Development of mRNA Vaccines at Lightspeed… A Regulatory Perspective

CMC Strategy for mRNA-LNP Vaccines:
Challenges and Regulatory Considerations

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Overview

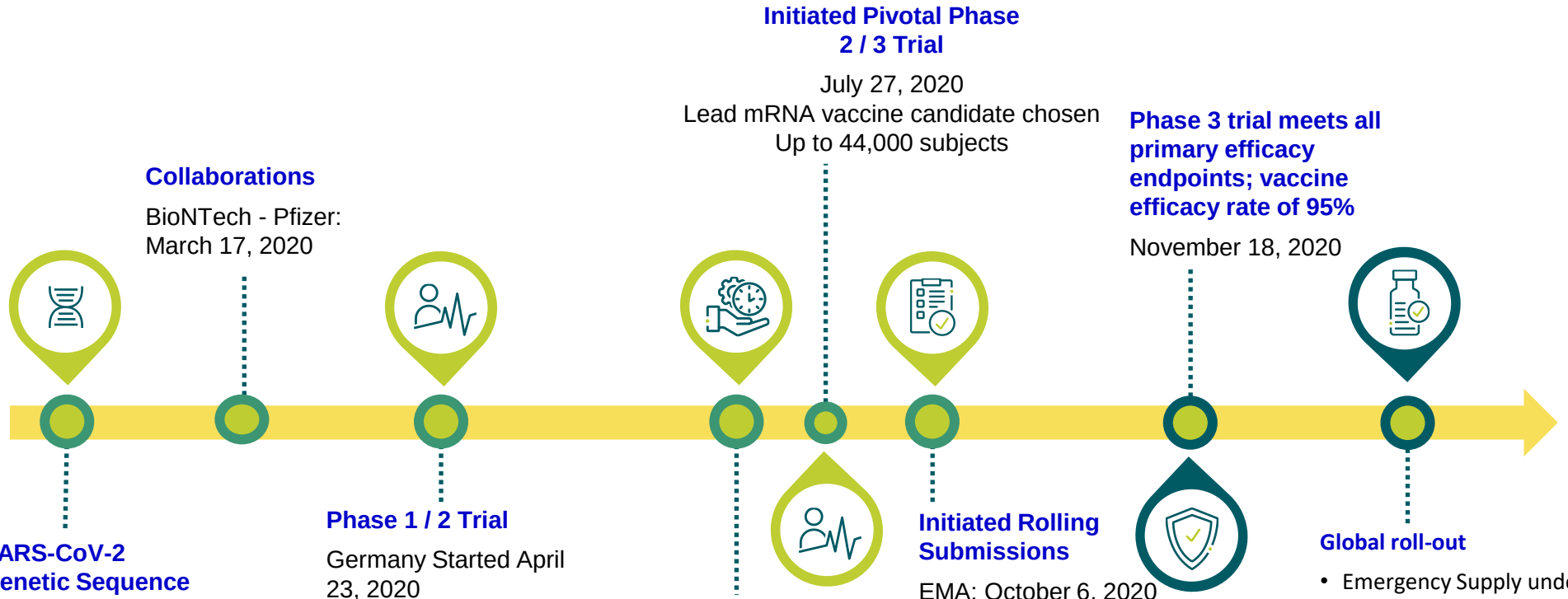
- Rapid Development and Acceleration of Production
- Global Authorizations of Comirnaty:
  Regulatory Innovation and Flexibilities
- Experience with Rapid Updates
- Opportunities to Provide Benefits of Vaccines to Patients Earlier and More Efficiently

The Challenge

The unprecedented stress that COVID-19 has imposed on the global biopharmaceutical supply chain necessitates *urgent action to implement flexible, but predictable, regulatory tools and approaches that will allow manufacturers to rapidly increase manufacturing capacity* for the production of COVID-19 therapeutics and vaccines to meet global demand and avoid or mitigate drug shortages for non-COVID-19-related products, without compromising patient safety or product quality.

Source: WHO, *Recommendations to Support the Rapid Increase of Manufacturing Capacity for the Production of COVID-19 Therapeutics*

