

## The Potential Pandemic Influenza Research Enterprise: An Existential Risk to Humanity?

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### ABSTRACT

The President Obama ordered [deliberative process](#) did not allow time to develop carefully crafted arguments regarding risk of lab-created potential pandemic pathogens. Moreover, new data is available that calls for a new calculation of risk.

This study focuses mainly on lab-created avian-influenza viruses that have been modified to be transmissible in mammals through the air. These are the most worrisome potential pandemic pathogens, because a highly transmissible strain released from a laboratory into the community *could* seed a pandemic with massive world-wide fatalities, creating an existential risk to humanity. Just the possibility of a pandemic dictates that we must proceed with the upmost caution.

There are at least fourteen entities world-wide that have created airborne-transmissible avian influenza viruses, here dubbed the "Research Enterprise." From Federal Select Agent Program (FSAP) data, it is calculated that there is a probability of 16% to 21% for at least one community release from the Research Enterprise conducting research for five years. From NIH incident reports, this same probability is much higher, 68% to 87%. The reasons for the large difference between FSAP and NIH can only be guessed at. While the analysis here employs the much more conservative FSAP numbers, the high percentage from the NIH incident reports is real so can't be entirely ignored in discussions of community releases.

Combining probability of release into the community with the not-insignificant 5% to 40% probability such a virus could seed a pandemic, we have an alarming situation. The one qualifier is that we really do not know how virulent or air-borne transmissible in humans these potential pandemic viruses would be when released into the community. In the best-case scenario, they would soon die out with little to no sickness and no deaths; however, just the possibility of a pandemic dictates that we must proceed with the upmost caution.

Likelihood-weighted-consequence analysis (likelihood times consequences) is a standard method for assessing risk and should be at the center of the potential pandemic influenza research debate. Considering only fatalities as consequences, two example calculations, using two case fatality rates, find likelihood-weighted-fatalities to be 8,700 or 109 for *a single lab in a single year*. In the first example, the case fatality rate was picked to be similar to the 1918 pandemic flu; in the second example, it was picked to be similar to a typical seasonal influenza.

To help put this fatality burden in perspective, no Institutional Review Board (IRB) tasked with assessing human-subject research would approve a research project with a potential of a hundred to perhaps thousands of fatalities, unless it could be assured with almost absolute certainty that there will never be a release into the community.

Those who support this dangerous research either believe the probability of community release is infinitesimal or the benefits in preventing a pandemic are great enough to justify the risk. It would take extraordinary benefits and significant risk reduction via extraordinary biosafety measures to correct such a massive overbalance of highly uncertain benefits to too-likely risks. Whatever number we are gambling with, it is clearly far too high a risk to human lives.

### **Case-fatality rates from infections with H5N1 and H7N9 viruses**

Research of Highest Concern (RoHC) is defined as lab-creation of or subsequent research with mammalian-airborne-transmissible (mat) or mammalian-contact-transmissible (mct) highly pathogenic influenza viruses.<sup>1</sup> The viruses include highly pathogenic avian influenza (HPAI) that are easily airborne or contact transmissible in mammals, and also include past human pandemic influenza viruses for which population immunity (herd immunity) may have been lost. In particular, the highly pathogenic H5N1 and H7N9 avian influenza viruses are of the most concern.

The H5N1 avian flu virus has killed [nearly 60 percent](#) of humans infected<sup>2</sup> from handling poultry, but it is [rarely transmissible among humans](#). Over the last year or so, human H5N1 fatalities [have almost disappeared](#), but we don't know if this will continue. Our concern is over a release of the older lab-created highly pathogenic strains into the community.

For H7N9, as of April, 2014, there had been about [30%](#)<sup>3</sup> to [40%](#) fatalities. There are also many fewer H7N9 infections in chickens, a vector for human infections, which is likely due to a [successful chicken vaccination program](#) in China.

### **Number of entities in the Research Enterprise**

The number of entities (facilities)<sup>4</sup> with laboratories creating and conducting RoHC must be estimated to quantify the potential risk to the community. The greater the number of entities in the Research Enterprise, the greater the risk of release into the community; and subsequently, the greater the risk that the release seeds an outbreak or pandemic. A minimum estimate is all that is required to make the argument that a release from the Research Enterprise is too likely.

