#### Potential Pandemic Severity Appraisals by Authoritative Sources, 2006 – 2019 Eric S. Starbuck, DrPH, MPH Advisor, Child Health & Pandemic Preparedness Department of Global Health Save the Children, Fairfield, Connecticut <u>estarbuck@savechildren.org</u> https://www.savethechildren.org/us/about-us/resource-library/influenza-library September 27, 2019

Influenza pandemics are worldwide epidemics caused by new flu viruses which evolve from birds or animals to allow <u>sustained person-to-person respiratory transmission</u>. Since the 16th century, there has been an average of about three flu pandemics per century. While the 1918 pandemic is estimated to have killed 50 to 100 million people,<sup>1,2,3</sup> the most recent pandemic, the 2009 "swine flu," was very much milder. The concern today is that another virus, such as the H5N1 or H7N9 avian flu virus, or the MERS coronavirus, could evolve to cause a severe pandemic. In such an event, vaccine and antiviral treatment would likely be unavailable for much or all of the world's population during at least the first several months. Although risk of onset in the next year, or in the next decade, of a severe pandemic involving <u>respiratory transmission of a novel virus</u> cannot be quantified, such an event is considered to be an important global threat by leading organizations. The following links to documents from various organizations (listed in chronological order) include appraisals of risk of a severe pandemic involving a novel respiratory virus, highlighting the importance of preparedness for such an event:

1. Influenza Research at the Human and Animal Interface: Report of a WHO Working Group, WHO, 2006, pages 15-16

(www.who.int/csr/resources/publications/influenza/WHO CDS EPR GIP 2006 3C.pdf): "One especially important question that was discussed is whether the H5N1 virus is likely to retain its present high lethality should it acquire an ability to spread easily from person to person, and thus start a pandemic. Should the virus improve its transmissibility by acquiring, through a reassortment event, internal human genes, then the lethality of the virus would most likely be reduced. However, should the virus improve its transmissibility through adaptation as a wholly avian virus, then the present high lethality could be maintained during a pandemic." .... "Concerning the potential high lethality of a wholly avian pandemic virus, some modelling studies have suggested that pandemic spread could not be fully sustained in the presence of very high mortality. All such matters remain difficult to predict."

<sup>&</sup>lt;sup>1</sup> Taubenberger JK, Morens DM. 1918 Influenza: The Mother of All Pandemics. Emerg Infect Dis 2006;12:20: <u>http://wwwnc.cdc.gov/eid/article/12/1/pdfs/05-0979.pdf</u>

<sup>&</sup>lt;sup>2</sup> Johnson NPAS, Mueller J. Updating the Accounts: Global Mortality of the 1918–1920 "Spanish" Influenza Pandemic, Bull. Hist. Med., 2002, 76: 105–115: <u>www.birdflubook.org/resources/NIALL105.pdf</u>

<sup>&</sup>lt;sup>3</sup> The world population was about 1.8 billion in 1918, about <sup>1</sup>/<sub>4</sub> of the 2014 population of about 7.2 billion.

- 2. WHO Strategic Action Plan for Pandemic Influenza, WHO, 2007, page 4 (http://www.who.int/csr/resources/publications/influenza/StregPlanEPR\_GIP\_2006\_2.pdf?u a=1). "Neither the timing nor the severity of the next pandemic can be predicted with any certainty. At the same time, however, the present threat to international public health is sufficiently serious to call for emergency actions calculated to provide the greatest level of protection and preparedness as quickly as possible." ...... "all concerned should keep in mind that no health emergency on the scale of a severe influenza pandemic has confronted the international community for several decades."
- 3. Interim Pre-Pandemic Planning Guidance: Community Strategy for Pandemic Influenza Mitigation in the United States - Early, Targeted, Layered Use of Nonpharmaceutical Interventions, US CDC, 2007, pages 17 & 32-34 (http://www.cdc.gov/nonpharmaceutical-interventions/guidance/index.html): "A severe pandemic in a fully susceptible population, such as the 1918 pandemic or one of even greater severity, with limited quantities of antiviral medications and pre-pandemic vaccine represents a worst-case scenario for pandemic planning and preparedness."
- 4. Pandemic: Potential Insurance Impacts, Lloyd's Emerging Risks Team Report, 2008, page 3 (http://www.lloyds.com/~/media/Lloyds/Reports/Emerging%20Risk%20Reports/ER Pande

<u>mic\_InsuranceImpacts\_V2.pdf</u>): "A pandemic is inevitable." "1918 may not be a worst case."

