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## IP Preparedness for Outbreak Diseases

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### ABSTRACT

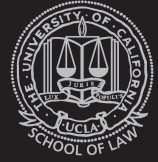
Outbreaks of infectious diseases will worsen in the coming decades, as illustrated by the recent back-to-back Ebola and Zika epidemics. The development of innovative drugs, especially in the form of vaccines, is key to minimizing the scale and impact of future outbreaks, yet current intellectual property (IP) regimes are ineffective in supporting this goal.

Scholarship has not adequately addressed the role of IP in the development of vaccines for outbreak diseases. This Article fills that void. Through case studies on the recent Ebola and Zika outbreaks, it provides the first descriptive analysis of the role of IP from the pre- to the post-outbreak stages, specifically identifying IP inefficiencies.

The Article concludes that these inefficiencies result in a lack of “IP preparedness” that ultimately weakens our ability to respond effectively to outbreaks. To solve the problem, we need a blend of new and existing legal tools. This Article surveys existing solutions and proposes a new legal mechanism: a dormant license, agreed upon in the pre-outbreak period, that would become active once a public health emergency is declared. This solution addresses transactional IP inefficiencies during the early stages of an outbreak and helps get vaccines to the market more efficiently to save lives.

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## TABLE OF CONTENTS

INTRODUCTION.....	1202
I. INEFFICIENCIES AND LACK OF IP PREPAREDNESS IN THE PRE-OUTBREAK PERIOD.....	1207
A. R&D Shortcomings of Outbreak Diseases.....	1207
B. IP as Incentives: The Problem of Underfunded Diseases.....	1213
C. Evidence from the 2014–16 Ebola and Zika Outbreaks.....	1218
1. Pre-Outbreak R&D.....	1218
a. Ebola.....	1218
b. Zika.....	1222
2. Impact of the 2014–16 Outbreaks on Incentives and R&D Frameworks.....	1224
a. The Ebola Vaccine Race.....	1224
b. The Zika Vaccine Race.....	1235
II. INEFFICIENCIES AND LACK OF IP PREPAREDNESS AFTER AN OUTBREAK STARTS.....	1244
A. Transactional IP Inefficiencies.....	1244
B. Lack of IP Preparedness in the Early Stages of an Outbreak.....	1245
C. Lack of IP Preparedness in Post-Outbreak Period.....	1248
III. IMPROVING IP PREPAREDNESS FOR FUTURE OUTBREAKS.....	1253
A. IP Preparedness for Future Outbreak Diseases.....	1253
B. IP Preparedness in Pre- and Inter-Outbreak Periods.....	1254
C. IP Preparedness in Early-Stage Outbreaks.....	1258
1. The Need for Streamlined IP Frameworks.....	1259
2. Benefits of a Dormant License.....	1261
D. IP Preparedness in the Post-Outbreak.....	1264
CONCLUSION.....	1266

## INTRODUCTION

Outbreaks<sup>1</sup> of infectious diseases<sup>2</sup> have risen exponentially from the late twentieth century onward,<sup>3</sup> impacting populations across the globe and producing devastating effects on domestic and regional health systems.<sup>4</sup> Increased travel and connectivity, quick expansion of urban centers, and the ongoing worldwide population boom have all contributed to the increased frequency and magnitude of outbreaks.<sup>5</sup> These same factors now lead scientists to predict that known infectious diseases will erupt more often in the foreseeable future with potentially catastrophic effects.<sup>6</sup> In addition to this, the World Health Organization (WHO) estimates that, in the short-run, a

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1. The World Health Organization defines outbreaks as “the occurrence of cases of disease in excess of what would normally be expected in a defined community, geographical area or season.” *Disease Outbreaks*, WORLD HEALTH ORG. [http://www.who.int/topics/disease\\_outbreaks/en](http://www.who.int/topics/disease_outbreaks/en) [<https://perma.cc/29AC-VBUY>] (noting that an outbreak may be geographically limited or extend to multiple countries).
  2. The World Health Organization defines infectious diseases as those “caused by pathogenic microorganisms, such as bacteria, viruses, parasites or fungi; the diseases can be spread, directly or indirectly, from one person to another.” *Infectious Diseases*, WORLD HEALTH ORG., [http://www.who.int/topics/infectious\\_diseases/en](http://www.who.int/topics/infectious_diseases/en) [<https://perma.cc/5WM6-ULF5>]. This Article focuses on infectious diseases traditionally prevalent in the developing world, but now posing a risk to populations all over the globe. The recent outbreaks of 2014–16, which led to the first Ebola and Zika-related deaths in the United States, illustrate the spread of these diseases.
  3. See Kate E. Jones et al., *Global Trends in Emerging Infectious Diseases*, 451 NATURE 990, 990–91 (2008) (noting a rise in infectious disease outbreaks already in the 1980s); Katherine F. Smith et al., *Global Rise in Human Infectious Disease Outbreaks*, 11 J. ROYAL SOC’Y INTERFACE 1, 3–4 (2014) (mapping the rise in worldwide outbreaks between 1980–2009).
  4. Jones et al., *supra* note 3, at 990. See generally Peter Daszak, *Anatomy of a Pandemic*, 380 LANCET 1883 (2012) (describing the evolution of pandemics in human history).
  5. See Meera Senthilingam, *Seven Reasons We’re at More Risk Than Ever of a Global Pandemic*, CNN (Apr. 10, 2017), <http://www.cnn.com/2017/04/03/health/pandemic-risk-virus-bacteria/index.html> [<https://perma.cc/ZK8B-JTZV>]; Julia Belluz, *4 Reasons Disease Outbreaks Are Erupting Around the World*, VOX (May 31, 2016, 7:00 AM), <https://www.vox.com/2016/5/31/11638796/why-there-are-more-infectious-disease-outbreaks> [<https://perma.cc/7E9A-YSKN>] (adding climate change to the list of factors that contribute to an accelerated pace and magnitude of infectious disease outbreaks); Bahar Gholipour, *What 11 Billion People Mean for Disease Outbreaks*, SCI. AM. (Nov. 26, 2013), <https://www.scientificamerican.com/article/what-11-billion-people-mean-disease-outbreaks> [<https://perma.cc/KM3V-J56S>] (describing the role of population growth as one of the key factors in the emergence of outbreak diseases).
  6. See Belluz, *supra* note 5.

novel pathogen is likely to result in the outbreak of “a new severe infectious disease.”<sup>7</sup>

Against this backdrop, health systems are faced with insurmountable challenges in anticipating and proactively addressing future outbreaks. Chief among these challenges is the fact that outbreaks remain inherently unpredictable.<sup>8</sup> Even in the case of pathogens that are well-known or that have erupted recently—take the 2014–16 case of Ebola—the general consensus is that we are scarcely prepared to respond to upcoming outbreaks.<sup>9</sup>

Currently, one of the key strategies to help reduce the scale and public-health impact of future outbreaks is the development of new vaccines.<sup>10</sup> This strategy leverages existing predictive information on emerging pathogens, however imperfect and limited that information might be, and it directs vaccine research and development (R&D) toward diseases for which there is a probability of outbreak in the near future.<sup>11</sup> As of mid-2017, the WHO lists six diseases that need to be “urgently addressed” from an R&D perspective, including all strains of Ebola, the Middle East respiratory syndrome coronavirus (MERS-CoV), and severe acute respiratory syndrome (SARS).<sup>12</sup> A second tier of three outbreak diseases, deemed to be in need of increased R&D “as soon as possible,” includes the congenital and neurological problems caused

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7. WORLD HEALTH ORG., AN R&D BLUEPRINT FOR ACTION TO PREVENT EPIDEMICS 22 (2016) [hereinafter R&D BLUEPRINT] (describing diseases that need “to be urgently addressed”); see also Marie Paule Kieny et al., *The Need for Global R&D Coordination for Infectious Diseases With Epidemic Potential*, 388 LANCET 460, 460–61 (2016); Christopher Black, *WHO Publishes List of Top Emerging Diseases Likely to Cause Major Epidemics*, WORLD HEALTH ORG. (Dec. 10, 2015), <http://www.who.int/medicines/ebola-treatment/WHO-list-of-top-emerging-diseases/en> [<https://perma.cc/9BUY-3Y2Y>] (noting that the list was based on multidisciplinary calculations, including “virology, microbiology, immunology, public health, clinical medicine, mathematical and computational modelling, product development, and respiratory and severe emerging infections”).
  8. See, e.g., Stephen S. Morse et al., *Prediction and Prevention of the Next Pandemic Zoonosis*, 380 LANCET 1956, 1956 (2012) (“The emergence of novel pandemic agents often seems to be inherently unpredictable.”); see also *infra* notes 39–41, and accompanying text (describing advances in predictive technology and its limitations).
  9. See CTR. FOR INFECTIOUS DISEASE RESEARCH & POLICY, COMPLETING THE DEVELOPMENT OF EBOLA VACCINES 29–31 (2017), [http://www.cidrap.umn.edu/sites/default/files/public/downloads/ebola\\_team\\_b\\_report\\_3-011717-final\\_0.pdf](http://www.cidrap.umn.edu/sites/default/files/public/downloads/ebola_team_b_report_3-011717-final_0.pdf) [<https://perma.cc/HS46-PD92>] [hereinafter CIDRAP] (describing lack of preparedness for future Ebola outbreaks); see also Helen Branswell, *We’re Not Prepared for Future Ebola Outbreaks, Experts Warn*, STAT (Jan. 17, 2017), <https://www.statnews.com/2017/01/17/ebola-vaccine-warning> [<https://perma.cc/AWA6-UM8M>].
  10. See John Arne Rottingen et al., *New Vaccines Against Epidemic Infectious Diseases*, 376 NEW ENG. J. MED. 610, 610–11 (2017).
  11. The WHO is the main aggregator of this type of information, used to create a list of “priority pathogens.” See R&D BLUEPRINT, *supra* note 7, at 21–22.
  12. *Id.* at 22.

by the Zika virus.<sup>13</sup> A significant portion of ongoing vaccine R&D thus targets some of these diseases, with Ebola and Zika R&D attracting the bulk of resources since the 2014–16 outbreaks.<sup>14</sup>

However, vaccine development in this context faces hurdles that vastly surpass the unpredictability of outbreaks and insufficient levels of R&D. Even when regarded through a specific lens (as in the case of this Article, which focuses solely on intellectual property (IP)),<sup>15</sup> the development of vaccines targeting outbreak pathogens encompasses several IP stages. These stages stretch well beyond the problems surrounding R&D<sup>16</sup> and correspond to markedly different stages of an outbreak. For instance, and as described in greater detail in the two case studies below, IP is not relevant merely as a means to incentivize risky and costly R&D on uncertain outbreak pathogens, although it undoubtedly performs this function in the pre-outbreak stages.<sup>17</sup> Rather, it often surfaces in the early stages of an outbreak, when preexisting IP (such as vaccine technology that has not been fully developed) is used<sup>18</sup> by entities that possess the capabilities to develop it in a short period of time.<sup>19</sup> Later still, toward the end of the R&D process—and typically in late- or post-outbreak periods—IP may play yet another role if a successful vaccine developer lacks manufacturing capacity and decides to license it to another entity, as happened most recently (and controversially) in the case of the Zika vaccine developed by the U.S. Army.<sup>20</sup>

IP literature dealing with drug development is becoming increasingly specialized in a salutary and fertile way,<sup>21</sup> even though the tandem IP/vaccines

13. *Id.*

14. *Infra* note 165 and accompanying text (noting a 258 percent increase in funding for Ebola R&D in 2014 and 2015).

15. For a perspective on how this problem unfolds with regard to the larger question of whether IP as a system of incentives is even appropriate to spur innovation in fields like outbreak diseases, see Douglas Lichtman, *The Central Assumptions of Patent Law*, 65 UCLA L. REV. 1268 (2018).

16. As in roles that IP plays in drug development in general, and vaccine development in particular. For instance, and as detailed below, some of the roles of IP include establishing a set of incentives to biopharmaceutical innovation, conferring exclusive rights to drug innovators, the role of incentivizing innovation, and the role ensuring access to biopharmaceutical inventions by the public at large. *See infra* Part II.

17. For a description of limitations of the role of IP as an incentives mechanism in the context of infectious diseases, see *infra* Subpart I.B.

18. Or unused, as was the case of one vaccine candidate during the Ebola outbreak. *See infra* notes 284–292 and accompanying text.

19. *See infra* notes 282–292 and accompanying text.

20. *Infra* notes 300–306 and accompanying text.

21. *See, e.g.*, Jacob S. Sherkow, *Cancer's IP*, 96 N.C. L. REV. 297 (2018) (analyzing cancer from the IP and information policy perspectives); Rachel E. Sachs, *The Unpatentable Microbiome*, 116

remains significantly underexplored. Literature, policy, and practice alike tend to focus disproportionately on the incentives side of IP,<sup>22</sup> paying far less attention to other IP effects on the development of vaccines.<sup>23</sup> More importantly, the different—yet interdependent—roles that IP plays in vaccine development in the context of infectious disease outbreaks need to be addressed both separately and collectively. This Article is the first to address and analyze all IP angles in vaccine development, highlighting different types of inefficiencies that emerge at each stage of an outbreak and addressing solutions for each type of inefficiency. It does so by turning to case studies on vaccine development prompted by the 2014–16 Ebola and Zika outbreaks.

These back-to-back outbreaks provide a clear illustration of the multiple ways in which IP intersects with vaccine development and, more broadly, how IP ultimately helps shape the response to infectious disease outbreaks. These case studies illustrate all types of IP inefficiencies at play during a complex outbreak<sup>24</sup> and point to paths forward in the next outbreaks. Looking ahead, some of the informal mechanisms that arose during the Ebola and Zika crises (such as streamlined IP negotiation models) can be adapted, and even formalized, for future use.<sup>25</sup>

Yet, in applying the lessons from Ebola and Zika to future outbreaks in general, the Article goes one step further and makes an overarching point: Failure to address the differentiated roles of IP in vaccine development ultimately hinders our ability to respond effectively to outbreaks. This is what I call a lack of IP preparedness. Much has been written about pandemic preparedness<sup>26</sup> and, more recently, R&D preparedness, which has been

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MICH. L. REV. (forthcoming 2018) (manuscript on file with author) (describing the IP challenges surrounding emerging technologies based on bacteria, viruses and protozoa living inside the human organism); Amy Kapczynski, Contagion: Between Property and the Commons in the WHO's Global Influenza Surveillance Network (Sept. 23–24, 2011) (draft paper for Commons Conference), [http://www.law.nyu.edu/sites/default/files/ECM\\_PRO\\_069673.pdf](http://www.law.nyu.edu/sites/default/files/ECM_PRO_069673.pdf) [<https://perma.cc/9F49-HLFZ>] (describing the global flu network as part of the scientific commons).