From an analysis of Pub Med abstracts from 2012 through November 2018, 17 RoHC publications from laboratories in 14 different Research Enterprise entities were found. The three influenza RoHC categories used in the Pub Med search to find the number of Enterprise entities were:

- RoHC 1. Highly-pathogenic-avian-influenza (HPAI) H5N1 and H7N9 viruses that are mammalian-airborne-transmissible (math5N1 and math7N9) or are mammalian-contact-transmissible (mctH5N1 and mctH7N9).
- RoHC 2. Other HPAI that were made mammalian-airborne-transmissible or contact transmissible (mathHPAI and mctHPAI). The avian viruses are restricted to those that have caused human infections in the past (H5N6, H10N8, H6N1, H1N2, H3N2, H10N7, H7N3, H7N2, H1N2, H7N7, H9N2, H1N2, H1N1, H2N2).
- RoHC 3. Human influenza viruses that have caused past pandemics and for which there is little immunity in the population at present (1918 H1N1, 1957 H2N2), or have been modified (enhanced) to escape immunity and vaccines (2009 H1N1 or 1968 H3N2).

Details of the Pub Med search to identify influenza RoHC publications through a lengthy, multistep process may be found in [the unpublished paper](#) "Minimum Estimate of Number of Laboratories in the Influenza PPP Research Enterprise."

The Pub Med search employing over a dozen search words should have identified most RoHC publications, but could miss a few. What might be missed?

- Unpublished research will be missed.
- Publications in languages other than English may not always be listed in Pub Med. In particular, some Chinese and other Asian research might be missed. Asia is the source of human fatalities from H5N1 and H7N9 avian influenza infections, so much of the recent RoHC seems to be carried out there.

The weeks of extra effort to identify more Research Enterprise entities is not necessary as the risk of a pandemic is already intolerably high in an Enterprise with as few as fourteen entities. In business plans, unexplored markets are often called "upside market potential." In keeping with this language, unidentified RoHC entities might be appropriately called "upside RoHC entities," indicating that it would be nice to have the data but not necessary to make the intolerable-risk case.

There are publications relevant to the RoHC focus from years before 2012; but a limit is necessary as to what this project will focus on. The focus here is the recent past as an indicator of the future Research Enterprise. With this focus in mind, the pre-2012 research will not be discussed.

### **The probability of a uuLAI from the Research Enterprise**

There are two main sources of data to determine the number of uuLAIs, the CDC/FSAP yearly reports to Congress and more recently their annual reports, and the NIH laboratory incident reports obtained from a FOIA request to the NIH Office of Science Policy.

*Analysis of FSAB/CDC Reports to Congress*

The official name of the [summary reports to Congress](#) is “The Department of Agriculture and the Department of Health and Human Services Report to Congress on Thefts, Losses, or Releases of Select Agents or Toxins.” The reports cover the years 2003 through 2015 and were provided to The Black Vault by the CDC under FOIA. The Black Vault is a non-government clearing house for FOIA documents. The years 2015, 2016 and 2017 are covered by the [new Annual Reports](#) of the Federal Select Agent Program.

Both the FSAP reports to Congress and the FSAP Annual Reports provide only brief descriptions of laboratory-acquired infections (LAIs) and no explicit discussion of which LAIs are undetected or unreported LAIs (uuLAIs). Whether a LAI is indeed a uuLAI must be inferred from the brief FSAP descriptions. The FSAP descriptions and this author’s italicized comments on the descriptions are presented in PART 1 of the Supplementary Material. As indicated in the author’s comments, a few FSAP descriptions are not clear enough to decide whether those LAIs can be classified as uuLAIs.

A summary of the FSAP LAI data is presented in Table 1.

