The Biopharmaceutical Supply Chain and COVID-19

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Overview

- Industry role in combatting COVID-19
- Helping ensure continuity in drug supply chain
- Range of uncertainties posed by COVID-19
- Select FDA actions to help ensure continuity of clinical trials
- Myths and facts regarding the supply chain
- Concerns regarding “Buy America”-type proposals
- Increasing resiliency in the supply chain

Industry Commitment to *Beat* Coronavirus

We **are rapidly screening our vast global libraries of medicines** to identify potential treatments and have numerous clinical trials underway to test new and existing therapies

We are **dedicating our top scientists and using our investments in new technologies** to speed the development of safe and effective vaccines

We are **sharing the learnings from clinical trials in real time** with governments and other companies to advance the development of additional therapies

We are **expanding our unique manufacturing capabilities and sharing available capacity** to ramp up production once a successful medicine or vaccine is developed

We are **collaborating with government agencies, hospitals, doctors and others** to donate supplies and medicines to help those affected around the world

We are **working with governments and insurers** to ensure that when new treatments and vaccines are approved they will be available and affordable for patients

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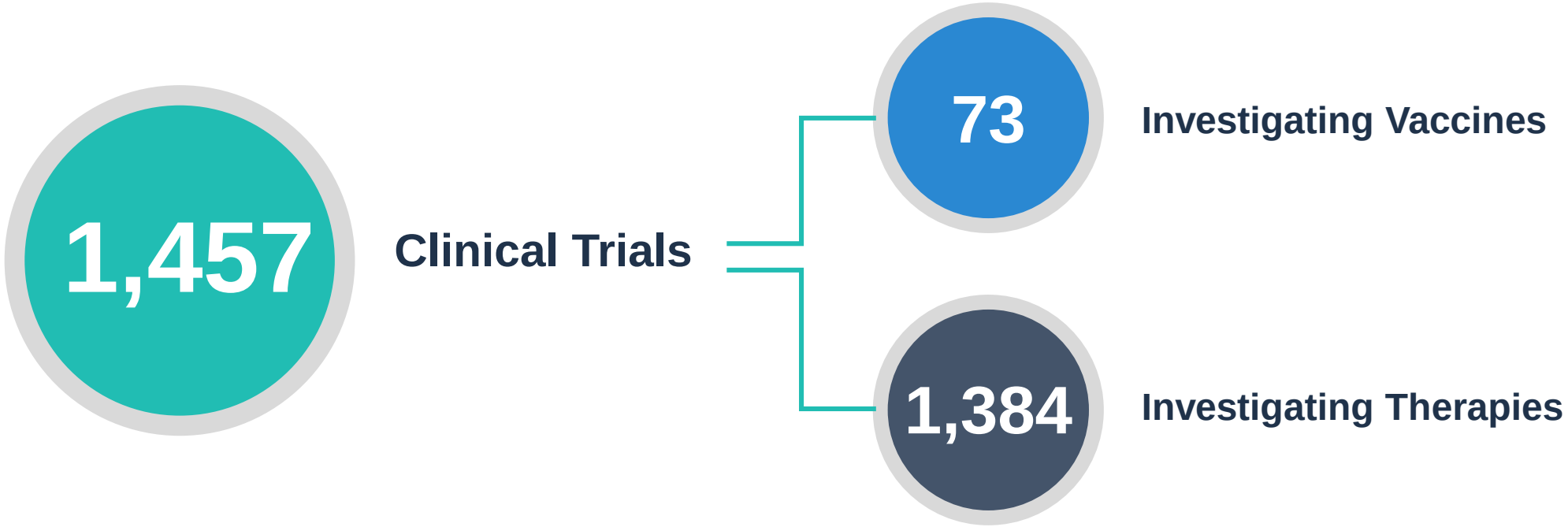
Factors Contributing to the Industry's Response

Armed with experience garnered from previous outbreaks and a vast storehouse of knowledge about infectious diseases like influenza, malaria and HIV, researchers are working to develop and deliver diagnostics, treatments and vaccines to save lives and restore the rhythms of daily life for billions of people.

Developing Treatments and Vaccines to Fight COVID-19

There are **1,457 clinical trials under way across the globe** for vaccinations and treatments.