22. The scholarly focus on IP qua incentives is matched by the overwhelming focus on strategies to increase vaccine R&D in non-IP literature. See, e.g., Røttingen, *supra* note 10, at 611.
23. The ongoing controversy surrounding the Army-developed Zika vaccine is now calling attention to one of these other effects, albeit separately from other IP aspects that affected Zika R&D. See *infra* notes 303–304 and accompanying text.
24. These inefficiencies include incentives problems (described in Part I) and transactional IP problems (described in Part II), which break down into two subtypes: inefficiencies related to preexisting IP during the early stages of an outbreak, and inefficiencies related to emerging IP after an outbreak subsides.
25. See *infra* Part III.
26. See, e.g., R&D BLUEPRINT, *supra* note 7; CIDRAP, *supra* note 9; WORLD HEALTH ORG., WHOLE-OF-SOCIETY PANDEMIC READINESS (2009), <http://www.who.int/influenza/>

described as the quest for “a novel R&D model” supporting the development of vaccines, treatments, and diagnostics before an outbreak occurs.<sup>27</sup> At the same level, in the IP field there are widespread concerns surrounding the patent system as a mechanism of incentivizing biopharmaceutical R&D.<sup>28</sup> To be sure, nuanced understandings of IP as a system of incentives, as well as a search for new incentives streams beyond the sphere of IP, are critically needed.<sup>29</sup> But we also need to address the role of IP comprehensively in scenarios like infectious disease outbreaks, and so far we have failed to do so.

As the case studies below illustrate, this failure may come at a hefty cost. Neglecting to consider certain aspects of transactional IP (such as transfer of certain IP rights from the original rights-holder to others) in the pre-outbreak stage might result in delays in technology-transfer during the early stages of an outbreak, when additional funding is often temporarily made available to develop a vaccine.<sup>30</sup> To give but one example, further developed below, the licensing of the first-ever Zika vaccine, which has been shrouded in controversy, led Senator Bernie Sanders to publicly plead with the Trump administration to “avoid a bad Zika vaccine [licensing] deal” in early 2017.<sup>31</sup> The problems surrounding the Zika vaccine licensing deal are largely attributable to an overemphasis on IP rights as incentives to R&D, with little consideration being paid to the availability and affordability of the resulting vaccine(s) before the outbreak occurs.

This Article advocates for an expanded focus on the multifaceted roles of IP in vaccine-development, as well as a corresponding tailoring of existing IP mechanisms—and the creation of new ones—to better suit the public health needs triggered by infectious disease outbreaks. The Article begins by providing an overview and categorization of IP-related inefficiencies that specifically affect outbreak diseases. Through case studies on the IP of the recent Ebola and Zika outbreaks, Parts I and II illustrate the public health impact of these inefficiencies, while also providing the first scholarly IP-based

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preparedness/pandemic/2009-0808\_wos\_pandemic\_readiness\_final.pdf [https://perma.cc/VDV4-2NGH] (laying a framework for pandemic preparedness at the economic, humanitarian and societal levels).

27. R&D BLUEPRINT, *supra* note 7, at 6.

28. *See infra* Subpart I.B.

29. *See generally* Nancy Gallini & Suzanne Scotchmer, *Intellectual Property: When Is It the Best Incentive System?*, 2 INNOVATION POL’Y & ECON. 51 (2002) (surveying non-patent mechanisms to incentivize R&D processes).

30. *See, e.g., infra* note 165 and accompanying text.

31. *See* Bernie Sanders, *Bernie Sanders: Trump Should Avoid a Bad Zika Deal*, N.Y. TIMES (Mar. 10, 2017), <https://www.nytimes.com/2017/03/10/opinion/bernie-sanders-trump-should-avoid-a-bad-zika-deal.html?smid=tw-nytopinion&r=0>.

narrative of the vaccine races triggered by the Ebola and Zika crises. Part III concludes by both surveying existing tools and developing new ones to reduce inefficiencies and thus increase our IP preparedness in future infectious disease outbreaks.

## I. INEFFICIENCIES AND LACK OF IP PREPAREDNESS IN THE PRE-OUTBREAK PERIOD

### A. R&D Shortcomings of Outbreak Diseases

Outbreak diseases present unique challenges to systemic and sustained R&D. The lengthy and costly<sup>32</sup> traditional model for developing vaccines and therapies is ill-suited to this specific type of disease. As an outbreak occurs, funding for R&D on the offending pathogen often balloons, only to wane as the outbreak scales back. Temporarily enhanced funding streams and resource mobilization might result in scientific and medical advancements<sup>33</sup> or help push existing products through the development pipeline.<sup>34</sup> But as these short-lived streams diminish, R&D slows down and in some cases all but ceases.<sup>35</sup>

In spite of the considerable burden outbreak diseases place on public health and regional economies<sup>36</sup>—and, in some cases, potentially on national security as well<sup>37</sup>—it is not hard to see why incentives to R&D in this field remain low. Unlike mainstream diseases,<sup>38</sup> outbreak diseases are, by definition, difficult to predict. Although there are increasingly sophisticated early-detection tools<sup>39</sup>—from GPS-based tracking technology

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32. There is no agreement on the average cost of biopharmaceutical R&D. See Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 VA. L. REV. 1575, 1581 (2003) (noting the problems associated with statistical cost estimation in pharmaceutical R&D).

33. This happened during the 2015–16 Zika outbreak, during which causal relationships between viral infection and neurological or congenital diseases were discovered. See *infra* note 153 and accompanying text.

34. That was the case with the leading Ebola vaccine candidate. See *infra* Subpart II.B.

35. See, e.g., *infra* note 325 and accompanying text.

36. R&D BLUEPRINT, *supra* note 7, at 5 (describing how outbreak diseases affect “global health, security, and economic prospects”).

37. *Infra* notes 122–123 and accompanying text.

38. For example, cardiovascular diseases are the leading cause of death in both the developed and the developing worlds. See, e.g., *Cardiovascular Diseases*, WORLD HEALTH ORG., <http://www.who.int/mediacentre/factsheets/fs317/en> [<https://perma.cc/4G4N-LK3T>] (last updated May 2017).

39. See Eirini Christaki, *New Technologies in Predicting, Preventing and Controlling Emerging Infectious Diseases*, 6 VIRULENCE 558 (2015) (surveying the most common methods and technologies employed in global surveillance and modeling of infectious diseases); Michael



to complex predictive models<sup>40</sup>—anticipating an outbreak remains an elusive task.<sup>41</sup>

Results from pre-outbreak R&D on a specific disease may also be of limited application when an actual outbreak occurs, as previously unknown strains of known pathogens present different characteristics. Take the case of Ebola virus disease (EVD), which was first identified in 1976 in Sudan (*Sudan ebolavirus*) and Zaire (now the Democratic Republic of the Congo) (*Zaire ebolavirus*). It was not until 1994 that a third EVD strain causing disease in humans was identified (*Tai Forest ebolavirus*). And in 2007 yet another strain was discovered in Uganda (*Bundibugyo ebolavirus*). In the meantime, a strain affecting nonhuman primates, and so far not known to cause disease in humans, was detected in Philippine macaques in 1989 in a lab in Virginia (*Reston ebolavirus*).<sup>42</sup>

In addition to strain-specificity, pathogens also mutate over time.<sup>43</sup> Emerging research is now correlating the geographical spread of Zika (from Africa to Asia) to mutations in the viral genome.<sup>44</sup> To be sure, pathogen mutation on its own does not account for the dearth of incentives surrounding outbreak diseases (for example, for the cost and risks associated with R&D in the field). Research on many other diseases, both mainstream and neglected,<sup>45</sup>

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M. Wagner et al., *The Emerging Science of Very Early Detection of Disease Outbreaks*, 7 J. PUB. HEALTH MGMT. PRAC. 51 (2001).

40. See, e.g., Xia Jiang & Gregory F. Cooper, *A Bayesian Spatio-Temporal Method for Disease Outbreak Detection*, 17 J. AM. MED. INFO. ASS'N 462 (2010) (describing a probabilistic modeling system for emerging outbreak diseases).
41. See John M. Drake, *Limits to Forecasting Precision for Outbreaks of Directly Transmitted Diseases*, 3 PLOS MED. 57, 57 (2006).
42. D'Vera Cohn, *Deadly Ebola Virus Found in Va. Laboratory Monkey*, WASH. POST (Dec. 1, 1989), [https://www.washingtonpost.com/archive/politics/1989/12/01/deadly-ebola-virus-found-in-va-laboratory-monkey/d6d94b90-b44e-4fa6-a9d0-d67cc0970aca/?utm\\_term=.dcc687543032](https://www.washingtonpost.com/archive/politics/1989/12/01/deadly-ebola-virus-found-in-va-laboratory-monkey/d6d94b90-b44e-4fa6-a9d0-d67cc0970aca/?utm_term=.dcc687543032).
43. This is also true of viruses associated with milder symptoms, such as the rhinovirus (which triggers common cold).
44. See Leslie Goo et al., *A Single Mutation in the Envelope Protein Modulates Flavivirus Antigenicity, Stability, and Pathogenesis*, 13 PLOS PATHOGENS 1 (2017) (describing mutations in flaviviruses, the genus to which Zika belongs); John H.-O. Pettersson et al., *How Did Zika Virus Emerge in the Pacific Islands and Latin America?*, 7 MBIO 1, 1–2 (2016) (reporting amino acid changes in the viral genome as Zika spread from Africa, where it was first identified, to Asia, where the 2015–16 is likely to have started); Adriano de Bernardi Schneider et al., *Molecular Evolution of Zika Virus As It Crossed the Pacific to the Americas*, 33 CLADISTICS 1 (2017).
45. The concept of “neglected diseases” often coincides with the category of “neglected tropical diseases,” which is described by the WHO as encompassing “a diverse group of communicable diseases that prevail in tropical and subtropical conditions in 149 countries.” See *Neglected Tropical Diseases*, WORLD HEALTH ORG., [http://www.who.int/neglected\\_diseases/diseases/en](http://www.who.int/neglected_diseases/diseases/en) [https://perma.cc/MSZ3-XJHQ].

must contend with mutation variables. The same can be said of disease complexity, as many other types of diseases present even greater degrees of complexity—consider the case of cancer<sup>46</sup> or Alzheimer's disease.<sup>47</sup>

However, when outbreak unpredictability, pathogen mutation, and disease complexity are coupled with the fact that outbreak markets have historically emerged in economically challenged areas, incentives for pre-outbreak R&D become especially problematic. Private-sector companies engaging in costly and risky<sup>48</sup> R&D have greater motivation to focus resources on diseases more likely to generate enough revenue to recover R&D costs and turn a profit. For this reason, industry funding for R&D on neglected diseases (of which outbreak diseases are a subset) amounts to only 15 percent of global funding,<sup>49</sup> with most of the money being channeled into R&D on the “top-tier” neglected diseases: HIV/AIDS, tuberculosis, and malaria.<sup>50</sup>

Other players in the field, such as international organizations, health-oriented public-private partnerships (such as the Medicines for Malaria Venture,<sup>51</sup> a Gates-funded vaccine alliance), and nonprofits (such as DNDi,<sup>52</sup> the Drugs for Neglected Diseases Initiative), face multiple limitations.<sup>53</sup> Even when allocating the bulk of their resources to R&D on neglected diseases,

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46. See, e.g., Sherkow, *supra* note 21.

47. See David A. Bennett, *Mixed Pathologies and Neural Reserve: Implications of Complexity for Alzheimer Disease Drug Discovery*, 14 PLOS MED. 1 (2017).

48. R&D is risky in the sense that investment of large amounts of resources and time might not translate into the development of a drug that will gain regulatory approval and be sold on the market.

49. See POLICY CURES RESEARCH, *NEGLECTED DISEASE RESEARCH AND DEVELOPMENT: A PIVOTAL MOMENT FOR GLOBAL HEALTH 5* (2016), <http://www.policycuresresearch.org/downloads/Y9%20GFINDER%20full%20report%20web.pdf> [<https://perma.cc/4WW6-DMLJ>].

50. *Id.* at 4.

51. The Medicines for Malaria Venture (MMV) is a nonprofit public-private partnership solely focused on malaria R&D. *About MMV*, MEDS. FOR MALARIA VENTURE, <https://www.mmv.org/about-us/about-mmv> [<https://perma.cc/W38R-R8NJ>]. The posterchild for public-private partnerships is Gavi, the Vaccine Alliance, a Gates-funded vaccine partnership; due to Gates's financial support, Gavi's funding is unusually high when compared to other players in the same field. See also Robert G. Ridley, *Product R&D for Neglected Diseases*, 4 EMBO REPS. S43 (2003). (surveying the role of the WHO/Special Programme for Research and Training in Tropical Diseases (WHO/TDR) in supporting product research and development through public-private partnerships over the span of nearly three decades).

52. The Drugs for Neglected Diseases Initiative (DNDi) is a nonprofit dedicated to R&D in underfunded diseases. *About Us*, DRUGS FOR NEGLECTED DISEASES INITIATIVE, <https://www.dndi.org/about-dndi> [<https://perma.cc/G6L3-6KSS>]; see *infra* note 367 and accompanying text.

53. See Richard T. Mahoney, *Product Development Partnerships: Case Studies of a New Mechanism for Health Technology Innovation*, 9 HEALTH RES. POL'Y & SYS. 1, 2 (2011) (describing the emergence of the so-called “era of partnerships” in health technology innovation).

funding remains a major constraint.<sup>54</sup> According to data from Policy Cures Research, in 2015 global investment on neglected-disease R&D totaled U.S. \$3 billion, a number in steady decline since 2012.<sup>55</sup> Of this amount, 71 percent (U.S. \$2.15 billion) was directed toward R&D on top-tier diseases.<sup>56</sup> These numbers illustrate how marginal the funding for outbreak and other neglected diseases remains.

In addition to insufficient funding, most of these players face a range of other problems, such as the lack of support from coordinating institutions in the global health arena (including the WHO), insertion into siloed networks, lack of experience in partnering with private-sector entities, and, in some cases, lack of experience in navigating national and international political economies.<sup>57</sup>

Moreover, smaller players—most saliently nonprofits, but a significant number of public-private partnerships as well—tend to focus on, and are often designed around, ad hoc projects that favor R&D on specific types of pathogens. While focused on neglected diseases, these organizations are more likely to work with mainstream diseases on which there is a preexisting and somewhat robust chain of R&D.<sup>58</sup> Take the case of the Medicines for Malaria Venture, a relatively well-funded public-private partnership that engages in the discovery, development, and delivery of affordable antimalarial drugs.<sup>59</sup> Among underfunded diseases, malaria R&D falls into the category of sustained R&D: the U.S. government has been funding malaria R&D since the WWII

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54. See POLICY CURES RESEARCH, *supra* note 49. In recent years, shrinking public-sector funding for neglected-disease R&D became a major concern.

55. *Id.* at 4. Data also show that the drop in overall funding is largely attributable to a decline in public-sector R&D funding.

