

THE NIH VACCINE

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INTRODUCTION

The U.S. government may jointly own a potential coronavirus vaccine. The National Institutes of Health (NIH) has played a critical role in coronavirus research for years.¹ Building off this work, federal scientists have helped design and test mRNA-1273—a vaccine candidate developed in partnership with Moderna.²

The federal government has filed multiple patents covering mRNA-1273. In this report, we describe two patent applications that list federal scientists as co-inventors.³ If the government successfully pursued its patent filings, the resulting patents would likely confer significant rights. We also review recently disclosed contracts between NIH and Moderna. The agreements suggest that NIH has not transferred its rights, but instead maintains a joint stake.

The federal government should use this authority to expand affordable access around the world. Moderna so far has committed publicly to supplying 500 million doses per year, potentially up to one billion.⁴ With two doses required per person, this could be enough for 250 million to 500 million people.⁵ Moderna’s CEO reportedly has acknowledged that “We won’t have enough supply at the global level.”⁶ He also has pledged to set a price in line with other respiratory vaccines—which cost up to \$800.⁷ If the vaccine proves safe and effective, nobody should be left behind. The U.S. government must take responsibility for timely access to mRNA-1273.

¹ Public Citizen, Blind Spot (2020), available at <https://www.citizen.org/article/blind-spot/> (noting that the NIH alone had spent nearly \$700 million on coronavirus research between the SARS outbreak and February 2020)

² NIH Clinical Trial of Investigational Vaccine for COVID-19 Begins (March 16, 2020), <https://tinyurl.com/wcy127j> (“Scientists at [NIH] and Moderna were able to quickly develop mRNA-1273 because of prior studies of related coronaviruses that cause severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS). Coronaviruses are spherical and have spikes protruding from their surface, giving the particles a crown-like appearance. The spike binds to human cells, allowing the virus to gain entry. VRC and Moderna scientists already were working on an investigational MERS vaccine targeting the spike, which provided a head start for developing a vaccine candidate to protect against COVID-19.”)

³ One application is provisional, and one application is nonprovisional.

⁴ Moderna Advances Late-Stage Development of its Vaccine (mRNA-1273) Against COVID-19 (June 11, 2020), <https://tinyurl.com/y7cyg3vq>

⁵ The Phase II trial is currently administering two vaccinations 28 days apart. *Id.*

⁶ <https://twitter.com/ZacharyBrennan/status/1260264559492960256> (tweet from Politico reporter at media event)

⁷ Evi Fordham, Coronavirus vaccine will be affordable, Moderna CEO says (March 5, 2020), <https://tinyurl.com/y9hbcxye> and CDC, Vaccine Price List, <https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html> (the standard 4-dose course of treatment with the pneumococcal vaccine costs up to \$800)

METHODS

Many scientific publications require authors to disclose conflicts of interest, including relevant patent ownership and applications. On June 15th, 2020, we searched the scientific literature for terms related to mRNA-1273. We collected information about disclosures that appeared relevant to the vaccine and, where possible, searched for full patent applications. Assessing whether the applications met patentability requirements was beyond the scope of this report.

We also reviewed the NIH-Moderna agreements disclosed by *Axios* to supplement our analysis. We selected documents based on their relevance to mRNA-1273 and assessed terms related to ownership.

FINDINGS: THE CASE FOR OWNERSHIP

Patent Applications

We found two patent application disclosures by federal scientists that appear relevant to a COVID-19 vaccine candidate. One application is provisional and remains unpublished. The other is nonprovisional and has been published. Provisional applications are easier to file and represent an initial step towards seeking patent protection.⁸ Nonprovisional applications serve as the basis for patent examination.

1. “2019-nCoV Vaccine.”⁹

U.S. Application no. 62/972,886

A provisional application has been filed for a patent that appears to claim the vaccine.¹⁰ From publicly available documents, it appears that the list of inventors at least includes several federal scientists, along with academic researchers based at University of Texas, Austin.¹¹ Notably, the scientific paper that disclosed this

⁸ To obtain a patent, inventors must convert provisional applications into nonprovisional applications. US Patent and Trademark Office, Provisional Application for Patent, <https://www.uspto.gov/patents-getting-started/patent-basics/types-patent-applications/provisional-application-patent>

⁹ Corbett et al., SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness, bioRxiv (preprint) (2020), <https://www.biorxiv.org/content/10.1101/2020.06.11.145920v1.full>

¹⁰ Due to a lack of publicly available information, it is not possible to discern with more precision the particular technology claimed. It may overlap with the second patent application described.

