Topics

- Phases of Vaccine Development
- Clinical Trial Status
- Other Vaccine Developments
- Issues that influence making vaccinations available and effective for the workforce
- Geographic Considerations
  - US
  - EMEA
  - Approach for other countries
  Note: Since many clients have a footprint that spans 2 or more countries, it is helpful to understand differences
- Appendix
  - Immunity, Dosing and Coverage Considerations
  - Sourcing, Manufacturing and Distribution Considerations
  - Operationalizing at Scale – Simultaneous Workstreams for Vaccine Development, Manufacturing and Distribution
  - Contacts for more information
  - Disclaimer
Phases of Vaccine Development

- **Pre-clinical phase** (135+ vaccines in this stage)
  - Small sample of healthy people
  - Purpose is to evaluate the immune response to drug
  - This process in typical drug development can take up to 2 years, for COVID-19 testing purposes it is taking 3 months
  - “An experimental drug or treatment in a small group of people (20–80) for the first time. The purpose is to evaluate its safety and identify side effects”

- **Clinical Phase I** (18 vaccines in this stage)
  - Study of 1000’s of people
  - Safety and efficacy continue to be studied
  - This process usually takes 2-4 years, phases II and III are being combined for COVID-19 vaccine development purposes
  - “The experimental drug or treatment is administered to large groups of people (1,000–3,000) to confirm its effectiveness, monitor side effects, compare it with standard or equivalent treatments”

- **Clinical Phase II** (12 vaccines in this stage)
  - “The experimental drug or treatment is administered to a larger group of people (100–300)”

- **Clinical Phase III** (6 vaccines in this stage)
  - Government Agency reviews the results of trials and lab results
  - Manufacturing can occur concurrently
  - Process expedited to a few months for COVID-19

- **Regulatory Review (RR)**
  - Testing begins after drug is released to the general public
  - Monitor effectiveness in real-world environments
  - “After a drug is licensed and approved by the FDA researchers track its safety, seeking more information about its risks, benefits, and optimal use”

- **Clinical Phase IV**
  - Government Agency reviews the results of trials and lab results
  - Manufacturing can occur concurrently
  - Process expedited to a few months for COVID-19

Sources:
1. [https://www.covid-19vaccinetracker.org/](https://www.covid-19vaccinetracker.org/)
3. [National Institutes of Health (for Clinical Trial Phase definitions)](https://www.nih.gov/)

Clinical Trial Status for top 10 vaccine candidates  
*Based on phase of testing and promising lab results as of August 10th 2020*

<table>
<thead>
<tr>
<th>Phase of Testing</th>
<th>Clinical Trial Testing Lab</th>
<th>Projected Advancement to Next Clinical Trial Phase</th>
<th>Company estimated timeline for transition to Manufacturing Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>III</td>
<td>Univ. Of Oxford/AstraZeneca</td>
<td>Plans for distribution have begun</td>
<td>End of 2020</td>
</tr>
<tr>
<td>III</td>
<td>Wuhan Inst./Sinopharm</td>
<td>Phase III in United Arab Emirates</td>
<td>End of 2020</td>
</tr>
<tr>
<td>III</td>
<td>Sinovac/Instituto Butantan</td>
<td>Just approved for Phase III in Brazil</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>Moderna</td>
<td>Just started Phase III</td>
<td>End of 2020</td>
</tr>
<tr>
<td>III</td>
<td>Beijing Inst./Sinopharm</td>
<td>Just started Phase III</td>
<td>End of 2020</td>
</tr>
<tr>
<td>II</td>
<td>CanSino Biologics</td>
<td>Set to initiate Phase III in Saudi Arabia; currently approved for use by Chinese military as a specially-needed drug</td>
<td>End of 2020</td>
</tr>
<tr>
<td>II</td>
<td>Inst. Of Medical Biology Academy of Medical Sciences</td>
<td>Phase II began in June</td>
<td></td>
</tr>
<tr>
<td>II</td>
<td>BioNtech/Fosun/Pfizer</td>
<td>Seeking RR as early as October</td>
<td>October 2020</td>
</tr>
<tr>
<td>I/II</td>
<td>Imperial College of London</td>
<td>Phase III to begin ASAP</td>
<td></td>
</tr>
<tr>
<td>I/II</td>
<td>Novavax</td>
<td>Plan to have Phase III trials in the fall</td>
<td>End of 2020</td>
</tr>
</tbody>
</table>