- Future Global Shocks, OECD, 2011 (<u>www.oecd.org/governance/48256382.pdf</u> & <u>http://www.oecd.org/governance/48329024.pdf</u> Several references throughout the documents. Future Global Shocks: Pandemics: <u>http://www.oecd.org/governance/risk/46889985.pdf</u>)
- 6. Scientific Summary of Pandemic Influenza and its Mitigation, UK Dep. of Health, March 2011, page 13

(https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/215666/dh 125333.pdf): ..... "given the current Case Fatality Ratio of over 50% for H5N1, compared with around 2% for 1918, more severe pandemics than 1918 may be entirely feasible at present, even with 21st century improvements in healthcare and interventions."

- 7. Strengthening Response to Pandemics and Other Public Health Emergencies: Report of the Review Committee on the Functioning of the International Health Regulations (2005) and on Pandemic Influenza (H1N1) 2009, WHO, 2011, page xxiv (www.who.int/ihr/publications/RC report/en/): "The world is ill-prepared to respond to a severe influenza pandemic or to any similarly global, sustained, and threatening public health emergency." ..... "the unavoidable reality is that tens of millions of people would be at risk of dying in a severe pandemic."
- Experimental adaptation of an influenza H5 HA confers respiratory droplet transmission to a reassortant H5 HA/H1N1 virus in ferrets, Yoshihiro Kawaoka, et. al., Nature, 2 May 2012 (<u>http://www.nature.com/nature/journal/v486/n7403/full/nature10831.html</u>): Four mutations and H5N1 reassortment with H1N1 led to droplet transmission between ferrets. .... "as H5N1 viruses continue to evolve and infect humans, receptor-binding variants of H5N1 viruses with pandemic potential, including avian-human reassortant viruses as tested here, may

emerge. Our findings emphasize the need to prepare for potential pandemics caused by influenza viruses possessing H5 HA" .....

# 9. Airborne Transmission of Influenza A/H5N1 Virus Between Ferrets, Ron A. M. Fouchier, et. al., Science, 22 June 2012

(http://www.sciencemag.org/content/336/6088/1534.full): H5N1 viruses which achieved respiratory transmission between ferrets had 5 mutations in common. "Our findings indicate that HPAI A/H5N1 viruses have the potential to evolve directly to transmit by aerosol or respiratory droplets between mammals, without reassortment in any intermediate host, and thus pose a risk of becoming pandemic in humans."

10. Weekly Epidemiological Record, WHO, 29 March 2013, page 143, paragraph 3 (www.who.int/wer/2013/wer8813.pdf): "Although influenza A(H5N1) infection in humans seems rare, the prospect that A(H5N1) viruses circulating in animals might evolve and acquire the ability to spread with ease from person to person, while retaining capacity to cause severe disease, is a serious public health concern. During 2011, 2 groups of researchers (one in the Netherlands and the other a joint Japan/USA group) conducted studies to understand better the transmissibility of A(H5N1) influenza viruses. These studies resulted in the creation of laboratory-modified A(H5N1) viruses that can easily transmit in ferrets and demonstrated that relatively few genetic changes in A(H5N1) viruses might enable transmission via the respiratory route. As humans lack immunity to influenza viruses possessing an H5 HA protein, a transmissible H5 virus would likely have pandemic potential."