Year	No. Registered Entities	Is confirmed release a BSL3 uuLAI?	How many infected?	Pathogens Involved and likely risk-group
2003-2006	241.3	no		Newcastle disease virus, RG2
2003-2006		no		Newcastle disease virus, RG2
2003-2006		yes	3	<i>Francisella tularensis</i> , RG3
2003-2006		maybe	1	<i>Brucella melitensis</i> , RG3
2003-2006		yes	1	<i>Brucella melitensis</i> , RG3
2007	283	yes	1	<i>Brucella melitensis</i> , RG3
2008	279	not relevant		<i>Brucella sp.</i> , RG3
2008		yes	1	<i>Brucella melitensis</i> , RG3
2009	285	no		<i>Francisella tularensis</i> , RG3
2010	285	maybe	1	<i>Brucella suis</i> , RG3
		maybe	1	<i>Brucella suis</i> , RG3
		not relevant		Classical Swine Fever virus, RG unk
2011	285	no		<i>Francisella tularensis</i> , RG3
2012	285	no		no reported confirmed releases
2013	285	maybe	1	<i>Burkholderia pseudomallei</i> , RG3
		no		<i>Brucella melitensis</i> , RG3
2014	285	no		<i>Coxiella burnetii</i> , RG2, RG3
		yes	1	<i>Coxiella burnetii</i> , RG2, RG3
2015	291	yes	2	<i>Coxiella burnetii</i> , RG2, RG3
		yes	1	<i>Brucella abortus</i> , RG3
2016	276	no		no reported confirmed releases
2017	263	no		no reported confirmed releases

**Table 1.** Summary of FSAP data on confirmed releases from registered laboratories for the years 2003 through 2017. A confirmed release in FSAP terminology is a laboratory-acquired infection. See PART 1 in the Supplementary Material for reasons why confirmed releases are classified as “yes” (for an uuLAI)<sup>5</sup>, or “maybe” (where the confirmed releases may or may not be an uuLAI). The three *M. tuberculosis* uuLAIs in 2004 were being researched in a BSL2 lab, but should have been in BSL3, so are counted as a “yes” in the table. A fully annotated version of this table may be found in PART 2 of the Supplementary Material.

The key number to be calculated from Table 1 is the probability,  $p_1$ , of a community release through a uuLAI per entity per year (entity-years). From  $p_1$ , it is a simple matter to find the probability  $p_{NY}$ , the probability of at least one community release from N Research Enterprise labs in Y years (see below).

The most conservative calculation assumes the number of uuLAIs for the “yes” entries in Table 1, which is 10. The total number of entity-years for the years 2003 through 2017 is the sum<sup>6</sup> of the No. Registered Entity column in Table 1, which is EY=4,067. Then

$$p_1 = \text{uuLAI}/\text{EY} = 10/4,067 = 0.00246 \text{ or } 0.246\% \text{ per entity-year}$$

The less conservative calculation assumes the number of uuLAI is the number of “yes” entries plus the number of “maybe” entries in Table 1, which is 14. Then,

$$p_1 = 14/4,067 = 0.00344 \text{ or } 0.344\%.$$

From most conservative to less conservative, the calculation of  $p_1$  from the FSAP data falls in a small range.

#### *Analysis of FOIA-obtained incidents reported to the NIH Office of Science Policy*

The incident reports from the NIH Office of Science Policy cover the period from 2004 through 2017<sup>7</sup> and include BSL3 and BSL4 labs only, not BSL2. The reports provide extremely detailed descriptions of incidents from the entities where they occurred.

There were 13 uuLAIs from 187 incident reports over that period. Detailed descriptions of the uuLAIs are presented in PART 3 of the Supplementary Material.

Next, the number of entity-years for the denominator of  $p_1$  must be determined. Since reporting to NIH in past years has been sporadic, it is likely that some entities have not reported any incidents despite NIH’s efforts to have all recombinant DNA labs report. In contrast, since the FSAP has strict requirements for compliance to Select Agent rules enforced by the FBI, the reporting percentage is likely high.

To estimate the number of entity-years (EY), one assumption is that once an entity files its first incident report, it will report all future incidents as required by NIH. Here are two examples of calculating entity years from this assumption:

(1) Suppose entity, 1, first reported an incident in 2010. Thus, through 2017  $\text{EY}(1) = 2017 - 2010 + 1 = 8$  entity-years.