¹¹ The list may not be exhaustive. It includes Kizzmekia Corbett (NIAID), Olubukola Abiona (NIAID), Geoffrey B. Hutchinson (NIAID), Barney Graham (NIAID), Nianshuang Wang (UT Austin), Jason McLellan (UT Austin), Daniel Wrapp (UT Austin). For the role of University of Texas researchers, see Francis Collins, Structural Biology Points

patent included Moderna scientists, but they were not named as co-inventors.¹² If the patent is granted and covers the vaccine, then the NIH has an ownership stake.

2. “Prefusion Coronavirus Spike Proteins and Their Use.”¹³

U.S. Application No. 16/344,774

In 2016, federal scientists in partnership with academic researchers developed a new way to stabilize coronavirus spike proteins. The approach required substituting two amino acids, known as prolines, between the central helix and heptad repeat 1 (“the 2P approach”).¹⁴ The stabilized spike protein for an earlier coronavirus produced a stronger immune response at lower doses than the naturally occurring protein.¹⁵ The scientists filed a patent application. The patent application, in relevant part, claims:

- Stabilized proteins produced using the 2P approach across a group of coronaviruses (Claims 1 and 5);
- Nucleic acid molecules (e.g., RNA) encoding those proteins (Claims 39-41); and
- Methods for generating an immune response and inhibiting infection with the coronavirus (Claims 45-49).¹⁶

Moderna describes mRNA-1273 as an “mRNA vaccine against SARS-CoV-2 encoding for a prefusion stabilized form of the Spike (S) protein.”¹⁷ The vaccine uses the 2P approach to produce stabilized spike proteins.¹⁸ If the ‘744 patent is

Way to Coronavirus Vaccine (March 3, 2020), <https://directorsblog.nih.gov/2020/03/03/structural-biology-points-way-to-coronavirus-vaccine/>

¹² See Corbett et al. (2020).

¹³ Application US16/344,774, Prefusion coronavirus spike proteins and their use, <https://tinyurl.com/y9n4azwx>

¹⁴ Corbett et al., SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness, bioRxiv (preprint) (2020) (“Subsequently, we identified 2 proline substitutions (2P) at the apex of the central helix and heptad repeat 1 that effectively stabilized MERS-CoV, SARS-CoV and HCoV-HKU1 S proteins in the prefusion conformation.”)

¹⁵ *Id.* (“Similar to other prefusion-stabilized fusion proteins, MERS S-2P protein is more immunogenic at lower doses than wild-type S protein.”)

¹⁶ Claim 1, Claim 5, Claims 39-41 and Claims 45-49 appear relevant. The patent application references the betacoronavirus genera, which includes SARS-CoV2, the virus that causes COVID-19. Application US16/344,774, Claim 5.

¹⁷ Moderna Announces Positive Interim Phase 1 Data for its mRNA Vaccine (May 18, 2020), <https://tinyurl.com/y7j7hs2g>

¹⁸ Corbett et al., SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness, bioRxiv (preprint) (2020). (“[T]he 2P mutations were substituted into S positions aa986 and 987 to produce prefusion-stabilized SARS-CoV-2 S (S-2P) protein for structural analysis and serological assay development in silico without additional experimental validation. Within 5 days of sequence release, current Good Manufacturing Practice (cGMP) production of mRNA/LNP expressing the SARS-CoV-2 S-2P as a transmembrane-anchored protein with the native furin cleavage site (mRNA-1273) was initiated in parallel with preclinical evaluation.”) Positions aa986 and 987 are

granted, we believe it likely would cover mRNA-1273. This means the patent owners could exclude Moderna from using the invention. The application lists several inventors at the National Institutes of Health, along with other researchers.¹⁹ The application states that it is owned by the U.S. government, Dartmouth College, and the Scripps Research Institute.²⁰ If the patent is granted, then the NIH likely has an ownership stake.

NIH-Moderna Agreements

We found two agreements that appear relevant to a COVID-19 vaccine candidate. Both had some information redacted.