The Journey of Developing the Pfizer/BioNTech mRNA Vaccine



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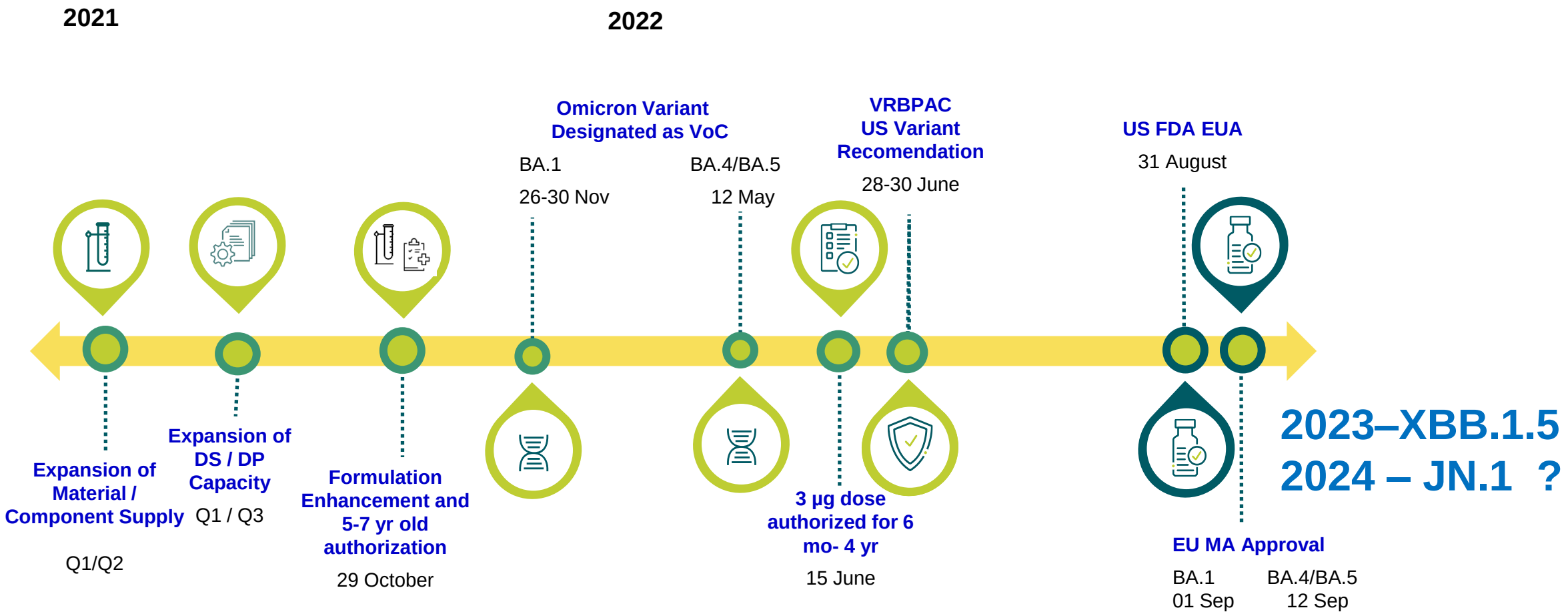
Previous Vaccines: Average is about 2,500 Days

COVID-19 Vaccine: 266 Days

Ongoing Development



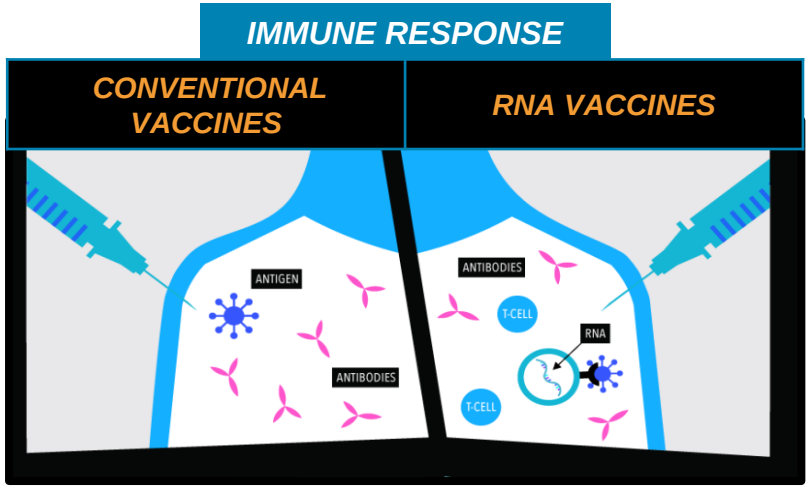
Authorization / Approval for >350 licenses / applications

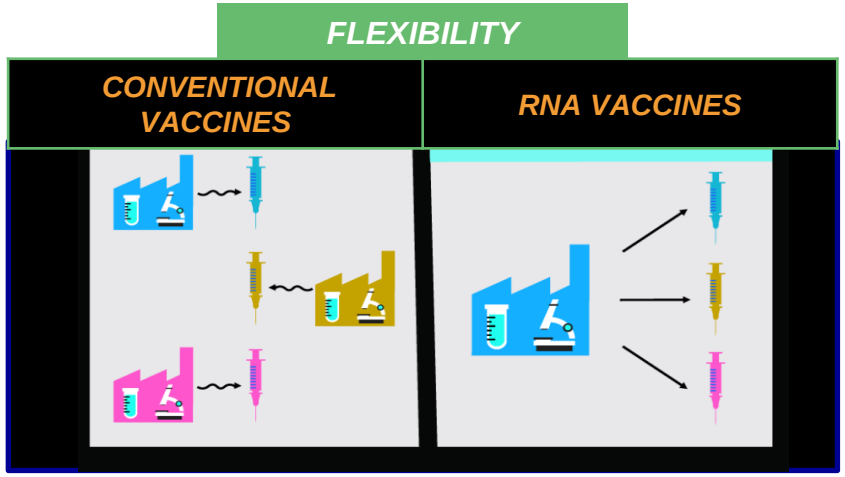
in >80 countries + WHO / COVAX / USAID distribution

