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Sharing the Burden of Ebola Vaccine-Related Adverse Events

Sam Halabi*
John Monahan†

On December 9, 2014, United States Secretary of Health and Human Services Sylvia Burwell issued a declaration under the U.S. Public Readiness and Emergency Preparedness (PREP) Act to provide immunity from legal claims related to manufacturing, testing, development, distribution, and administration of three candidate Ebola vaccines.¹ At an earlier meeting of major stakeholders held at the World Health Organization (WHO), the management of legal liabilities related to vaccines was an important subject of the global response to Ebola addressed by national governments, the World Bank, and others.² That discussion, however, has faded as the epidemic has been brought under control even as clinical trials for vaccine candidates commence.³ This Essay argues that planning for the management of adverse event costs associated with rapidly developed vaccines is in fact a critical opportunity in public health emergency preparedness and recommends six options available to governments of countries afflicted by outbreaks of infectious disease, governments in countries where vaccines are likely to be developed, major global vaccine manufacturers, and major third-party sponsors such as the Bill and Melinda Gates Foundation, the Global Alliance for Vaccines and Immunization (GAVI Alliance), the World Bank, and WHO.

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1. Notice of Declaration Under the Public Readiness and Emergency Preparedness Act, 79 Fed. Reg. 73,314 (Dec. 10, 2014).

2. World Health Org. [WHO], *Summary Report of a WHO High-Level Meeting on Ebola Vaccines Access and Financing*, at 2, 7 (Oct. 23, 2014), http://apps.who.int/iris/bitstream/10665/137184/1/WHO_EVD_Meet_EMP_14.2_eng.pdf?ua=1.

3. Sarah Boseley, *Experimental Ebola Vaccine Shipped to Liberia*, GUARDIAN (Jan. 23, 2015, 5:34 EST), <http://www.theguardian.com/world/2015/jan/23/ebola-vaccine-liberia-gsk-glaxosmithkline-trials>.

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I. INTRODUCTION

There are real and perceived liability risks of adverse events relating to Ebola vaccines. The challenge facing partners in the Ebola response is to allocate, whether explicitly by action or implicitly by nonaction, such liability risks between vaccine manufacturers, supporting governments, beneficiary governments (Guinea, Liberia, and Sierra Leone), individuals who may experience adverse events, and populations in the affected countries and elsewhere who will benefit from widespread vaccination.

This challenge is compounded by the fact that such risks and accompanying legal liabilities are difficult to project in advance, are based upon imperfect information, and are potential precedents for treatment of liability risks in future public health emergencies. Guinea, Liberia, and Sierra Leone have histories of relatively weak judicial systems, which increase the potential legal risks.⁴ Even in the context of stronger judicial systems, there is no way to effectively assess how large liability exposure might be. Liability for GlaxoSmithKline's ASO3- adjuvanted pandemic influenza vaccines during the 2009 H1N1 episode ran into the tens of millions of dollars if not more.⁵ The influenza vaccine is generally manufactured according to well-known processes and over its life enjoys a strong safety profile. There are, by contrast, few, if any, licensed vaccines based on current approaches to Ebola

4. United Nations Dev. Programme [UNDP], *Improving Access to Justice in Sierra Leone*, at 3 (2009) http://www.sl.undp.org/content/dam/sierraleone/docs/projectdocuments/demgov/undp_sle_A2Jprodod.pdf; Report of the Special Adviser to the Secretary-General on the Prevention of Genocide on His Mission to Guinea from 7 to 22 March 2010, at 1 (2010), http://www.un.org/en/preventgenocide/adviser/pdf/osapg_mission_report_guinea_mar_2010.pdf.

5. Nick Paul Taylor, *Report: U.K. Facing \$100M Compensation Payout Relating to GSK's Swine Flu Vaccine*, FIERCE VACCINES (Mar. 4, 2014), <http://www.fiercevaccines.com/story/report-uk-facing-100m-compensation-payout-relating-gsk-swine-flu-vaccine/2014-03-04>.

vaccine development. Ebola vaccines will potentially be administered to a large population after limited development and unusual circumstances.

