

# Actionable Information - Research Briefs - 1 - Vaccination

March 24, 2021

## Contents



2

<b>Actionable Information - Research Briefs - 1 -Vaccination</b>	<b>2</b>
U.S. COVID-19 Vaccines Key Takeaways . . . . .	2
Pfizer . . . . .	2
Moderna . . . . .	3
J&J Janssen . . . . .	3
U.S. Vaccination Overview and Supply Chain . . . . .	4
Pfizer and BioNTech . . . . .	4
Moderna . . . . .	6
Moderna’s Manufacturing Facilities and Supply Chain Overview	6
Moderna’s Cold-Chain Distribution and packaging . . . . .	9
Moderna Distribution Efforts as of February 23, 2021 . . . . .	9
Johnson and Johnson Janssen COVID-19 Vaccine . . . . .	9
J&J’s Janssen Vaccine Distribution Efforts as of March 12, 2021 . . . . .	9
COVID-19 Vaccination Landscape . . . . .	12
References . . . . .	13

## Actionable Information - Research Briefs - 1 - Vaccination

*Last updated: March 24, 2021*

Suggested citation:

Medina-Cetina, Z., Pompelli, G., Cochran, M., Olivares, M., Perez-Patron, M., Alvarado, J., Duran, G., & Z-Losoya, E.. (2021). CBTS-R13: U.S.-Mexico Risk Taskforce to Support the Health Supply Chain Systems for Infrastructure and Workforce Threatened by the COVID19 Pandemic. <https://r13-cbts-sgl.engr.tamu.edu/>

Table

---

### U.S. COVID-19 Vaccines Key Takeaways

- Pfizer, Moderna, and J&J's Janssen COVID-19 Vaccines have been granted emergency use authorization in the United States (see Table tbl. 1)
- U.S. Vaccine wholesale prices have been reported to range from 10 to \$50 dollars per patient as shown in Fig. 1.

Table 1: U.S. Emergency Authorized COVID-19 Vaccines Comparison as of March 14, 2021.

Vaccine	Type	Doses	Reported Efficacy	Cold Supply Storage
Pfizer and BioNTech	mRNA	2x - 21 days apart	95%	-75°C
Moderna	mRNA	2x - 28 days apart	94%	-20°C
Johnson & Johnson	Adenovirus-based	1x	72%	7°C

### Pfizer

- *Expected to deliver* a total of **320 million doses** to the U.S. Government:
  - 120 million by end of **March 2021**
  - 100 million by the end of **May 2021**
  - 100 million by end of **2021**
- Pfizer's U.S. vaccine production is vertically integrated
- The most critical manufacturing step of its supply chain is combining

mRNA production with lipids which occurs during the first half of the manufacturing process

- **Pfizer** is producing DNA for the U.S. Market with plants located in Kalamazoo, Michigan, St. Louis, Missouri and Andover, Massachusetts
- Critical infrastructures updates during February, 2021 caused a ~40% drop in weekly supply for that month but has since recovered

### **Moderna**

- *Expected to deliver* a total of **300 million doses** to the U.S. Government:
  - 100 million by the end of **March 2021**
  - 100 million by the end of **May 2021**
  - 100 million by end of **July 2021**
- The most critical manufacturing step of its supply chain is the combining mRNA production with lipids which occurs during the first half
  - **Moderna** and **Lonza** are producing DNA for the U.S. Market with plants located in Norwood, Massachusetts and Portsmouth, New Hampshire respectively
- Moderna is subcontracting several U.S. Pharmaceutical manufacturers to handle drug production and filling
  - Lonza
  - Corden Pharma
  - Catalent Pharma

### **J&J Janssen**

- *Expected to deliver* a total of **200 million doses** to the U.S. Government:
  - 20 million by the end of **March 2021**
  - 80 million by the end of **June 2021**
  - 100 million by the end of **December 2021**
- JJ's manufacturing cycle is the longest ranging from 60 to 80 days
- The most critical manufacturing step of its supply chain is the cell culture growth which occurs at the beginning of the manufacturing process
  - **Emergent Bio Solutions** and **Merck Pharmaceutical** are producing DNA for the U.S. Market with plants located in Baltimore, MD and Philadelphia, PA respectively
- J&J is collaborating with 5 U.S. Pharmaceutical manufacturers to handle drug production and filling
  - Emergent Bio Solutions
  - Merck Pharmaceutical
  - Grand River Aseptic Manufacturing (GRAM)
  - Catalent, Inc
  - PCI Pharma Services