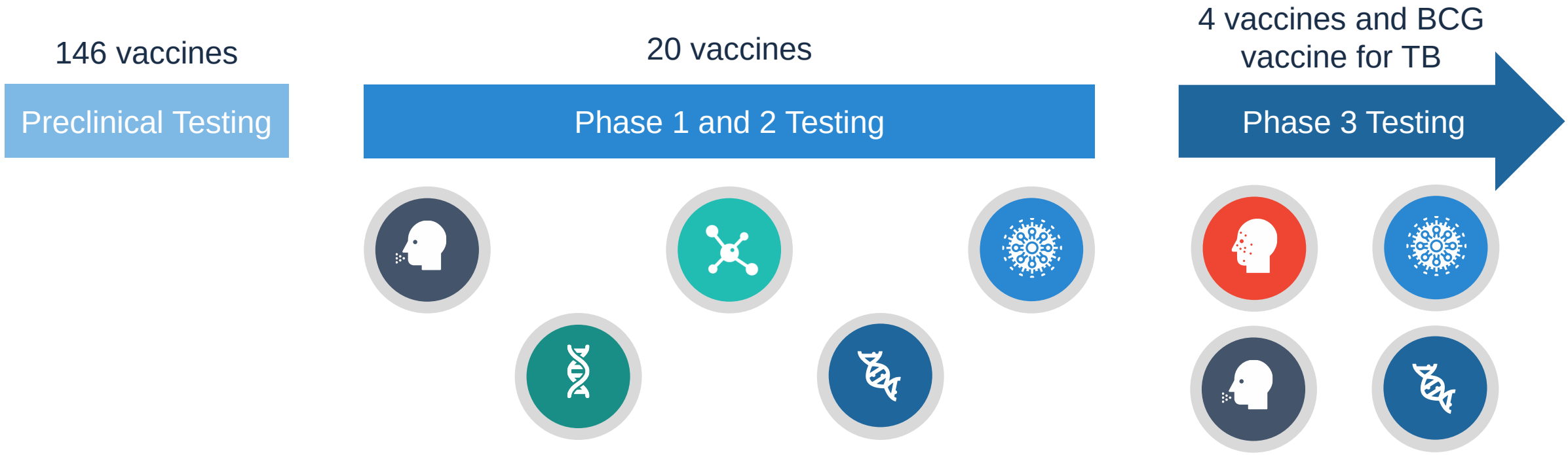


Data as of 7/24/2020

Source: World Health Organization International Clinical Trials Registry Platform (ICTRP)

Developing and Testing Vaccines to Prevent COVID-19

COVID-19 vaccines currently under investigation include **over 170 unique "shots on goal"**



Data as of 7/24/2020

Source: World Health Organization International Clinical Trials Registry Platform (ICTRP)

It Will Take a Minimum of 18 to 24 Months for Potential FDA Approval of a COVID-19 Vaccine

Faster Timeline & Ramp Up

- In 2003, it took 20 months from sequencing SARS to the first human study of a vaccine-today, leveraging prior experience it has been **less than 4 months from sequencing SARS-CoV-2** to the first human study of a vaccine
- **Manufacturing ramp up** occurring concurrent with clinical trials
- Public-private collaborations to **increase manufacturing capacity,** access to materials (e.g., vials), and support tech transfer
- Efforts to **facilitate regulatory review and approval** with regulators around the globe

Differing Approaches

- **Some approaches offer speed**

  Knowing the virus's genetic sequence, companies can synthesize and manufacture clinical study supplies of an RNA or DNA-based vaccine in a matter of weeks

- **Some approaches can boost the impact of a potential vaccine**

  Adjuvants can boost the immune response and minimize the amount of vaccine needed

Failure Rate

- **There is a historical high failure rate**

  Only 5-10% are likely to succeed

  We need lots of shots on goal to assure a few shots in goal

  Unclear how historical attribution rates will apply

Ensuring Continuity in the Medicine Supply Chain

Biopharmaceutical Companies

- **Companies report substantial data on certain types of potential shortages to FDA and other regulatory authorities internationally** and work closely with FDA to prevent and mitigate shortages
- **Manufacturers continuously monitor their supply and distribution lines to ensure sufficient supply, anticipate risk, and avert potential disruptions.**
- **Companies have robust inventory management systems** that typically include:
  - Data on anticipated demand reflecting historical demand and supply data
  - Risk management plans that address additional or alternate manufacturing sites, inventory reserves, and/or a range of global external suppliers
  - Logistics planning to help ensure continuity in shipping of supplies

