NSABB meeting

January 7, 2016

Scope of RBA too broad

- Assessment included “gain of function” experiments outside area of greatest concern
- Substantial discussion on manipulation of seasonal strains: not discussed as major concern in last few yrs
- Using GOF techniques to increase vaccine virus yield: this is logical and beneficial as these techniques attenuate strains while enhancing growth
- Expanded scope leads to understated risks and overstated benefits

Would narrow focus of process to proposed creation of novel strains that are highly virulent and highly transmissible

On potential consequences of accident

- Consequences of accident/misuse much more explicit than USG reports
  - "An accident that starts a pandemic with 1918-like influenza strain could cause 80 million deaths."
  - "Creation of strains that are human transmissible would greatly increase the risk that such an outbreak could occur, which could cause millions of illnesses. "

- Don't agree: implications that 1918 level pandemic be considered upper bound, or that PPP induced epidemic < 1918 be considered less alarming

- Global pandemic induced by PPP accident or misuse with a case fatality anywhere above a normal flu season would be shocking global event that would kill many and deeply damage science

Would not use 1918 influenza as threshold of acceptable risk. Without extraordinary, unique benefit, experiments where accidents could start pandemics that lead to thousands or millions of deaths should not be performed

On biosecurity risks

- Disagree that biosecurity assessment should be so focused on risks in US--this is global issue, not a US one.
- Don’t think it is possible to predict future misuse of biology or pandemic pathogens by studying past events.
- Notable conclusion in report: biosecurity risks pose as much threat as biosafety
- **Focus on what the biosecurity risks would be internationally (not only in US) if the norm were set that this work should be approved and funded**
- **Other recommendations as per EMBO paper with D Relman**

On laboratory accidents

- "Data are lacking on how often humans will make mistakes of a variety of kinds in a biological laboratory (epistemic uncertainty)…Lab workers are humans and some humans are more prone than others to errors due to carelessness, unfamiliarity with protocols, distraction or stress." (p 124)

- "Increasing transmissibility of coronaviruses could significantly increase the chance of a global pandemic due to a lab accident." (p 3)

- *Also says that even if coronaviruses modified to be as transmissible as influenza, the susceptibility to control measures would still contain a majority of outbreaks.* But if virus spreads as efficiently as flu, it's not susceptible to control measures

- SARS contained only after months of intense effort, infecting thousands, killing hundreds. Crashed Asian economy. Big cities look like ghost towns. **Even if coronavirus transmission only minimally increased, should be very concerned**

- **Given absence of rigorous reporting of human errors in life sciences, danger in pursuing experimental work where consequences of accidents could be pandemics**

On ‘control’ of PPP induced epidemics

- Report implies that human behavior will reduce risk of transmission during a PPP outbreak(p 9) –
  - But in the case of influenza, there is no evidence that human behavior (e.g. social distancing, p 131) could change the course of a pandemic

- Report cites the reproductive number of SARS to be 1.4, but more authoritative sources calculate it at 3

- **Planning should assume that human behavior will not substantially change course of pandemic flu**
- **Human behavior could affect outcome of coronavirus spread, but not if it were made as transmissible as flu**

On information risks

- Don’t agree: “Little information risk remains from GOF research….”or that “methods to produce these strains have already been published and so no information risk remains.”
- More PPP work is being proposed which will carry new immediate risks and information risks.
- Possibility of new approaches to create novel pathways to PPP strains, perhaps more efficient techniques
- Interest in creating PPP strains with major flu strains across spectrum

New PPP research will carry new information risks

International repercussions

- The RBA focuses on risks in the US. If this funding pause is lifted now, other governments will see this as a green light to fund this work elsewhere.
- Based on past case studies, RBA says this kind of work may proliferate to as many as 70 labs in the next 10-15 years(p 4)
- No international consensus effort going on now that would seek a different outcome.

USG needs to make these decisions with international research community and global impact in mind

Benefit Assessment

- Majority interviewed were proponents of this research, or came from institutions supporting it
- Benefit claims in RBA are made as if fact (as opposed to opinions)
- Should be public forum with companies who make relevant vaccines. Do they need PPP work in critical path for making new vaccines? Almost none have commented publicly, some have said opposite
- RBA implies that PPP research might have identified molecular markers in the 2009 H1N1 strain that would have accelerated vaccine production and saved hundreds of thousands of cases(p 328). No evidence this is true.
- Agree with comments submitted by Plotkin and by Lipsitch

Benefits claims overstated and need external validation. Should be public forums with vaccine companies and impartial surveillance experts

Other notable elements

- RBA statement: "Other pathogens that lie outside the framework could be manipulated to cause a global outbreak" (p 8)
  - Of note - in earlier NSABB meeting, one research scientist prepared a slide justifying creation of making Ebola airborne transmissible

- RBA: Other traits of influenza or coronaviruses not covered by the Framework (e.g. environmental stability or other mechanisms of transmission) could increase the possibility of global pandemic

- RBA judges risk in 5 yr time horizons, but benefits w/out time constraints

- **Other risks will emerge that USG will need to deal with outside framework**
- **Judge risks and benefits without time constraints -- once a risk is created, it will endure**

NSABB Draft Working Paper

Agree:

- Finding 3 – Current oversight insufficient for all GOF studies of concern
- Finding 4- Some research should not be conducted at all on ethical or PH grounds if potential risks not justified by benefits
- Finding 5 – Subset of GOF studies have potential to generate high, potentially unknown risks

- Rx 1: Studies of greatest concerns generate highly transmissible, highly virulent virus (highly transmissible **by definition will be resistant to PH controls** so would NOT add that as separate criterion).

NSABB Draft Working Paper

Don't agree:

- …That existing oversight mechanisms for this work are robust or sufficient;

Funding criteria listed in NSABB document useful but insufficient:

- Benefits should be > than Risks – who determines that?
- Proposed research is ethically justifiable – who decides that?

Doesn't make sense for USG funding to be only vehicle discussed for control of experiments. USG should decide whether to fund **or approve**

Overall recommendation to USG

- Benefits of PPP are not so crucial and singular that they are worth the high risks. Potential number of people affected globally by an accident or deliberate use is more extreme than most dangers that humans could willingly choose to take

- Would not fund or allow PPP research (aka “GOF research of concern”) unless highly compelling case for benefits validated that merit such extraordinary risks (including vaccine companies)

- Seek international consensus on how to proceed