(2) Another entity, 2, first reported an incident in 2014, so  $\text{EY}(2) = 2017 - 2014 + 1 = 4$  entity-years.

For the two entities,  $\text{EY} = 8 + 4 = 12$  entity-years. In total, there have been 58 different entities that have reported incidents over the years. Summing the EY values over those 58 entities gives a total of 458.3 entity-years. Windows metafile images of the spreadsheet used to calculate total entity-years for all entities is in PART 4 of the Supplementary Material. This spreadsheet also contains additional information on all 187 reported incidents.

The probability of a uuLAI per entity-year,  $p_1 = \text{uuLAI}/\text{EY} = 13/458.3 = 0.0284$  or 2.84% uuLAIs per entity per year.

Many of the thirteen uuLAIs were first incident reports. These entities may have had a number of reportable incidents before they experienced a uuLAI, but didn’t start reporting incidents until a serious

incident occurred such as a uuLAI. Thus, the denominator for calculating  $p_1$  would be larger if they had reported earlier. In this regard, the calculation of  $p_1$  is not conservative, in that  $p_1$  could be smaller.

Toward a more conservative estimate of  $p_1$ : If we assume that each of the 58 BSL3 entities have been conducting research since 2004, the total entity-years would be  $EY = 58 \times (2017-2004+1) = 812$  entity-years. Further, assume that they had no uuLAIs over their earlier non-reporting years, then  $p_1 = 13/812 = 0.016$  or 1.6%. This is the most conservative calculation over the years 2004 through 2017. So, the range for  $p_1$  is 1.6% to 2.8% per facility-year.

This range is about 5-times to 10-times greater than the  $p_1$  values found from the FSAP data. How can that be? While there is no obvious reason in the data that would explain this large difference, some possibilities come to mind:

- (1) Perhaps laboratory workers working with less dangerous BSL3 pathogens become infected more easily as they are not being as cautious as they should be. The recombinant DNA in some of the NIH incident reports is designed to make the pathogens less virulent.
- (2) Of the thirteen uuLAIs, four were exposure and subsequent latent infection with *M. tuberculosis*, but no active infections.<sup>8</sup> Tuberculosis is highly contagious by the airborne route, so it might be easier to acquire a TB infection in the lab. Unfortunately, TB infections in the FOIA NIH data might be an indicator of what could occur in research on other airborne-contagious pathogens like matHPAI.
- (3) Only two incidents (with 4 uuLAIs) were select agents so were also reported to FSAP. Nine were reported to only NIH. Since some FSAP enforcement is conducted by the FBI, there may be more diligent biosafety practices for labs that research select agents.

The reasons for this large difference between  $p_1$  for the FSAP and NIH data remains a mystery. But the high  $p_1$  value from the NIH incident reports is real, so must be kept in mind.

### **Human error is the main cause of community releases**

The major route to release into the community are uuLAIs. The [biggest source of uuLAIs is human error](#), which cannot be prevented by careful laboratory design. Depending on data source, the percentage of entity incidents due to human error is 67 percent and 79.3 percent. In a 2015 publication, [Fouchier describes](#) the careful design of his BSL3+ laboratory in Rotterdam and its standard operating procedures, which he contends should increase biosafety and reduce human error. Most of Fouchier's discussion, however, addresses mechanical systems in the laboratory. Given the many ways by which human error can occur, it is doubtful that Fouchier's human-error-prevention measures can eliminate release of airborne-transmissible avian flu into the community through uuLAIs.

### **Calculation of probability of community release from the Research Enterprise**

As found before, the probability of a community release from a single Enterprise entity in a single year is  $p_1=0.00246$  to  $0.00344$  from the FSAP data, and  $p_1=0.016$  to  $0.028$  from the NIH data. The number of entities,  $N$ , in the Research Enterprise is at least fourteen.

The probability of at least one community release from a uuLAI for  $N$  Enterprise labs in  $Y$  years is

$$p_{NY} = 1 - (1-p_1)^{NY} \quad (1)$$

Some examples are presented in Table 2 for the minimum estimate of N=14 labs in the Enterprise.

