Novel Approaches to Manufacturing to Enable Rapid Response

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A World At Risk: annual report on global preparedness

"Between 2011 and 2018, WHO tracked 1483 epidemic events in 172 countries. Epidemic-prone diseases such as influenza, severe acute respirator syndrome (SARS), Middle East respiratory syndrome (MERS), Ebola, Zika, plague, yellow fever and others are harbingers of a **new era of high-impact, potentially fast-spreading outbreaks that are more frequently detected and increasingly difficult to manage**."

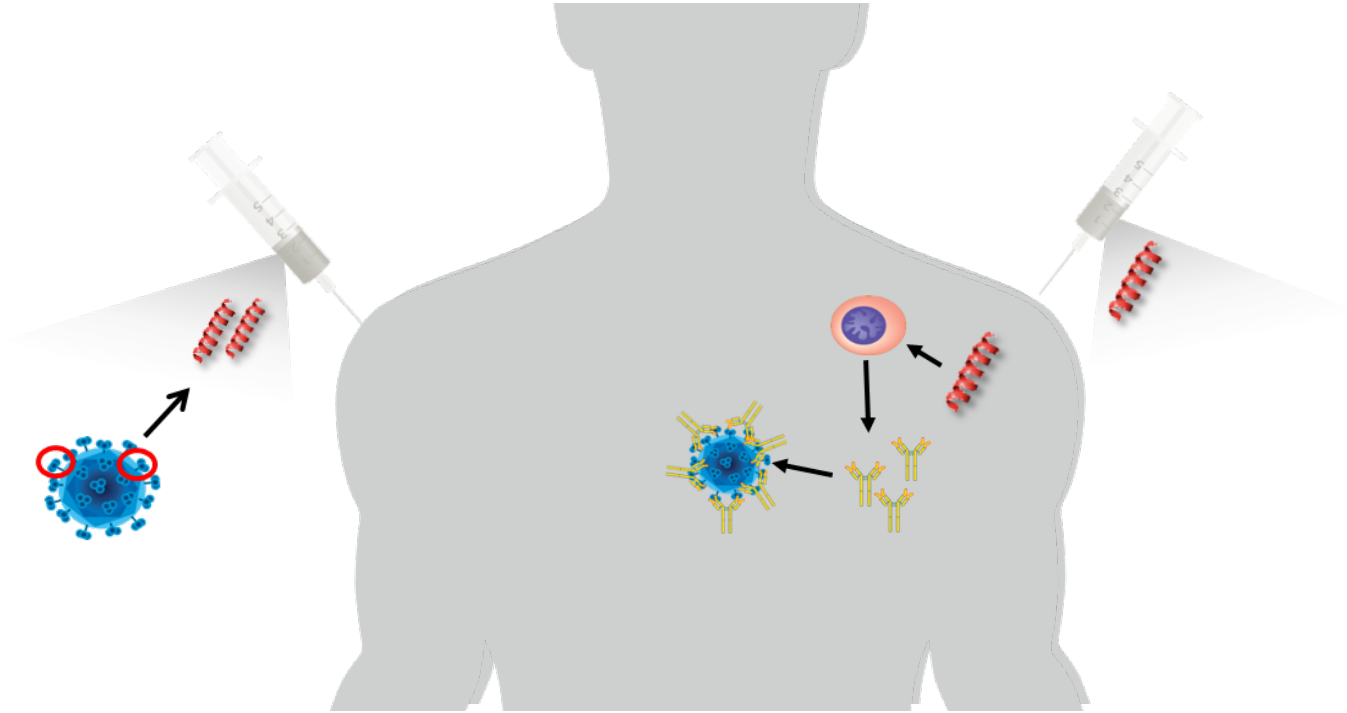
"Negative impacts are particularly profound in fragile and vulnerable settings where poverty, poor governance, weak health systems, lack of trust in health services, … and sometimes ongoing armed conflict greatly complicate outbreak preparedness and response."

Ultimate objectives:

"The tools and systems needed to respond effectively to a fast-moving and lethal respiratory pathogen are in place: A universal influenza vaccine is effective and routinely used to protect the global population new therapeutics and broad-spectrum antivirals are widely available to treat and reduce mortality from a range of viruses; novel pathogens are routinely identified and sequenced, and the sequences are shared on a globally accessible website. **Distributed manufacturing of vaccines (including nucleic acid types) begins within days of obtaining the new sequencing and effective vaccines are pre-tested and approved for use within weeks.**"