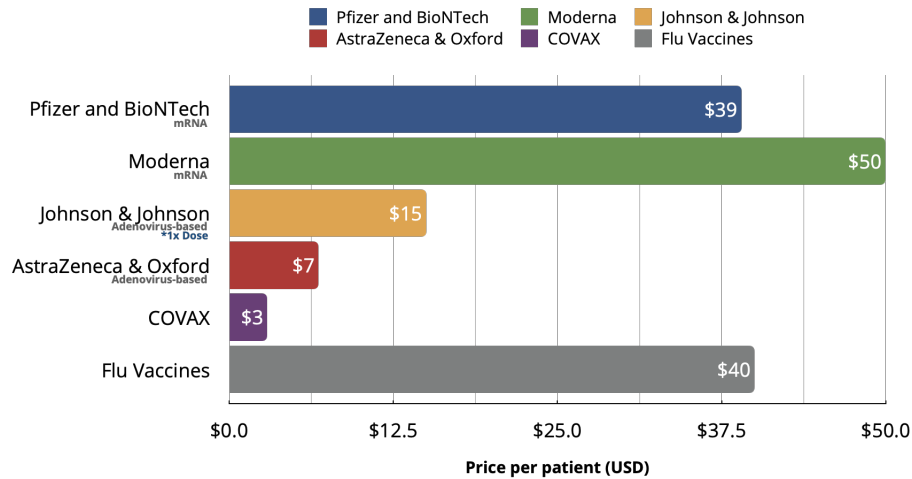


Figure 1: Approximate wholesale prices listed by vaccine manufacturer, adapted from (Cohen, 2020; Dooling et al., 2020; Dooling, 2020; Lewis, 2020 ; Nature, 2020 ; Quentin, 2020 ; Ries, 2020 ; Romero, 2020)

## U.S. Vaccination Overview and Supply Chain

The most important manufacturing, and distribution sites involved in the COVID-19 supply chain in the U.S. are shown in Fig. 2.

Figure 2: Top U.S. COVID-19 Vaccine Supply Chain Suppliers Facilities

**Pfizer and BioNTech** Pfizer can integrate most of its manufacturing and distribution in the United States. The company, however, was part of operation warp speed for distribution (Slaoui & Hepburn, 2020). According to the company’s yearly review, the company has ten manufacturing facilities and two distribution centers, as shown in Fig. 3 . (Inc., 2018), However, only a handful of sites are directly involved in manufacturing its Pfizer-BioNTech COVID-19 Vaccine, as highlighted in Fig. 4 and Fig. 5.

### 1. St. Louis, Missouri plant

1. The process starts at this manufacturing plant in the DNA production and raw materials of their COVID-19 Vaccine.

### 2. Drug Formulation in Andover, Massachusetts or Germany facility

1. RNA messenger through DNA incubation with genetic building blocks takes place in the Andover facility for the U.S. market while international market is supplied by facilities located in Germany
2. Fast shipment to next facility in helicopters or jets at the beginning of the manufacturing process

