Re-imagining vaccine manufacturing

Shifting the paradigm of vaccine process development and manufacturing to address global health challenges

DCVMN AGM 2020

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Process Solutions
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Agenda

01 Introduction
02 A Paradigm Shift
03 Re-imagining vaccine manufacturing
04 Take away messages
Our mission

Enabling the industry to produce better faster safer vaccines to improve access, globally

Vaccines are a major contribution to overall Global Health
We contribute
to global vaccine access

1. Technology, Services & expertise
2. Collaborations
3. Training curricula

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1. Re-imagining vaccine manufacturing - Josephine Cheng
Overview of Vaccines

Vaccine Market Growth Drivers

- Increased population & immunization coverage
- Expansions & decentralization
- Innovative vaccines
- Emerging & re-emerging diseases
- Platforms & Manufacturing innovations

Major Challenges of the Vaccine Industry

- Vaccine type and process diversity
- Economies of scale
- Funding processes
- Global capacity
- Outbreaks and pandemics
A Paradigm Shift with Pandemics

Major Challenges with Outbreak and Pandemic Vaccines

**Time**
The typical vaccine paradigm doesn’t allow adequate response to tackle outbreaks

**Cost**
- Vaccine development & licensure requires $>500$ million
- No guaranteed long-term market

**Scalability**
- Need to be able to produce huge amount of doses in a short time
- Global vaccine manufacturing capacity may not be sufficient for COVID19
A paradigm shift

Time is compressed, phases overlap

Traditional paradigm
+10 years

Target ID, development partner selection & Pre-clinical trials

Go or no-go decision to invest in candidate

Small-scale clinical trial material

Phase 1
First trial in humans

Manufacturing scale-up, commercial scale, process validation

Phase 2a
Efficacy trial in humans

Large-scale manufacturing

Phase 3
Evaluation trial in humans

Outbreak paradigm
2-4 years

Target ID, development partner selection & Pre-clinical trials

Go or no-go decision to invest in candidate

Clinical development

Safety/Dose selection
First in humans (safety)

Safety/efficacy
Efficacy trial

Manufacturing development, scale up, clinical lots, commercial scale, validation of process

Regulatory pathway for emergency authorization

Large-scale manufacturing

Adapted from NEJM, Lune et al., March 30th, 2020
Pandemics and outbreaks
How they have influenced vaccine manufacturing

The Evolution of Vaccine Production in Response to Pandemics and Outbreaks

**H1N1 Influenza**
- 214 countries
- 762 million cases
- 284,000 deaths

**MERS-COV**
- 27 countries
- 2,500 confirmed cases
- 866 deaths

**Ebola**
- 10 countries
- 15,283 confirmed cases
- 11,325 deaths

**Zika**
- 87 countries
- 5,000 cases

**COVID-19 (SARS-COV2)**
- YTD June 8, 2020
- 186 countries
- 7 million cases
- 405,000 deaths

2009
- Single-use final fill

2012
- Development of full single-use platforms

2014
- Process development time can be complete in two months -
- Process can be scaled up to 2009 & using single-use technologies

2015
- Increase of platforms mRNA & viral vectors

2020
- +6 billion doses planned for manufacturing in 2020-2021

Millipore
- Preparation, Separation, Filtration & Monitoring Products

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COVID-19 pandemic has boosted development and capacity building
Unprecedented activities around a vaccine

Fastest human vaccine development in history

- 42 days 1st vaccine created after novel virus sequencing
- $6.7 billion global investment
- 213 candidates in the pipeline
- 37 already in human studies
- 9 candidates in Phase III

Between 7-9 vaccines could obtain regulatory approval within the next 2 years

Unprecedented capacity building in short period of time

- 1 Billion COVID-19 vaccine doses in 2020 & 8-9 billion doses by 2021 announced by the industry vs 1 billion doses by 2022 predicted by experts with current capacity.

Source: Milken Institute COVID vaccine tracker, Oct. 22, 2020
Global capacity is constrained to respond to COVID19 need

The “unknown” preparedness remain the biggest challenge

Next time, how can we minimize risks and be better prepared?”

• Acceleration of development is needed.