		$p_{NY} = 1 - (1-p_1)^{NY}$							
		N =	14	(number of Enterprise entities)					
						Y=years			
<u>Data Source</u>		<u>p<sub>1</sub></u>		<u>1</u>	<u>2</u>	<u>5</u>	<u>10</u>		
FSAP			0.00246	0.0339	0.0666	0.1584	0.2917		
FSAP			0.00344	0.0471	0.0920	0.2143	0.3827		
NIH			0.01600	0.2021	0.3634	0.6767	0.8955		
NIH			0.02840	0.3319	0.5537	0.8669	0.9823		
Fouchier (FSAP min/10)			0.00025	0.0034	0.0069	0.0171	0.0339		

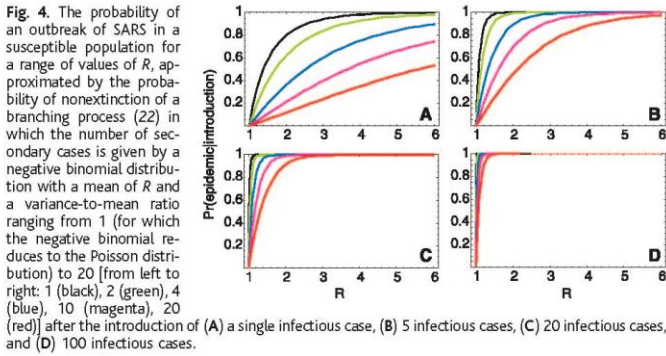
**Table 2.** The body of the table is probability,  $p_{NY}$ , of at least one community release from an uuLAI for a Research Enterprise of N=14 entities for various values of the probability of release for a single entity in a single year,  $p_1$ , and for various years, Y, of research. The Fouchier row-entries are from his guess that his BSL3+ laboratory is at a minimum ten-times safer than the average BSL3 lab researching surrogate data. Then, for the Fouchier entry,  $p_1=0.000246$  was used for the calculation of  $P_{NY}$ .

Taking the conservative estimate  $p_1=0.00246$ , the probability of at least one community release from an Enterprise entity is  $p_{NY}=0.1584$  or 16% in five years of research, the typical length of a research project. This likelihood of a release is uncomfortably high.

The Fouchier 10-fold minimum reduction guess for  $p_1$  would be a reasonable guess for mechanical failure, but it is likely too large a reduction when human-error is considered. Thus, the  $p_{NY}=0.0171$  or 1.7% is likely much too conservative but still uncomfortably high given the possible millions of fatalities from a lab release.

### Probability of a lab-created pandemic

The next step is to determine the probability of a pandemic from a release into the community from a uuLAI. For this probability, Figure 4 in the [Lipsitch \*et al.\* \(2003\) paper](#) was consulted. The figure is reproduced below for convenience to the reader.



**Figure 1.** Reproduction of Figure 4 from *Transmission Dynamics and Control of Severe Acute Respiratory Syndrome* in [Transmission Dynamics and Control of Severe Acute Respiratory Syndrome](#).

The graphs were generated using branching theory, a purely mathematical construct, which requires only two parameters, the mean  $R_0$  (the reproductive number; i.e., the mean number of people infected by an infected person) and the variance to mean ratio  $k$ , which measures the variation in number of people infected.

Assume that a lab-created PPP (e.g., matHPAI) is as capable of human-to-human airborne transmission as an historical pandemic strain; that is,  $R_0 \sim 1.5$ . The probability that a pandemic is seeded from a single release might be as high as 40% (green curve in Figure 4a where the variance to mean ratio  $k/R_0=1$ , for  $R_0=1.5$ ). Or being more conservative taking  $k/R_0=10$ , the probability that a pandemic is seeded from a single release is about 10% (magenta curve in Figure 4a for  $R_0=1.5$ ).

In a very different approach, where progress of infection from person to person through the community is simulated, Merler, *et al.*, found that “that there is a non-negligible probability (5% to 15%), strongly dependent on reproduction number, and probability of developing clinical symptoms, and that the release event is not detected at all” that a pandemic results.