U.S. Food and Drug Administration

- **FDA is working with individual companies to facilitate ramping up manufacturing** to address surges in demand and expediting approvals of changes in the drug supply chain
- **FDA is working closely with companies to expedite development and availability of COVID-19 treatments and vaccines**, including helping companies to leverage scientific and clinical trial data from the United States and other countries
- **FDA is working with companies to provide increased flexibilities in the conduct of ongoing clinical trials**

Range of Challenges Posed by COVID-19

- Travel bans and import/export restrictions impacting costs and timeliness of transport
- Patchwork of essential worker policies resulting in uncertainty for R&D, manufacturing, and distribution
- Pandemic resulting in disruptions in clinical trials
- Immigration EO limiting transfer of key company personnel
- Localized surges in demand leading to shortages of generic ICU medicines
- Potential Buy America EO/legislative proposals diverting focus from COVID-19 efforts
- Challenges of needing to have as many shots on goal as possible and many different vaccine modalities from R&D perspective while simultaneously increasing manufacturing capacity
- Unprecedented cybersecurity threats posed by foreign actors
- Uncertainties around projected demands, particularly in mid to long term and impact of and magnitude of vaccine reluctance & interplay with flu season
- Concerns regarding adoption of nationalist policies and impact on supply chain resiliency
- Worker safety concerns, including workforce impact of COVID cases

Selected FDA Actions During COVID-19

Providing appropriate regulatory flexibility in conduct of clinical trials to ensure protection of human subjects and to promote both trial continuity and trial integrity

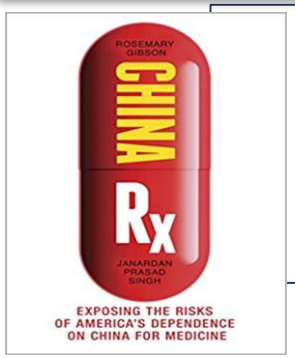
Participation in ACTIV partnership and Operation Warp Speed to inform clinical trial design and conduct and relevant FDA regulatory standards to help ensure efficient use of clinical resources and more efficient reviews

Expediting quality assessments for products to treat COVID-19 patients and transferring manufacturing to new or multiple sites to avoid supply disruptions

Ongoing individual outreach to manufacturers and others in supply chain around potential shortages and mitigation

Additional flexibilities for generics and expediting of generic approvals related to essential medicines in shortage due to localized increases in demand, e.g., generic inhalers

The Drug Supply Chain: Rhetoric vs. Facts



"China could potentially weaponize our medicines." "China can't be trusted…what if China were the anthrax attacker?"—*Rosemary Gibson*

"FDA Commissioner Stephen Hahn reported in Feb. that only 20 drugs used in the United States come solely from China in finished drug form or contain an "active pharmaceutical ingredient" made solely in China. None of those drugs are considered critical, he said." via @politico

Judith A. McMeekin, Associate Commissioner for Reg. Affairs, FDA:
"American consumers should know that the U.S. drug supply is safe, and supply chains are secure."
Sen. John Cornyn (R-TX): "Excuse me just a second, did you say our supply chains are secure?"
McMeekin: "Yes."

