

Meeting summary: Vaccine Research for Pathogen X

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A scientific framework for epidemic and pandemic research preparedness
Scientific opportunities to achieve fast and equitable access to high-quality
and trusted vaccines for future pandemics.

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Meeting summary: Platforms

Nanoparticles are very versatile and can be used for multimeric antigen display. Manufacturability is a difficulty, and an important research question.

mRNA may not be the solution to all problems— especially need for very robust CD8 responses. Gap: improve cold chain storage

Live vaccine platforms can recapitulate natural infection. Can produce quickly, broad cross protection is possible, and can stop transmission, move towards platform approach

Vectored vaccines can produce native, functional proteins, be produced quickly and at scale, potentially also can be delivered mucosally. Technology & infrastructure is needed for rapid scale up. Improve in vivo safety testing. Can responses be broadened with additional antigens? Need: Durability of response.

Adjuvanted subunit proteins can be highly effective, thermostability, scalability, safety (during production & AEs). Challenges speed, breadth of protection (feasible with more work)

DNA vaccines have great potential: thermostability, cost. Increase potency & combination approaches, including prime boost.

Computational protein design is becoming a platform. Can be used to design better antigens. Self assembling nanoparticles. ML & AI are critical tools to improve vaccines including Ags and platforms.

Need research and investment across platforms. Goals: confidence, accessibility, manufacturability (scalable) and programmable. Alternate delivery, dose sparing, thermostability. Need for collaboration. Compare across products needed. Learn from platforms for other biologics.

Broadly accessible Adjuvants

Meeting summary: Adjuvants

Goals: increase antibody titer, increase breadth of response, provide appropriate bias (usually Th1), CMI, enable immunization in weakened immune system. Priming response induction is critical. Can reduce vaccine dose or number of doses of pandemic vaccines, enable protein subunit vaccines. E.g., pandemic flu vaccines.

Adjuvants can be stockpiled. Adjuvants need to be aligned with antigens in context of concrete need.

Challenges: is there experience in an approved vaccine (addressing safety concerns)? GMP supply? Formulation questions (how and when is adjuvant added, appropriate ratios by age)?

In pandemic: time to product protein subunits delayed evaluation of adjuvanted vaccines.

Regulatory comment: adjuvants do not necessarily carry higher safety burden than other platforms, but requires methodical evaluation. Study of AEFI mechanism is important (still don't understand narcolepsy after flu vaccines). Rely on excellent post-vaccination surveillance mechanisms. No pathway to approve adjuvants independently of antigens.

Meeting summary: Manufacturing

Diversity of mfg. capability is essential; need for global end-to-end research for multiple platforms; evolved ecosystem (reg, market, finance, IP, etc.) needed for sustainable production; research investment in mfg capacity. Diversifying RNA platforms (circular, saRNA, mRNA) provide opportunity for research-enabled manufacturing development. Afrigen milestone: make GMP mRNA vaccine comparable to standard.

Sustainability requires capability/markets for routine vaccines. All capabilities may not be applicable to all pandemic vaccines.

Centralized adjuvant facility can increase efficiency of production and support sustainable vaccine manufacture.

Incentives and risks need to be balanced for manufacturers. Predictable regulatory and QA processes can reduce risks.

Automation can improve portability/decentralization and scalability of technology. RNA is especially amenable including in non-vaccine areas, with innovation.

Meeting summary: Regulatory

What can be borrowed within/across platforms? Tox, reprotox, enhanced disease, biodistribution, etc. What cross reliance with other regulators can be done, collaboration? Seamless master protocols, more efficient clinical trial approvals.

FDA: early interactions and communications are critical. Don't wait for disease X. New programs allow increased communication re: manufacturing.

HC: Specifics matter, but much can extend within platforms. Learning from COVID: Patient-centric specifications based on dose-ranging studies supported broad specifications to allow rapid scaleup. Using all available data to address reg requirements. We could be faster in the future e.g., for mRNA platform especially with cross-agency collaboration.