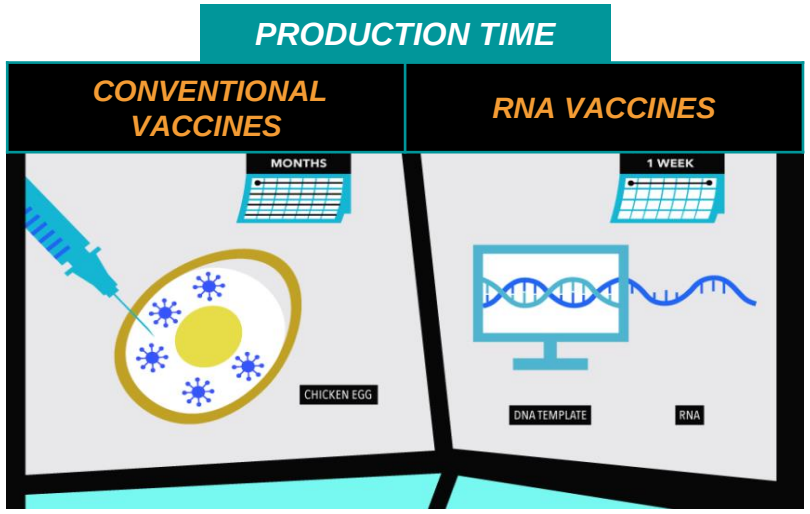
How was this Rapid Development & Acceleration of Production Possible?

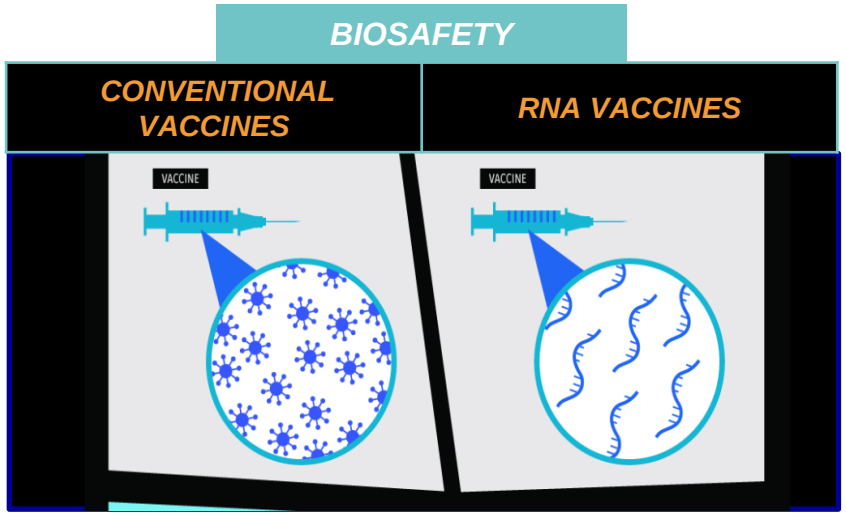
- Leveraged mRNA flu development program
  - Team established
  - Expertise in technology
  - Process and Analytical Development transferrable
- RNA platform lends itself to rapid development
  - Proven Repeatedly in Capacity Expansion
  - Proven Again with Variant Vaccines
- “Lightspeed” Designation
  - Mindset
  - Procedures
- Frequent Communication
- Clarity of Common Objectives with Regulators
- Hard Work and Sacrifice

mRNA Vaccine Approach









Lightspeed Designation

- Don’t let bureaucracy get in the way
- Streamlined justification for requests of resources & capital
- Decisions to use additional resources at the edge of normal vaccine network
  - Colleagues with related expertise
  - Facilities with sterile products or other related API expertise
- Risk-based decisions with bias toward high probability of success, sometimes with acknowledgement of trade-offs
  - Examples; -80° C storage, MDV, etc.
- Perform many product and process development activities in parallel rather than sequentially
  - Overlapping stages of development
  - Build capabilities for global production prior to clinical proof of success
  - Repeated with Formulation Enhancement and Variant Vaccine Development