In most countries, a plaintiff (whether individual or governmental) is required to prove causation between an injury and the vaccination that preceded it. The method by which causation is established under products liability law differs in key respects from the accepted method of establishing causation in science and medicine. In law, there is generally no requirement that a decision maker, typically a judge, apply a scientific standard to the causation determination, only that some evidence exists to support a finding of causation.

If supporting governments accept all liabilities for adverse events attributed to Ebola vaccines, they are potentially responsible for substantial claims that might erode their credibility when undertaking future vaccination or access-to-medicines programs. On the other hand, effective risk-sharing may set a useful precedent for future public health emergencies. There is a public health preparedness value in agreeing to compensate individuals through predefined legal or regulatory mechanisms. In the vaccination context generally, the traditional argument is that the public health benefits of vaccination so far outweigh the risks that we, as a community, compensate individuals who pay the price in experiencing adverse events. The argument is also true for public health emergencies where rapid response to an evolving threat in the face of imperfect information counsels toward aggressive action.

From the standpoint of vaccine manufacturers, the risks associated with potential legal liability cannot be fully separated from other more general business risks and opportunities:

- (1) Under prevailing legal norms, product manufacturers are expected to pay for injuries caused by their products, which in the case of rapidly developed medicines may result in potentially substantial liability;
- (2) The perception that a firm's vaccines may be unsafe or cause injury may threaten its reputation across multiple product lines; and
- (3) Firms compete globally, and there is a strong incentive for firms to produce the first safe and effective Ebola vaccine given the potential market likely to be formed by governments seeking to secure access to an Ebola vaccine as part of their health security preparedness plans.

This Essay focuses specifically on vaccine injury, a specific type of product liability that is likely to subject manufacturers to "litigation risk," i.e., the possibility that legal action will be taken because of a defendant's

actions, inactions, products, services or other events. It outlines preliminary options for addressing manufacturers' litigation risk for injuries attributed to experimental Ebola vaccines.

II. PRODUCT LIABILITY AND EBOLA VACCINES

"Products liability" refers to any action against a manufacturer or seller for recovery of damages arising out of personal injury, death, or property damage allegedly caused by a defective product. For vaccine manufacturers, litigation risk for product liability attaches any time there is an association between an injury suffered by a recipient and the place, time, and specifics of the vaccine administration. These risks are particularly relevant for manufacturers because, even if the injury is wrongly associated with the vaccination, the manufacturer must nevertheless incur costs in reputation, time, and money to establish the falsity of the allegation.

Liability will depend upon the laws applied by the court hearing the case. Key questions as to jurisdiction, choice of law, venue, and enforceability of judgments are complex and will depend upon the facts of particular cases. Moreover, the rapid circumstances under which current Ebola vaccine candidates have been or are being developed have necessarily compressed typical drug development protocols. The window to discover adverse events will be narrower for Ebola vaccines, raising the risk that delayed adverse events may not be revealed until a mass vaccination campaign is already underway.

A. *Real and Unknown Risks*

Even vaccines that are generally regarded as safe and effective will still typically generate adverse events among those inoculated, ranging from (common) soreness at the injection site, to fever, discomfort, and muscle pain, to more serious problems like seizures, severe allergic reactions, and brain damage.⁶ On December 11, 2014, the Merck-NewLink experimental Ebola vaccine (rVSV-ZEBOV) phase 1 trial was temporarily suspended because four of fifty-nine participants reported joint pain in the hands and feet, both delayed-onset and away from the injection site.⁷ The candidate vaccine (cAd3-ZEBOV) developed by

6. *Possible Side-Effects from Vaccines*, CTRS. DISEASE CONTROL & PREVENTION, <http://www.cdc.gov/vaccines/vac-gen/side-effects.htm> (last visited Nov. 6, 2015).