56. Predictably, funding for Ebola R&D skyrocketed after 2014 and 2015, totaling \$574 million. *Id.* at 6.

57. See Denise Roland, *Experts Criticize World Health Organization's 'Slow' Ebola Outbreak Response*, WALL STREET J. (May 12, 2015, 12:32 PM), <https://www.wsj.com/articles/experts-criticize-world-health-organizations-slow-ebola-outbreak-response-1431344306>. Additional problems arise into the outbreak stages, with several well-established institutions often having flawed policies in place to cope with the spread of the disease. See, e.g., Robert Gatter, *Ebola, Quarantine, and Flawed CDC Policy*, 23 U. MIAMI BUS. L. REV. 375, 375 (2015) (noting that institutions like the Centers for Disease Control and Protection in the United States have interim guidance that “disregards the science of Ebola transmission”).

58. A notable exception is Gavi, working in areas that range from R&D on Yellow Fever (a neglected outbreak disease) to Human Papillomavirus (HPV). Gavi, as pointed out above, remains however an isolated case. See *Vaccine Support*, GAVI: THE VACCINE ALLIANCE, <http://www.gavi.org/support/nvs> [<https://perma.cc/2FZ2-LMF5>].

59. MEDS. FOR MALARIA VENTURE, *supra* note 51.

era;<sup>60</sup> the Food and Drug Administration has approved two antimalarial drugs;<sup>61</sup> and in 2016, PATH<sup>62</sup> (another Gates-funded, international nonprofit) and pharmaceutical company GlaxoSmithKline, reported the successful development of the first malaria vaccine (RTS,S).<sup>63</sup> As this example illustrates, smaller players tend to orbit areas where basic research has already been done or is currently underway, and a significant component of their work is to ensure affordability of existing or emerging technologies.<sup>64</sup>

At least until now, outbreak diseases like Ebola and especially Zika have been in R&D limbo. They have failed to attract substantial private-sector, public, and public-private attention.<sup>65</sup> The economic footprint of the regions where outbreaks occurred in the past have been too small to trigger strong private-sector R&D investment, while interest from other players has been overshadowed by more visible neglected diseases like malaria or HIV/AIDS.<sup>66</sup> Beyond the cases of Ebola and Zika, outbreak diseases in general do not fit well into any R&D mold. The unpredictability of outbreaks makes investment in a specific disease especially risky, as the pathogen may lie dormant for variable periods of time.<sup>67</sup> And in many cases, lack of knowledge about certain pathogens may lead scientists (and consequently, funders) to underestimate the

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60. See Paul M. Arguin & Alan J. Magill, *For the Record: A History of Malaria Chemoprophylaxis*, CDC (June 12, 2017), <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/for-the-record-a-history-of-malaria-chemoprophylaxis> [https://perma.cc/657C-GNDS] (last updated June 12, 2017).

61. Lariam and Malarone. *Id.*

62. PATH, <http://www.path.org> [https://perma.cc/L5L8-JXZC].

63. RTS,S Clinical Trials P'ship, First Results of Phase 3 Trial of RTS,S/AS01 Malaria Vaccine in African Children, 365 NEW ENG. J. MED. 1863, 1863 (2011); RTS,S Clinical Trials P'ship, Efficacy and Safety of RTS,S/AS01 Malaria Vaccine With or Without a Booster Dose in Infants and Children in Africa: Final Results of a Phase 3, Individually Randomised, Controlled Trial, 386 LANCET 31, 31 (2015). See also David C. Kaslow & Sophie Biernaux, *RTS,S: Toward a First Landmark on the Malaria Vaccine Technology Roadmap*, 33 VACCINE 7425, 7425 (2015).

64. See *infra* Subpart II.C. See also Annette Choi, *First Malaria Vaccine, 30 Years in the Making, To Be Trialled in Africa*, PBS (Apr. 25, 2017), <http://www.pbs.org/wgbh/nova/next/body/first-malaria-vaccine-30-years-in-the-making-to-be-trialed-in-africa>.

65. *Infra* Subpart I.C.1.a.

66. See Marco Vitoria et al., *The Global Fight Against HIV/AIDS, Tuberculosis, and Malaria: Current Status and Future Perspectives*, 131 AM. J. CLINICAL PATHOLOGY 844 (2009) (identifying malaria, HIV/AIDS and tuberculosis as “the 3 major global public health threats”).

67. This has happened several times in the chronology of Ebola outbreaks. See *Outbreaks Chronology: Ebola Virus Disease*, CDC, <http://www.cdc.gov/vhf/ebola/outbreaks/history/chronology.html> [https://perma.cc/V4F2-N3F5] (last updated July 28, 2017) (listing the different strains of Ebola that have caused known outbreaks since 1976).

potential damage that a pathogen may cause, as was the case with the recent Zika outbreak.<sup>68</sup>

Finally, from an incentives perspective, outbreak diseases present one more challenge. As illustrated in the case studies on Ebola and Zika below, incentives for R&D on this type of disease peak during the early stages of an outbreak. But the R&D triggered by an outbreak will at best result in vaccines and therapies that will target the next (unpredictable) outbreak. There is therefore an intrinsic misalignment between outbreak-induced incentives and the product of the corresponding R&D. As described below, any resulting diagnostics, prophylactics, or therapies may become less efficient (or even useless) if the pathogen mutates considerably during the inter-outbreak period.

Considered together, these factors render R&D on pathogens associated with outbreak diseases particularly risky and costly.<sup>69</sup> Although imposing great burdens on health systems across the globe, outbreak diseases attract low levels of pre-outbreak R&D,<sup>70</sup> a phenomenon that has led the World Health Organization to talk about a “lack of R&D preparedness”<sup>71</sup> in this area, as opposed to suboptimal R&D incentives *tout court*. The expression emphasizes how R&D for these diseases tends to occur at a particularly depleted level of the suboptimal spectrum, at least until an outbreak occurs.

As described in the following Part, the default system to spur innovation in costly areas, or in areas characterized by a heightened risk of failure, relies on IP incentives. Nevertheless, as far as outbreak diseases are concerned, IP routinely fails to achieve this goal.<sup>72</sup> Furthermore, as Part II shows, existing IP might function as a deterrent to expedited R&D when incentives peak during the early stages of an outbreak.<sup>73</sup> Similarly, IP emerging from outbreak-induced R&D might function as a barrier to widespread availability and affordability of drugs and therapies, an issue to which I return in Part III.

It is possible that, in the long run, incentives for R&D on outbreak diseases will grow as tourism routes broaden and fear of a pandemic becomes more global, creating new markets from both a geographic and an economic point of view.<sup>74</sup> There was a period during the recent Ebola and Zika outbreaks in which speculation over a possible catastrophic impact of both diseases in the United

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68. See *infra* Subpart I.C.1.b.

69. *R&D Blueprint*, *supra* note 7, at 18.

70. *Id.* at 5.

71. *Id.* at 6.

72. *Infra* Subpart I.B.

73. *Infra* Subpart II.B.

74. See Belluz, *supra* note 5.

States was in vogue.<sup>75</sup> But a significant change in incentives and funding models for outbreak diseases is unlikely to take place for decades, which makes the need to address both the current lack of pre-outbreak incentives and IP-related inefficiencies more pressing.<sup>76</sup>

## B. IP as Incentives: The Problem of Underfunded Diseases

The previous Part outlined the shortcomings of R&D on diseases with complex profiles and limited patient populations. This Part turns to the role of IP—specifically, the patent system—in incentivizing R&D for this type of disease.

Patents have long been regarded as the default mechanism to incentivize R&D in areas with imperfect incentives.<sup>77</sup> The patent bargain establishes that, in exchange for the disclosure of information, the state grants the patentee a set of exclusive rights for a certain period of time, currently set at twenty years.<sup>78</sup> This is a market-based approach to spurring innovation in underfunded technical and scientific fields<sup>79</sup>: Absent some form of incentive, would-be innovators are likely to shy away from or underinvest in R&D for two reasons. First, there are the costs and risks inherent to the R&D process, which can be particularly daunting in complex or specialized areas. And second, without IP rights, an invention that was costly and time-consuming to develop tended to be disproportionately easy to replicate,<sup>80</sup> allowing second-comers to

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75. See, e.g., Tara C. Smith, *America's Ebola Panic*, SLATE (Oct. 6, 2015, 8:00 AM), [http://www.slate.com/articles/health\\_and\\_science/medical\\_examiner/2015/10/ebola\\_panic\\_an\\_niversary\\_predictions\\_of\\_a\\_u\\_s\\_epidemic\\_didn\\_t\\_come\\_true.html](http://www.slate.com/articles/health_and_science/medical_examiner/2015/10/ebola_panic_an_niversary_predictions_of_a_u_s_epidemic_didn_t_come_true.html) [<https://perma.cc/8DTC-QRMH>] (summarizing predictions made in 2014 about the scope of the Ebola outbreak and its impact on U.S. soil).

76. See *infra* Part III.

77. See generally Kenneth J. Arrow, *Economic Welfare and the Allocation of Resources for Invention*, in *THE RATE AND DIRECTION OF INVENTIVE ACTIVITY* 609 (1962) (examining cost efficiency in the use of monopolies to incentivize innovation). Other approaches to patents emphasize efficiency arguments. See, e.g., Edmund W. Kitch, *Elementary and Persistent Errors in the Economic Analysis of Intellectual Property*, 53 VAND. L. REV. 1727, 1727–28 (2000). See generally Petra Moser, *Patents and Innovation in Economic History*, 8 ANN. REV. ECON. 241 (2016).

78. The U.S. Constitution adopts an instrumental view of patent rights, which are granted for limited periods of time “[t]o promote the Progress of . . . useful Arts.” U.S. CONST. art. I, § 8, cl. 8.

79. See generally Benjamin N. Roin, *Intellectual Property Versus Prizes: Reframing the Debate*, 81 U. CHI. L. REV. 999, 1017–20 (2014) (noting that the “primary benefit of the intellectual property system has always been viewed as its ability to offer a market-based incentive for innovation tied to consumers’ willingness to pay”).

80. There are, of course, exceptions, including macromolecular drugs such as vaccines and other biologics, which are difficult to replicate. See W. Nicholson Price II & Arti K. Rai, *Manufacturing Barriers to Biologics Competition and Innovation*, 101 IOWA L. REV. 1023,

compete with the innovator by incurring only the marginal cost of copying.<sup>81</sup>

In theory, the prospect of obtaining a patent lessens the burden associated with costly and risky R&D in two ways. On the one hand, this cost reflects the economic investment in producing scientific or technical knowledge, developing an innovative product, and, when necessary, obtaining regulatory approval to market the invention.<sup>82</sup> On the other hand, it also factors in the risk associated with the R&D endeavor, as R&D successes (the revenue generated by an innovator's patent portfolio) are expected to absorb the cost of R&D failures.<sup>83</sup> In this sense, patent exclusivity functions as a carrot given to innovators as a means to encourage the production of socially valuable inventions.<sup>84</sup>

Several scholars have likened the twenty-year patent exclusivity to a monopoly,<sup>85</sup> a traditionally disfavored figure in both economic and noneconomic literature.<sup>86</sup> Patent-based exclusivity may also be supplemented by other features that further enhance the economic reward of the invention, like regulatory market exclusivities (such as those arising from the approval of certain types of drugs by the Food and Drug Administration),<sup>87</sup> data

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1026 (2016) (describing the difference between small-molecule drugs and biologics) ("In terms of size and rough complexity, if an aspirin were a bicycle, a small biologic would be a Toyota Prius, and a large biologic would be an F-16 fighter jet.").

81. See Suzanne Scotchmer, *Standing on the Shoulders of Giants: Cumulative Research and the Patent Law*, 5 J. ECON. PERSP. 29, 30 (1991) (noting that patent applicants often seek to obtain broad patents in order to shield their inventions from as much competition as possible).
82. For an overview of the drug approval process, see Erika F. Lietzan, *The Drug Innovation Paradox* 8–17 (Univ. of Mo. Sch. of Law Legal Studies Research Paper Series, Paper No. 2017-12), <https://ssrn.com/abstract=2948604> [<https://perma.cc/VG92-PWF6>].
83. That is, products that generate considerable R&D expenditures but that never make it to market.
84. See Michael J. Meurer & Katherine J. Strandburg, *Patent Carrots and Sticks: An Economic Model of Nonobviousness*, 12 LEWIS & CLARK L. REV. 547, 558–65 (2008) (noting that patents should incentivize socially optimal levels of innovation, not only via the patent carrot but also through use of the nonobviousness threshold stick mechanism).
85. E.g., Roin, *supra* note 79, at 1001.
86. See generally THOMAS BABINGTON MACAULAY, *SPEECHES OF LORD MACAULAY: CORRECTED BY HIMSELF* 112 (1877) ("[T]he effect of monopoly generally is to make articles scarce, to make them dear, and to make them bad."); SANFORD V. BERG & JOHN TSCHIRHART, *NATURAL MONOPOLY REGULATION: PRINCIPLES AND PRACTICE* (1988).
87. For instance, six months of market exclusivity may be granted to drugs treating certain pediatric diseases, five years to new chemical entities and seven years to orphan drugs (drugs treating a disease that affects "fewer than 200,000 people in the U.S., or that affect more than 200,000 persons but are not expected to recover the costs of developing and marketing a treatment drug"). *Developing Products for Rare Diseases & Conditions*, FDA, <http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm2005525.htm> [<https://perma.cc/A2AP-AN2U>] (last updated Feb. 23, 2018); *How Can I Better*

exclusivity,<sup>88</sup> or post-patent brand prestige derived from a product that entered the market first.<sup>89</sup>

Even in a scenario where the patent bargain is successful and the prospect of patent exclusivity leads to the production of an innovation, detrimental effects are still likely to occur. When a patent holder is allowed to commercialize the invention at heightened prices for twenty years, deadweight loss—in the form of would-be consumers that value the invention above marginal cost but cannot afford it—is probable.<sup>90</sup> This leads to a reduction in social welfare that is undesirable but arguably tolerable, if the social benefit expected from the invention outweighs the cost of deadweight loss.<sup>91</sup>

A successful patent bargain comes therefore at a cost, although one that society is in theory willing to accept in exchange for the promotion of scientific knowledge and welfare-maximizing innovation.<sup>92</sup> However, patents as incentive mechanisms may fail in two different forms. Even when leading to the production of innovation, exclusivity arising from a patent may be ill-calibrated and reward the inventor beyond socially acceptable levels of deadweight loss.<sup>93</sup> In this case, patents over-reward innovation. But the patent bargain may collapse altogether at an earlier stage, by failing to encourage sufficient innovative R&D to begin with. If the patent exclusivity is not calibrated in a way that aligns expected returns with R&D costs and risk, then IP does not truly operate as a system of incentives. In this scenario, even

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*Understand Patents and Exclusivity?*, FDA, <https://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm238582.htm> [<https://perma.cc/4LXM-AX7Z>] (last updated May 22, 2016).