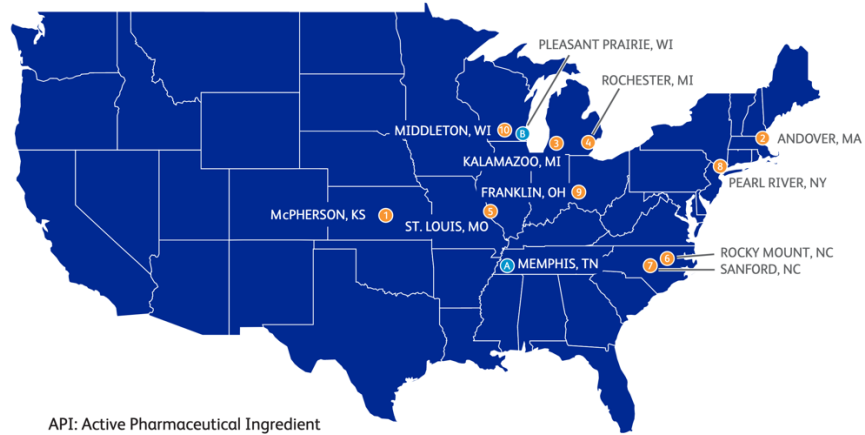


Figure 3: Pfizer's Facilities in the United States

- |  |   |   |
|--|---|---|
| <ul style="list-style-type: none"> <li>1 <b>McPherson, KS</b><br/>Biologics, biosimilars and sterile injectables</li> <li>2 <b>Andover, MA</b><br/>Biologics and Vaccines; clinical trial development products</li> <li>3 <b>Kalamazoo, MI</b><br/>API and sterile injectables</li> <li>4 <b>Rochester, MI</b><br/>Penicillin</li> <li>5 <b>St. Louis, MO</b><br/>Sterile injectable drug and device combination products</li> </ul> | <ul style="list-style-type: none"> <li>6 <b>Rocky Mount, NC</b><br/>Sterile injectables</li> <li>7 <b>Sanford, NC</b><br/>Vaccines; clinical trial development products</li> <li>8 <b>Pearl River, NY</b><br/>Biologics; clinical trial development products</li> <li>9 <b>Franklin, OH</b><br/>API</li> <li>10 <b>Middleton, WI</b><br/>API</li> </ul> | <ul style="list-style-type: none"> <li>A <b>Memphis, TN</b><br/>Distribution center</li> <li>B <b>Pleasant Prairie, WI</b><br/>Distribution center</li> </ul> <p>Major office locations are Collegeville, PA; Lake Forest, IL; New York, NY; and Peapack, NJ (PGS global headquarters).</p> |
|--|---|---|

Figure 4: Pfizer's Manufacturing and Distribution Locations in the United States

Figure 5: Pfizer's Manufacturing and Distribution Locations in the United States

### 3. Lipids production & other raw materials

1. U.K. Croda International

### 4. Formulation, Fill and Finish in Kalamazoo, Michigan

1. LNP production step in Kalamazoo is reported to be the bottleneck of the U.S. supply chain. “Combining mRNA and lipids into lipid nanoparticles is the biggest hurdle in the manufacturing process” (Lowe, 2021)
2. Two production lines producing 600 vials/min

**Moderna** Moderna is a U.S.-based pharmaceutical company founded in 2010 with primary headquarters located in Cambridge, MA, and specialized in the research and development of mRNA-based therapeutics. The company is part of Operation Warp Speed and backed by Venture Capital investments (Moderna, 2021); other takeaways about the company are shown in Fig. 6. The company’s workforce has grown 80% over the past two years, according to LinkedIn data (LinkedIn, 2021).

### Moderna’s Manufacturing Facilities and Supply Chain Overview

**Catalent Pharma** is Moderna’s main subcontractor for COVID-19 Vaccine manufacturing in the U.S. (Moderna, 2021),(Neubert, 2021). All U.S. supply comes from Moderna’s dedicated supply chain in the U.S. Supply to locations outside of the U.S. comes from dedicated supply points based outside of the U.S.” (Moderna, 2021)

#### 1. Moderna’s Main Plant in Massachusetts

1. This plant is involved in the mRNA production phase of the COVID-19 vaccine (Carolyn, 2020)

#### 2. DNA Production in Portsmouth, New Hampshire

1. Moderna is subcontracting **Lonza** to produce DNA for their vaccines, one of the world’s largest contract development and manufacturing companies.
2. It is reported that at least 3 other production lines located in Visp, Switzerland with a capacity of 600k/day are supplying the international market

#### 3. Lipid’s production in Boulder, Colorado

1. Moderna is subcontracting **Corden Pharma**, the largest U.S. pharmaceutical manufacturer to produce enough lipids for its vaccine
2. At least 2 production lines were installed in Liestal, Switzerland and Chenôve, France for international market