Sources:
https://www.covid-19vaccinetracker.org/
Other Vaccine Development

- **Russia vaccine**
  - Russia has fast-tracked their own vaccine candidate produced by Gamaleya Institute (named Sputnik V), which has not yet undergone Phase III Clinical Trials. Limited information is currently available regarding Clinical Trial results, safety and efficacy.
  - According to news reports in Washington Post, Bloomberg and other outlets, the Russian government has now given this vaccine conditional registration, which will open the door to manufacturing and civilian use. These reports also state that less than 100 people had officially received the inoculation against the epidemic by early August.1, 2
  - WHO spokesman Tarik Jasarevic was quoted as saying “We are in close contact with Russian health authorities and discussions are ongoing with respect to possible WHO prequalification of the vaccine” and continued on to say “prequalification of any vaccine includes the rigorous review and assessment of all required safety and efficacy data”.1

- **Purpose of the Clinical Trial process – why it matters in the discussion of Sputnik V**
  - Clinical Trial process is necessary to establish a balance between speed and safety. The purpose of Phase III, in particular, is to test on large populations of volunteers to confirm its effectiveness and monitor side effects. Phase III studies generally assess clinical outcomes, and are designed to determine whether the demonstrated benefits of the product outweigh its risks.
    - Note: The WHO still lists the Gamaleya vaccine as being in Phase I as of August 10.1
  - Even if Sputnik V is ineffective (as opposed to harmful), populations may lose faith in the ability of any vaccine to prevent disease. This could result in the inability to vaccinate sufficient numbers of people to achieve herd immunity.
  - Russia’s push to manufacture and distribute an insufficiently tested vaccine could potentially impel other countries to bypass appropriate Clinical Trial procedures.

Sources:
Note: Herd immunity levels can be more quickly achieved if people accept vaccination when it becomes available to them.

For more details, see Appendix.
Geography Considerations – US Overview

Coronavirus Aid, Relief, and Economic Security (CARES) Act for US

CARES Act Requires Coverage of COVID-19 Vaccine/Immunization

- **What’s required?**
  - An employer-sponsored group health plan must cover (without cost-sharing) any Qualifying Coronavirus Preventive Service

- **What is the deadline for coverage?**
  - Within 15 business days of the recommendation by the USPSTF or the ACIP

- **Any additional information?**
  - No guidance from the agencies to date, but based on statutory language, it appears that the requirement will apply to most employer-sponsored medical/Rx plans and likely will apply only in-network.
  - Pending guidance to the contrary, we anticipate that the following types of plans will not be required to cover the vaccine/immunization without cost sharing:
    - Retiree only (fewer than 2 current employees in legal plan on first day of plan year)
    - Grandfathered group health plans

Qualifying Coronavirus Preventive Service means an item, service or immunization that mitigates COVID-19 AND is:

An evidence based item or service that has a rating of “A” or “B” in the U.S. Preventive Services Task Force recommendations (USPSTF)

OR

An immunization that has a recommendation from the Advisory Committee on Immunization Practices (ACIP)
Operation Warp Speed is a collaborative effort to accelerate vaccine development, manufacturing and distribution for US

- Entities involved: HHS (Dept. of Health and Human Services), CDC, FDA, NIH, DOD (Dept. of Defense), and BARDA (Biomedical Advanced Research and Development Authority)
- Goal: Invest in and streamline COVID-19 vaccination development efforts and deliver a safe and effective drug to the general US public by the end of 2020
  - Note: It is not certain that all vaccine candidates will be effective; too early to tell
- Funding: $10 billion of funding ($6.5 billion for countermeasure efforts and $3.5 billion for research)