88. See generally Rebecca S. Eisenberg, *The Role of the FDA in Innovation Policy*, 13 MICH. TELECOMM. & TECH. L. REV. 345, 359–61 (2007) (discussing the role of FDA regulation in biopharmaceutical innovation).

89. Frederic Sherer, *First Mover Advantages and Optimal Patent Protection*, *The Journal of Technology Transfer*, 2015, vol. 40, issue 4, 559–80.

90. Roin, *supra* note 79, at 1023; Steven Shavell & Tanguy van Ypersele, *Rewards Versus Intellectual Property Rights*, 44 J.L. & ECON. 525, 529 (2001). But see Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 843–44 (1990) (discussing how a patent-based incentives system should still attempt to foster competition on the margins).

91. See Shavell & van Ypersele, *supra* note 90, at 529–30 (noting the loss of social welfare caused by lack of competition during the period of patent exclusivity).

92. See *supra* note 78 and accompanying text.

93. For instance, in the field of pharmaceutical R&D, the pharmaceutical industry has traditionally pushed for levels of strong patent protection that are often at odds with welfare-maximization goals. See Eisenberg, *supra* note 88, at 346–47 (describing the role of big pharma in perpetuating the myth of a strong patent-based system as a *sine qua non* of drug R&D).



when the IP reward is available, the innovator deems it too small to offset the cost and risk associated with R&D.<sup>94</sup>

Historically, one of the areas in which the patent bargain has been especially inept at spurring appropriate levels of innovation is the biopharmaceutical arena.<sup>95</sup> Biopharmaceutical R&D is especially resource-intensive, consuming outstanding amounts of money and time. It is also an area where several fields are still in the early stages of development and where basic complex research is needed on multiple fronts. For instance, ongoing R&D characterized by informational complexity (for example, cancer<sup>96</sup> or antimicrobial resistance<sup>97</sup>) or opacity (for example, algorithm-based precision medicine)<sup>98</sup> presents especially salient challenges.

To counteract the insufficiencies of patent-based levers in stimulating biopharmaceutical innovation, scholars and policymakers have increasingly turned their attention to non-IP forms of incentives,<sup>99</sup> such as grants,<sup>100</sup> prizes,<sup>101</sup> and R&D tax credits.<sup>102</sup> Recent examples of efforts to increase both funding and new approaches to problem-solving in biopharmaceutical R&D include the creation of the Cancer Moonshot,<sup>103</sup> the Precision Medicine

94. There are alternative systems of rewards available to innovators. See generally Daniel J. Hemel & Lisa Larrimore Ouellette, *Beyond the Patents-Prizes Debate*, 92 TEX. L. REV. 303 (2013) (analyzing prizes, patents, government grants and tax incentives).

95. See Michael A. Heller & Rebecca S. Eisenberg, *Can Patents Deter Innovation? The Anticommons in Biomedical Research*, 280 SCIENCE 698, 698 (1998).

96. See Jacob S. Sherkow, *Cancer's IP*, 96 N.C. L. REV. 297, 297 (2018).

97. See generally Aaron S. Kesselheim & Kevin Outterson, *Improving Antibiotic Markets for Long Term Sustainability*, 11 YALE J. HEALTH POL'Y L. & ETHICS 101 (2011) (describing different types of challenges posed by multidrug resistant bacteria); Kevin Outterson, *The Legal Ecology of Resistance: The Role of Antibiotic Resistance in Pharmaceutical Innovation*, 31 CARDOZO L. REV. 613 (2010) (framing antibiotic resistance as a process of depletion of a common good); Kevin Outterson et al., *Will Longer Antimicrobial Patents Improve Global Public Health?*, 7 LANCET INFECTIOUS DISEASES 559 (2007) (arguing against the creation of new IP rights as a way to incentivize R&D on antimicrobial resistance).

98. See e.g., W. Nicholson Price II, *Black-Box Medicine*, 28 HARV. J.L. & TECH. 419, 421–22 (2015); see also *The Precision Medicine Initiative*, WHITE HOUSE, <http://obamawhitehouse.archives.gov/node/333101> [<https://perma.cc/H7QW-E4YD>].

99. See Gallini & Scotchmer, *supra* note 29.

100. See Shavell & van Ypersele, *supra* note 90, at 525–31.

101. Roin, *supra* note 79.

102. Hemel & Ouellette, *supra* note 94.

103. *Cancer Moonshot*, NAT'L CANCER INST., <http://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative> [<https://perma.cc/8N9Y-3QC4>]; see also Joe Biden, *Inspiring a New Generation to Defy the Bounds of Innovation: A Moonshot to Cure Cancer*, CANCER MOONSHOT (Jan. 12, 2016), <http://medium.com/cancer-moonshot/inspiring-a-new-generation-to-defy-the-bounds-of-innovation-a-moonshot-to-cure-cancer-fbdf71d01c2e> [<https://perma.cc/F3MA-EJQA>]. But see Vinay Prasad, *Why a Cancer 'Moonshot' Is Unlikely to Find Us a Cure*, WASH. POST (Jan. 29, 2016), <http://www.washingtonpost.com/opinions/why-a-cancer->

Initiative (including the *All of Us* Research Program),<sup>104</sup> and the Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (Carb-X), a public-private partnership aimed at expediting the preclinical development of new antibiotics and antimicrobial vaccines and diagnostics.<sup>105</sup> These initiatives, however, are outliers in an era in which funding streams have consistently shrunk.<sup>106</sup>

While incentives for biopharmaceutical R&D in general tend to be suboptimal, incentives for outbreak-disease R&D in particular are especially scarce. As seen above, there are several factors that make R&D on this group of diseases highly risky: strain-specificity, possible genomic mutation between outbreaks, lack of basic research, the impossibility of determining when the following outbreak will occur, and unpredictability as to the size of the following outbreak and the corresponding market for certain types of drugs. Outbreak diseases as a whole are therefore prone to a first type of inefficiency: The amount of IP-based incentives available to would-be innovators falls substantially below the cost-risk threshold.

Public-sector funding, which plays a preponderant role in stimulating R&D in this area,<sup>107</sup> is becoming increasingly thinner. In the United States, which funds nearly three-quarters (72 percent) of global public R&D on neglected diseases,<sup>108</sup> federal funding for basic research has recently reached a post-WWII low,<sup>109</sup> a situation that is unlikely to change in the near future.<sup>110</sup>

For some outbreak diseases, R&D is bolstered to a certain extent by collaborative models that minimize—although they do not eradicate—the shortcomings of IP-based incentives. This is the case of pathogen-specific partnerships like the ones surveyed in the previous Part, which add some

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moonshot-is-unlikely-to-find-us-a-cure/2016/01/29/08cc66dc-c545-11e5-8965-0607e0e265ce\_story.html [https://perma.cc/DUD9-J8CM] (addressing funding and scientific shortcomings of the Cancer Moonshot).

104. *About the All of Us Research Program*, NAT'L INST. HEALTH, <http://allofus.nih.gov/about/about-all-us-research-program> [https://perma.cc/JJ86-3NRR].

105. *About CARB-X*, CARB-X, <http://www.carb-x.org/about> [https://perma.cc/9EPB-TH27]; Sara Rimer, *Law School Guides Global Effort to Create New Antibiotics*, B.U. TODAY (July 28, 2016), <http://www.bu.edu/today/2016/carb-x> [https://perma.cc/XU9Q-PH8J].

106. See Jeffrey Mervis, *Data Check: Federal Share of Basic Research Hits New Low*, 355 SCIENCE 1005, 1005 (2017).

107. *Id.*

108. POLICY CURES RESEARCH, *supra* note 49, at 5.

109. Mervis, *supra* note 106.

110. See Ingrid T. Katz & Alexi A. Wright, *Scientific Drought, Golden Eggs, and Global Leadership—Why Trump's NIH Funding Cuts Would Be a Disaster*, 376 NEW ENG. J. MED. 1701, 1703–04 (2017) (noting recent cuts to the budget of the National Institutes of Health and their potential long-lasting impact).

muscle to pre- and inter-outbreak R&D for certain diseases (for example, malaria).<sup>111</sup> Nevertheless, their funding volume and funding streams pale when compared to those available to non-outbreak diseases.<sup>112</sup>

Conversely, other types of outbreak diseases lack virtually any support, be it in the form of IP incentives, non-IP rewards, or partnership models. This was the case of Zika between 1947, when it was first discovered, and the start of the 2015–16 outbreak.<sup>113</sup>

Even when an outbreak triggers investment in an otherwise underfunded disease, R&D may still remain at low levels. Consider the case of Ebola vaccines, for which incentives spiked at the beginning of the 2014–16 outbreak.<sup>114</sup> Even though there had been multiple Ebola outbreaks in the past (with mortality rates of up to 89 percent),<sup>115</sup> until 2013 the possibility of “properly controlled clinical trials seemed impossible”<sup>116</sup> due to low enrollment of eligible patients. Outbreak diseases with low case numbers, high mortality rates, or both, have the potential to generate low-quality clinical trial data that may not benefit follow-on innovation.

In the following Part, I turn to the specificities of the pre-Ebola and pre-Zika R&D landscapes, both of which reflect IP inefficiencies in the form of low levels of pre-outbreak incentives to R&D. Part III, while addressing issues related to post-outbreak IP generated by R&D on Zika vaccines, illustrates yet another type of IP inefficiency identified above: over-rewarding of a vaccine innovator and its potential impact on social welfare.

## C. Evidence from the 2014–16 Ebola and Zika Outbreaks

### 1. Pre-Outbreak R&D

#### a. Ebola

Even though we still lack a fully developed Ebola vaccine, the Ebola virus has been known to scientists since 1976.<sup>117</sup> Until the 2014–16 outbreak, fatality

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111. *Supra* notes 59–63 and accompanying text.

112. *Id.*

113. *Infra* Subpart I.C.1.b.

114. *Infra* Subpart I.C.2.a.

115. CTRS. FOR DISEASE CONTROL & PREVENTION, *supra* note 67.

116. Karen A. Martins et al., *Ebola Virus Disease Candidate Vaccines Under Evaluation in Clinical Trials*, 15 EXPERT REV. VACCINES 1101, 1101 (2016).

117. This first registered outbreak took place in Sudan and Zaire, collectively infecting around 600 people. CTRS. FOR DISEASE CONTROL & PREVENTION, *supra* note 67. The Sudan outbreak had a fatality rate of 53 percent, while the one in Zaire registered the second-highest Ebola fatality

rates ranged from 25 percent to close to 90 percent, for an estimated average of 50 percent.<sup>118</sup> These numbers make the Ebola virus frightful from a public health perspective and yet unappealing from the R&D and incentives perspectives. While the disease burden has been considerable over the past thirty-five years, the intermittent nature of outbreaks, an Ebola-free decade (the 1980s), and the geography of the outbreaks—affecting non-affluent, mostly rural populations in the developing world—consistently kept R&D efforts at very low levels.<sup>119</sup>

While manifestly insufficient, R&D was nonetheless somewhat sustained: Basic research was conducted in the late twentieth and early twenty-first centuries by the public sector, primarily in the United States and Canada.<sup>120</sup> By the time the extent and burden of the 2014–16 outbreak became apparent and funding streams opened up, enough Ebola-related research had been conducted to support expedited R&D of multiple vaccines and therapies.<sup>121</sup>

Part of the public-sector interest in funding Ebola R&D was tied to concerns of bioterrorism, especially in the wake of 9/11.<sup>122</sup> In 2006, the Department of Homeland Security declared that Ebola “presented a material threat to the U.S. population sufficient to affect national security.”<sup>123</sup> The virus

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rate in history, at 89 percent. *Id.* For over a decade after 1979, there were no reported cases of Ebola (this includes four of the five known strains of Ebola; excluded is Ebola-Reston, which is asymptomatic in humans). *Id.* The outbreaks resumed in 1994, but between then and the 2014–16 outbreak, there were never more than 425 cases in any year. *Id.*

118. Case numbers per outbreak have also varied widely. For instance, in 2000–01 there was an Ebola outbreak (Sudan virus) in Uganda, with 425 reported cases and 224 deaths, for a 53 percent mortality rate. By contrast, in 2004 there was an outbreak in Sudan (now South Sudan) of the same strain of Ebola with much lower numbers: 17 cases and 7 deaths (41 percent mortality rate). *Id.*

119. See generally POLICY CURES RESEARCH, *supra* note 49.

120. See William W. Fisher III & Katrina Geddes, Learning From Ebola: How Drug-Development Policy Could Help Stop Outbreaks of Infectious Diseases 28 (Oct. 14, 2015), [https://cyber.harvard.edu/people/tfisher/Learning\\_from\\_Ebola.pdf](https://cyber.harvard.edu/people/tfisher/Learning_from_Ebola.pdf) [<https://perma.cc/NH7Z-NQ3E>]. See NIH, Ebola Vaccines, <https://www.niaid.nih.gov/diseases-conditions/ebola-vaccines> (detailing the participation of the US government in Ebola vaccine R&D).

121. Fisher & Geddes, *supra* note 120, at 28, 38 (listing the different partnerships formed to develop Ebola vaccines and therapies shortly after the beginning of the 2014 outbreak).

122. Before 9/11, there were already concerns surrounding the potential use of the Ebola virus in a bioterrorism attack, but these concerns were largely assuaged by the fact that it is extremely difficult to access samples of infectious diseases like Ebola. Although there have been episodic attempts—like the one perpetrated by Japanese doomsday cult Aum Shinrikyo, which tried (and failed) to obtain Ebola cultures—gathering samples for bioterrorism purposes remains notoriously difficult. See Dina Fine Maron, *Weaponized Ebola: Is It Really a Bioterror Threat?*, SCI. AM. (Sept. 25, 2014), <https://www.scientificamerican.com/article/weaponized-ebola-is-it-really-a-bioterror-threat> [<https://perma.cc/VU7U-H7QU>].

123. U.S. DEP’T OF HEALTH & HUMAN SERVS., 2015 PUBLIC HEALTH EMERGENCY MEDICAL COUNTERMEASURES ENTERPRISE (PHEMCE) STRATEGY AND IMPLEMENTATION PLAN 15

was added to the Department of Health and Human Services's high-priority threat list, where it remains.<sup>124</sup> The linkage between Ebola and bioterrorism also co-involved institutional players that do not necessarily invest in R&D for other types of outbreak diseases, such as the Department of Defense and the Biomedical Advanced Research and Development Authority (BARDA).<sup>125</sup>

The effect of linking Ebola to national security concerns thus tempered the generalized lack of R&D incentives, although paradoxically the costs of engaging in Ebola R&D remain higher than for more severely underfunded outbreak diseases, like Zika. This is due to the fact that Ebola R&D must be performed in facilities conforming to the most stringent type of biosafety requirements (biosafety level 4, or BSL-4).<sup>126</sup> Creating and maintaining BSL-4 facilities is expensive, with initial building costs estimated at around U.S. \$350 million.<sup>127</sup> These costs are supported by the public sector, which until the 2014–16 outbreak was virtually the sole funder of Ebola R&D.<sup>128</sup>

Pre-outbreak incentives for Ebola were low, but sustained. Private-sector interest, however, was almost nonexistent. A chronology of the pre-outbreak development of what was deemed to be a promising Ebola vaccine illustrates this trend. In the early 2000s, the Canadian government funded R&D at the National Microbiology Laboratory<sup>129</sup> on experimental vaccines targeting the Ebola virus (EBOV) and Marburg virus (MARV).<sup>130</sup> The Ebola vaccine was

(2015), <https://www.phe.gov/Preparedness/mcm/phemce/Documents/2015-PHEMCE-SIP.pdf> [<https://perma.cc/F2DB-E8SY>] [hereinafter PHEMCE].