#### 4. Formulation & Fill finishing

1. Moderna is utilizing the vast manufacturing network of **Catalent** formulation and fill finishing.

#### 5. Packaging and Distribution



<p><b>FOUNDING YEAR:</b> 2010</p>	<p><b>TEAM MEMBERS:</b> 1000+ (As of August, 2020)</p> <p><a href="#">Current Job Openings &gt;</a></p>	<p><b>HEADQUARTERS:</b> Cambridge, MA</p>
<p><b>CEO:</b> Stéphane Bancel</p> <p><a href="#">Learn About Stéphane &gt;</a></p>	<p><b>HEALTHY VOLUNTEERS &amp; PATIENTS ENROLLED:</b> 2,000+ (prior to enrolling 30,000 participant Phase 3 trial of mRNA-1273)</p>	<p><b>LOCATIONS:</b> 200 Technology Square, Cambridge, MA One Upland Road, Norwood, MA</p>
<p><b>THERAPEUTIC AREAS:</b></p> <ul style="list-style-type: none"> <li>• Infectious Diseases</li> <li>• Immuno-Oncology</li> <li>• Rare Diseases</li> <li>• Cardiovascular Diseases</li> <li>• Autoimmune Diseases</li> </ul>	<p><b>CAPITALIZATION:</b></p> <ul style="list-style-type: none"> <li>• Cash, cash equivalents, and investments in marketable securities: \$3.07 billion (unaudited as of June 30, 2020)</li> <li>• No Debt</li> </ul>	<p><b>PARTNERS:</b></p> 
<p><b>PIPELINE:</b></p> <ul style="list-style-type: none"> <li>• 23 development candidates; 12 in clinical studies</li> </ul>	<p><b>FOUNDING INVESTOR:</b></p> <ul style="list-style-type: none"> <li>• <a href="#">Flagship Pioneering</a></li> </ul>	

Figure 6: Moderna’s company profile

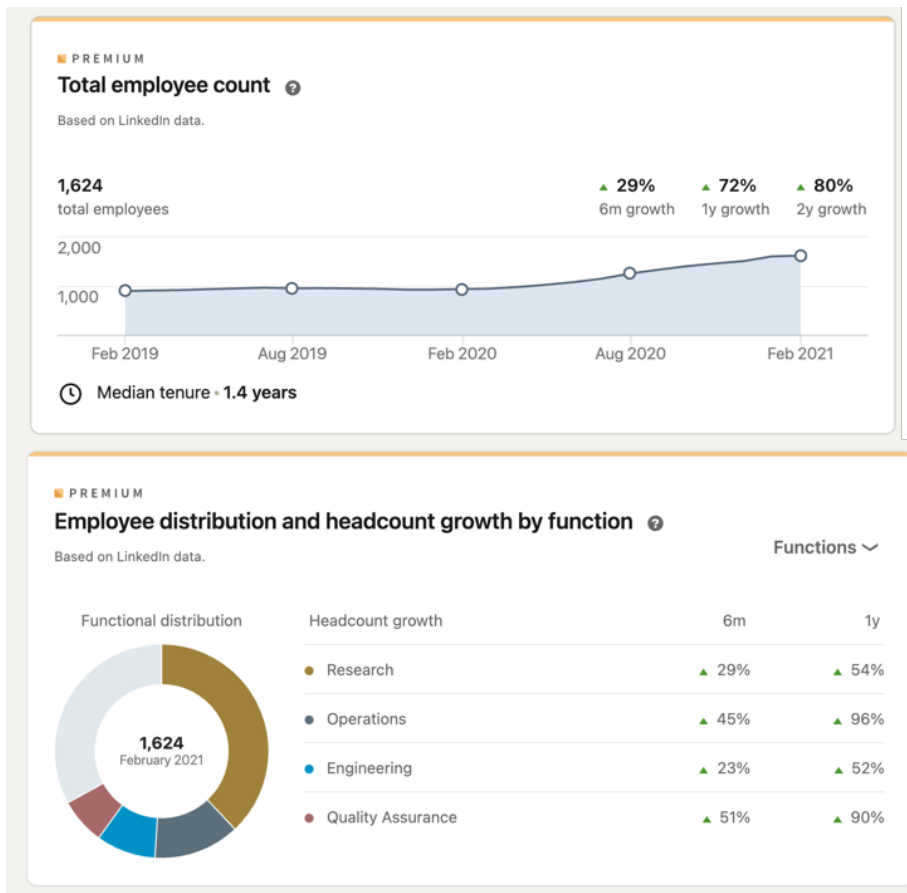


Figure 7: Moderna's workforce growth according to linkedin data as of Feb. 22, 2021 (LinkedIn, 2021)



1. Moderna is part of the U.S. Operation warp speed for both development and distribution. The company uses the central distribution facility