1. “Research Collaboration Agreement 2017-1179”²¹

In May 2019, NIH and Moderna entered into a “research collaboration agreement” to develop vaccine candidates against Middle East Respiratory Syndrome coronavirus (MERS-CoV) and Nipah virus.²² The project was focused on evaluating candidates in animal models.²³ NIH signed an amendment to the document on January 13, 2020—the day the agency and Moderna finalized the design of their novel coronavirus vaccine.²⁴ The amendment is significantly redacted and does not mention the new coronavirus. However, the close proximity suggests the terms of the contract may have been expanded to apply to this new project. At the very least, the terms may have been instructive for the mRNA-1273 project.

The document notes that ownership of inventions in the performance of the research project will “follow inventorship” in accordance with U.S. law.²⁵ It

near the end of heptad repeat 1. *See* Xia et al., Fusion mechanism of 2019-nCoV and fusion inhibitors targeting HR1 domain in spike protein, *Nature* (2020).

¹⁹ The co-inventors include Hadi Yassine (NIAID), Barney Graham (NIAID), Masaru Kanekiyo (NIAID), M. Gordon Joyce (NIAID), Kizzmekia Corbett (NIAID), Jason McLellan (previously at Dartmouth, now UT Austin), Andrew Ward (Scripps), Robert Kirchdoefer (Scripps), Christopher Cottrell (Scripps), Jesper Pallesen (Scripps), Hannah Turner (Scripps). *See* NIH, Prefusion Coronavirus Spike Proteins and Their Use, <https://www.ott.nih.gov/technology/e-234-2016>

²⁰ Application US16/344,774, Prefusion coronavirus spike proteins and their use, <https://tinyurl.com/y9n4azwx>.

²¹ Corbett et al., SARS-CoV-2 mRNA Vaccine Development Enabled by Prototype Pathogen Preparedness, *bioRxiv* (preprint) (2020).

²² Research Collaboration Agreement 2017-1179, Pg. 72 of Axios disclosures, <https://www.documentcloud.org/documents/6935295-NIH-Moderna-Confidential-Agreements.html>

²³ Research Collaboration Agreement 2017-1179, Pg. 83 of Axios disclosures, <https://www.documentcloud.org/documents/6935295-NIH-Moderna-Confidential-Agreements.html>

²⁴ Moderna’s Work on a COVID-19 Vaccine Candidate, <https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19>

²⁵ The Federal Circuit has held that “Making the invention requires conception and reduction to practice. While conception is the ‘formation, in the mind of the inventor, of a definite and permanent idea of a complete and

provides that “inventions made in the performance of the Research Project that are invented jointly by employees of both Parties will be owned jointly.”²⁶ It does not contain a requirement to license the technology developed to the private collaborator, suggesting the government maintains its full rights – including the right to use the technology as it sees fit.

2. “Material Transfer Agreement”²⁷

NIH and Moderna agreed to transfer materials to a coronavirus scientist at the University of North Carolina for animal testing in an agreement executed December 16, 2019.²⁸ Notably, the materials were described as “mRNA coronavirus vaccine candidates developed and jointly-owned by [NIH] and Moderna.”²⁹ This likely refers to work done on an earlier coronavirus, MERS-CoV. It nonetheless provides further evidence that the federal government was developing coronavirus candidates with Moderna that it jointly owned.³⁰

In addition to potentially sharing the same collaboration agreement, the nature of the MERS and new coronavirus collaborations appear similar. In both cases, the NIH worked with Moderna to develop a coronavirus vaccine that expressed a stabilized spike protein.³¹

operative invention,’ reduction to practice ‘requires that the claimed invention work for its intended purpose.’” Solvay S.A. v. Honeywell International Inc., 742 F.3d 998 (2014). Although publicly available information is limited, federal scientists played a critical role in designing and testing the vaccine, and likely meet this test. Indeed, NIH scientists are named as inventors on a patent application that appears essential to the vaccine. U.S. Application no. 62/972,886.

²⁶ Research Collaboration Agreement 2017-1179, Pg. 75 of Axios disclosures,

<https://www.documentcloud.org/documents/6935295-NIH-Moderna-Confidential-Agreements.html>

²⁷ Material Transfer Agreement, Pg. 105 of Axios disclosures, <https://www.documentcloud.org/documents/6935295-NIH-Moderna-Confidential-Agreements.html>

²⁸ The timing of the transfer may be a coincidence, or it may represent an earlier than previously reported effort to prepare for the new coronavirus. The outbreak was publicly reported in late December. But U.S. intelligence officials were reportedly warning of the outbreak in late November. <https://abcnews.go.com/Politics/intelligence-report-warned-coronavirus-crisis-early-november-sources/story?id=70031273>

²⁹ The agreement states the National Institute of Allergy and Infectious Diseases (NIAID), one of the institutes that comprises the NIH.

