at Innovations in Reproductive Health Access, a

non-profit organization based in Emeryville, California. It was designed to block progesterone, a hormone needed for pregnancy to continue. Misoprostol was originally approved for preventing gastric ulcers. But researchers realized that it causes the uterus to contract, bleed and expel any embryo inside.

So it is an option for medication abortion, says Heidi Moseson, an epidemiologist based in Oakland, California, who works at Ibis Reproductive Health, a global research organization that supports abortion rights. “It’s just that clinicians in the United States have less experience providing it, because for so long the default has been the combined regimen,” she says.

“Make no mistake, the plan here is to end access to medication abortion for everyone in this country.”

Moseson was the first author of a study published last year that looked into the effectiveness and safety of medication abortion with misoprostol alone or in combination with mifepristone (H. Moseson *et al. Lancet Glob. Health* **10**, E105–E113; 2022). The study, which followed 961 people who self-managed abortions in Argentina and Nigeria, found that 99% of those who used misoprostol alone had a complete abortion without needing surgical intervention. Among those who used the combined regimen, the rate was 94%.

Another reason why misoprostol isn’t often administered on its own is that some clinical trials have shown that it has a lower success rate, Moseson says. But that’s probably

because of differences in study design and local conditions, she adds. In some studies, if after a few days of taking misoprostol the abortion is not complete, participants are offered a surgical abortion. This would then be registered as an unsuccessful use of the drug. In settings where surgical intervention isn’t readily available, the success rates tend to be higher, Moseson says.

The other issue is that some of the previous studies that evaluated misoprostol alone did not use the dosing scheme that is currently endorsed by the WHO. “There’s a lot of variation both in the results and in the regimens that are used,” says Daniel Grossman, director of Advancing New Standards in Reproductive Health, a social-sciences research group at the University of California, San Francisco.

Could misoprostol eventually be banned?

It’s possible. In addition to requesting the ban of mifepristone, the Texas lawsuit invokes an 1873 law, the Comstock Act, which is still a part of the US Code. This act made it illegal to send obscene materials or articles intended for “producing abortion” through the mail. The legal team for the plaintiffs hopes to use this to prohibit the distribution of all abortion drugs by mail.

“Their first stop in this lawsuit is to go after mifepristone. But, make no mistake, the plan here is to end access to medication abortion for everyone in this country,” says Allen.

The precedent set by a court overturning an FDA approval could endanger misoprostol, too – as well as many other medications, including birth-control pills, COVID-19 vaccines and more.

“This really threatens the FDA’s authority over the approval process for medications across the board,” says Allen. “It really kind of flies in the face of the idea that the FDA is there because they’re the ones who have the scientific and medical expertise to make these decisions, not courts.”

What happens next?

As *Nature* went to press, Kacsmaryk was poised to deliver a decision. What happens next will depend on the ruling. If Kacsmaryk agrees with the plaintiffs, it could trigger an immediate ban on mifepristone, or he could order the FDA to take certain steps. In the latter case, “nothing would really happen until those steps were taken. So, we’re really in a state of just waiting and seeing,” Allen says.

If such a decision were to be appealed, it would land in the US Court of Appeals for the Fifth Circuit, “one of the most conservative appellate courts in the country”, according to Allen. Assuming that the court upheld this theoretical decision by Kacsmaryk to ban mifepristone, the next option would be for the FDA to take the case to the Supreme Court.