Frequent Communication and Rapid Decision Making

- Within Pfizer and BioNTech
  - Frequency of Standard meetings
  - Digital platforms
- Between Sponsors & Regulators
  - Rapid decision making enabled by IND protocol / amendment reviews within days
  - Delivery of scientific advice in real-time
  - Alternative approaches & flexibility in data submissions; Rolling submissions allowed regulators to view real-time data and shorten review duration from last data submission
  - Clear prioritization of changes based on quality enhancement and supply impact

Standardized, Global Product and Registration Dossier

- Global approach to product configuration and control strategy
  - “Any customer can have a car painted any color that they want, so long as it is black” – Henry Ford
  - Example: Testing and Specifications
- Waivers for Many Ancillary Documents, Normative Documents, Pre-Certification, etc.
- Single Product License for Different Configurations, or Multiple Sites
- Real time data submission and review for CMC
- Reliance on other Stringent Regulatory Authority/Rest of World approvals
  - Formal or Informal
  - Sharing of queries and responses
- Acceptance of potential for post approval commitment(s) as outcome of query / response process

Standardized, Global Product and Registration Dossier

- 2022-2024 has brought some reversion toward ‘normal’
- Movement away from conditional or emergency authorizations

Pros

- Improved rapport with some agencies
- Enabled us to Deliver 2 different variant vaccines
- Some agencies have requested less duplication between licenses / dossiers

Cons

- Continued extensive resources to address queries and commitments
- Speed of rollout of pediatric formulation and variant vaccines not matching initial rollout
- Waste of some vaccine that has become obsolete
- Uncertainty of requirements & timelines for transition

Additional Flexibilities

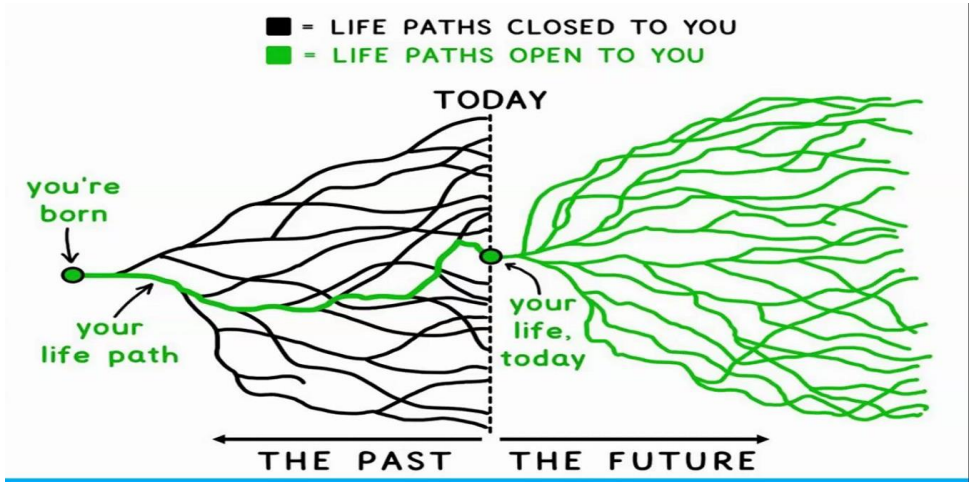
- Matrix and other Enhanced Validation Approaches
  - Acceptance of knowledge / data gained from similar products manufactured with the same well-characterized platform technology
  - Extension of product specific data produced to support development or production at earlier sites
- Realize Benefits of Advanced platforms
  - Demonstrated ability to update vaccine and even apply to other vaccines
  - Scalability and Replication
- Science & risk-based approaches to enable rapid changes and improvements
- Remote facility GMP inspection: A useful mechanism for verifying GMP compliance
- Streamlined Processes for Batch Release by Regulators

Opportunities to Provide Benefits of Vaccines to Patients Earlier and More Efficiently

- Enhance communication between industry and regulators
- Reduce or standardize ancillary documentation
- Greater utilization of enhanced platform technologies
- Potential to maintain greater flexibility of rolling submissions for data that must come relatively late in development cycles such as Stability, Process and Cleaning Validation
- Risk-based and fit for purpose CMC requirements
- Applicability of distant assessments to augment inspections for verifying GMP compliance
- Expansion of Reliance Practices as a goal
  - Reduce duplicative import & release testing
- Establish a harmonized global pathway for EUA/conditional marketing authorization

Some Personal Lessons Learned

GET COMFORTABLE BEING UN-COMFORTABLE



Announced Friday May 5, 2023

WHO says Covid-19 is no longer a global health emergency

By Jamie Gumbrecht, Jacqueline Howard and Deidre McPhillips, CNN
Updated 11:26 AM EDT, Fri May 5, 2023

Getty Images

The World Health Organization declares an end to the Covid-19 global health emergency

Only took 3 years, 1 month, 23 days, 20 hours and 58 minutes!!

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Thank You!

Questions?