#### 11. H7N9: Is This Flu Something to Worry About? US CDC, May 2013

(http://www.cdc.gov/features/h7n9flu/index.html): ...... "a big concern is that this H7N9 virus might gain the ability to spread easily from person to person. This can happen when animal and flu viruses mix genetic information (reassort) and produce a new influenza virus that can spread easily between people but that is still very different from human viruses, and so people would have little or no immunity against it. Such "reassortment" events are believed to have happened before the influenza pandemics of 1918, 1957, 1968 and 2009. CDC doesn't know if this change will occur. But if this change happens with H7N9, the severity of illness associated with this virus is concerning. The world could face a pandemic with a high toll in illnesses, hospitalizations and deaths."

- 12. H7N9 Influenza Emergency Use Authorization, U.S. Food & Drug Administration, April 2013 (<u>http://www.phe.gov/emergency/news/healthactions/phe/Pages/H7N9-influenza-virus.aspx</u>): ...... "I hereby determine that a there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad and that involves the avian influenza A (H7N9) virus."
- 13. MERS-CoV Emergency Use Authorizations, U.S. Food & Drug Administration, May 2013 (<u>http://www.phe.gov/emergency/news/healthactions/phe/Pages/mers-cov.aspx</u>): ...... "I hereby determine that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad and that involves Middle East respiratory syndrome coronavirus (MERS-CoV)."
- 14. National Risk Register of Civil Emergencies, UK Cabinet Office, 2013, page 7 (https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/211867/Na

tionalRiskRegister2013 amended.pdf): "The following are considered by the Government to be the highest priority risks of emergency, taking both likelihood and impact into account: Pandemic influenza – This remains the most significant civil emergency risk."

#### 15. The Actuary, Institute and Faculty of Actuaries, December 2013

(http://www.theactuary.com/news/2013/11/global-pandemic-tops-poll-of-insurance-industryrisks/): "Global pandemic tops poll of insurance industry risks. Insurers from around the world have ranked the risk of a global pandemic as the most extreme event that could impact the industry."

#### 16. The World Development Report 2014, The World Bank, pages 248-249

(http://siteresources.worldbank.org/EXTNWDR2013/Resources/8258024-1352909193861/8936935-1356011448215/8986901-1380046989056/07a--Spotlight 7.pdf): "a severe flu pandemic could more than double the total burden of disease" and "trigger a global recession." ..... "pandemics are an undermanaged risk. Pandemic prevention and preparedness tend to be sidelined, especially in the health sector, where the responsibility often rests."

17. Statement for the Record: Worldwide Threat Assessment of the US Intelligence Community, Senate Select Committee on Intelligence, January 29, 2014, page 12 (http://www.dni.gov/files/documents/Intelligence%20Reports/2014%20WWTA%20%20SFR SSCI 29 Jan.pdf) "If H7N9 influenza or any other novel respiratory pathogen that kills or incapacitates more than 1 percent of its victims were to become easily transmissible, the outcome would be among the most disruptive events possible. Uncontrolled, such an outbreak would result in a global pandemic with suffering and death spreading globally in fewer than six months and would persist for approximately two years."

#### 18. Communicable Disease Threats Report, European CDC, May 2014 (http://ecdc.europa.eu/en/publications/Publications/communicable-disease-threats-report-04may-2014.pdf, with regard to Avian Influenza H7N9) "the continued transmission of a novel reassortant avian influenza virus, in one of the most densely populated areas in the world, capable of causing severe disease in humans, is a cause for concern due to the pandemic potential of the virus."

19. Warning signals from the volatile world of influenza viruses, WHO, February 2015 (http://www.who.int/influenza/publications/warningsignals201502/en/) "The current global influenza situation is characterized by a number of trends that must be closely monitored. These include: an increase in the variety of animal influenza viruses co-circulating and exchanging genetic material, giving rise to novel strains; continuing cases of human H7N9 infections in China; and a recent spurt of human H5N1 cases in Egypt." ......... "The diversity and geographical distribution of influenza viruses currently circulating in wild and domestic birds are unprecedented since the advent of modern tools for virus detection and characterization. The world needs to be concerned." ....... "The highly pathogenic H5N1 avian influenza virus, which has been causing poultry outbreaks in Asia almost continuously since 2003 and is now endemic in several countries, remains the animal influenza virus of greatest concern for human health. From end-2003 through January 2015, 777 laboratory-confirmed human cases of H5N1 virus infection have been reported to WHO from 16 countries. Of these cases, 428 (55.1%) have been fatal." ....... "The sudden increase in the number of H5N1 human infections in Egypt that began in November 2014 and continued during January and February 2015 awakened concern. From the start of November to 23 February, Egypt reported 108 human cases and 35 deaths. The number of cases over this period is larger than yearly totals reported by any country since human H5N1 virus infections re-emerged in late 2003." ………… "According to a recent estimate, the maximum annual global manufacturing capacity has risen to 1.5 billion doses of seasonal influenza vaccines and the potential of 6.2 billion doses in the event of a pandemic." ………… "Though the world is better prepared for the next pandemic than ever before, it remains highly vulnerable, especially to a pandemic that causes severe disease." ……… "An influenza pandemic is the most global of infectious disease events currently known. It is in every country's best interests to prepare for this threat with equally global solidarity."

