# A conversation with George Poste on February 12, 2014

## Participants

- George Poste — Chief Scientist, Complex Adaptive Systems Initiative and Professor of Health Innovation at Arizona State University
- Alexander Berger — Senior Research Analyst, GiveWell

**Note**: These notes were compiled by GiveWell and give an overview of the major points made by Professor Poste.

## Summary

GiveWell spoke to Professor Poste as part of its ongoing investigation in biosecurity. Conversation topics included the risks posed by different kinds of biological threats, areas for improvement in biosurveillance, vaccine production, the organization of genetic data, the publication of dual-use research, and the "select agents" approach to regulation.

## Overview of biological threats

Biological threats fall into three main categories: natural infectious diseases, synthetic biology/engineered pathogens, and bioterrorism. Each threat could lead to serious consequences, though at the moment natural diseases seem to present the greatest threat.

Synthetic biology could cause harm either intentionally (e.g. an engineered pathogen used in a bioterrorist attack) or accidentally (e.g. through the accidental release of dangerous agents from a lab conducting dual use research).

Of the three kinds of threats, natural infectious diseases are currently the most likely to occur, followed by bioterrorism, followed by accidents related to synthetic biology. Risks related to synthetic biology are likely to increase over the next five to fifteen years as technologies become more advanced. The risk of bioterrorism is also likely to increase. It is difficult to predict whether natural or man-made biological hazards will pose a greater risk in the future.

Influenza (commonly known as the flu) is the world's most dangerous organism. It is appropriate to expect that a highly virulent and transmissible flu strain will eventually evolve, though it is difficult to anticipate when that might occur or which strain it might be. The impact of pathogens such as malaria and dengue are also likely to increase, in part due to expansion of the geographic range of the insect vectors involved in their spread as a consequence of climate.

**Opportunities to improve biosecurity**

Opportunities include:

1. Improving global biosurveillance capabilities.
2. Improving vaccine production methods.

3. In silico modeling to produce vaccine candidates more quickly.
4. Regulating the dissemination of dual-use research.

*Biosurveillance*

Diagnosing outbreaks before large numbers of people or animals show symptoms can save lives. U.S. biosurveillance systems still face serious performance problems, despite billions of dollars in continued funding from the government. For example, BioWatch, a federal biosurveillance program, recently received another $3 billion in funding despite its many limitations. The continued funding of BioWatch is largely the result of lobbying efforts by the companies that receive funding from the program. On an international scale, more sophisticated and better-connected biosurveillance systems are needed. This is a high priority because existing systems are inadequate.

New technologies may allow for far more effective biosurveillance. For example, the capability to sequence genes of infectious agents could eliminate the need to grow them in labs, enabling more rapid diagnoses, and allow the relationships between strains to be tracked. Ensuring the widespread adoption of new technologies would also reduce the lag time between initial sample collection and confirmed diagnosis.

In the global public health space, there is a reasonable amount of funding for the surveillance of human health, but there is less funding for the surveillance of animal health. Because animals often play a critical role in spreading diseases, it is important to increase

funding for the surveillance of animal health, particularly animals (e.g. birds and pigs) known to spread high-priority diseases such as influenza. Assessing the risks of different zoonotic diseases will help prioritize the surveillance of certain animals over others.

*Vaccine production*

Current vaccine production processes involve growing infectious agents on a large scale, via eggs or cells. These agents, or their immunizing proteins, are then injected into humans as vaccines. This "biological" process is outdated and inefficient and the ability to chemically synthesize immunizing proteins would represent a major technological advance. Chemical production would be faster and cheaper than biological production. Switching to chemical production could increase the number of facilities that produce vaccines, because chemical production does not require facilities of the same level of sophistication as manufacturing facilities for biolgoicals. The approval process of the U.S. Food and Drug Administration (FDA) would also be less protracted for chemically-produced vaccines than biologically-produced vaccines, which may vary from batch to batch and therefore require regulatory approval for each batch.

Chemical production would not eliminate the need for clinical trials, which demonstrate the efficacy and safety of vaccines, though there may be opportunities to make clinical trials more efficient. For example, the E.U. does not require effectiveness trials for new influenza vaccines – they only check that the new vaccines are safe and efficacious and trigger the appropriate level of antibodies in immunized individuals

Chemical vaccine production would require identifying genes that code for immunogenic proteins, i.e. proteins that are likely to be recognized by human immune systems. Currently, this capability is limited because the relevant data is not well-organized.

Recent efforts by the Biomedical Advanced Research and Development Authority (BARDA) to accelerate flu vaccine production has focused on switching from conventional egg-based vaccines to more efficient cell-based methods, but still require specialized facilities.

*Database to enable in silico modeling*

By combining large datasets on virus genetics and protein immunogenicity, researchers may be able to better predict which proteins and epitopes will be immunogenic on the basis of pathogen sequence, which would again facilitate more rapid development of a chemical vaccine production process.

Creating the database required for such a project might cost around $25 million. This could be a good opportunity for philanthropists, because the work is unlikely to be funded by the National Institutes of Health (NIH), the National Science Foundation (NSF), academic institutions, or the pharmaceutical industry. Infectious disease researchers may be reluctant to support chemical vaccine production because of their academic interests in biological methods.

The capability to predict virulence based on genetic sequences is currently limited but growing. As more genetic data becomes available, researchers may be able to use computer-based modeling to correlate changes in organisms' genetic sequences with changes in virulence. RNA viruses, such as influenza and HIV, are good candidates for this kind of analysis because they mutate at faster rates than DNA viruses.

*Regulating the dissemination of dual-use research*

Academics need to be cautious when disseminating research that could enable bioterrorists. Examples of such research include influenza recombination experiments and experiments to develop molecular probes capable of targeting specific proteins in the human body. Although it is difficult to keep research completely confidential, it is possible and appropriate to share it in constrained ways in some cases. Debates about publishing dual-use research will likely become more common as biotechnology becomes more advanced.

**Thoughts on the possibility of a universal flu vaccine**

The development of a universal flu vaccine may be conceptually possible but seems unlikely. In the mid 1980s, Dr. Poste launched a program to find common regions on the hemagglutinin proteins (HA) of different influenza viruses. Although such regions were found, none were immunogenic enough for use in vaccine development. If influenza strains had highly-immunogenic regions in common, then a person infected by one seasonal flu

would be protected from others (which is generally not the case). The quest for a universal flu vaccine continues but the technical challenges are formidable.

**Thoughts on "select agents" approach**

*GiveWell asked Dr. Poste about criticisms of the "select agents" approach, which involves regulating a list of identified pathogens.*

Criticisms of the "select agents" approach are legitimate, but it would not be practical to abandon the approach. The select agents list is appropriate so long as it is routinely updated and efforts are made to address unidentified threats. For example, a better understanding of human immunology could lead to the development of broader-spectrum drugs and vaccines.

**Who else to talk to about these issues**

- David Relman — Professor, Stanford University; Co-Director, Center for International Security and Cooperation
- Michael Osterholm — Director, Center for Infectious Disease Research and Policy (CIDRAP), University of Minnesota
- Tom Inglesby — Director, UPMC Center for Health Security
- Alan Rudolph — Vice President of Research, Colorado State University
- Robin Robinson — Director, Biomedical Advanced Research and Development

Authority (BARDA)

- Andrin Oswald — Division Head, Vaccines and Diagnostics, Novartis International

*All GiveWell conversations are available at http://www.givewell.org/conversations/*