124. *See id.*

125. *Id.* at 16–17.

126. *See* CTR. FOR DISEASE CONTROL AND PREVENTION, BIOSAFETY IN MICROBIOLOGICAL AND BIOMEDICAL LABORATORIES 251 (5th ed. 2009), <https://www.cdc.gov/biosafety/publications/bmbl5/bmbl.pdf> [<https://perma.cc/XWZ8-H4L8>]. The Centers for Disease Control and Prevention require BSL-4 for “work with dangerous and exotic agents that pose a high individual risk of aerosol-transmitted laboratory infections and life-threatening disease that is frequently fatal, for which there are no vaccines or treatments, or a related agent with unknown risk of transmission.” *Id.* at 45.

127. Helen Branswell, *CDC requests funds to build new maximum-security laboratory*, STAT (Feb. 23, 2018), <https://www.statnews.com/2018/02/23/cdc-bsl4-laboratory/> [<https://perma.cc/H5UV-5XCP>] (noting that the Centers for Disease Control and Prevention requested U.S. \$350 million in early 2018 to support the costs of a new building to house BSL-4 laboratories).

128. POLICY CURES RESEARCH, *supra* note 49, at 93 and accompanying text.

129. The National Microbiology Laboratory is part of the Public Health Agency of Canada. *See National Microbiology Laboratory*, PUB. HEALTH AGENCY CAN., <https://www.nml-lnm.gc.ca/index-eng.htm> [<https://perma.cc/5597-VWPC>] (last modified July 31, 2015).

130. *See* Stephen M. Jones et al., *Live Attenuated Recombinant Vaccine Protects Nonhuman Primates Against Ebola and Marburg Viruses*, 11 NATURE MED. 786 (2005). The development of the rVSV-EBOV vaccine built itself on preexisting research. *See, e.g.,*

based on an attenuated recombinant vesicular stomatitis virus (rVSV) and became known as rVSV-ZEBOV.<sup>131</sup>

The Canadian government was granted a patent on rVSV-ZEBOV in 2003.<sup>132</sup> Further R&D for this vaccine was done by scientists in Canada between 2003 and 2005, with animal tests being run by the U.S. Army's Medical Research Institute of Infectious Diseases (USAMRIID).<sup>133</sup> The tests run on nonhuman primates confirmed the safety of the vaccine candidates and showed them to be "highly efficacious."<sup>134</sup> The achievement was hailed as groundbreaking.<sup>135</sup> Researchers initially hoped to start human clinical trials around 2008 and to start licensing the vaccine in 2010 or 2011.<sup>136</sup>

By 2011, however, scientists involved in the development of rVSV-ZEBOV were still making the case that the vaccines should be moved along in the R&D pipeline:

Given the efficacy profile in preventive and treatment approaches and the safety record in several immune-competent and immune-compromised animal species, this vaccine platform is ready to be considered for investigational drug licensure. We further propose to consider the rVSV platform for preinvestigational drug use in cases of laboratory exposures with EBOV . . .<sup>137</sup>

In spite of promising preclinical results, private-sector interest in licensing the vaccines was virtually nonexistent.<sup>138</sup> The pace of R&D on rVSV-ZEBOV slowed considerably. Eventually the vaccine was licensed to NewLink Genetics,

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Anjeanette Roberts et al., *Attenuated Vesicular Stomatitis Viruses As Vaccine Vectors*, 73 J. VIROLOGY 3723 (1999).

131. See Andrea Marzi et al., *Vesicular Stomatitis Virus-Based Ebola Vaccines With Improved Cross-Protective Efficacy*, 204 J. INFECTIOUS DISEASES 1066 (2011).

132. Recombinant Vesicular Stomatitis Virus Vaccines for Viral Hemorrhagic Fevers, Can. Patent No. WO 2004/011488 A2 (filed July 28, 2003).

133. USAMRIID is the "lead laboratory for medical biological defense research" for the Department of Defense. See *About USAMRIID*, U.S. ARMY MED. RES. INST. INFECTIOUS DISEASES, <http://www.usamriid.army.mil/aboutpage.htm> [<https://perma.cc/8YBW-WUY8>] (last modified Dec. 4, 2016).

134. Jones et al., *supra* note 130.

135. See Richard Knox, *Scientists Race to Find Vaccine for Ebola*, *Marbug*, NPR (June 6, 2005, 12:00 AM), <http://www.npr.org/templates/story/story.php?storyId=4681932>.

136. See Denise Grady, *Ebola Vaccine, Ready for Test, Sat on the Shelf*, N.Y. TIMES (Oct. 23, 2014), <https://www.nytimes.com/2014/10/24/health/without-lucrative-market-potential-ebola-vaccine-was-shelved-for-years.html>.

137. See Thomas W. Geisbert & Heinz Feldmann, *Recombinant Vesicular Stomatitis Virus-Based Vaccines Against Ebola and Marburg Virus Infections*, 204 J. INFECTIOUS DISEASES 1075, 1079 (2011).

138. See Dan Lett, *Wanted: Manufacturer for Ebola and Marburg Vaccines*, 173 CAN. MED. ASS'N J. 472 (2005); Grady, *supra* note 136.

a small Iowa-based pharmaceutical company.<sup>139</sup> The agreement reached with the Canadian government granted NewLink a “sole, worldwide, revocable and royalty-bearing license.”<sup>140</sup> The license required NewLink to commercialize the vaccine “for . . . maximum commercial return.”<sup>141</sup> NewLink, however, did not prioritize Ebola R&D, and rVSV-ZEBOV was not moved to clinical trials. As one commentator put it, “the vaccine sat on a shelf” for years.<sup>142</sup> It would take the violent outbreak of 2014–16 for interest in the rVSV-ZEBOV line of R&D to rekindle, as described in Part II.

The pre-outbreak R&D landscape for Ebola was thus characterized by sustained yet low public-sector incentives, as well as by virtually nonexistent incentives in the private sector. This asymmetry negatively impacted the pace of Ebola R&D, as the private sector remains the main driver behind clinical drug development.<sup>143</sup> When a catalyst event—the 2014–16 outbreak—sparked the need for Ebola vaccines and therapies, there was a wide market failure. No approved vaccine or treatment for the disease existed.<sup>144</sup> Experimental medicines were also in short supply.<sup>145</sup> Even today, during the inter-outbreak period following the largest and most lethal Ebola pandemic in recorded history, it is not clear that the vaccines currently in advanced clinical development will have a “clear commercial market.”<sup>146</sup>

## b. Zika

The discovery of Zika, dating back to 1947 in Uganda, predates that of Ebola.<sup>147</sup> Before the 2015–16 outbreak, the only known symptoms associated

139. NEWLINK GENETICS, <http://www.newlinkgenetics.com> [<https://perma.cc/V8GT-46JW>].

140. *Sole Licensing Agreement for Recombinant Vesicular Stomatitis Virus Vaccines for Viral Hemorrhagic Fevers*, GOV'T OF CAN., <https://www.canada.ca/en/public-health/services/infectious-diseases/viral-haemorrhagic-fevers/sole-license-agreement-recombinant-vesicular-stomatitis-virus-vaccines-viral-hemorrhagic-fevers.html> [<https://perma.cc/A7VJ-AA7U>] (last modified Oct. 13, 2014). NewLink was, at the time, a subsidiary of BioProtection Corp.

141. *Id.* The full provision required NewLink to work the patent for full profit of “the Company and Canada.”

142. Grady, *supra* note 136.

143. Once the outbreak began, the private sector did enter the Ebola vaccine race. *Infra* Part II.

144. *See Statement on the WHO Consultation on Potential Ebola Therapies and Vaccines*, WORLD HEALTH ORG. (Sept. 5, 2014), <http://www.who.int/mediacentre/news/statements/2014/ebola-therapies-consultation/en> [<https://perma.cc/F8JW-AX6C>].

145. *Id.*

146. CIDRAP, *supra* note 9, at 25.

147. *See* Oumar Faye et al., *Molecular Evolution of Zika Virus During Its Emergence in the 20th Century*, 8 PLOS NEGLECTED TROPICAL DISEASES 1 (2014); A. J. Haddow et al., *Twelve Isolations of Zika Virus From Aedes (Stegomyia) Africanus (Theobald) Taken in and Above a Uganda Forest*, 31 BULL. WORLD HEALTH ORG. 57 (1964). A year after the Ugandan outbreak, scientists

with Zika were considered mild: cutaneous rash, malaise, fever, and headache.<sup>148</sup> Given the similarities between these and the symptoms triggered by influenza, it is probable that Zika outbreaks went largely undetected through history.<sup>149</sup> At the turn of the century, there were only fourteen documented cases of Zika infection in humans worldwide.<sup>150</sup> That number more than tripled in 2007 during an outbreak on a small Micronesian island. There were forty-nine confirmed cases, and it is estimated that nearly three quarters (74 percent) of the island's residents over the age of three had been infected by the virus at some point.<sup>151</sup>

Research concluded in 2012 showed that there were now two different lineages of Zika virus, African and Asian.<sup>152</sup> A 2013–14 outbreak in the South Pacific, caused by a virus belonging to the Asian lineage, raised the first suspicions that Zika infection could be connected to Guillain-Barré syndrome, a rare neurological disorder.<sup>153</sup> That hypothesis remained unconfirmed until the 2015–16 outbreak in Latin America, but it has now been established that the virus that emerged during the South Pacific outbreak is likely to be the same or related to the one that caused the 2015–16 outbreak in Brazil.<sup>154</sup>

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succeeded in isolating the virus from *Aedes africanus* mosquitos and, in 1952, the first cases of Zika infections in humans were reported in Uganda and Tanzania. See *The History of Zika Virus*, WORLD HEALTH ORG., <http://www.who.int/emergencies/zika-virus/timeline/en> [https://perma.cc/E2TJ-YGJT]. While most prevalent in Western Africa, Zika expanded across the continent during the 1970s and reached Asia by the end of the decade. See Jon Cohen, *Zika's Long, Strange Trip Into the Limelight*, SCIENCE (Feb. 8, 2016, 5:45 PM), <http://www.sciencemag.org/news/2016/02/zika-s-long-strange-trip-limelight> [https://perma.cc/QL28-X3CF] (tracing the evolution of Zika R&D).

148. For an overview of the most common symptoms caused by Zika infection, see *Zika Virus*, WORLD HEALTH ORG., <http://www.who.int/mediacentre/factsheets/zika/en> [https://perma.cc/5N53-6Y8E] (last updated Sept. 6, 2016); see also Cohen, *supra* note 147.

149. Cf. *Zika Virus Spread Undetected for Many Months, NIH-Supported Study Finds*, NAT'L INST. HEALTH (May 24, 2017), <https://www.niaid.nih.gov/news-events/zika-virus-spread-undetected-many-months-nih-supported-study-finds> [https://perma.cc/5RBA-Z5TR] (noting that even during the recent outbreak in Latin America the virus went undetected for several months).

150. See Cohen, *supra* note 147.

151. *Id.*

152. *Id.*

153. See Van-Mai Cao-Lormeau et al., *Guillain-Barré Syndrome Outbreak Associated With Zika Virus Infection in French Polynesia: A Case-Control Study*, 387 LANCET 1531 (2016).

154. Research carried out during the 2015–16 outbreak confirmed the linkage between Zika and Guillain-Barré syndrome. See Michael A. Johansson et al., *Zika and the Risk of Microcephaly*, 375 NEW ENG. J. MED. 1 (2016); Thais dos Santos et al., *Zika Virus and the Guillain-Barré Syndrome—Case Series From Seven Countries*, 375 NEW ENG. J. MED. 1598 (2016). Outbreak-induced research also discovered connections between Zika and congenital defects. See Fernanda R. Cugola et al., *The Brazilian Zika Virus Strain Causes Birth Defects in Experimental Models*, 534 NATURE 267 (2016) (describing additional Zika complications).



Research on Zika thus predates R&D on Ebola, but given the apparent lesser severity of Zika infection, allocation of resources toward Zika R&D was understandably not a priority until 2015, even by the incentives standards that normally apply to outbreak diseases. R&D efforts were further along in other diseases in the Zika family (flavivirus). For instance, this was true of Japanese encephalitis, for which vaccine technology was developed in the United States in 2009.<sup>155</sup> As described in Part II, existence of R&D in the genus to which a virus belongs might be helpful in speeding R&D for that virus once an outbreak occurs.

Due to the profile and burden of the Zika virus throughout the 20th century, at the time of the 2015–16 outbreak the market failure for Zika was quantitatively and qualitatively different from the one observed with Ebola. Incentives to R&D were low and intermittent, resulting in the complete lack of R&D efforts aimed at generating a vaccine or treatment for Zika infection in humans.<sup>156</sup> The incentives landscape changed in 2015 with the outbreak in Latin America, much in the same way it did for Ebola with the West Africa outbreak in 2014.

## 2. Impact of the 2014–16 Outbreaks on Incentives and R&D Frameworks

### a. The Ebola Vaccine Race

The large-scale outbreaks of 2014–16 had a profound impact on the R&D landscape, with different players coming together exceptionally quickly to support the development of vaccines for the outbreak diseases.

In the case of Ebola, this was “the largest and most complex” outbreak ever recorded.<sup>157</sup> There were more reported cases and deaths during this period than in all the previous outbreaks combined.<sup>158</sup> The WHO declared it a Public

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155. *Testing of Investigational Inactivated Zika Vaccine in Humans Begins*, NAT’L INST. HEALTH (Nov. 7, 2016), <https://www.nih.gov/news-events/news-releases/testing-investigational-inactivated-zika-vaccine-humans-begins> [<https://perma.cc/7SJZ-P5PY>].

156. See WORLD HEALTH ORG., R&D BLUEPRINT, *supra* note 7. See also WORLD HEALTH ORG., WHO/UNICEF Zika Virus (ZIKV) Vaccine Target Product Profile (TPP): Vaccine to protect against congenital Zika syndrome for use during (sic) an emergency, [http://www.who.int/immunization/research/development/Zika\\_vaccine\\_TPP\\_QandA\\_feb17.pdf?ua=1](http://www.who.int/immunization/research/development/Zika_vaccine_TPP_QandA_feb17.pdf?ua=1) (detailing the timeline of the product profile for Zika vaccines).