OWS is only choosing the manufacturers of the top 7 contenders who show promising results in initial trials, research, and technology capabilities:

- Novavax ($1.6 billion)
- Pfizer Inc ($1.9 billion)
- AstraZeneca ($1.2 billion)
- Moderna ($430 million)
- Merck and IAVI ($38 million)
- Protein Sciences, A Sanofi co. ($30 million)
- Janssen ($457 million)

Sources:

Geography Considerations – US

Operation Warp Speed (OWS) for US
Provider Delivery Considerations and Pricing – US

Enable any/all options:
- Provider Office,
- Community Pharmacy* or Clinic,
- Local Public Health Event, or a
- Contracted COVID-19 Screening/Testing Partner

* Community pharmacies may offer most convenient access

Coverage Arrangement
- Medical Plan,
- Voucher,
- Direct Contract or Reimbursement,
- PBM Network

Incentivize or Mandate
Whether optional or mandatory, consider use of wellness credits or full coverage if not available under the medical or pharmacy coverage

Sampling of Potential Vaccine Providers and Pricing
- Pfizer/BioNtech- $19.50 a dose (two doses necessary)¹
- Moderna- $37 a dose (two doses necessary)²
- Janssen- $10 a dose³

In an article published by the Wall Street Journal, it is speculated that most doses of the COVID-19 vaccine will be between $10 and $37, with most manufacturers requiring a 2 dose series. ⁴

Sources:
Geography Considerations – EMEA

Strategy approach

- **EU Strategy for COVID-19 vaccines**
  
  Mid-June, the European Commission presented a strategy to accelerate the development, manufacturing and deployment of vaccines against the SARS-CoV-2. Under this strategy the commission is supporting efforts to accelerate the development & availability of safe and effective vaccines in a timeframe of 12-18 months:

  - Initial investment of €2.7 billion has been committed in advanced purchase commitments
  - European commission is envisaging a contract with Sanofi-GSK for COVID-19 vaccines which would provide an option for all EU Member States to purchase the vaccine. Commission would have a contractual framework in place for the purchase of 300 million doses once an effective vaccine has been developed.
  - European Commission is also currently in negotiations with the following organizations for advanced purchase commitments for vaccine, Sanofi, Moderna, Johnson & Johnson, BioNtech and CureVac

- **Inclusive Vaccine Alliance**
  
  France, Germany, Netherlands and Italy have joined together to form the Inclusive Vaccine Alliance. The alliance is focused on achieving faster vaccine development and that pharma companies promise that such vaccine development must be accessible, available and affordable. The alliance is also working on making a portion of vaccines available to low-income countries, including those in Africa:

  - This alliance has reached an agreement with AstraZeneca to supply up to 400 million doses of Univ. of Oxford’s COVID-19 vaccine with an advance purchase commitment of € 750 million.

**Sources:**
Geography Considerations – EMEA
EMEA & Public Health Organizations Overview

- **UK**:
  - Sanofi and GSK have reached an agreement, subject to final contract, with the UK government for the supply of up to 60 million doses of a COVID-19 vaccine
  - 90 million vaccine doses from the BioNTech/Pfizer alliance and Valneva with more in the pipeline as part of its strategy to build a portfolio of promising new vaccines to protect the UK from COVID-19
  - In addition, treatments containing COVID-19-neutralising antibodies have been secured from AstraZeneca to protect those who cannot receive vaccines

- **COVAX Facility**
  - Lead by Gavi, World Health Organization (WHO) & Coalition for Epidemic Preparedness Innovations (CEPI) - The COVAX Facility has been created to guarantee rapid, fair & equitable access to COVID-19 vaccination worldwide. Their goal is to deliver 2 billion doses of vaccines with regulatory approval and WHO prequalification, with prioritization of healthcare workers of the participating 165 countries, followed by rest of the population
  - COVAX Facility is an important part of ACT- Accelerator is a dedicated framework the European Commission helped establish for enhancing global collaboration in speeding up the development and universal deployment of the tools required to fight COVID-19
  - 7 partners have been supported by COVAX, with an advanced market commitment of US $2 billion
  - AstraZeneca has committed COVAX a supply of 300 million doses of COVID-19 vaccine