³⁰ The vaccine candidate relies on the genetic sequence of the virus, which was not publicly disclosed until January 11. Moderna’s Work on a COVID-19 Vaccine Candidate, <https://www.modernatx.com/modernas-work-potential-vaccine-against-covid-19>

³¹ Moderna, Form 10-K, pg. 60-61. (compare “in collaboration with the VRC, we have selected the viral Spike protein as the antigen for our SARS-CoV-2 vaccine (mRNA-1273)” and “in an existing collaboration with the VRC to develop a vaccine against MERS, we designed an mRNA-based vaccine targeting the prefusion-stabilized Spike protein.”) <https://investors.modernatx.com/node/8346/html>

ANALYSIS

The U.S. government may jointly own a potential COVID-19 vaccine. At least two patent applications that appear essential to the vaccine name federal scientists as inventors, giving the U.S. government ownership if the patents are granted. Collaboration agreements also support the government's ownership stake in mRNA-1273.

Co-ownership provides significant rights.³² For example, assuming there were no other monopolies, the government could make, use, or sell the technology without the consent of Moderna.³³ It could also license the technology to others, including other vaccine manufacturers or the World Health Organization, without the consent of Moderna.³⁴

Our analysis is limited by a lack of transparency. We do not have the provisional patent application. We do not know whether the U.S. government will continue to pursue its patent applications, or if the disclosed agreements between Moderna and NIH capture all terms related to their collaboration. Nor do we know if other applications exist that may cover the vaccine and potentially block production, or if the U.S. government has ownership interests beyond what is outlined in this report.

Moderna has benefited significantly from federal support. As we described in *The People's Vaccine*, the U.S. government provided millions of dollars to Moderna as early as 2013 to help develop its mRNA technology.³⁵ The NIH meanwhile was also developing new methods to target coronavirus spike proteins. When the new coronavirus emerged in Wuhan, the NIH worked with Moderna to design and test a

³² 35 U.S.C. § 262 (“In the absence of any agreement to the contrary, each of the joint owners of a patent may make, use, offer to sell, or sell the patented invention within the United States, or import the patented invention into the United States, without the consent of and without accounting to the other owners.”). These rights would complement the existing authority the U.S. government has to use patents that it does not own. See e.g., 28 U.S.C. § 1498.

³³ The government could eliminate other patent barriers by using its existing patent use authority. This would allow the government to license technologies in exchange for reasonable compensation. The government would not need to use the patent use authority—or provide compensation—for technologies it co-owned. See 28 U.S.C. § 1498. Brennan et al., *A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health*, *Yale Journal of Law & Technology* (2017).

³⁴ Notably, the U.S. government appears to have nonexclusively licensed the coronavirus spike protein technology. Form 8-K Orogenics Inc (2020), <https://sec.report/Document/0001493152-20-008008/>

³⁵ PUBLIC CITIZEN, *THE PEOPLE'S VACCINE* (2020), <https://www.citizen.org/article/the-peoples-vaccine/> (“Many investors initially considered the [mRNA] idea too speculative. But the Department of Defense took significant risk early-on. In 2013, the agency awarded the corporation \$25 million to test the approach. In 2016, BARDA awarded Moderna \$125 million to develop a Zika vaccine, which helped increase confidence in the new technology.”)

vaccine.³⁶ The U.S. Biomedical Advanced Research Development Authority has provided Moderna an additional \$483 million to further develop the vaccine and scale-up manufacturing.

In general, the federal government has the authority to use any patent (not only those it owns), in exchange for reasonable compensation, under existing law.³⁷ Yet another set of rights attach to many federally-funded and federally-supported technologies.³⁸ In some cases, federal scientists working on a project meet the requirements of inventorship, resulting in U.S. government ownership of the patents.³⁹ This case appears to support the claim of public ownership.