157. See WORLD HEALTH ORG., *supra* note 41.

158. The outbreak originated in a village in Guinea, and patient zero has been traced back to late 2013. The disease expanded quickly, and by March 2014 the Ministry of Health of Guinea confirmed an outbreak of Ebola virus disease, reporting 49 cases and 29 deaths (a mortality rate of 59 percent). See *Ebola Viral Disease Outbreak—West Africa, 2014*, CTRS. FOR DISEASE CONTROL & PREVENTION (June 27, 2014), <https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6325a4.htm> [<https://perma.cc/54TX-99GR>]. Between late March and

Health Emergency of International Concern (PHEIC) on August 8, 2014.<sup>159</sup> By this point, there were 1711 reported cases and 932 deaths.<sup>160</sup>

PHEIC status for Ebola lasted until March 29, 2016.<sup>161</sup> By the time it was lifted, there had been 28,610 reported cases and over 11,000 deaths in three countries.<sup>162</sup> As of late-2016, there were over 10,000 Ebola survivors from the Western Africa outbreak and subsequent flare-ups.<sup>163</sup> The only fatality outside West Africa occurred in the United States, where a total of eleven patients were treated for Ebola virus disease.<sup>164</sup>

Even though R&D sparked by the emergence of a pathogen is of no avail to at-risk populations during an ongoing outbreak, the magnitude of the 2014–16 events in Western Africa—coupled with fear of a worldwide pandemic fueled by globalized travel—introduced important changes to the incentives landscape for Ebola R&D. Funding for Ebola R&D increased by 258 percent between 2014 and 2015.<sup>165</sup> Looking at global investment in African viral hemorrhagic fevers<sup>166</sup> for 2015, 91 percent (U.S. \$574 million) was directed

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May 2014, Ebola expanded into Liberia and Sierra Leone, prompting Médecins Sans Frontières/Doctors Without Borders (MSF) to state that the outbreak was “out of control.” See *Ebola: Massive Deployment Needed to Fight Epidemic in West Africa*, DOCTORS WITHOUT BORDERS (June 23, 2014), <http://www.doctorswithoutborders.org/news-stories/press-release/ebola-massive-deployment-needed-fight-epidemic-west-africa> [<https://perma.cc/WG33-GW7M>].

159. See *Statement on the 1st Meeting of the IHR Emergency Committee on the 2014 Ebola Outbreak in West Africa*, WORLD HEALTH ORG. (Aug. 8, 2014), <http://www.who.int/mediacentre/news/statements/2014/ebola-20140808/en> [<https://perma.cc/TMG9-BEN5>]. The WHO has the authority to declare a PHEIC under the International Health Regulations, a binding set of rules for the WHO Member States. Article 2 of the regulations defines its “purpose and scope” as follows: “to prevent, protect against, control and provide a public health response to the international spread of disease in ways that are commensurate with and restricted to public health risks, and which avoid unnecessary interference with international traffic and trade.” WORLD HEALTH ORG., INTERNATIONAL HEALTH REGULATIONS 10 (2d ed. 2005) (emphasis added).

160. *Ebola Virus Disease Update—West Africa*, WORLD HEALTH ORG. (Aug. 6, 2014), [http://www.who.int/csr/don/2014\\_08\\_06\\_ebola/en](http://www.who.int/csr/don/2014_08_06_ebola/en) [<https://perma.cc/J9UA-DL2M>].

161. See Helen Branswell, *The Ebola Public Health Emergency Is Over, WHO Declares, but Concerns Linger*, STAT (March 29, 2016), <https://www.statnews.com/2016/03/29/ebola-who-end-of-emergency> [<https://perma.cc/ZR62-NLVZ>].

162. *Ebola Data and Statistics*, WORLD HEALTH ORG., <http://apps.who.int/gho/data/view.ebola-sitrep.ebola-summary-20160330?lang=en>.

163. *Ebola Outbreak 2014–2015*, WORLD HEALTH ORG. (Dec. 23, 2016), <http://www.who.int/csr/disease/ebola/en> [<https://perma.cc/942A-LCZG>].

164. Liberian citizen Thomas Eric Duncan died in Dallas on October 8, 2014. See *Press Briefing Transcript*, CTNS. FOR DISEASE CONTROL & PREVENTION (Oct. 8, 2014, 4:00 PM), <https://www.cdc.gov/media/releases/2014/t1008-ebola-confirmed-case.html> [<https://perma.cc/4VU6-2THS>].

165. See POLICY CURES RESEARCH, *supra* note 49, at 6.

166. *Id.* This category of diseases includes Ebola and other diseases in the Ebola family, like Marburg. It also includes a wide range of other types of diseases, such as Lassa fever, Crimean-Congo

toward Ebola R&D. Of this amount, 61 percent (U.S. \$388 million) was used to fund vaccine R&D.<sup>167</sup> Investment in drug development accounted for 16 percent (U.S. \$103 million); basic research, 9.4 percent (U.S. \$59 million); and diagnostics, 4.4 percent (U.S. \$28 million).<sup>168</sup>

While the public sector remained the largest funder of Ebola R&D, the role of the private sector increased significantly. Data referring to overall funding for Ebola and other African viral hemorrhagic fevers shows that pharmaceutical companies were responsible for 36 percent (U.S. \$226 million) of R&D expenditures, vis-à-vis 61 percent (U.S. \$383 million) coming from the public sector.<sup>169</sup> Philanthropic contributions were modest at 3.4 percent (U.S. \$22 million) and product-development partnerships “played little to no role.”<sup>170</sup>

The outbreak-induced funding mosaic suggests that, although pandemic events may cause a quantitative increase in R&D expenditures, they are unlikely to affect the primacy of the public sector in ensuring both reactive R&D and long-term R&D. But the private sector emerges as a powerful force in the late- and post-outbreak periods, particularly in the clinical development context.<sup>171</sup> This dynamic was at play during the Ebola vaccine race that began during the early stages of the 2014–16 outbreak.

Before the outbreak, moderately low incentives resulted in a fragmented R&D landscape covering different strains of Ebola. The outbreak sped up existing R&D and triggered new R&D at an extraordinary pace. By 2015, there were twenty-one ongoing R&D projects.<sup>172</sup> Of these, twelve were vaccines<sup>173</sup> and nine antiviral therapies.<sup>174</sup> With nearly two-thirds of R&D<sup>175</sup> being directed toward vaccine development—and given the pivotal role of vaccines in decreasing the public health impact of future outbreaks<sup>176</sup>—it is worth taking a closer look at how the Ebola vaccine race unfolded, as well as at the consequences of that race from an IP perspective.

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hemorrhagic fever, and Rift Valley fever. See *Haemorrhagic Fevers, Viral*, WORLD HEALTH ORG., [http://www.who.int/topics/haemorrhagic\\_fevers\\_viral/en](http://www.who.int/topics/haemorrhagic_fevers_viral/en) [<https://perma.cc/RL7K-XZUR>].

167. See POLICY CURES RESEARCH, *supra* note 49, at 89.

168. *Id.*

169. *Id.* at 90.

170. *Id.* at 93.

171. See *infra* Figure 1 (showing both private and public-sector players in the development of an Ebola vaccine).

172. See Fisher & Geddes, *supra* note 120, at 13.

173. *Id.* at 13–28.

174. *Id.* at 29–38.

175. POLICY CURES RESEARCH, *supra* note 49, at 6.

176. Röttingen et al., *supra* note 10 and accompanying text.

With the sudden spike in incentives to conduct R&D on Ebola, several vaccine candidates emerged, displaying pluralistic R&D approaches as shown in Table 1. As of early 2017, there were five types of Ebola vaccine candidates, most of them with multiple ongoing projects.<sup>177</sup> In addition to different types of vaccines, there are emerging studies evaluating the possibility of extending R&D for a specific strain of Ebola into other strains.<sup>178</sup>

Type of Vaccine	Candidates <sup>179</sup>
Replication-competent, vectored vaccines	rVSV-ZEBOV, VesiculoVax, HPIV3-EBOVZ
Replication-incompetent, adenovirus-vectored	cAd3-EBOZ, Ad26.ZEBOV, Ad5-EBOV
Replication-incompetent poxvirus-vectored	MVA-BN-Filo, MVA-EbolaZ
DNA vaccines	INO-4201, INO-4202, INO-4212
Subunit vaccines	EBOV GP nanoparticle vaccine with Matrix-M adjuvant

**Table 1:** Ebola Vaccine Candidates (2017)<sup>180</sup>

As of mid-2017, seven vaccines have entered clinical trials. Three of them have moved to advanced trials: rVSV-ZEBOV, cAd3-EBOZ and Ad26-EBOV/MVA-EBOV.<sup>181</sup>

rVSV-ZEBOV is the Canada-developed recombinant vesicular stomatitis virus-based vaccine, which was patented in 2003 but subsequently failed to

177. Figure 1 follows the taxonomy used by the Center for Infectious Disease Research and Policy at the University of Minnesota in January 2017. See CIDRAP, *supra* note 9, at 10. Other categorizations are possible; for instance, Keshwara et al. have proposed the following breakdown: DNA vaccines; virus-like particles and nanoparticle vaccines; replication-deficient Ebola; adenovirus-based vaccines; vesicular stomatitis virus; and recombinant rabies virus. See Rohan Keshwara et al., *Toward an Effective Ebola Virus Vaccine*, 68 ANN. REV. MED. 371 (2017).

178. See Martins et al., *supra* note 116.

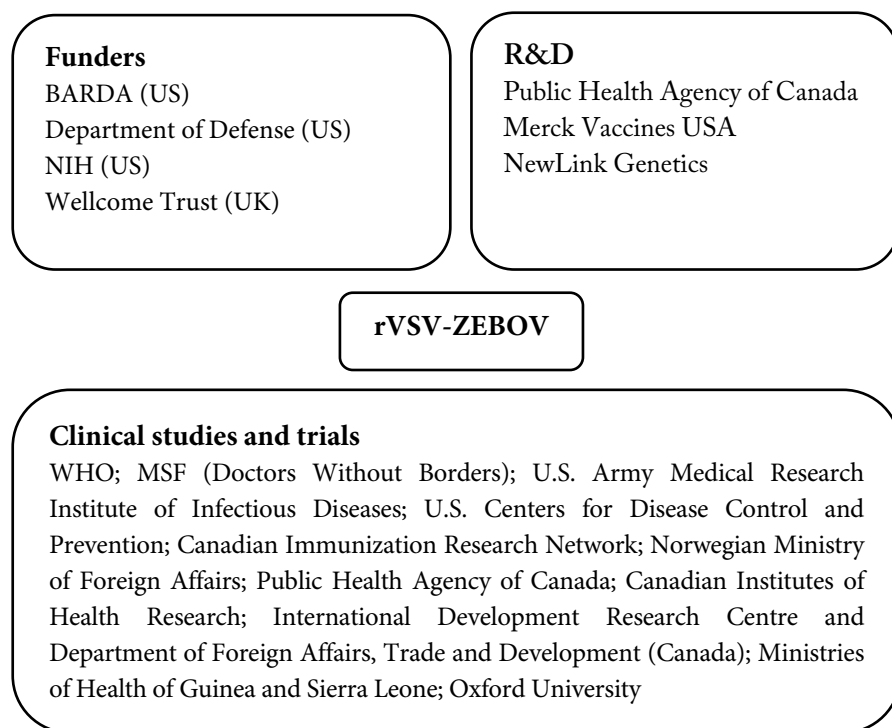
179. As of early 2017.

180. See CIDRAP, *supra* note 9, at 10.

181. See Keith J. Chappell & Daniel Watterson, *Fighting Ebola: A Window for Vaccine Re-evaluation?*, 13 PLOS PATHOGENS 1 (2017); see also Yuxiao Wang et al., *Ebola Vaccines in Clinical Trial: The Promising Candidates*, 13 HUM. VACCINES & IMMUNOTHERAPEUTICS 153 (2017); Keshwara et al., *supra* note 177, at 379; Martins et al., *supra* note 116.

attract sufficient private-sector support.<sup>182</sup> It quickly became widely considered the most advanced of the Ebola vaccine candidates.<sup>183</sup>

A few months after the start of the outbreak, this vaccine was pushed through the R&D pipeline by NewLink Genetics, now in partnership with a large U.S. pharmaceutical company, Merck.<sup>184</sup> Funding poured in quickly as different types of players joined the network supporting expedited R&D on rVSV-ZEBOV. Figure 1 below provides an overview of this network according to the role taken on by each player.



**Figure 1:** rVSV-ZEBOV Vaccine Candidate

The most noticeable difference brought about by the outbreak-induced change in the incentives landscape was the entry of the private sector into vaccine R&D. This occurred not only in the case of the current leading vaccine

182. See *supra*, note 141.

183. See Chappell & Watterson, *supra* note 181.

184. This was not a smooth transition, however. See *infra* Part II.

candidate, rVSV-ZEBOV, but with other candidates that emerged during the outbreak.<sup>185</sup> Small pharmaceutical companies played a role in bringing preexisting vaccine technology into expanded collaborative R&D models, while big pharma drove follow-on R&D, mostly at the level of clinical development. The case of rVSV-ZEBOV illustrates this point, as NewLink had acquired the IP rights to the vaccine three years before the outbreak, but it was the collaboration with Merck that pushed the vaccine through the R&D pipeline.<sup>186</sup>

The breadth of institutions involved in clinical studies and trials is consistent with trends observed in other infectious disease outbreaks.<sup>187</sup> Both Canadian research institutions and the USAMRIID were involved in pre-outbreak R&D, having participated in preclinical R&D for rVSV-ZEBOV a decade before the outbreak.<sup>188</sup> The other players listed in Table 1 show a blend of international players that is common to vaccine candidates,<sup>189</sup> as well as the geographical focus of the 2014–16 outbreak (with Guinea and Sierra Leone being among the most affected countries).

Given the status of Ebola as a “material threat” to U.S. national security,<sup>190</sup> it should come as no surprise that two dominant funding players were the Biomedical Advanced Research and Development Authority (BARDA) and the U.S. Department of Defense.<sup>191</sup> BARDA is part of the Office of the Assistant Secretary for Preparedness and Response, created after Hurricane Katrina with the goal of “preventing, preparing for, and responding to the adverse health effects of public health emergencies and disasters.”<sup>192</sup> BARDA engages in both development and procurement of medical countermeasures<sup>193</sup> for chemical,

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185. See *infra* Figure 2, a propos the cAd3-EBOZ vaccine example. It also occurred in the case of non-vaccine R&D, such as for Ebola therapeutic drugs.

186. See *infra* Subpart II.B.

187. See, e.g., Daniel Lucey & Lawrence O. Gostin, *A Yellow Fever Epidemic: A New Global Health Emergency?*, 315 JAMA 2661 (2016) (noting the role of the WHO in the response to Yellow Fever outbreaks).