#### **Moderna's Cold-Chain Distribution and packaging**

- 10 doses of 0.5 each into tray
  - 12 trays per package
- Up to 192 packages can be shipped per pallet for a total of 230,400 doses
- Moderna uses UPS, FEDEX, DHL and commercial airlines
- Part of OWS for development and distribution

**Moderna Distribution Efforts as of February 23, 2021** • *Company has supplied 45.4 million doses of Moderna COVID-19 Vaccine to U.S. Government*

- *CDC Reports that approximately 30.7 million doses of the Moderna Vaccine has been administered*
- *Additional 33.2 million doses have been produced and are filled in vials and in the final stages of final production and testing*
- *Expected to deliver 100 million doses to the U.S. Government by end of March 2021*
- *Expected to deliver 100 million additional doses by end of May 2021 (moved one month forward) followed by another 100 million additional doses by end of July 2021*

Figure 8: Main Moderna's COVID-19 Vaccine U.S. Manufacturing and Distributions locations

#### **Johnson and Johnson Janssen COVID-19 Vaccine Production & Shipments**

- *March 2021 - 20 million doses*
- *April to June 2021 – at least 20 million doses per month*

#### **J&J's Janssen Vaccine Distribution Efforts as of March 12, 2021**

- *FDA Emergency Use Authorization Granted – Feb. 27, 2021*
- Company has supplied **2.9 million doses** of J&J's Janssen COVID-19 Vaccine to the U.S. Government
  - Plans to distribute **16 million** of doses more by the end of March (Services, 2021)

- Johnson & Johnson hopes to have partnerships with a total of 10 manufacturing plants by the end of 2021 (House, 2021)
  - 5 U.S. and 3 international partnerships announced as of March 8, 2021 Brody (2020)
- Merck will use two of its facilities to produce drug substance, formulate and fill vials (Services, 2021)
- Expected to deliver **100 million doses to the U.S. Government by end of June 2021**(House, 2021)
- Expected to deliver **100 million additional doses by end of 2021**

J&J is using a global network of collaborators to scale up production of its COVID-19 vaccine as seen in Fig. 9, and highlighted in Fig. 10 and Fig. 11.

### Production & Shipments

- March 2021 - 20 million doses
- April to June 2021 – at least 20 million doses per month



Figure 9: J&J's Janssen COVID-19 Vaccine Global Drug substance, product, and fill-finish manufacturing partners (House, 2021)

### J&J Supply Chain Overview

1. Drug Substance - Linear DNA Molecules from cells are grown in a bioreactor
  1. Subcontracting Brody (2020)
    1. Emergent Bio Solutions in Baltimore, MD