Sources:
Geography Considerations – Global

Approach

- Combination of approaches available for countries throughout the world:
  - Pursue their own contract arrangements with Clinical Trial labs/manufacturers/distributors (such as Oxford/AstraZeneca), and/or
  - Participate in WHO’s ACT-Accelerator (“ACT” is “Access to COVID-19 Tools”) and have access to vaccines available to the world (also acts as a safety net in case the vaccine candidates involved in a country’s own contract arrangements do not prove effective)

Note: It is not certain that any vaccine candidates being considered will be effective; too early to tell

- ACT-Accelerator¹
  - Participating global health organizations include the Bill & Melinda Gates Foundation, CEPI, FIND, Gavi, The Global Fund, Unitaid, Wellcome, the WHO, the World Bank and Global Financing Facility
  - ACT-Accelerator is a framework for collaboration; it is NOT a decision-making body. It has 4 pillars: Diagnostics, Treatment, Vaccines, Health System Strengthening
  - Vaccine pillar is the COVAX discussion described on the previous slide

Source:
1. https://www.who.int/initiatives/act-accelerator/
Appendix
Immunity, Dosing and Coverage Considerations

- **Immunity considerations:**
  - 2 paths to achieving immunity: (1) Vaccines, (2) Infections
  - Herd immunity – Occurs when large portion of a community becomes immune to a disease, thereby making the further spread of disease unlikely. As a result, the whole community becomes protected; not just those who are immune
    - To achieve herd immunity, community’s target % immune threshold varies with how contagious a disease is; for instance, typical view is 70% immunity needed, but for measles (which is highly contagious), 94% is needed; targeting 70% for COVID-19
  - It is not certain these vaccine candidates will be successful in producing immunity; Clinical Trial process helps gauge success, but even vaccine candidates that pass might not achieve the same success in a real-world community with a large illness burden
  - If immunity is produced, it is not certain how long such immunity will be sustained
    - It is too early to tell how long immunity resulting from infections lasts
    - Not clear how long vaccine-induced immunity will last – will it be durable, or will re-vaccination be needed? If so, how soon?

- **Dosing and coverage considerations:**
  - Experts expect 1 or 2 doses will be required, depending on the vaccine
  - Coverage implications, using US as example and assuming an estimated 2-dose regimen:
    - Estimated number of doses to achieve herd immunity (70% of US population): 462 million doses for US (estimate only)
    - Estimated number of doses to achieve full coverage (100% of US population): 660 million doses for US (estimate only)
  - Global need (not just a US need), so coverage implications exponentially larger than just for US

Sources:
Sourcing, Manufacturing and Distribution Considerations

- Fill-finish process is important to achieving necessary coverage:\(^1\):
  - Fill-finish is process of filling vials and syringes and packaging them in highly sterile conditions
  - Fill-finish is a major hurdle on the path to vaccine distribution

- Components for fill-finish, and sourcing concerns for these components:\(^1\):
  - Glass vials and stoppers:
    - Shortage of sand to make glass vials – takes 2 years to produce # of glass vials needed for COVID-19 vaccines\(^1\)
    - Stoppers (rubber or latex components) can’t interact with chemicals inside the vial\(^1\)
  - Needles and syringes
  - Chemicals and vaccine components
    - Adjuvants (adjuvant strengthens the body’s immune response to inoculation)\(^1\)
      - Note: one adjuvant comes from bark of a special tree in South America that is only harvested November-January\(^1\)
    - Many of the needed chemicals come from China and India\(^1\)

- Additional concern: Segregate COVID-19 needs from needs of other medicines to minimize disruption to other medicines\(^1\)