188. See *supra* note 133 and accompanying text.

189. See *infra* Figure 2 and Figure 3.

190. See *supra* note 123 and accompanying text.

191. See PHEMCE, *supra* note 123, at 16–17.

192. Office of the Assistant Secretary for Preparedness and Response, PUB. HEALTH EMERGENCY, <https://www.phe.gov/about/aspr/pages/default.aspx> [<https://perma.cc/2FVC-FYG5>] [hereinafter ASPR]. ASPR operates under the umbrella of the Department of Health and Human Services. *Id.*

193. Medical countermeasures are drugs used to respond to bioterrorism, naturally occurring emerging diseases, or natural disasters. See *What Are Medical Countermeasures?*, FDA, <https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/AboutMCMi/ucm431268.htm> [<https://perma.cc/5HFW-DTL9>] (last updated Feb. 5, 2018).

biological, radiological, and nuclear defense.<sup>194</sup> From the onset of the outbreak, BARDA was involved with different types of Ebola R&D. Besides funding clinical development of rVSV-ZEBOV, BARDA also collaborated with companies and institutions developing other vaccine candidates. For instance, in December 2014 it awarded GlaxoSmithKline U.S. \$12.9 million for the manufacturing of cAd3-EBOZ, a monovalent vaccine derived from a recombinant chimpanzee adenovirus.<sup>195</sup> In addition to investing in vaccine R&D, BARDA collaborated with companies and institutions involved in non-vaccine R&D. This was the case with the experimental drug ZMapp, a monoclonal antibody cocktail used as a therapeutic agent for acute Ebola virus disease.<sup>196</sup> BARDA co-funded the clinical development of the drug alongside the National Institute of Allergy and Infectious Diseases (NIAID) and the Department of Defense (through the Defense Threat Reduction Agency).<sup>197</sup> BARDA entered into an eighteen-month, U.S. \$24.9 million contract (extendable to U.S. \$42.3 million) with Mapp Biopharmaceutical, a small company based in Southern California.<sup>198</sup> This multipronged approach to early-outbreak Ebola R&D was followed by several public-sector institutions, especially U.S. government agencies, as Figure 2 below illustrates.<sup>199</sup>

The other leading Ebola vaccine candidates, as of early 2017, rely on a different type of technology: Both cAd3-EBOZ and Ad26-EBOV/MVA-EBOV

194. This is known as CBRN defense and the U.S. Army is the leading player in the response to CBRN crises. In addition to contributing to CBRN defense through drug development, procurement, and stockpiling, BARDA develops and procures drugs for pandemic influenza and emerging infectious diseases. See *Biomedical Advanced Research and Development Authority (BARDA)*, MED. COUNTERMEASURES.GOV, <https://www.medicalcountermeasures.gov/barda.aspx> [<https://perma.cc/NR8A-VBAW>].

195. See Figure 2 below, mapping the other players involved in the development of the cAd3-EBOZ vaccine candidate). See also Fisher & Geddes, *supra* note 120, at 18; *infra* Figure 3.

196. See G. Marshall Lyon et al., *Clinical Care of Two Patients With Ebola Virus Disease in the United States*, 371 NEW ENG. J. MED. 2402 (2014).

197. See PHEMCE, *supra* note 123, at 15–17.

198. Press Release, U.S. Dep't of Health & Human Servs., HHS Contracts With Mapp Biopharmaceutical to Develop Ebola Drug (Sept. 2, 2014), <https://web.archive.org/web/20160116072625/http://www.hhs.gov/about/news/2014/09/02/hhs-contracts-with-mapp-biopharmaceutical-to-develop-ebola-drug.html> [<https://perma.cc/G856-WP6D>]. Clinical trials for ZMapp were considered promising but missed the statistical threshold. See Stephanie Soucheray, *Trial Offers Mixed View of Ebola Drug ZMapp*, CIDRAP (Oct. 12, 2016), <http://www.cidrap.umn.edu/news-perspective/2016/10/trial-offers-mixed-view-ebola-drug-zmapp> [<https://perma.cc/AD56-KC4C>] (noting that the drug ZMapp demonstrated efficacy in 91.2 percent of cases, below the current standard of 97.5 percent).

199. See *infra* Figure 2. Other institutions that played a prominent role in funding multiple R&D projects include the Department of Defense and National Institute of Allergy and Infectious Diseases (NIAID).

are adenovirus-based vaccines.<sup>200</sup> In the case of cAd3-EBOZ, the initial bulk of funding for the expedited development of the vaccine was provided by the European Commission and, to a smaller extent, by the Swiss government.<sup>201</sup> Supplemental funding was provided to the University of Oxford and the Jenner Institute by three U.K.-based institutions<sup>202</sup>: Wellcome Trust, the second largest nongovernmental funder of biomedical research in the U.K.;<sup>203</sup> the Medical Research Council, a government agency;<sup>204</sup> and the Department for International Development, a ministerial department.<sup>205</sup> NIAID funded and conducted clinical trials in the U.S.<sup>206</sup>

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200. See Vincent Pavot, *Leading Ebola Vaccine Candidates*, 1 VACCINATION RES. OPEN J. 1 (2016); see also Milagritos D. Tapia et al., *Use of ChAd3-EBO-Z Ebola Virus Vaccine in Malian and US Adults, and Boosting of Malian Adults With MVA-BN-Filo: A Phase 1, Single-Blind, Randomised Trial, a Phase 1b, Open-Label and Double-Blind, Dose-Escalation Trial, and a Nested, Randomised, Double-Blind, Placebo-Controlled Trial*, 16 LANCET 31 (2015).

201. The European Commission contributed around \$20 million and the Swiss government, U.S. \$2 million. Fisher & Geddes, *supra* note 120, at 18.

202. U.S. \$4.6 million. *Id.* at 17.

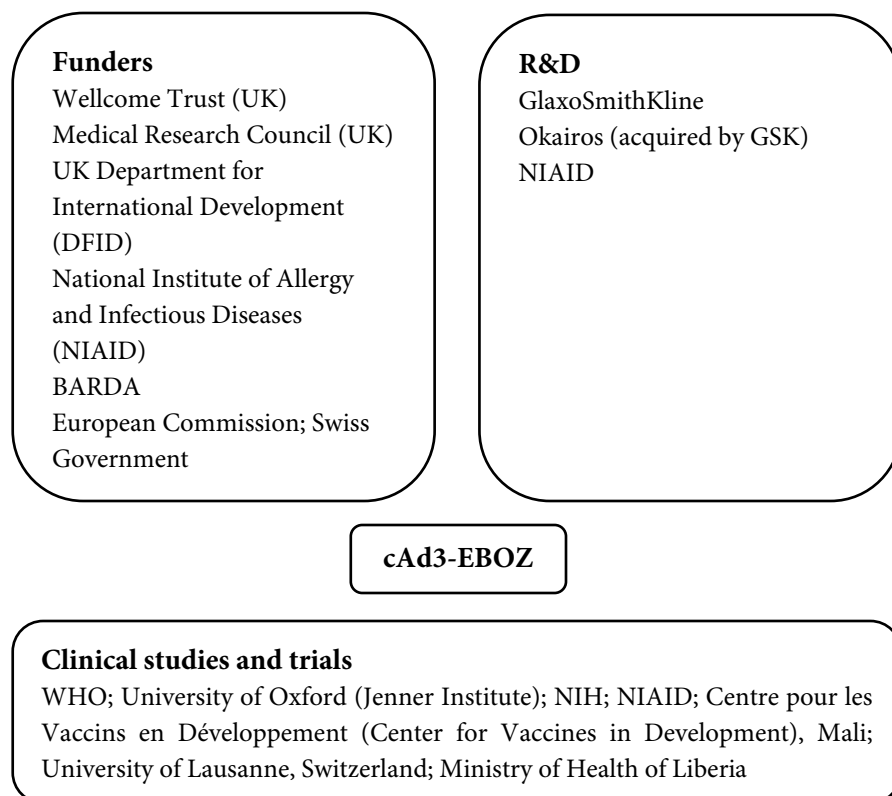
203. *About Us*, WELLCOME TRUST, <https://wellcome.ac.uk/about-us> [<https://perma.cc/44YS-CKHM>]; see also Emma Howard, *What Is the Wellcome Trust?*, GUARDIAN (Mar. 16, 2015, 8:51 AM), <https://www.theguardian.com/environment/2015/mar/16/what-is-the-wellcome-trust> [<https://perma.cc/H5UQ-2UVQ>]. See also Emma Howard, *What is the Wellcome Trust?*, The Guardian (Mar. 16, 2015), <https://www.theguardian.com/environment/2015/mar/16/what-is-the-wellcome-trust>.

204. *About Us*, MED. RES. COUNCIL, <https://www.mrc.ac.uk/about> [<https://perma.cc/DD56-KLHM>].

205. DEP'T FOR INT'L DEV., <https://www.gov.uk/government/organisations/departement-for-international-development> [<https://perma.cc/GQ5K-2ZG2>].

206. Fisher & Geddes, *supra* note 118, at 17.





**Figure 2: CAD3-EBOZ VACCINE CANDIDATE**

Private-sector R&D was led by GlaxoSmithKline (GSK), which had bought a small Swiss biotech company (Okairos) the year before the outbreak for strategic reasons that did not have much to do with Ebola R&D.<sup>207</sup> As it happened, Okairos's portfolio included rights over the then early-stage cAd3-EBOZ vaccine.<sup>208</sup> Unlike Merck and NewLink, which had to negotiate the IP

207. See Ben Hirschler, *GSK Bets on Chimp Virus With \$321 Million Vaccines Buy*, REUTERS (May 30, 2013, 8:35 AM), <http://www.reuters.com/article/us-glaxosmithkline-okairos-idUSBRE94T0O120130530> [<https://perma.cc/NMW7-WDLG>]. Okairos's portfolio included vaccines against hepatitis C and malaria that were undergoing phase II testing, as well as early vaccine technology targeting syncytial virus (RSV), tuberculosis, Ebola, and HIV. Some of Okairos's technology was also expected to be of use in cancer-related R&D. *Id.*

208. Press Release, GlaxoSmithKline, *GSK Strengthens Vaccines Business With Acquisition of Okairos* (May 29, 2013), [http://www.okairos.com/files/documents/3\\_GSK-strengthens-vaccines-business-with-acquisition-of-Okairos-29-05-13.pdf](http://www.okairos.com/files/documents/3_GSK-strengthens-vaccines-business-with-acquisition-of-Okairos-29-05-13.pdf) [<https://perma.cc/FDY6-NQT2>] ("Under the terms of the transaction, GSK will take full ownership of the company and thus assume ownership of early stage assets for diseases such as respiratory syncytial virus (RSV),

surrounding the rVSV-ZEBOV vaccine against the outbreak clock,<sup>209</sup> GSK was able to start clinical development of the vaccine immediately. That process was bolstered in late 2014 by funding from BARDA<sup>210</sup> and the Bill & Melinda Gates Foundation.<sup>211</sup>

The remaining frontrunner vaccine (Ad26-EBOV/MVA-EBOV), another adenovirus-based vaccine,<sup>212</sup> stands out for two reasons. First, it was funded primarily by a grant from the Innovative Medicines Initiative,<sup>213</sup> the world's largest public-private partnership in the life sciences, and the product of a collaboration between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA)<sup>214</sup> The recipient of the grant, the large pharmaceutical company Johnson & Johnson (J&J), thus received a substantial amount of funding from the private sector in the form of the European pharmaceutical industry represented by EFPIA.

The second reason this vaccine differs from the previous two candidates is that clinical development involved two large pharmaceutical companies: J&J partnered with Denmark-based Bavarian Nordic to “accelerate and scale up” clinical development of the vaccine.<sup>215</sup> This is a deviation from the small-big pharma collaboration model, in which a player with modest resources either develops or acquires IP on an early-stage vaccine targeting a relatively neglected disease. J&J did, however, rely on preexisting vaccine technology developed by the U.S. National Institutes of Health and NIAID (as indicated by Figure 2), reinforcing the idea that there is a lack of incentives to pre-outbreak R&D for private-sector companies.

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hepatitis C virus (HCV), malaria, tuberculosis, ebola [sic] and HIV, supplementing the company's existing vaccines pipeline.”).

209. See *infra* Subpart II.B.

210. In the amount of U.S. \$12.9 million. Fisher & Geddes, *supra* note 118, at 18.

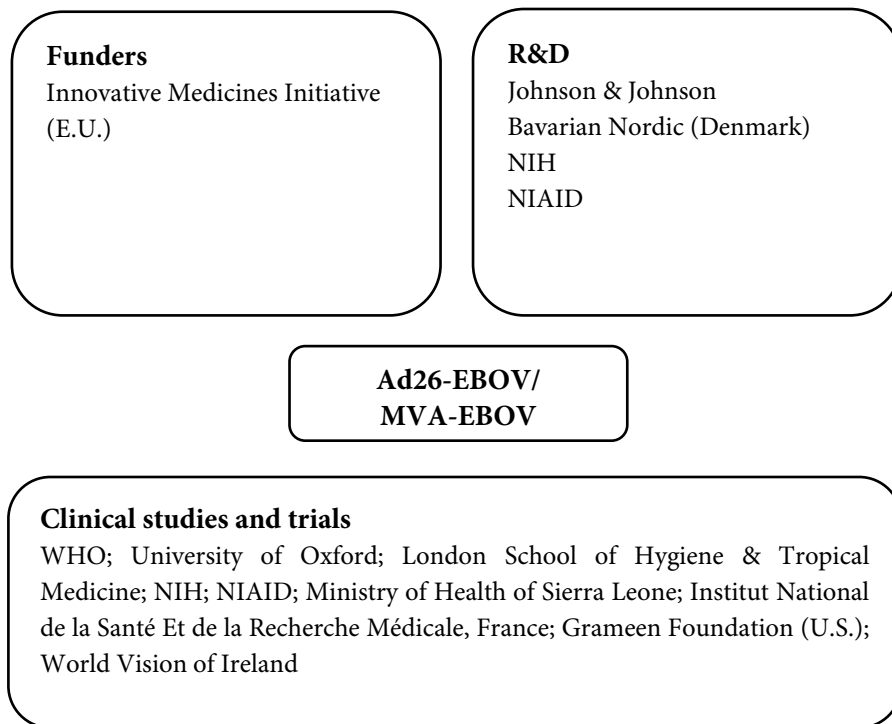
211. Approximately U.S. \$3 million. *Id.* at 17.

212. See Chappell, *supra* note 183.

213. The grant totaled over U.S. \$100 million. See Press Release, Johnson & Johnson, Johnson & Johnson Announces Formation of Ebola Vaccine Development Consortia, Gains Funding From Innovative Medicines Initiative (Jan. 16, 2015), <https://www.jnj.com/media-center/press-releases/johnson-johnson-announces-formation-of-ebola-vaccine-development-consortia-gains-funding-from-innovative-medicines-initiative> [<https://perma.cc/8M83-4DYN>].