#### 20. National Risk Register of Civil Emergencies, UK Cabinet Office, March 2015,

(https://www.gov.uk/government/uploads/system/uploads/attachment\_data/file/419549/201 50331\_2015-NRR-WA\_Final.pdf) "The following, as reflected within the risk matrices, are considered by the Government to be the highest priority risks. Pandemic influenza – This continues to represent the most significant civil emergency risk." ...... "The consensus view among experts is that there is a high probability of another influenza pandemic occurring. It is impossible to forecast its timing or the nature of its impact." ...... "Consequences may include: in the case of pandemic influenza, half the UK population potentially being infected, with between 20,000 and 750,000 additional deaths potentially by its end." ...... "in the absence of early or effective interventions to deal with a pandemic, significant social and economic disruption, significant threats to the continuity of essential services, lower production levels, and shortages and distribution difficulties." ...... "The UK Government plans to maintain a stockpile of antivirals sufficient to treat 50% of the population" ...... "Arrangements are in place for vaccines to be developed and supplied in the event of a pandemic, although delivery of the first batch of vaccine will not take place until four to six months after the pandemic's start."

#### 21. What Bill Gates is afraid of, Vox, May 27, 2015 (Gates in 4 <sup>1</sup>/<sub>2</sub> minute video) (http://www.news.com.au/finance/work/bill-gates-has-revealed-what-frightens-him-most-anepidemic-so-great-it-would-rapidly-wipe-out-millions-worldwide/story-fn5tas5k-1227372407389 & https://www.youtube.com/watch?v=9AEMKudv5p0) "The Ebola epidemic showed me that we are not ready for a serious epidemic, an epidemic that would be more infectious and would spread faster than Ebola did. This is the greatest risk of a huge tragedy. This is the most likely thing by far to kill over 10 million excess people in a year." The Next Epidemic — Lessons from Ebola, Bill Gates, New England Journal of Medicine, April 9, 2015

(http://www.nejm.org/doi/full/10.1056/NEJMp1502918) Also see http://www.npr.org/2016/03/04/468880150/how-can-we-prevent-the-next-global-healthepidemic NPR TED Radio Hour: How Can We Prevent The Next Global Health Epidemic? TED talk by Bill Gates from March 2015, in which he discusses disease outbreak preparedness.

22. US CDC, Public Health Threat of Highly Pathogenic Asian Avian Influenza A (H5N1) Virus, Updated June 2015, paragraph 2 (www.cdc.gov/flu/avianflu/h5n1-threat.htm): "If HPAI Asian H5N1 viruses gain the ability for efficient and sustained transmission among humans, an influenza pandemic could result, with potentially high rates of illness and death worldwide. Therefore, the HPAI H5N1 epizootic continues to pose an important public health threat."

# 23. Frequently Asked Questions on Middle East Respiratory Syndrome Coronavirus (MERS-CoV), WHO, July 2015

(http://www.who.int/csr/disease/coronavirus\_infections/faq/en/) "There have been clusters of cases in health-care facilities, where human-to-human transmission appears to be more efficient, especially when infection prevention and control practices are inadequate. Thus far, no sustained community transmission has been documented."