- Cold-chain distribution needs:\(^1\):
  - Most vaccines must be kept at 2 degrees to 8 degrees Celsius (35.6 degrees to 46.4 degrees Fahrenheit)
  - Each step in the distribution chain must maintain consistent temperature in that range without interruption

Sources:
2. [https://science.sciencemag.org/content/368/6494/948](https://science.sciencemag.org/content/368/6494/948)
Operationalizing at Scale – Vaccine Development, Manufacturing and Distribution

Importance of simultaneous workstreams; timing doesn’t allow for sequential process

<table>
<thead>
<tr>
<th>Workstream</th>
<th>Relative Timeframe (to illustrate concurrent workstreams)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccine Development</td>
<td></td>
</tr>
<tr>
<td>- Pre-Clinical Vaccine Development and non-human testing</td>
<td></td>
</tr>
<tr>
<td>- Phase I Clinical Trials with human testing to confirm safety and dosage</td>
<td></td>
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<tr>
<td>- Phase II Clinical Trials with human testing to confirm immunogenicity (does it provoke an immune response?)</td>
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<tr>
<td>- Phase III Clinical Trials with human testing to confirm large-scale efficacy (does it protect, and how long will it protect?)</td>
<td></td>
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<tr>
<td>- Review &amp; Approval Process</td>
<td></td>
</tr>
<tr>
<td>- Monitor effectiveness in real-world environment; continue to improve understanding of risks, benefits and optimal uses</td>
<td></td>
</tr>
<tr>
<td>Sourcing for Vaccine Delivery Components and commodities to produce those components</td>
<td></td>
</tr>
<tr>
<td>- Glass vials and stoppers (includes sourcing sand for use in manufacturing glass vials, and rubber and latex for stopper caps)</td>
<td></td>
</tr>
<tr>
<td>- Needles and syringes (includes sourcing for materials to create the needles and syringes)</td>
<td></td>
</tr>
<tr>
<td>- Chemicals (adjuvants to provoke immune response, etc.) (includes sourcing for materials to create the adjuvants)</td>
<td></td>
</tr>
<tr>
<td>Manufacturing facilities identified and readied</td>
<td></td>
</tr>
<tr>
<td>- Suitable manufacturing facilities identified</td>
<td></td>
</tr>
<tr>
<td>- Construction begun on new facilities for readiness in 2021 or later</td>
<td></td>
</tr>
<tr>
<td>- Capacity accelerated for existing purposes to develop stockpile of other medicines until COVID candidate(s) confirmed</td>
<td></td>
</tr>
<tr>
<td>- Preliminary customization work identified for existing facilities; readied for pivot to producing COVID-19 vaccine</td>
<td></td>
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<tr>
<td>Manufacturing at scale</td>
<td></td>
</tr>
<tr>
<td>- Production of the vaccine itself in a sterile environment in existing facilities</td>
<td></td>
</tr>
<tr>
<td>- Packaging of the vaccine and delivery components in a sterile environment in existing facilities</td>
<td></td>
</tr>
<tr>
<td>- Fill-Finish technology and process for the vaccine doses</td>
<td></td>
</tr>
<tr>
<td>- Blow-Fill-Seal technology for pre-filled syringes</td>
<td></td>
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<tr>
<td>Distribution Logistics and Planning</td>
<td></td>
</tr>
<tr>
<td>- Priority distribution chain: frontline healthcare, first responders, vulnerable populations, general population</td>
<td></td>
</tr>
<tr>
<td>- Destinations confirmed: continually updated</td>
<td></td>
</tr>
<tr>
<td>- Supply Chain planning utilizing cold chain approach; continually updated as new information becomes available</td>
<td></td>
</tr>
<tr>
<td>- Distribution begins and continues to evolve as greater coverage for demographic groups is achieved</td>
<td></td>
</tr>
</tbody>
</table>

Sources:
https://science.sciencemag.org/content/368/6494/948
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