What the Moderna–NIH COVID vaccine patent fight means for research

Vaccine collaborators are locked in a high-stakes dispute over which researchers should be named as inventors on a key patent application.

It was a testament to the power of collaboration: scientists at the biotechnology firm Moderna Therapeutics teamed up with government researchers at the US National Institutes of Health (NIH) to swiftly produce one of the world's first successful COVID-19 vaccines.

But a boiling patent dispute between the collaborators also showcases the complexities of teamwork, as the two groups battle over whether NIH researchers were unfairly left off as co-inventors on a pivotal vaccine patent application.

The stakes are high. Moderna, which is based in Cambridge, Massachusetts, has projected that it will make up to US$18 billion on its COVID-19 vaccine this year. Inventor status could enable the NIH to collect royalties — potentially recouping some of its investment of taxpayer money — and to license the patent as it sees fit, including to competing vaccine makers in low- and middle-income countries, where vaccines are still painfully scarce.

Nature looks at four key questions about the patent spat and its potential ripple effects for collaborations between government and industry.

Moderna's COVID-19 vaccine is at the centre of a patent dispute that could potentially affect future public–private collaborations.

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What are Moderna and the NIH fighting about?

Before the COVID-19 pandemic struck, the NIH and Moderna collaborated on the development of vaccines for other coronaviruses. So, when the news of the SARS-CoV-2 outbreak reached them, it was only natural that they work together on producing a vaccine.

The vaccine they created contains messenger RNA that encodes a modified form of the SARS-CoV-2 spike protein. The modifications were intended to hold the protein in a stable conformation that was deemed likely to trigger an immune response. The NIH has stated in the past that these modifications were developed by researchers at its National Institute of Allergy and Infectious Diseases and other collaborators, and it described analogous modifications in another coronavirus in 2017 (J. Pallesen *et al*. *Proc. Natl Acad. Sci. USA* **114**, E7348–E7357; 2017).

In drug and vaccine development, it is common for inventors to file multiple patents — often dozens or more — to cover different aspects of a single product. Moderna has filed several patent applications on its COVID-19 vaccine that name NIH investigators as co-inventors.

> **"With this patent, you could imagine the magnitude of the importance of making sure it is correct."**

But some of its patent applications do not, including at least one that claims the mRNA sequence used in the vaccine. In an August statement to the US Patent and Trademark Office, Moderna acknowledged that the NIH had submitted three of its researchers as co-inventors, but stood by its decision to exclude them from the application.

The company argues that its researchers developed the mRNA sequence for the vaccine independently. NIH researchers, however, have said that they helped to develop the sequence.

The patent in question could be particularly crucial because it covers the principal component of the vaccine, says Christopher Morten, who specializes in intellectual-property law at Columbia Law School in New York City: "A claim on the active ingredient in a pharmaceutical product is important, because it can be impossible for competitors to design around it."

Is it unusual for collaborators to fight over inventor status on a patent?

Disputes over who deserves to be credited on a patent are common, particularly in collaborations between institutions, says Rebecca Eisenberg, who studies patent law

and biopharmaceutical regulation at the University of Michigan Law School in Ann Arbor. There can be different ways of defining an invention, for example, or patents can be structured such that they include only one group's contribution. "Whoever drafts the application tends to draft around what they've done," she says.

An inventor is defined by US patent law as someone who aids in the conception of the invention. Individual inventors at universities and government agencies, and in company laboratories, often assign their patent rights to the institution that they work for. But when it comes to collaborations, it can be difficult to agree up front who will be named as an inventor on the patent. "You can address in advance who's going to own the patent rights, but you can't necessarily specify who is going to be an inventor," says Eisenberg.

In the 1990s, the NIH was involved in a patent dispute with industry collaborators over the development of the HIV drug AZT. Two generics makers that wanted to challenge AZT patents argued that NIH researchers had been unfairly omitted from some of them — in which case, the patents could have been rendered invalid, or the NIH would have had the right to license them. But the court sided with the pharmaceutical companies, which argued that they had already prepared their patent application before using the NIH's assay. The analysis, they said, simply confirmed the value of something that they had already invented.