#### 24. The Inclusive Cost of Pandemic Influenza Risk, March 2016, Victoria Y. Fan, Dean T. Jamison, and Lawrence H. Summers, the National Bureau of Economic Research, NBER Working Paper No. 22137 (http://larrysummers.com/wpcontent/uploads/2016/04/NBER\_The-Inclusive-Cost-of-Pandemic-Influenza-Risk.pdf) "The recent Ebola outbreak in Guinea, Liberia and Sierra Leone reminded the world that enormous economic and human costs result from the uncontrolled spread of deadly infection. Less noticed was that a pandemic with characteristics similar to that of influenza in 1918 would have killed about 10 times as many people in those three countries as did Ebola. Worldwide the death total from such a pandemic would be on the order of 2500 times higher than WHO's estimate of a little over 11,300 Ebola deaths through the end of the epidemic on March 17, 2016 (World Health Organization, 2016)" (page 3). "While the world may be expected to experience moderately severe to severe pandemics several times each century, there is consensus among influenza experts that an event on the very severe scale of the 1918 pandemic may be plausible but remains historically and biologically unpredictable." ..... "While a biological replica of the 1918 flu would no doubt result in lower mortality rates than occurred in 1918 (Madhav, 2013), both that study and other analysts point to the possibility that exceptionally transmissible and virulent viruses could lead to global death rates substantially higher than in 1918 (see McKibben and Sidorenko, 2006, or Osterholm, 2005)"(page 5).

### 25. Avian Influenza A (H7N9) Virus, US CDC, January 30, 2017

(https://www.cdc.gov/flu/avianflu/h7n9-virus.htm) "As of January 16, 2017, cumulative reported human infections with H7N9 totaled 918 with 359 deaths. Most human infections with H7N9 have occurred after exposure to poultry; H7N9 viruses continue to circulate in poultry in China. Most reported patients have had severe respiratory illness; about 40% have died. Rare, limited person-to-person spread of this virus has been identified in China, but there is no evidence of sustained person-to-person spread of H7N9." ....... "Most concerning about this situation is the pandemic potential of this virus. Influenza viruses constantly change and it's possible that this virus could gain the ability to spread easily and sustainably among people, triggering a global outbreak of disease (pandemic). In fact, of the influenza viruses rated by the Influenza Risk Assessment Tool (IRAT), H7N9 is ranked as having the greatest potential to cause a pandemic, as well as potentially posing the greatest risk to severely impact public health."

#### 26. Defense Civil Support: DOD, HHS, and DHS Should Use Existing Coordination Mechanisms to Improve Their Pandemic Preparedness. GAO-17-150: Publicly Released: Feb 10, 2017 (<u>https://www.gao.gov/products/GAO-17-150</u>) "The U.S. Army estimates that if a severe infectious disease pandemic were to occur today, the number of U.S. fatalities could be almost twice the total number of battlefield fatalities in all of America's wars since the American revolution in 1776." ...... "HHS and DHS have plans to guide their response to a pandemic, but their plans do not explain how they would respond in a resource-constrained environment in

which capabilities like those provided by DOD are limited." ...... "HHS and DHS plans do not specifically identify what resources would be needed to support a response to a pandemic in which demands exceeded federal resources."