Even if the reader is uncomfortable with mathematical approaches, observing how the 2009 H1N1 pandemic virus marched quickly throughout the world, no matter what attempts were made to slow it, should convince everyone that it is nearly impossible to stop an influenza pandemic once it appears in the community.

In what follows, an intermediate value of the probability of a pandemic,  $\text{pan} = 15\%$ , will be used. This probability was taken from a range of 5% to 40% from branching theory and simulation. Then, the probability that the Enterprise seeds a pandemic in a single year is

$$\text{pan}_{14,1}(\text{Enterprise}) = 0.15 \times 0.0339 = 0.0051 \text{ or } 0.51\% \text{ per year,}$$

where the 0.0339 probability is from Table 2 for an Enterprise of  $N=14$  entities and  $Y=1$  year.

For  $Y=5$  years, the probability of a pandemic increases to

$$\text{pan}_{14,5}(\text{Enterprise}) = 0.15 \times 0.1584 = 0.0238 \text{ or } 2.38\%,$$



much too high a percentage since the number of fatalities could be in the millions. Should we be willing to risk a 2.5% likelihood of a pandemic from the Research Enterprise for five years of research that may yield little practical results?

**Likelihood-weighted consequences and fatality burden**

Likelihood-weighted consequences (LWC) are defined as the product of the probability of the consequences times the consequences:

$$LWC = (\text{probability of the consequences}) \times (\text{consequences}).$$

LWC analysis is a standard method for assessing risk and should be at the center of the PPP influenza research debate.

Here for RoHC, only fatalities will be considered as the consequences. So for likelihood-weighted consequences, we substitute the term fatality burden,  $LWC = FB$ .

$$FB = (\text{probability of a release}) \times (\text{probability of a pandemic}) \times (\text{number of pandemic fatalities})$$

$$FB_{NY} = p_{NY} \times p_{an} \times F, \tag{2}$$

where F is the number of fatalities for the pandemic.

To calculate the number of fatalities, first note that the case-fatality rate could be as high as 60%, the rate for the highly pathogenic H5N1 strains used in creating math5N1. To be more conservative, assume that the case-fatality rate is 2%, similar to the 1918 pandemic flu.

The number of fatalities, F, is then

$$F = (\text{world population}) \times (\text{fraction of population infected}) \times (\text{case-fatality rate})$$

$$F = 7.7 \times 10^9 \times 0.15 \times 0.02 = 23.1 \text{ million}$$

where a typical seasonal influenza epidemic infects about 15% of the world’s population, and the 1918 pandemic flu had about a 2% case-fatality rate.

Consider three cases: The fatality burden for (1) a single Research Enterprise entity in a single year; (2) a 14-entity Enterprise for a single year; and (3) and an 14-entity Enterprise for 5 years of research. The fatality burdens for the three cases calculated using equations (1) and (2) are summarized in Table 3.

$p_{NY} = 1 - (1-p_1)^{NY}$			
$FB_{NY} = p_{NY} \times p_{an} \times F$			
	$p_1 = 0.0025$	(the FSAP minimum value)	
	$p_{an} = 0.15$		
	$F = 2.31E+07$		
	<b>N</b>	<b>Y</b>	<b>p<sub>NY</sub></b>
			<b>FB</b>
	<b>1</b>	<b>1</b>	0.00250
	<b>14</b>	<b>1</b>	0.03444
	<b>14</b>	<b>5</b>	0.16073
			8.7E+03
			1.2E+05
			5.6E+05

**Table 3.** Fatality burden for Research Enterprises of either 1 or 14 entities and for 1 or 5 years of research on matHPAI or mctHPAI. The body of the table is fatality burden, FB. N is the number of entities in the Research Enterprise and Y is the number of years the Enterprise is conducting research.

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Each entity in the Research Enterprise must bear the burden of its contribution to potential fatalities, that is, its fatality burden. Using the numbers in the top row of Table 3, each year that a single entity conducts research, it carries with it the burden of 8,700 fatalities.