Nucleic Acid Technologies

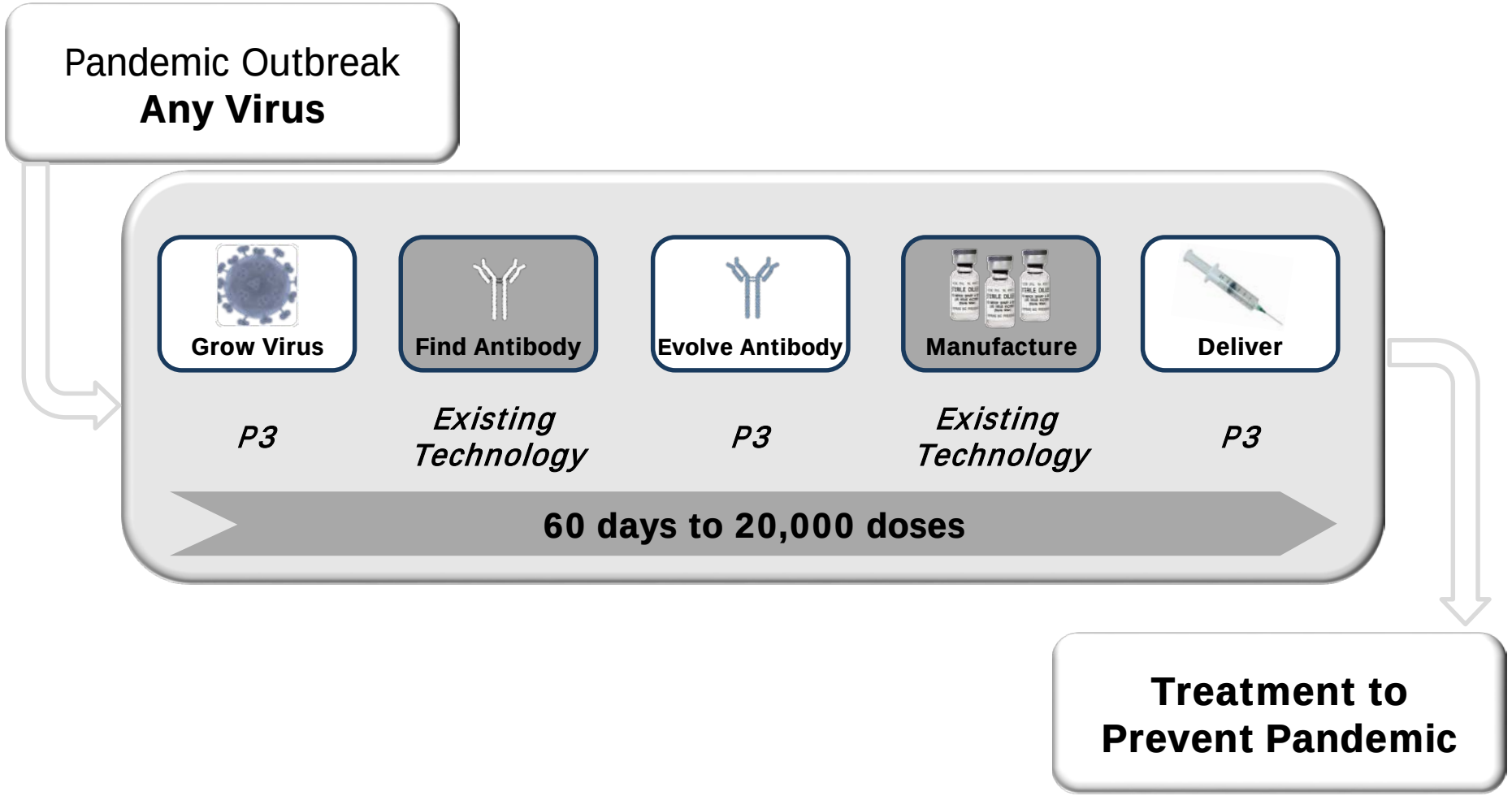
DARPA pioneered the use of the body as bioreactor to produce therapeutics



- **Gene-encoded vaccines** for long term protection
- **Gene-encoded antibodies** for near immediate, temporary protection
  - Potent antibody discovery
- **Distributed diagnostics** based on highly sensitive molecular assays