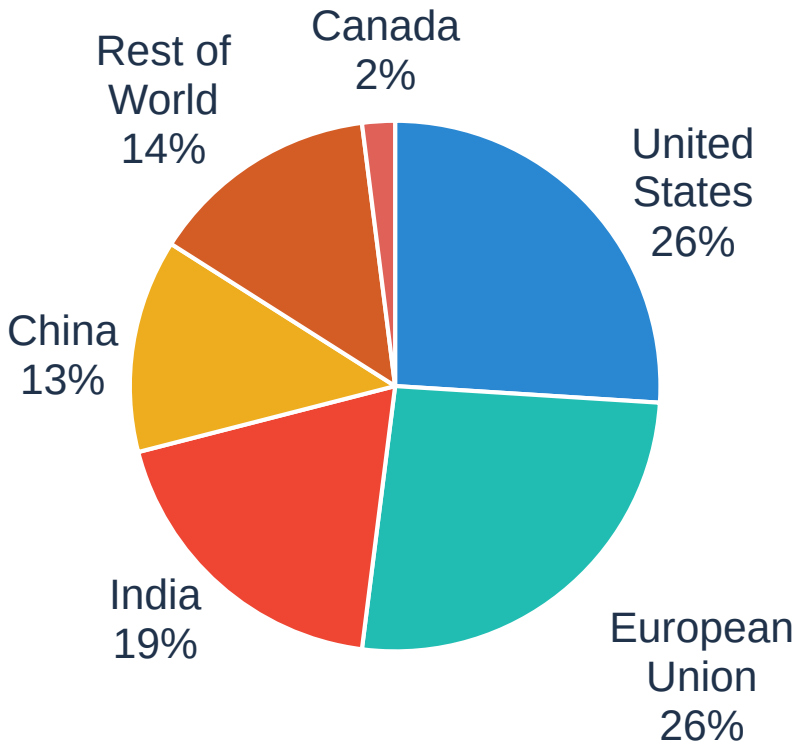
"What I can speak to is… how dependent the United States of America is on the global supply chain, not just for its medicines but for its medical supplies and medical equipment...The essence of the order … is to bring all of that home so that we don't have to worry about foreign dependency."
–WH Trade Advisor Peter Navarro

FDA has identified only *3 meds from WHO essential meds list used in U.S. solely dependent on China:*

- 2 meds to treat TB
- 1 medicine that treats two different types of bacterial infection

Fact: Industry relies on globally diverse supply chain

Myth: Industry solely reliant on other countries for its API



- **Data on location of API facilities reflects globally diverse supply chain**
- Data from Avalere shows that **54% of API measured in dollar value, consumed in the US came from the US in 2019**
- FDA determined there are **only three medicines** on the WHO Essential Medicines list whose API manufacturers are solely based in China (2 meds to treat TB & 1 medicine that treats two different types of bacterial infection)
- FDA has identified **only 20 medicines** that sole source their API or medicine from China, and none of these have been deemed critical medicines—**out of 20,000 medicines approved for marketing in the US**

Source: FDA, "COVID-19 and Beyond: Oversight of the FDA's Foreign Drug Manufacturing Inspection Process," June 2, 2020. https://www.fda.gov/news-events/congressional-testimony/covid-19-and-beyond-oversight-fdas-foreign-drug-manufacturing-inspection-process-06022020

Fact: Significant shifts in manufacturing cannot be implemented overnight

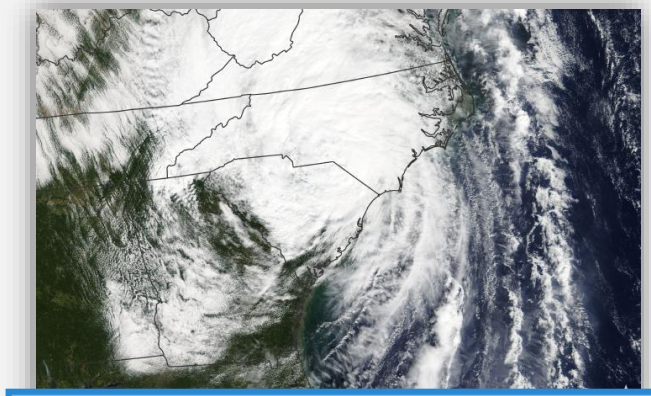
Myth: Changes can quickly be made to supply chains. Moving all manufacturing to the United States would be easy.