7. Joanna Lyford, *Ebola Clinical Trial Suspended After Volunteers Complain of Joint Pains*, PHARMACEUTICAL J. (Dec. 12, 2014), <http://www.pharmaceutical-journal.com/news-and-analysis/news/ebola-clinical-trial-suspended-after-volunteers-complain-of-joint-pains/20067418>. article.

GlaxoSmithKline and the United States National Institute for Allergy and Infectious Disease (NIAID) showed a mild, adverse event for some participants at a high dose.⁸

B. *Perceived and Falsely Attributed Risks*

In many developing countries, including Guinea, Liberia, and Sierra Leone, there have been campaigns asserting that vaccines may cause sterility or other adverse health effects.⁹ Such campaigns fuel suspicions that firms from developed countries use people as unwitting human subjects for research for a range of self-serving or even nefarious objectives. There have, in fact, been instances of improper human subject research in developing countries which influence these views.¹⁰ For a variety of reasons beyond the scope of this Essay, there are fears and rumors associated with vaccination campaigns and the testing of new medical products in many communities in the developing world. Indeed, common rumors in the three most Ebola-affected countries link the outbreak with preexisting vaccination drives and the presence of clinical trials in the region sponsored by pharmaceutical companies.¹¹

Establishing causation will be a key element of any action to recover money damages in the context of Ebola vaccines. Litigation risk is far more significant for perceived injuries or false attribution of background events to a vaccination. The beneficiary countries suffer from high background levels of morbidity and mortality, and coincidental deaths and injuries associated with vaccine administration may give rise to liability, even if objective data ultimately vindicates a manufacturer and its product. Similarly, vaccine-related injuries may be attributable to contamination or infection from vaccines or improperly used syringes, a risk that increases in low resource countries without the infrastructure to ensure proper handling, storage, distribution, and administration from facility to recipient.

8. NIAID/GSK *Experimental Ebola Vaccine Appears Safe, Prompts Immune Response*, NAT'L INSTS. HEALTH (Nov. 28, 2014), <http://www.nih.gov/news/health/nov2014/niaid-28.htm>.

9. James Fairchild, Melissa Leach & Mary Small, *Childhood Vaccination and Society in the Gambia: Public Engagement with Science and Delivery* 4 (Inst. of Dev. Stud., Working Paper No. 218, Jan. 2004), <http://www.ids.ac.uk/files/dmfile/Wp218.pdf>.

10. Remigius N. Nwabueze, *Ethical Review of Research Involving Human Subjects in Nigeria: Legal and Policy Issues*, 14 IND. INT'L & COMP. L. REV. 87, 88-89 (2003-2004).

11. Yoichi Shimatsu, *The Ebola Outbreak Coincided with UN Vaccine Campaigns*, LIBER. OBSERVER (Oct. 9, 2014), <http://www.liberianobserver.com/commentaries/ebola-breakout-coincided-un-vaccine-campaigns>.

C. Risk-Sharing Mechanisms

Product liability plays a large role in global public health emergency responses. In 2006, the IFPMA issued a statement in the wake of a potential H5N1 pandemic:

[I]n some countries, existing pharmacovigilance systems may fail to detect key signals until after the vaccines have already been administered to hundreds or thousands or millions of people. Many of the individuals vaccinated could develop medical conditions, by chance alone and unrelated to the vaccine, at some point following vaccination. It is inevitable that many will expect to be compensated. This is why [IFPMA] call(s) for a waiver of liability for the manufacturing and use of pandemic vaccines.¹²

In the 2009 H1N1 pandemic, manufacturers restated their concerns with potential product liability suits. In fact, negotiations regarding indemnification for manufacturers caused substantial delays.¹³