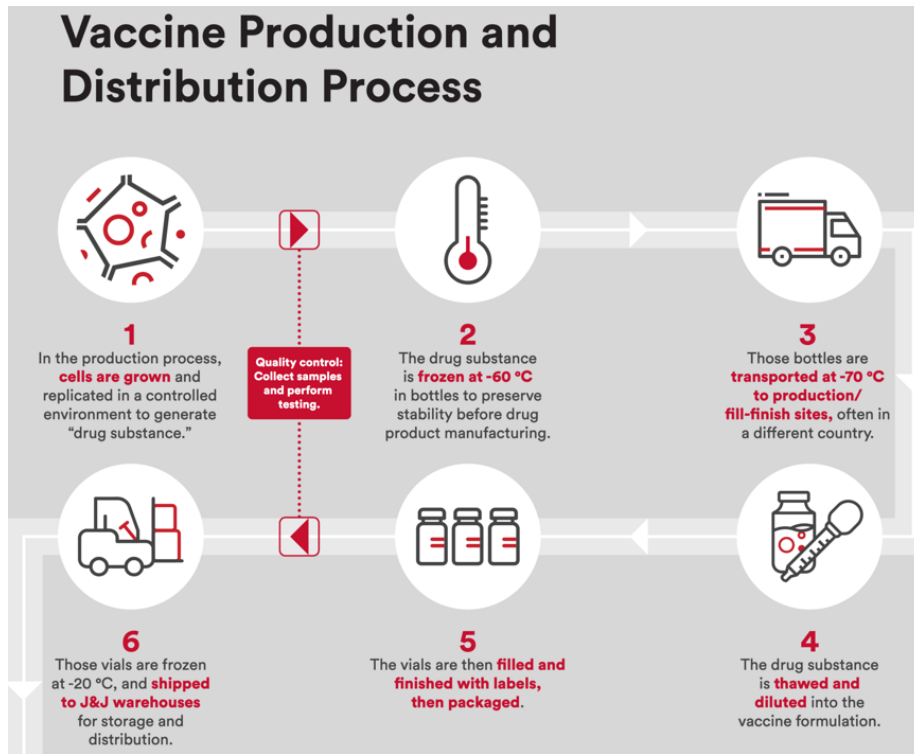


Figure 10: J&J's Janssen COVID-19 Vaccine Production and Distribution Process (House, 2021)

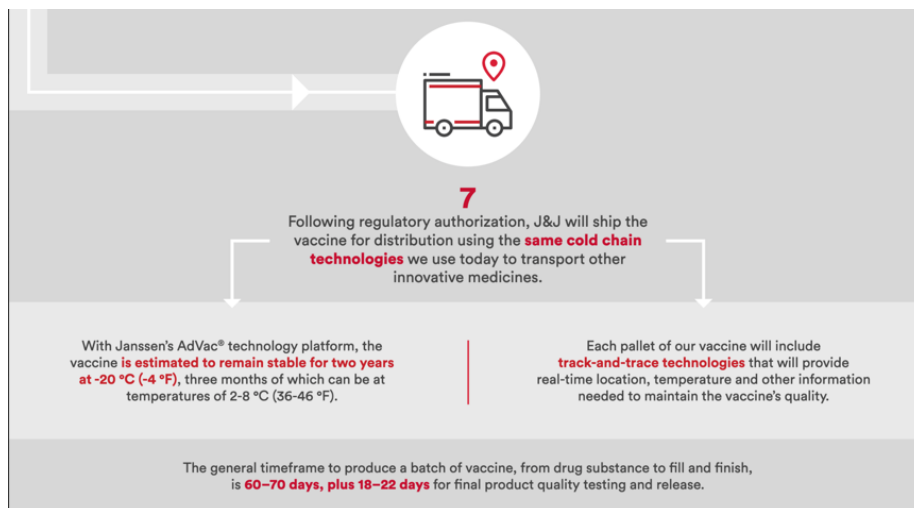


Figure 11: J&J's Janssen COVID-19 Vaccine Production and Distribution Process Continued (House, 2021)

Figure 12: U.S. J&J's Janssen COVID-19 Vaccine Supply Chain Suppliers Facilities

2. **Merck Pharmaceutical** in Philadelphia, PA
2. **Drug Product - Purification, Fill finishing, and packing**
  1. Subcontracting Kelly (2020)
    1. **Grand River Aseptic Manufacturing (GRAM)**, Grand Rapids, MI
    2. **PCI Pharma Services** *in Philadelphia, PA*
    3. **Catalent Inc**, *U.S.*
    4. **Merck Pharmaceutical** *in Philadelphia, PA*
  3. **Distribution McKesson's OWS Distribution plant**
    - **Cold-Chain Distribution**
      - 5 doses of 0.5ml each into one vial Kelly (2020)
      - UPS, FEDEX, DHL and commercial airlines
      - Part of OWS

The vaccine can be frozen at  $-4^{\circ}$  F for up to two years, and once it arrives at its final destination, can stay in a refrigerator at between  $35$  and  $46^{\circ}$  F for at least three months.

Each 0.5 mL dose of the Janssen COVID-19 Vaccine is formulated to contain 50 billion virus particles of the Ad26 vector encoding the S glycoprotein of SARS-CoV-2.

### COVID-19 Vaccination Landscape

The World Health Organization (WHO) provides weekly bulletins with the status of COVID-19 Vaccine clinical trials in the world. The bulletin is updated twice per week and includes information from several data sources such as Pubmed (Canese & Weis, 2013), the Cochrane vaccine mapping tool (Boutron et al., 2020), ClinicalTrials.gov (Medicine, 2021), WHO International Clinical Trials Registry Platform (ICTRP) (Organization, 2021) and other researchers in industries with registered trials for clinical information (R&D Blue Print, 2021). In addition, several news organizations and research teams have been reporting periodic updates and keeping track of changes, for instance, the New York Times (Carl Zimmer, 2021) and Bloomberg (Bloomberg, 2021), to mention some examples of such efforts to inform the general public.