What if the released virus is no more deadly than a typical seasonal influenza virus? According to the World Health Organization, for [a typical seasonal-influenza epidemic](#) “Worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290,000 to 650,000 respiratory deaths.” Using the lower number, F=290,000 fatalities, the fatality burden for a single Enterprise entity in a single year is

$$FB = p_1 \times 0.15 \times 290,000 = 0.0025 \times 0.15 \times 290,000 = 109 \text{ fatalities}$$

### Conclusion

Each entity in the Research Enterprise must bear the burden of its contribution to potential fatalities, that is, its fatality burden. Based on a case-fatality rate of 2%, similar to the 1918 influenza pandemic, the fatality burden for a single Research Enterprise entity each year it conducts research is 8,700 fatalities. Even if the case-fatality rate is as low as a typical seasonal influenza, the fatality burden is 109 fatalities.

To put this fatality burden in perspective, no Institutional Review Board (IRB) tasked with assessing human-subject research would approve a research project with a potential of a hundred to perhaps thousands of fatalities yearly. Clearly, no IRB would allow this research to be conducted unless it could be assured with almost absolute certainty that there will never be a release into the community.

Those who support this dangerous research either believe the probability of community release is infinitesimal or the benefits in preventing a pandemic are great enough to justify the risk. For this research, it would take extraordinary benefits and significant risk reduction via extraordinary biosafety measures to correct such a massive overbalance of highly uncertain benefits to too-likely risks. Whatever number we are gambling with, it is clearly far too high a risk to human lives.

## ENDNOTES

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<sup>1</sup> Contact transmissibility is determined by placing infected mammals in the same cage with uninfected mammals, then observing if the uninfected mammals become infected. Airborne transmissibility is determined by placing infected mammals in cages separated by a short distance from cages with uninfected mammals.

<sup>2</sup> 332 fatalities in 556 cases between 2003 and 2011

<sup>3</sup> 419 human infections with 127 unofficial number of deaths. The mortality rate in documented cases is high for both strains of avian influenza, about 60% for H5N1 and about 30% for H7N9. “However, the 30% mortality for H7N9 is [probably too high](#) because in contrast to H5N1, asymptomatic as well as mildly symptomatic cases of H7N9 have been observed. Therefore, cases are underreported.”

<sup>4</sup> Here, the words “entity” and facility have the same meaning. Entity or facility are the words used by the Federal Select Agent Program. Each entity may have a number of high-containment laboratories. It is usually an entity official, not laboratory principal investigators, who reports accidents and incidents to the FSAP and NIH.

<sup>5</sup> The number four uuLAIs identified for the years 2004-2010 in Table 1 is in exact agreement with the number four uuLAIs found by the CDC’s Henkel, *et al.* (Monitoring Select Agent Theft, Loss and Release Reports in the United States—2004-2010)

<sup>6</sup> Approximate total number of entities for the years 2003 through 2006 is estimated to be  $4 \times 241.3 = 965$ . The total number of entities for the years 2007 thru 2017 is 3,102. Thus, the total number of entities for the years 2003 thru 2017 entity-years is estimated to be  $965 + 3,102 = 4,067$ .

<sup>7</sup> The analysis is based on about 187 total FOIA reports delivered in three batches: December 2017, July 2018 and February 2019 with report dates ranging from 2008 through 2017. This third batch of over 60 reports is not incorporated into earlier analyses.

<sup>8</sup> TB is highly contagious and can be transmitted from an infected person to an uninfected person, mainly when a person with TB coughs, sneezes, or speaks (airborne transmission). Other people who breathe in the aerosolized bacteria can become infected. Some individuals have TB infections but show no symptoms because their bodies prevent TB bacteria from growing. Patients with this type of infection are described as having latent (dormant) TB. Individuals with latent TB suppress the bacteria and are not contagious. However, if someone with latent TB is no longer able to suppress the TB bacteria, that individual can then become contagious.

[https://www.medicinenet.com/is\\_tuberculosis\\_tb\\_contagious/article.htm#how\\_will\\_i\\_know\\_if\\_i\\_have\\_tuberculosis](https://www.medicinenet.com/is_tuberculosis_tb_contagious/article.htm#how_will_i_know_if_i_have_tuberculosis)