Manufacturers have expressed similar concerns with respect to Ebola vaccines under development.¹⁴ Some jurisdictions, like the United States, have extended immunity against legal claims related to the manufacturing, testing, development, distribution, and administration of Ebola vaccines.¹⁵ But even where such legal authorizations apply, they do not generally provide immunity for a claim brought in a court outside that country.¹⁶ Nor, of course, does immunity provide any relief for individuals harmed by vaccines administered as part of public health campaigns that respond to public health emergencies.¹⁷

Product liability, therefore, figures prominently in manufacturers' risk assessments, and it is on product liability that we will focus our discussion of potential mechanisms or processes that may ameliorate

12. Int'l Fed'n of Pharmaceutical Manufacturers & Ass'ns [IFPMA], *Pandemic Influenza Vaccines and Liability Protection for Manufacturers* (May 19, 2006), http://www.ifpma.org/fileadmin/content/Global%20Health/Influenza/Ref_56_IFPMA_IVS_Request_on_Liability_May_19_2006.pdf.

13. WHO, *Report of the Review Committee on the Functioning of the International Health Regulations, (2005) in Relation to Pandemic (H1N1) 2009*, A64/10 (May 5, 2011), http://apps.who.int/gb/ebwha/pdf_files/WHA64/A64_10-en.pdf?ua=1.

14. *Id.*

15. Notice of Declaration Under the Public Readiness and Emergency Preparedness Act, 77 Fed. Reg. 73,314 (Dec. 10, 2014).

16. HHS Notice of Declaration Under the Public Readiness and Emergency Preparedness Act, *supra* note 1.

17. Peggy Binzer, *The PREP Act: Liability Protection for Medical Countermeasure Development, Distribution and Administration*, 6 BIOSECURITY & BIOTERRORISM: BIODEFENSE STRATEGY, PRAC., & SCI. 1 (2008), http://www.wcsr.com/resources/pdfs/binzer_120709.pdf (noting that PREP Act only applies in the United States).

liability concerns if partners in the Ebola response wish to address these matters. We note at the outset that there are at least nineteen national, no-fault compensation regimes for adverse events attributed to vaccination, all of which are in well-resourced jurisdictions.¹⁸ We assume for purposes of this Essay that establishing similar regimes in target jurisdictions will be prohibitive due to resource constraints. Nevertheless, there are aspects of these regimes that inform our analysis of possible risk-sharing mechanisms.

1. Liability Remains with Manufacturer

Before considering risk-sharing and reallocating mechanisms, the global health community should assess the relationship between indemnification and the likelihood that the absence of a risk-sharing or reallocating mechanisms will deter or delay manufacturer participation. Before the current outbreak, manufacturers identified the market potential of being a first-mover on an effective Ebola vaccine.¹⁹ Seeking to do so makes sense for both low-income and developed country procurement markets. GAVI has established a \$300 million dollar procurement fund for a WHO-approved Ebola vaccine.²⁰ Moreover, there remains the possibility that manufacturers may be able to negotiate coverage of some sort from their traditional insurers. Similarly, while risk-shifting regimes are advantageous in minimizing the likelihood of delay or deterrence of manufacturer participation, they also signal that a manufacturer may lack confidence in its product and that it regards the chances of an adverse event as significant enough to seek maximum indemnity for such occurrences. Indeed, such broad protection could feed into already existing suspicions that European and North American firms are inappropriately or illegally testing their products on people in developing countries. Partners in the global Ebola response should assess whether mitigating or sharing liability is necessary or desirable as a threshold matter.

18. Clare Looker & Heath Kelly, *No-Fault Compensation Following Adverse Events Attributed to Vaccination: A Review of International Programmes*, 89 BULL. OF THE WHO 317, 317 (Mar. 21, 2011), <http://www.who.int/bulletin/volumes/89/5/10-081901/en/>.

19. MICHAEL KREMER & RACHEL GLENNERSTER, STRONG MEDICINE: CREATING INCENTIVES FOR PHARMACEUTICAL RESEARCH ON NEGLECTED DISEASES 38 (2004) (describing first-mover advantage in vaccine markets and circumstances under which that advantage will help innovators).