According to the sources mentioned before, there are **73** vaccines being researched around the world in clinical trials on humans, **16** have reached the final stages

of testing, known as Phase III. Of these, at least **182** pre-clinical vaccines are under active investigation in animals as of **Feb. 23, 2021**

Table 1 tbl. 2 highlights the leading vaccine manufacturers working in their clinical trials and Table tbl. 4 their corresponding vaccine administration medium.

Table 2: Vaccine landscape pipeline

Number of doses	Schedule	Candidate vaccines	Percentage
1 dose		12	16%
	Day 0	12	
2 doses		45	62%
	Day 0 + 14	6	
	Day 0 + 21	17	
	Day 0 + 28	22	
3 doses		1	1%
	Day 0 + 28 + 56	1	
TBD / No Data (ND)		15	21%
	<b>Total</b>	<b>73</b>	<b>100%</b>

Table 4: COVID-19 Vaccine landscape by route of administration

Route of administration		Candidate vaccines	Percentage
Oral		2	3%
Injectable		61	84%
SC	Sub cutaneous	2	3%
ID	Intra dermal	3	4%
IM	Intra muscular	56	77%
TBD / No Data (ND)		10	14%

## References

- Bloomberg. (2021). Bloomberg vaccine tracker. In *Bloomberg News*. Online. <https://www.bloomberg.com/graphics/covid-vaccine-tracker-global-distribution/>
- Boutron, I., Chaimani, A., Meerpohl, J. J., Hróbjartsson, A., Devane, D., Rada, G., Tovey, D., Grasselli, G., & Ravaud, P. (2020). *The COVID-NMA project: Building an evidence ecosystem for the COVID-19 pandemic*. American

College of Physicians.

- Brody, B. (2020). *4 high-tech tools johnson & johnson is using to get products to you during the pandemic*. <https://www.jnj.com/innovation/johnson-johnson-supply-chain-technology-during-coronavirus>
- Canese, K., & Weis, S. (2013). PubMed: The bibliographic database. In *The NCBI handbook [internet]. 2nd edition*. National Center for Biotechnology Information (US).
- Carl Zimmer, S.-L., Jonathan Corum. (2021). Coronavirus vaccine tracker. In *The New York Times*. Online. <https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html>
- Carolyn, T. W. P. Inc., Y. Johnson. (2020). *A vial, a vaccine and hopes for slowing a pandemic — how a shot comes to be*. <https://www.washingtonpost.com/health/2020/11/17/coronavirus-vaccine-manufacturing/> last accessed on 02/20/2021
- Cohen, J. (2020). As COVID-19 vaccines emerge, a global waiting game begins. *Science*. <https://doi.org/10.1126/science.abg1793>
- Dooling, K. (2020). The advisory committee on immunization practices' updated interim recommendation for allocation of COVID-19 vaccine—united states, december 2020. *MMWR. Morbidity and Mortality Weekly Report*, 69.
- Dooling, K., McClung, N., Chamberland, M., Marin, M., Wallace, M., Bell, B. P., Lee, G. M., Talbot, H. K., Romero, J. R., & Oliver, S. E. (2020). The advisory committee on immunization practices' interim recommendation for allocating initial supplies of COVID-19 vaccine—united states, 2020. *Morbidity and Mortality Weekly Report*, 69(49), 1857.
- (GRAM), G. R. A. M. (2021). *Development and manufacturing facilities*. <https://www.grandriverasepticmfg.com/facilities/butterworth/>
- House, U. S. (2021). *Statement of dr. Richard nettles, m.d. Vice president of u.s. Medical affairs, janssen infectious diseases and vaccines before the subcommittee on oversight and investigations, committee on energy and commerce [Congressional Hearing]*. <https://docs.house.gov/meetings/IF/IF02/20210223/111226/HHRG-117-IF02-Wstate-NettlesR-20210223.PDF>
- Inc., P. (2018). *American pharmaceutical innovation and job creation [Company Yearly Review]*. [https://www.pfizer.com/sites/default/files/investors/financial\\_reports/annual\\_reports/2017/assets/media/Pfizer-infographic-US-ManufacturingSites.pdf](https://www.pfizer.com/sites/default/files/investors/financial_reports/annual_reports/2017/assets/media/Pfizer-infographic-US-ManufacturingSites.pdf)
- Johnson, J. &. (2021). *Johnson & johnson COVID-19 vaccine authorized by u.s. FDA for emergency use - first single-shot vaccine in fight against global pandemic*. <https://www.jnj.com/johnson-johnson-covid-19-vaccine-authorized-by-u-s-fda-for-emergency-usefirst-single-shot-vaccine-in-fight->