The NIH lost the AZT case, but that does not mean it is at a disadvantage in this one, says Eisenberg: "Every case is idiosyncratic."

Will the debate affect future public–private partnerships?

The US government has a reputation for not aggressively enforcing its patent rights, says Chad Landmon, a patent attorney at the law firm Axinn, Veltrop & Harkrider in Hartford, Connecticut. Instead, the government often funds early-stage research, and then largely leaves it to industry partners to manage intellectual property on later stages of an invention. Pharmaceutical companies often invest heavily — sometimes hundreds of millions of dollars — in the final development of a therapy; the government has generally considered the benefit to taxpayers to be the main reward for funding early research.

But political sentiment on this could be shifting, Landmon says. Several of the Democratic candidates in the 2020 US presidential election — including Kamala Harris, now vice-president — pushed for the government to become more assertive about intellectual property, particularly if, by doing so, it could rein in the prices of prescription drugs. And in 2019, the government took the unusual step of suing Gilead Sciences in Foster City, California, for infringing government patents in the production of HIV-prevention drugs.

> **"It might lead companies to be pickier when deciding if they are going to collaborate with the government."**

Then came the COVID-19 pandemic, and concerns that patents could restrict vaccine production. At a meeting of the World Trade Association in May, the United States made a surprise announcement that it supported waiving patent protection on COVID-19 vaccines.

This, plus the NIH's outcry over its exclusion from the Moderna patent, could suggest that the government will take a more active stance in managing intellectual property, Landmon says: "My general sense is that it's pointing in that direction."

In 2020, Morten and a collaborator analysed patents on the antiviral drug remdesivir, which has been used as a treatment for COVID-19. They determined that government researchers had probably contributed to the drug's development but had been left off the patents. A subsequent government investigation, however, concluded that the scientists' work had not contributed to the inventions in the patents.

If the government does become tougher about licensing patents, "it might lead companies to be pickier in terms of deciding if they are going to collaborate with the government", says Landmon.

Any change in government policy is unlikely to happen rapidly, says Ana Santos Rutschman, who specializes in health law at Saint Louis University in Missouri. But she thinks that a change could be on the horizon. "At the end of the day, it's not just about this particular patent," she says. "Public scrutiny is as important as legal scrutiny."

What happens now?

In November, NIH chief Francis Collins was quoted by Reuters news agency as saying that the patent dispute was not yet over. "Clearly this is something that legal authorities are going to have to figure out," he said.

Moderna has said that it offered the NIH co-ownership of the patent in September, and that the agency could then license the patent "as they see fit". But this is different from inventor status: terms of co-ownership would need to be negotiated, and could come with strings attached, says Morten. The NIH might also want its scientists on the patent for scientific credit or political reasons, says Lisa Ouellette, who specializes in vaccine production and patent law at Stanford Law School in California.

The NIH could choose to bring a lawsuit and argue in court that Moderna inappropriately left off NIH researchers. If the court determines that the NIH is correct, and that the omission was an unintentional oversight, the patent might be corrected. But if the court finds that Moderna knowingly deceived the patent office about the NIH's contribution, the patent would no longer be valid.

Such a case could involve poring over lab notebooks to find out when Moderna investigators determined the mRNA sequence used in the vaccine, and whether this pre-dated the NIH team sharing its sequence with the company, says Morten.

The potential impact of the case on vaccine production is uncertain. Moderna has already said that it will not enforce its patents on its COVID-19 vaccine during the pandemic, and patents are generally not the key hurdle to vaccine production, says Ouellette.

Still, given the unusually high stakes in this dispute, it is likely that any decision would prompt an appeal — potentially all the way to the US Supreme Court — and the battle could drag out for years.

"With this patent, you could imagine the magnitude of the importance of making sure it is correct," says Joy Goswami, a technology-transfer officer at the University of Delaware in Newark. "This is probably going to be a long run."

By Heidi Ledford