20. Global Alliance for Vaccines and Immunization [GAVI], *GAVI Commits to Purchasing Ebola Vaccine for Affected Countries* (Dec. 11, 2014), <http://www.gavi.org/Library/News/Press-releases/2014/Gavi-commits-to-purchasing-ebola-vaccine-for-affected-countries/>.

2. Risk Sharing Between Beneficiary Governments and Manufacturers

If conventional insurance markets are not available or optimal for covering Ebola vaccine injury liabilities, manufacturers and procuring governments may enter into their own variations on existing insurance compensation schedules in place for pharmaceutical or other product sectors. For example, manufacturers could agree to pay up to a per claim limit as well as an aggregate limit for claims in a given jurisdiction with the beneficiary government (potentially supported by a multilateral agency or group of supporting governments) promising to pay any compensation above the designated individual or aggregate claims. Similarly, beneficiary governments may establish specific criteria (consistent with their constitutional principles) for which burden sharing is appropriate. For example, manufacturers may agree to compensate for “severe” injuries, injuries based on a period or level of disability, medical costs only, or perhaps other noneconomic losses.²¹ Some relevant models for this kind of risk sharing may be found in UNICEF procurement agreements which, depending on vaccine and registration, shift liabilities between the manufacturer and the beneficiary government.²² UNICEF and third-party financing entities are generally fully indemnified.²³ A second set of relevant models may be found in multilateral agreements addressing indemnification for national security or emergency vaccine deployments like smallpox.²⁴

3. Multilateral Agency or Supporting Government Approach

The World Bank, or a group of willing, supporting governments, may agree to cover any liabilities arising from vaccine injuries. Aside from the logistical questions that will confront a multilateral agency or supporting governments as to how claims are established, how losses and compensation are calculated, and what administrative body will be charged with undertaking those determinations, this approach requires either that manufacturers defend themselves initially and then seek

21. Looker & Kelly, *supra* note 18.

22. United Nations Children’s Fund [UNICEF], *Request for Proposal: United Nations Children’s Fund (UNICEF) Wishes To Receive Proposals for Inactivated Polio Vaccine (IPV)*, RFP-DAN-2013-501729 (Oct. 4, 2013), http://www.unicef.org/videoaudio/PDFs/RFP_DAN_2013_501729.pdf.

23. WHO, *Operational Framework for Monovalent Oral Poliovirus Type 2 (mOPV2) Deployment and Replenishment (During the Endgame Period)*, arts. 15-16 (Oct. 9, 2014), http://www.who.int/immunization/sage/meetings/2014/october/4_Polio_mOPV2_stockpile_v4_09_10_2014.pdf.

24. *See, e.g., id.*

reimbursement or that the supporting organization or group be substituted as the proper party as a threshold matter in any legal action.

4. Risk Mitigation Through Disclosure and Government Recommendations to Judicial Authorities

The principal litigation risk manufacturers face is the possibility of an individual or governmental party bringing suit against it for one of the aforementioned legal bases of liability in a judicial system with which the manufacturer is unfamiliar and/or whose processes may not be as transparent or well-resourced as in its home jurisdiction. This risk may be mitigated if manufacturers are given clear bases for liability in a given jurisdiction and are promised by beneficiary governments to appear in judicial proceedings to explain the reasons for deployment of vaccines. By lending a promise to participate in judicial processes, beneficiary governments may give manufacturers at least some assurance (indeed, relatively low cost assurance) that the beneficiary government will appear to explain legal positions. In the GAVI context, this may be encouraged by including ministries of justice (as well as ministries of health and finance) in country procurement plans or clarifying the ability of ministries of health and finance to appear in court to articulate government positions in specific cases. This has the additional benefit of allowing governmental legal experts the opportunity to present and shape epidemiological and medical evidence as courts and other tribunals are accustomed to hearing it.