- 27. National Risk Register of Civil Emergencies, 2017 edition, UK Cabinet Office, Sep. 2017 (https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment\_dat a/file/644968/UK\_National\_Risk\_Register\_2017.pdf) See: "Matrix A Hazards, diseases, accidents, and societal risks" on page 9 (showing pandemic influenza with the highest impact severity and likelihood). "It is difficult to forecast the spread and impact of a new flu strain or disease until it starts circulating. However, consequences may include: for pandemic flu: up to 50% of the UK population experiencing symptoms, potentially leading to between 20,000 and 750,000 fatalities and high levels of absence from work" (p. 34). "vaccines will be developed as soon as possible once new flu strains are identified. This will take at least four to six months after a pandemic begins" (p. 35).
- 28. "H7N9 influenza is both lethal and transmissible in animal model for flu," University of Wisconsin press release, October 19, 2017 (https://news.wisc.edu/h7n9-influenza-is-bothlethal-and-transmissible-in-animal-model-for-flu/): "In early 2017, Yoshihiro Kawaoka, professor of pathobiological sciences at the University of Wisconsin-Madison School of Veterinary Medicine, received a sample of H7N9 virus isolated from a patient in China who had died of the flu. He and his research team subsequently began work to characterize and understand it. The first of those results are published today in Cell Host & Microbe. For the first time, Kawaoka says, his team has identified an influenza virus strain that is both transmissible between ferrets (the best animal model proxy for human influenza infections) and lethal, both in the animal originally infected and in otherwise healthy ferrets in close contact with these infected animals. "This is the first case of a highly pathogenic avian virus that transmits between ferrets and kills them," Kawaoka says. "That's not good for public health."" ...... "Without additional mutations, the virus transmitted and killed ferrets," says Kawaoka, noting that further alterations to the virus may not be necessary to make it a potential public health threat, though human-to-human transmission has thus far remained limited." (Also see: http://www.cell.com/cell-host-microbe/fulltext/S1931-3128(17)30396-7 & http://www.cidrap.umn.edu/news-perspective/2017/10/study-details-pandemic-potentiallatest-h7n9-flu-strains: "Ferrets are thought to be the best animal model for studying flu viruses in humans, because clinical symptoms and transmissibility seem similar. However, some experts doubt how well ferret studies predict what will happen in humans." Similar findings were also reported in October 2017 by Hualan Chen and colleagues: http://www.nature.com/cr/journal/vaop/ncurrent/full/cr2017129a.html)
- 29. Statement for the Record: Worldwide Threat Assessment of the US Intelligence Community, Daniel R. Coats, Director of National Intelligence, February 13, 2018, page 17 (https://www.dni.gov/files/documents/Newsroom/Testimonies/2018-ATA---Unclassified-SSCI.pdf): "The increase in frequency and diversity of reported disease outbreaks—such as dengue and Zika—probably will continue through 2018, including the potential for a severe global health emergency that could lead to major economic and societal disruptions, strain governmental and international resources, and increase calls on the United States for support. A novel strain of a virulent microbe that is easily transmissible between humans continues to be a major threat, with pathogens such as H5N1 and H7N9 influenza and Middle East Respiratory Syndrome Coronavirus having pandemic potential if they were to acquire efficient human-to-

human transmissibility." ...... "The World Bank has estimated that a severe global influenza pandemic could cost the equivalent of 4.8 percent of global GDP—more than \$3 trillion—and cause more than 100 million deaths."