The federal government should use its authority to ensure the vaccine, if proven safe and effective, is available to everyone in the U.S. and around the world. Domestically, this includes:

1. In cases where the federal government has ownership rights but Moderna does not, it should nonexclusively license the rights and condition use of its technologies on ensuring reasonable pricing and sufficient supply;⁴⁰
2. In cases where there is joint ownership, the government should license the technologies to competitors; and
3. If there are patented technologies the U.S. government does not own needed to produce the vaccine, then the government should exercise its general, preexisting authority to use any patented invention in exchange for appropriate royalty payments to the patent holder.⁴¹

³⁶ Moderna Announces Funding Award from CEPI to Accelerate Development of Messenger RNA (mRNA) Vaccine Against Novel Coronavirus (Jan. 23, 2020), <https://tinyurl.com/v6g65mo>.

³⁷ Brennan et al., A Prescription for Excessive Drug Pricing: Leveraging Government Patent Use for Health, Yale Journal of Law & Technology (2017).

³⁸ See e.g., 35 U.S.C. § 202 (royalty free rights for government-funded inventions), 35 U.S.C. § 203 (march-in rights for government-funded inventions), 15 U.S.C. § 3710a (royalty free rights for federally-supported inventions). Because the disclosed research collaboration agreement between Moderna and NIH was explicitly described as not a funding agreement under 35 U.S.C. § 201(b) nor a cooperative research development agreement under 15 U.S.C. § 3710a, it is not immediately clear whether any of these rights would attach.

³⁹ 37 C.F.R. 501.6 (a)(1) (“The Government shall obtain, except as herein otherwise provided, the entire right, title and interest in and to any invention made by any Government employee . . .”).

⁴⁰ The U.S. government appears to have nonexclusively licensed the coronavirus spike protein technology so far without any reasonable pricing and supply conditions. Form 8-K Oragenics Inc (2020), <https://sec.report/Document/0001493152-20-008008/>.

⁴¹ See 28 U.S.C. § 1498 (“Whenever an invention described in and covered by a patent of the United States is used or manufactured by or for the United States without license of the owner thereof or lawful right to use or manufacture the same, the owner’s remedy shall be by action against the United States in the United States Court of Federal Claims for the recovery of his reasonable and entire compensation for such use and manufacture.”)

Globally, the government should share its intellectual property and know-how with the World Health Organization's COVID-19 Technology Access Pool.⁴² This would allow manufacturers from around the world to help scale-up production and prevent rationing. If the vaccine proves safe and effective, it should be available to everyone as quickly as possible.

⁴² World Health Organization, COVID-19 Technology Access Pool, <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool>

APPENDIX

Table 1: Axios Disclosures of NIH-Moderna Agreements

Title	Year	Disease Target	Page Number
Confidential Disclosure Agreement 2015-33448	2015	Multiple, including HIV, hPIV, Nipah virus influenza, Ebola, Zika virus, MERS-CoV	1 to 18
Cooperative Research and Development Agreement 2016-0005 and 2016-0262	2016	HIV-1	19 to 43
Material Transfer Agreement 2016-1228	2017	Zika virus	44 to 47
Research Collaboration Agreement 2016-1424	2017	Zika virus	47 to 57
Confidential Disclosure Agreement 2017-0492	2017	EBV and Herpes Simplex virus	58 to 60
Material Transfer Agreement 2017-0993	2017	Zika virus	61 to 71
Research Collaboration Agreement 2017-1179	2019	MERS-CoV and Nipah virus	72 to 82
Amendment to Research Collaboration Agreement 2017-1179	2020	MERS-CoV and Nipah virus	83 to 85
Material Transfer Agreement 2017-1210	2017	Zika virus	86 to 96
Confidential Disclosure Agreement	2017	N/A	97 to 100
Material Transfer Agreement 2018-0664	2018	Zika virus	101 to 104
Material Transfer Agreement 2019-1177	2019	Coronavirus	105 to 109
Non-Exclusive Patent License Agreement for Internal Research Use and Biological Materials License Agreement L-044-2018	2018	hMPV	110 to 128
Public Health Service L-44-2018	2019	hMPV	129 to 136
Non-Exclusive Patent License Agreement for Internal Research Use and Biological Materials License Agreement A-261-2018	2018	Zika virus	137 to 153

Source: <https://www.documentcloud.org/documents/6935295-NIH-Moderna-Confidential-Agreements.html>



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