5. Declarations of Immunity by Supporting and Beneficiary Governments

Taking as a model the U.S. declaration of immunity, under U.S. law for legal claims related to the manufacturing, testing, development, distribution, and administration of specified vaccines for the Ebola virus, allow beneficiary governments and supporting governments issue similar declarations pursuant to whichever statutory and regulatory frameworks might serve as bases to circumscribe, limit, or prohibit litigation based on Ebola vaccine injury.²⁵ This option is complex, not only because of the internal constitutional and statutory process that may need to mobilize in support of such a declaration, but because judicial or administrative authorities in jurisdictions which lack clear authority for such declarations may deem those acts void under law. Externally (and

25. Notice of Declaration Under the Public Readiness and Emergency Preparedness Act, 79 Fed. Reg. 73,314 (Dec. 10, 2014).

relatedly) if beneficiary and supporting governments do not issue relatively uniform declarations in relatively similar timeframes, it may open additional areas of legal uncertainty.

6. Contractual Indemnities Provided by Third-Party Procurement Entities or Supporting Governments

It is also possible to construct a regime that is entirely or almost entirely risk shifting from manufacturers to procuring governments or to third parties through the procurement agreements themselves. This was effectively the approach adopted for donations and discounted sales of vaccines by manufacturers during the 2009-2010 H1N1 pandemic as well as fully commercial sales to high-income countries.²⁶ Manufacturers agreed to produce vaccines under the condition that all supporting governments indemnify them from liability “for any adverse events arising from the use of pandemic H1N1 vaccine, except to the extent that such adverse events were caused by a failure to comply with cGMP or to meet agreed specifications.”²⁷ This would effectively expand current measures by some governments, like the United States, to shield manufacturers from liability and to effectively cover similar judgments arising in other jurisdictions. As a practical matter, this may end up in negotiated agreements with beneficiary governments where a lump payment is paid to discharge all claims for individuals a beneficiary government represents.²⁸ This arrangement is supported by a long set of international legal precedent.

As the aforementioned discussion noted, such comprehensive promises of indemnification may be both expensive for supporting governments and erode their credibility in attempting to undertake other public health support or emergency measures in the future. Additionally,

26. Sam F. Halabi, *Obstacles to pH1N1 Vaccine Availability: The Complex Contracting Relationship Between Vaccine Manufacturers, WHO, Donor and Beneficiary Governments*, THE PUB. HEALTH RESPONSE TO 2009 H1N1 (2015), http://digitalcommons.law.utulsa.edu/cgi/viewcontent.cgi?article=1469&context=fac_pub.

27. WHO, *Report of the WHO Pandemic Influenza A (H1N1) Vaccine Deployment Initiative*, at 9 (2009), http://www.who.int/influenza_vaccines_plan/resources/h1n1_deployment_report.pdf.

28. Letter from Maxim Litvinov to the President of the United States of America (Nov. 16, 1933), <http://nsarchive.gwu.edu/coldwar/documents/episodes-1/fdr-ml.htm>; Declaration of the Government of the Democratic and Popular Republic of Algeria Relating to the Commitments made by Iran and the United States, 20 I.L.M. 223, 1 (Iran-U.S. Cl. Trib. 1981); Declaration of the Democratic and Popular Republic of Algeria Concerning the Settlement of Claims by the Government of the United States of America and the Government of the Islamic Republic of Iran, 20 I.L.M. 223, 9 (Iran-U.S. Cl. Trib. 1981).

a preexisting promise of indemnity may increase meritless claims as well as reduce the optimal risk manufacturers should bear.

III. CONCLUSION

There are legal risks involved with the current vaccine development effort that is now under way that need to be managed by the relevant actors in the response to the Ebola outbreak in the beneficiary countries. The lack of a global plan for legal risk means a solution must be cobbled together at each step in the response when it is precisely the kind of predictable, resolvable issue that lends itself to advance planning. Doing so provides an opportunity for the global community to use the current Ebola vaccine development and distribution effort as a precedent for dealing with related issues in future global emergencies.