PhRMA member company invested $2 billion in new API manufacturing facility for diabetes and obesity medicines expected to be operational in 2020

- Biopharmaceutical manufacturers must begin setting up the manufacturing supply chain for a medicine years before that medicine is approved for use by patients…in fact companies' long-term global supply chains are planned over the course of decades
- Overall facility and supply chain planning often occurs decades in advance
- Building a new biopharmaceutical manufacturing facility can take 5 years or more before it is operational and can cost $1 to $2 billion, including time and costs for regulatory compliance
- Can take 2-3 years to establish and obtain approval for existing API facility
- Need to address infrastructure gaps in US:
  - Current STEM worker shortfall of over 2 million in US
  - US produces 10% of overall STEM bachelor's degrees---China 50% (labor costs 40% or more less expensive ex-US)
  - Need to build advance manufacturing and other key capacities to support innovation in manufacturing to help offset substantial cost differentials with other countries

Fact: Diverse Supply Chains Help Prevent and Mitigate Supply Disruptions

Myth: Geographic diversity doesn't really matter when setting up supply chains. It is just an excuse manufacturers use.



When Hurricanes caused significant flooding in North and South Carolina, having alternate packaging capabilities for vaccine products in Europe allowed several large biopharmaceutical companies to continue supply to the U.S. market.

- Diversity across the drug supply chain reduces the potential impact of disruptions that may result from natural disasters or other public health emergencies.
- Having sources of supply of crucial drug substances in the US and abroad allowed companies to respond to unprecedented demand in a way that would not have been possible without the multiple sources of capacity.
- Having the ability to redirect supply from other sites has helped ensure there have been no significant ongoing disruptions in US supply chain for innovator medicines during the COVID-19 pandemic.

Concerns with Certain “Buy American” and/or Related Policy Proposals

1

Any policy changes that seek to unravel the global drug supply chain developed over decades should be based on the facts.

- Need comprehensive study of the supply chain to seek to identify a narrow set of medicines for which there may be undue reliance on countries that pose significant national security concerns and solutions should be targeted based on the facts in each case.

2

Policy proposals ignore the strengths and benefits of a globally diverse supply chain.

- Maintaining flexibility in the supply chain protects against shortages by allowing manufacturers to redirect potential supply from other facilities and increase capacity in other sites to respond to increases in demand.

➢ When Hurricane Maria struck Puerto Rico, approximately 50 pharmaceutical manufacturing facilities were impacted. Despite this, companies were able to work with the FDA to source from facilities in several different countries, limiting the number of resulting shortages.

➢ Similarly, following severe flooding in North Carolina, manufacturers were able to redirect supply from other countries to avoid disruption in supply.

Concerns with “Buy American” or Other Similar Policies

3

Mandating the entire supply chain be solely based in the United States overnight ignores fundamental feasibility and practical challenges.

- The United States lacks critical advanced manufacturing capabilities.
- The United States currently faces a STEM worker gap in the millions—we need long-term STEM investments.
- The United States lacks sufficient manufacturing capacity—It can take 5-10 years and $1 to $2 billion for a company to build a single new facility, secure supplies, and comply with various government regulations.

4

These policies risk creating large-scale disruptions including shortages.

- Unworkable, large-scale mandates, such as immediate domestic sourcing of countermeasures and essential medicines, could fundamentally disrupt the supply chain and production of medicines for the United States and globally.
- Raising the cost of doing business through mandates will make the United States less globally competitive, slow U.S. economic growth, potentially shrink the generic industry’s footprint and potentially result in higher drug prices.
- Compelling U.S.-only production of certain medicines could lead to retaliatory actions by our trading partners that could further inhibit resiliency in the supply chain.

Meaningful Policies Are Needed To Foster Increased Manufacturing In The United States Without Disrupting The Drug Supply Chain

- We should ensure America remains at the forefront of biopharmaceutical innovation by expanding advanced manufacturing and related technologies capabilities and capacity in the U.S. and investing in a 21st century workforce.
- We should pursue policies that support resiliency in the supply chain through increased diversity in supply chain sourcing and investment in the U.S. to decrease reliance on countries that pose a significant public health or national security risk.
- We should level the playing field for Americans by using all available trade tools to prevent other countries from using harmful practices that undermine U.S. intellectual property rights and violate existing trade deals.
- We should review and assess the adequacy and role of the Strategic National Stockpile in responding to pandemics.
- We should ensure that any policies are based on the facts not rhetoric and ensure we don't implement policies that could lead to major disruptions in the supply chain and disadvantage U.S. global competitiveness