against-global-pandemic#:~:text=The%20Company%20has%20begun%20shipping,the%20first%20half%20of%202021.

- Kelly, K. (2020). Critical to vaccines, cold storage is wall street’s shiny new thing. *The New York Times*.
- Lewis, T. (2020). Pfizer-BioNTech COVID vaccine is first to win u.s. authorization. *Scientific American*. <https://www.scientificamerican.com/article/pfizer-biontech-covid-vaccine-is-first-to-win-u-s-authorization/>
- LinkedIn. (2021). *LinkedIn company profile, premium insights*. <https://www.linkedin.com/company/pfizer/insights/> last accessed on 02/22/2021
- Lowe, D. (2021). *Myths of vaccine manufacturing*. <https://blogs.sciencemag.org/pipeline/archives/2021/02/02/myths-of-vaccine-manufacturing> last accessed on 02/18/2021
- Medicine, U. S. N. L. of. (2021). ClinicalTrials.gov, a database of privately and publicly funded clinical studies conducted around the world. In *U.S. National Library of Medicine*. U.S. National Library of Medicine. <https://www.clinicaltrials.gov/>
- Moderna. (2021). *Moderna provides u.s. COVID-19 vaccine supply update*. <https://investors.modernatx.com/news-releases/news-release-details/moderna-provides-us-covid-19-vaccine-supply-update-0#:~:text=16%2C%202021%2D%2D%20Moderna%2C%20Inc,the%20U.S.%20Government%20to%20date>. last accessed on 02/16/2021
- Nature. (2020). The COVID vaccine challenges that lie ahead [Magazine Article]. *Nature*, 587, 522. <https://doi.org/https://doi.org/10.1038/d41586-020-03334-w>
- Neubert, J. (2021). *Exploring the supply chain of the pfizer/BioNTech and moderna COVID-19 vaccines*. <https://blog.jonasneubert.com/2021/01/10/exploring-the-supply-chain-of-the-pfizer-biontech-and-moderna-covid-19-vaccines/> last accessed on 02/22/2021
- Organization, W. H. (2021). International clinical trials registry platform (ICTRP). In *World Health Organization*. Online. <https://www.who.int/clinical-trials-registry-platform/>
- Quentin, B. M. C. (2020). Europe is paying less than u.s. For many coronavirus vaccines. *The Washington Post*. [https://www.washingtonpost.com/world/eu-coronavirus-vaccines-cheaper-than-united-states/2020/12/18/06677e34-4139-11eb-b58b-1623f6267960\\_story.html](https://www.washingtonpost.com/world/eu-coronavirus-vaccines-cheaper-than-united-states/2020/12/18/06677e34-4139-11eb-b58b-1623f6267960_story.html)
- R&D Blue Print, W. (2021). Draft landscape and tracker of COVID-19 candidate

vaccines. *World Health Organization*. <https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines>

Ries, J. (2020). How much will it cost to get a COVID-19 vaccine? *Healthline*. <https://www.healthline.com/health-news/how-much-will-it-cost-to-get-a-covid-19-vaccine>

Romero, C., J. (2020). ACIP presentation slides: December 19 and 20, 2020 meeting. *CDC Advisory Committee on Immunization Practices (ACIP)*. <https://www.cdc.gov/vaccines/acip/meetings/slides-2020-12-19-20.html>

Services, U. S. D. of H. & H. (2021). *Biden administration announces historic manufacturing collaboration between merck and johnson & johnson to expand production of COVID-19 vaccines*.

Slaoui, M., & Hepburn, M. (2020). Developing safe and effective covid vaccines — operation warp speed’s strategy and approach. *New England Journal of Medicine*, 383(18), 1701–1703. <https://doi.org/10.1056/NEJMp2027405>