Example: Pandemic Prevention Platform (P3) Program

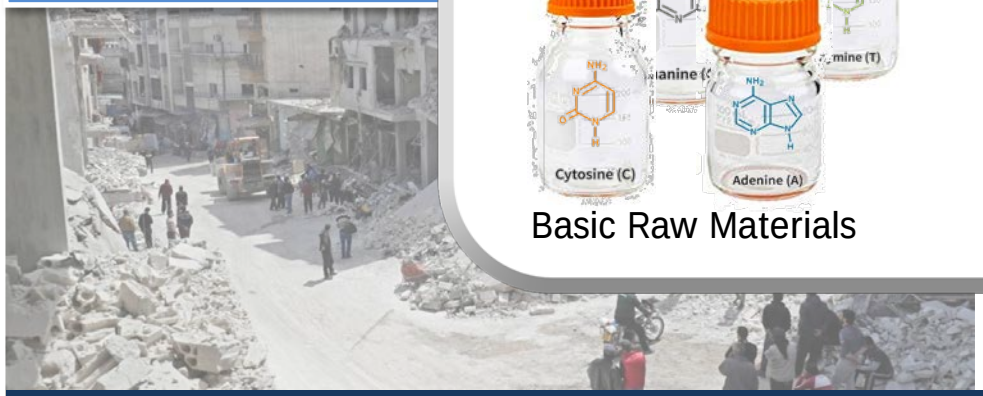
P3 is developing a functionally integrated platform to deliver pandemic prevention treatments in <60 days



DARPA vision for distributed medical countermeasure manufacturing

The DoD relies on an outdated manufacturing paradigm that limits rapid access to medical countermeasures (MCMs) against CBRN threats in austere environments

Leverage DoD MCM discovery pipeline



Protect warfighters and civilians

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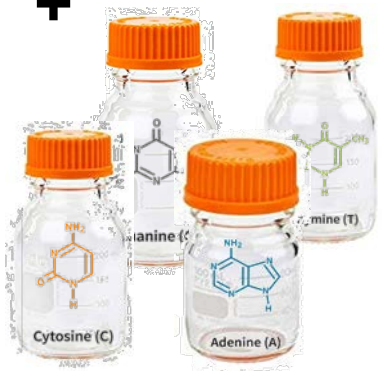


Basic Raw Materials

Synthesis of MCM

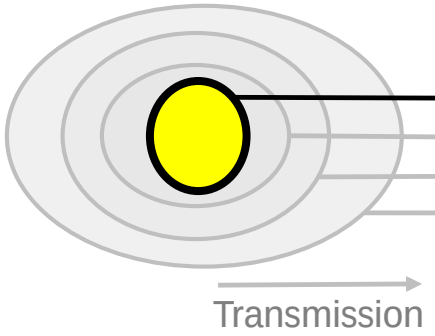
Vials of MCM

Vision: Integrated MCM manufacturing platform that synthesizes any nucleic-acid based prophylactic in military stabilization operations

What Is New About Our Approach?

World-wide response capability for stabilization operations

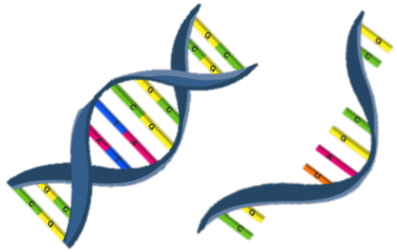
- *Fast*
- *Distributed*
- *Adaptable/flexible*
- *Deployable device*



100s of doses needed to **prevent** outbreak

Nucleic Acids Worldwide (NOW) Technical Approach

TA1: Upstream Process



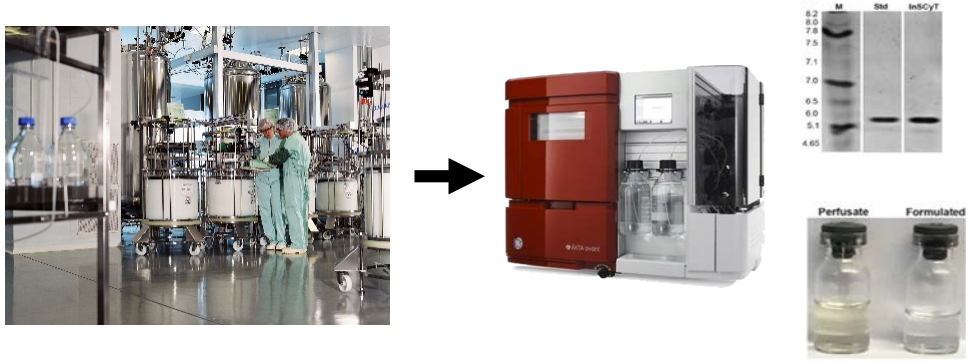
New/improved methods for DNA **and/or** RNA synthesis

Performers can choose DNA or RNA synthesis; however **both** is preferred

Key Challenges

- Polymer length
- Error-free synthesis
- Ensuring simplified starting materials

TA2 : Downstream Process



End-to-end platform for continuous DNA and RNA manufacturing

Key Challenges

- Automated production
- Integrated quality control/product identity assessment
- Systems engineering