• Platform Technology to reduce changes & increase production capabilities.

• Prepare for scalability once vaccine is developed.
re-imagining
Vaccine manufacturing
Re-imagining vaccine manufacturing

Opportunity to Shift the Development and Manufacturing Paradigm

- Establishing multiple platforms to accelerate Development
- Flexible & next generation manufacturing
- Decentralized manufacturing
Establishing platforms to accelerate vaccine development and manufacturing

**Collaboration with the Jenner Institute**

- **Collaboration with the Jenner Institute, started in 2017: Objective:** Develop a cost effective, rapid platform for adenovirus vector using a Rabies vaccine candidate for clinical phase 1 material, using single use and filtration technologies.

- The platform is currently leveraged for **COVID-19 efforts**

**Key achievements**

- Development of a platform at 4L batch scale for 2000 doses
- Process *simplification* and single use implementation
- Increased process efficiency
- Platform was leveraged for COVID-19 and allowed significant time saving

*Publication: Fedosyuk et al, Vaccine, 2019*
Flexible & next generation manufacturing

Flexible Manufacturing Will Be Required to Accelerate and De-risk Vaccine Manufacturing Preparedness

Implementation of Single use in Final filling – GSK case study H1N1, 2009

<table>
<thead>
<tr>
<th></th>
<th>Traditional</th>
<th>Single use</th>
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<tbody>
<tr>
<td>Clean and set-up</td>
<td>14 hrs</td>
<td>&lt;1 hr</td>
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<tr>
<td>Cleaning validation</td>
<td>Extensive</td>
<td>Zero</td>
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<tr>
<td>Filling time</td>
<td>24 hrs</td>
<td>10 hrs</td>
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<tr>
<td>Average vials/hr</td>
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<td>10,000</td>
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<tr>
<td>Aseptic connections</td>
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<td>0</td>
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<tr>
<td>Operator training</td>
<td>2 weeks</td>
<td>2 days</td>
</tr>
<tr>
<td>Equipment utilization</td>
<td>35%</td>
<td>82%</td>
</tr>
<tr>
<td>Total time</td>
<td>38 hrs</td>
<td>12 hrs</td>
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</table>

Faster deployment
Flexibility to change scale or process
Reduces time to market
Accelerate response to high surge of vaccines

Traditional large vaccine manufacturing facilities

Manufacturing facility using single-use technologies

<table>
<thead>
<tr>
<th></th>
<th>Traditional stainless facility</th>
<th>Single-use facility</th>
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</thead>
<tbody>
<tr>
<td>Capex required</td>
<td>~$500M to $1B</td>
<td>$20-100M</td>
</tr>
<tr>
<td>Time to construct</td>
<td>5-10 years</td>
<td>1.5 years</td>
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<tr>
<td>Change over time</td>
<td>4 weeks</td>
<td>0.5 days</td>
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<tr>
<td>Footprint</td>
<td>~70,000 m²</td>
<td>~11,000 m²</td>
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Re-imagining vaccine manufacturing - Josephine Cheng
Flexible & next generation processing
Facility of the future

Revisiting vaccine manufacturing through the integration of next generation processing concepts

Upstream intensification
Better cell culture platforms, scale out strategies

Downstream intensification
De-complexification and efficient processing

Enabling smart manufacturing
Increased automation & digitalization
Several LMICs have developed local vaccine capacities to « own their vaccination strategy »

- Emerging vaccine manufacturers represent now almost ~20% of the market, led by India, China and Brazil.

- Additional countries have expressed their desire to localize and expand current vaccine manufacturing in different regions in the globe.

- COVID19 pandemic is urging governments to fill their current gaps and reduce weaknesses when it comes to pandemic preparedness.
Re-imagining vaccine manufacturing for the future

Conclusions

1. Pandemic and outbreaks are **inevitable and unfortunately** difficult to predict

2. Past occurrences have **improved vaccine manufacturing** and the response speed

3. **Efforts** are still needed to **simplify and accelerate** manufacturing

4. **Global capacity increase, flexibility, evolving towards template 4.0 and decentralization** will be key to respond better to pandemics
Josephine Cheng
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Thank You for listening!

For more information about Vaccine Production: please visit

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