China: learnings from existing platforms will speed us up in the future, standardization of requirements around the world may be helpful.

India: agility, flexibility, engagement is essential

Potential improvements: cross-reliance/collaboration: consider ICMRA, sometimes can be facilitated by sponsors (e.g., sharing assessments). Modelling to adjust dosing based on emerging data (impeded by resistance)

Can reliance be increased in a future pandemic? Work towards that in formal/informal ways

Meeting summary: Post declaration research

Rapid sharing of data is essential. GISAID provides a clearinghouse for sequence and related data essential for vaccine development. New computational tools will further improve predictions and can enable structural surveillance.

Diagnostics can now be developed via PCR almost instantly when a new pandemic pathogen is identified. Need cultured pathogens, reagents to validate assays & share reference materials. Key challenge is implementation, including commercialization. Other assay needs include immune response assays.

WHO mediated international collaboration on animal models sped preclinical development of COVID vaccines. Sharing failures (which aren't published) was as important as sharing successes and helped to standardize successful approaches.

WHO mediated international collaboration on assays led to international standards and increased ability to evaluate immune responses with credible assays to quantify antibody responses, including for Th1/Th2 response, NP based assays to detect prior infection. Discovery that Vero cells generated furin cleavage mutations came out of the group, saving substantial effort. Knowledge sharing included training, webinars for calibrating secondary standards. Repositories were important and worked well.

Meeting summary: What research could have been done better?

Could have started Ph 1 sooner, gotten into Ph 3 faster with **clinical trial networks**, better reg preparedness/coordination could have saved a few weeks etc., so a few months could have been saved. Goal: Vaccinate the world within 6 months.

Rapid sharing of data is important. could be strengthened (especially where background rates aren't available). **Global vaccine safety systems**. Community engagement could be improved in some countries. Coordination between IT platforms could help.

Imperfect coordination and planning led to duplication and uninterpretable results. Don't have enough resources in developing world to address a future pandemic. Significant equity issue in how researchers could respond. Developing world was late to receive vaccines. Better and more sustained investments in **surveillance networks**.

Need systems and processes: sharing, networks, etc.

Discussing regulatory and legal "barriers" and potential improvements in coordination/collabobration openly could help. Faster approval of trials by international ethics committees. Models of collaboration with private sector.

But also need to identify key research topics. **Evaluation of interventions in large multicenter international studies**.

Themes from Pathogen X meeting

Existing platforms are valuable, but it is important to keep improving, introducing new technologies

Adjuvants: Huge potential advantages but limited by need to manufacture proteins

Finding ways to combine technologies that may be “owned” by different entities may improve outcomes. Mix and match may require adjustment by companies and regulators.

Availability without access is not helpful— manufacturing vaccine to scale is also critically important. Technology, integration of research, and attention to sustainability/markets are essential, recognizing that it may be difficult to predict exact manufacturing needs for a future pandemic vaccine. Viable vaccine industry also supports regulatory capacity.

Optimism re: lessons learned from COVID and ability to extrapolate data within/across platforms and ability to plan for future pandemics, enthusiasm for continued regulatory discussions on how this can be accomplished.

Diagnostics early in a pandemic are critically important. Main challenges are in implementation and commercialization—assay research is nonetheless critical for response.

Themes from Pathogen X meeting (2)

WHO-sponsored animal models and Assays groups during Covid greatly accelerated vaccine research and enhanced access and collaboration. Positive and negative findings were discussed. Could additional or expanded groups help even more in a future pandemic?

Success with COVID on speed (but could have been faster). Failure on equity. Uninformative clinical research could be addressed via larger, better coordinated multicenter international trials. More research on combinations, fractional dosing & schedules. Enhanced surveillance/epidemiology research, global vaccine safety surveillance systems. Research in field settings to obtain and analyze local data, including more research into public engagement and communication, health systems capacity. Don't work in silos!