- 30. Vulnerability to Pandemic Flu Could Be Greater Today Than a Century Ago. Interview with Michael Osterholm, Director, Center for Infectious Disease Research and Policy, University of Minnesota. (Voelker R. JAMA. Published online September 28, 2018. doi:10.1001/jama.2018.12966: https://jamanetwork.com/journals/jama/fullarticle/2705303) "I would say that we are much more vulnerable today to a catastrophic influenza pandemic than we were in 1918." ....... "In the future, vaccines still are going to have only a limited impact." ...... "If anything causes a disruption in drugs and medical devices that come here from around the world, it doesn't matter how modern our health care system is if we don't have basic drugs or equipment like mechanical ventilators ...... The second piece is that we're going to have a lot of health care workers that are going to be put at risk for influenza by going to work. We will run out of N95 respirators very quickly. We will not have vaccine available in a timely manner in our hospitals. We won't have anywhere near enough antiviral drugs." ..... "We used to talk about vaccine hesitancy where people were reluctant to get vaccines. Today it's much greater than that. It's a hesitancy to adopt any kind of science-based approach."
- 31. Statement for the Record: Worldwide Threat Assessment of the US Intelligence Community, Daniel R. Coats, Director of National Intelligence, January 29, 2019, page 21 (https://www.dni.gov/files/ODNI/documents/2019-ATA-SFR---SSCI.pdf): Global Health: "We assess that the United States and the world will remain vulnerable to the next flu pandemic or large-scale outbreak of a contagious disease that could lead to massive rates of death and disability, severely affect the world economy, strain international resources, and increase calls on the United States for support. Although the international community has made tenuous improvements to global health security, these gains may be inadequate to address the challenge of what we anticipate will be more frequent outbreaks of infectious diseases because of rapid unplanned urbanization, prolonged humanitarian crises, human incursion into previously unsettled land, expansion of international travel and trade, and regional climate change."
- 32. Risk Communication Strategies for the Very Worst of Cases: How to Issue a Call to Action on Global Catastrophic Biological Risks, Johns Hopkins Center for Health Security, March 2019 (http://www.centerforhealthsecurity.org/about-thecenter/pressroom/press\_releases/2019-03-04\_risk-communications-global-catastrophicbiological-risks.html): "In 2017-18, the Johns Hopkins Center for Health Security conducted a multiphase research project to help inform the development of a strategic approach for communicating about global catastrophic biological risks (GCBRs). In brief, we define a GCBR as a biological development that could adversely affect the human species as a whole or radically change the course of human civilization—for instance, a severe pandemic involving a naturally occurring or deliberately engineered pathogen" (page 3). ..... "For most subject matter experts who are thinking about GCBRs, that which comes readily to mind are well-known naturally occurring pandemics, such as the Spanish Flu and the Black Death, and the certain prospect of another influenza pandemic. Yet, individuals who are familiar with advances in bioscience and biotechnology warn that engineered pathogens have an even greater potential to threaten the human species" (page 4). ...... "Among naturally occurring pathogens, many felt influenza was the most likely culprit for a GCBR, since it was "much likelier to go global" and

"reach pandemic levels very quickly" because of the rapid transmissibility of the virus that regularly mutates" (page 12).

33. A world at risk: annual report on global preparedness for health emergencies. Global Preparedness Monitoring Board. Geneva: WHO; September 2019, page 5 (http://apps.who.int/gpmb/annual report.html): "The chances of a global pandemic are growing. While scientific and technological developments provide new tools that advance public health (including safely assessing medical countermeasures), they also allow for diseasecausing microorganisms to be engineered or recreated in laboratories. A deliberate release would complicate outbreak response; in addition to the need to decide how to counter the pathogen, security measures would come into play limiting information-sharing and fomenting social divisions. Taken together, naturally occurring, accidental, or deliberate events caused by high-impact respiratory pathogens pose "global catastrophic biological risks." The world is not prepared for a fast-moving, virulent respiratory pathogen pandemic. The 1918 global influenza pandemic sickened one third of the world population and killed as many as 50 million people - 2.8% of the total population. If a similar contagion occurred today with a population four times larger and travel times anywhere in the world less than 36 hours, 50-80 million people could perish. In addition to tragic levels of mortality, such a pandemic could cause panic, destabilize national security and seriously impact the global economy and trade."

### 34. **Preparedness for a High-Impact Respiratory Pathogen Pandemic**, Johns Hopkins University Center for Health Security, September 2019

(http://www.centerforhealthsecurity.org/newsroom/center-news/2019-09-18-GPMBreport.html): "The IHR core capacities are unlikely in their current formulation to

<u>GPMBreport.html</u>): "The IHR core capacities are unlikely in their current formulation to adequately prepare countries and the international community for high-impact respiratory events" (page 7). ..... "we define "high-impact respiratory pathogens" as pathogens that are readily transmissible by the respiratory route (via droplets and airborne transmission); that, due to their typically short incubation periods and high probability of person-to-person transmission, have the potential for widespread (possibly pandemic) spread; and, due to their high observed percent mortality (generally on the order of at least 1%, possibly substantially higher), may have significant public health, economic, social, and political consequences. We expect that, were such a pathogen to emerge, either naturally, or as the result of accidental or deliberate release, many countries would be affected at once, which would require different international approaches than typically occur in geographically limited events" (page 15). "The potential for an epidemic or pandemic caused by a high-impact respiratory pathogen is increasing." (page 18). "Guidelines from public health authorities such as WHO exist regarding the use of NPIs, but they do not provide sufficient information to guide the appropriate use of these measures" (page 72).