214. *IMI Mission and Objectives*, INNOVATIVE MEDS. INITIATIVE, <https://www.imi.europa.eu/content/mission> [<https://perma.cc/WA8G-W6GD>].

215. See Cormac Sheridan, *Johnson & Johnson, Bavarian Nordic Ink \$187M Deal for Ebola Virus Vaccine*, BIO WORLD, <http://www.bioworld.com/content/johnson-johnson-bavarian-nordic-ink-187m-deal-ebola-virus-vaccine> [<https://perma.cc/U8DM-RT3K>].



**Figure 3: AD26-EBOV/MVA-EBOV VACCINE CANDIDATE**

Clinical trials for these three Ebola vaccine candidates and several others are ongoing. The latest wave of trials began in April 2017.<sup>216</sup> While results appear promising,<sup>217</sup> there is not a reliable timeline to predict when the first approved vaccines will enter the market. The 2014–16 outbreak created incentives for Ebola R&D that will benefit post-outbreak populations and potentially minimize the burden caused by future outbreaks. Nevertheless, this temporary spike in incentives is not enough to guarantee the necessary levels of sustained Ebola R&D in the future. Already in late 2015, when Ebola and Zika raged concomitantly, several institutions began moving existing Ebola resources

216. *Ebola: New Trial Launched in West Africa to Evaluate Three Vaccination Strategies*, NAT'L INST. OF ALLERGY & INFECTIOUS DISEASES (Apr. 6, 2017), <https://www.niaid.nih.gov/news-events/ebola-new-trial-launched-west-africa-evaluate-three-vaccination-strategies> [https://perma.cc/E6YB-9TEK].

217. See News Release, World Health Org., Final Trial Results Confirm Ebola Vaccine Provides High Protection Against Disease (Dec. 23, 2016), <http://www.who.int/mediacentre/news/releases/2016/ebola-vaccine-results/en> [https://perma.cc/4LG4-89SP]; see also Donald G. McNeil Jr., *New Ebola Vaccine Gives 100 Percent Protection*, N.Y. TIMES (Dec. 22, 2016), <https://www.nytimes.com/2016/12/22/health/ebola-vaccine.html>.

toward the response to Zika.<sup>218</sup> In the United States, of the U.S. \$589 million that were used to fund the response to Zika in 2016, U.S. \$500 million were diverted from Ebola funds.<sup>219</sup> This suggests that the combination of IP rights and outbreak-induced incentives is not enough to generate desirable levels of systemic R&D for most outbreak diseases. Scholars analyzing biopharmaceutical innovation in areas with severe market failures have proposed different mechanisms to create supplemental incentives streams. A short survey of these types of incentives can be found in Part III, alongside a brief discussion of measures aimed at reducing IP inefficiencies during the early- and post-outbreak periods.

### b. The Zika Vaccine Race

As with Ebola, the Zika R&D landscape was bolstered by the impact of the 2015–16 outbreak. The WHO declared it a Public Health Emergency of International Concern in February 2016.<sup>220</sup> Research conducted during the early stages of the outbreak confirmed suspicions of a link between Zika infection and Guillain-Barré syndrome.<sup>221</sup> It also showed that, if contracted during pregnancy, the virus might cause microcephaly in newborns.<sup>222</sup>

Even though the Zika virus was identified nearly two decades earlier than Ebola, science on Zika was significantly less developed at the beginning of the outbreak.<sup>223</sup> Until 2015, Zika “was not considered to be a major pathogen.”<sup>224</sup> Since the outbreak began, close to one thousand scientific publications on Zika

218. This was the case, for instance, of the WHO. See Dylan Scott, *Millions in Ebola Funding, A Casualty of Zika Virus, May Not Be Replenished*, STAT (June 1, 2016), <https://www.statnews.com/2016/06/01/ebola-zika-virus-funding> [https://perma.cc/6UY6-WWYR].

219. See Andrew Joseph, *Obama Administration Diverts \$500 Million From Ebola Response to Zika Fight*, STAT (Apr. 6, 2016), <https://www.statnews.com/2016/04/06/white-house-zika-call> [https://perma.cc/833Y-FC66].

220. See WORLD HEALTH ORG., ZIKA STRATEGIC RESPONSE PLAN 8 (2016). By the time the WHO lifted the Public Health Emergency in November 2016, over sixty countries and territories had reported cases of Zika infection. See *Zika Cumulative Cases—16 November 2017*, WORLD HEALTH ORG., [http://www.paho.org/hq/index.php?option=com\\_content&view=article&id=12390&Itemid=42090&lang=en](http://www.paho.org/hq/index.php?option=com_content&view=article&id=12390&Itemid=42090&lang=en). Nearly five thousand cases were reported in the United States alone. See *2016 Case Counts in the US*, CTRS. FOR DISEASE CONTROL & PREVENTION, <https://www.cdc.gov/zika/reporting/2016-case-counts.html> [https://perma.cc/QP4F-VGWF].

221. See Cao-Lormeau et al., *supra* note 153 and accompanying text.

222. Johansson et al., *supra* note 154.

223. See Jeff Lyon, *Zika: Worse Than Thalidomide?*, 316 JAMA 1246, 1248 (2016) (discussing the areas on which long-term Zika research is still needed).

224. Alan D. T. Barrett, *Zika Vaccine Candidates Progress Through Nonclinical Development and Enter Clinical Trials*, NPJ VACCINES (Nov. 10, 2016), <http://www.nature.com/articles/npjvaccines201623>.

have appeared.<sup>225</sup> The discovery of the relationship between the Zika infection and its severe symptoms spiked incentives to R&D on multiple fronts. The most prominent is, unsurprisingly, vaccine development: As of mid-2017, there were at least forty entities involved in Zika R&D on different types of vaccines.<sup>226</sup> On a smaller scale, the outbreak also directed a portion of R&D efforts into the development of diagnostics, therapeutics, and vector-control methods.<sup>227</sup>

One of the main R&D strategies to develop Zika vaccines was to build on preexisting vaccine technology targeting similar viruses like Yellow Fever or dengue (both flaviviruses like Zika).<sup>228</sup> This was the approach taken by the Walter Reed Army Institute of Research (hereinafter the Army) in the United States, which produced the world's leading vaccine candidate in the Zika race.<sup>229</sup>

Nevertheless, given the scientific unknowns surrounding the Zika virus, the vaccine race has been characterized by multiple approaches, with several funding institutions supporting parallel and competing R&D strategies.<sup>230</sup> According to the most recent data collected by the WHO, the Zika R&D pipeline includes four different categories of products:<sup>231</sup> Zika diagnostics (of which there are three types: nucleic acid test kits,<sup>232</sup> ELISA-based tests<sup>233</sup> and RDT-type tests<sup>234</sup>); therapeutics;<sup>235</sup> vaccines;<sup>236</sup> and vector-control methods.<sup>237</sup> While diagnostics and vaccines are deemed strategic areas, R&D on Zika-related therapeutic products is not considered a priority due to the “complexity of testing and using novel therapeutic drugs in pregnant women,”<sup>238</sup> the most

225. *Id.*

226. *See infra* Table 2.

227. *See* WORLD HEALTH ORG., CURRENT ZIKA PRODUCT PIPELINE 5 (2016), <http://www.who.int/blueprint/priority-diseases/key-action/zika-rd-pipeline.pdf> [<https://perma.cc/8X7D-AGKB>].

228. *Id.*

229. *See* Cheryl Pellerin, *Walter Reed Scientists Test Zika Vaccine Candidate*, U.S. DEP'T OF DEF. (June 9, 2016), <http://www.defense.gov/News/Article/Article/795226/walter-reed-scientists-test-zika-vaccine-candidate> [<https://perma.cc/Y5RG-7D8J>]; *see also infra* Part II (discussing transactional IP inefficiencies that have affected the licensing of the Army's vaccine).

230. WORLD HEALTH ORG., *supra* note 227. Most pharmaceutical companies, however, have chosen to pursue a single approach (such as purified vaccines or DNA-based vaccines, but not both).

231. *Id.* The WHO collected, but did not verify this data. *Id.* at 7.

232. *Id.* at 7–8.

233. *Id.* at 9–10.

234. *Id.* at 10–11.

235. *Id.* at 12–13.

236. *Id.* at 14.

237. *Id.* at 15–16.

238. *Id.* at 4. *See also* CENTERS FOR DISEASE CONTROL & PREVENTION, Zika Virus—Pregnancy, <https://www.cdc.gov/zika/pregnancy/index.html> [<https://perma.cc/L6GF-UTYB>] (noting that the Zika virus can be transmitted from a pregnant person to the fetus).

at-risk population for Zika infection. Even with a potentially small market, at least ten companies are engaged in diagnostic development for the Zika virus.<sup>239</sup>

As far as vaccines are concerned, by the time the WHO declared the end of the Zika Public Health Emergency in November of 2016, there were close to twenty active projects.<sup>240</sup> Over a dozen private-sector entities were involved in Zika R&D, as well as several research institutions.<sup>241</sup> Additional entities are still announcing early-stage product development<sup>242</sup> as noted in the overview of Zika R&D projects listed below in this Part.

Similar to what happened in Ebola R&D, the bulk of Zika R&D is taking place in the United States and Europe. However, there are also three projects that have been initiated by entities in more affluent and technically sophisticated developing countries: In India, Bharat Pharmaceuticals,<sup>243</sup> a large private-sector company, is currently developing two different types of vaccine; in Brazil, Bio-Manguinhos/Fiocruz, a scientific research unit within a Ministry of Health–sponsored foundation,<sup>244</sup> has three active Zika vaccine projects; and also in Brazil, Butantan, a research institute and one of the world’s leading centers for dengue vaccine R&D,<sup>245</sup> is developing two different Zika vaccines.

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239. According to data collected by the WHO, these companies include bioMerieux, Alere, Cepheid, Hema Diagnostic Systems, Atomo Diagnostics, OraSure, Access Bio, Chembioio, DiaSorin, and Siemens. *Id.* at 11.

240. This list has been updated to reflect changes that took place after the WHO updated its own data for the most recent time. Some of the players involved in Zika vaccine development are working collaboratively. *Id.* at 3–5. Some of the funders are involved in more than one project (this is especially true of government funding in the United States).

241. *Id.* at 5.

242. See *infra* Table 2.

243. BHARAT PHARMACEUTICALS, <http://www.bharatpharmaceuticals.com/#&panel1-1> [<https://perma.cc/4BU6-C6WU>].

244. BIO-MANGUINHOS/FIOCRUZ, <https://www.bio.fiocruz.br> [<https://perma.cc/Q94T-Y7CZ>].

245. See Marcelo De Franco & Jorge Kalil, *The Butantan Institute: History and Future Perspectives*, 8 PLOS NEGLECTED TROPICAL DISEASES 1 (2014).

Institution	Country	Vaccine Type
Bharat (pharma)	India	(1) inactivated purified virus (2) VLP <sup>246</sup>
Bio-Manguinhos/Fiocruz (research institution; manufacturing)	Brazil	(1) inactivated purified virus (2) VLP (3) DNA
Butantan (research institution)	Brazil	(1) live dengue recombinant (vaccine technology licensed from NIAID) (2) inactivated purified
Centers for Disease Control and Prevention (CDC)	U.S.	(1) VLP (2) live recombinant adenovirus
GeoVax (pharma)	U.S.	MVA-VLP platform
GlaxoSmithKline (pharma)	U.S.	RNA
Hawaii Biotech (pharma)	U.S.	insect cell line produced recombinant proteins
Inovio/GeneOne (pharma)	U.S./ South Korea	DNA
Institut Pasteur (private research foundation)	France	2 vectored vaccines
Moderna/Valera, Biomedical Advanced Research and Development Authority (BARDA)	U.S.	mRNA
NewLink Genetics (pharma)	U.S.	purified inactivated virus
NIH: Vaccine Research Center (VRC) at the National Institute of Allergy and Infectious Diseases (NIAID)	U.S.	(1) Zika-targeted mutation live vaccine (2) DNA (3) VSV recombinant
Novavax (pharma)	U.S.	E protein

246. VLP stands for virus-like particles, multiprotein structures commonly used in vaccine development. See Antônio Roldão et al., *Virus-Like Particles in Vaccine Development*, 9 EXPERT REV. VACCINES 1149, 1149 (2010).

Institution	Country	Vaccine Type
Replikins (pharma)	U.S.	synthetic peptides
Sanofi (pharma)	France	(1) chimera (2) undisclosed
Takeda (pharma)/BARDA	Japan/U.S.	inactivated whole virion vaccine
Themis Bioscience (pharma)	Austria	vector vaccine
Valneva (pharma)	France	purified inactivated virus
Walter Reed Army Institute of Research (Army), National Institutes of Health (NIH); National Institute of Allergy and Infectious Diseases (NIAID); Biomedical Advanced Research and Development Authority (BARDA); Sanofi (pharma; funding recipient)	U.S.	purified inactivated virus (ZPIV)
Inactive or early stage projects: CureVac, Johnson & Johnson, Merck, Oxford University, Pax Vax, Pfizer, Profectus Biosciences, Protein Sciences, Sementis, Sinergium		

**Table 2:** Zika Vaccine R&D Projects<sup>247</sup>

In addition to the Army's leading candidate (an inactivated vaccine known as ZPIV), as of mid-2017 there are two other advanced vaccine candidates: a DNA vaccine developed by Inovio, a small Pennsylvania-based biotech company, in partnership with GeneOne Life Science, a South Korean biopharmaceutical company; and a DNA vaccine developed by the Vaccine Research Center at the National Institute of Allergy and Infectious Diseases (NIAID).<sup>248</sup> In this group, the Inovio vaccine is the only one that was not funded by the NIH. All candidates in the group are currently in clinical development. The Army-developed vaccine has been undergoing

247. Updated and adapted from: WORLD HEALTH ORG., *supra* note 227.

248. GLOBAL RESEARCH COLLABORATION FOR INFECTIOUS DISEASE PREPAREDNESS, ZIKA VACCINE WORKING GROUP OVERVIEW 1 (2016), [https://www.glopid-r.org/wp-content/uploads/2016/12/zika\\_working\\_group\\_vaccines\\_overview\\_november\\_2016.pdf](https://www.glopid-r.org/wp-content/uploads/2016/12/zika_working_group_vaccines_overview_november_2016.pdf) [<https://perma.cc/U7ZZ-CXRR>] [hereinafter GLOPID-R].



phase I trials since late 2016, with phase II planned for early 2018.<sup>249</sup> Inovio concluded phase I in June 2015 and is conducting phase II trials in Puerto Rico.<sup>250</sup> NIAID launched phase I in late 2016 and scheduled phase II for 2017.<sup>251</sup>

The group of advanced vaccine candidates in the Zika race splits into two very different categories in terms of vaccine type. Two candidates are DNA-based vaccines: the vaccine developed by Inovio in partnership with GeneOne; and one of the vaccines developed at the Vaccine Research Center, which is part of the NIH.<sup>252</sup> The remaining vaccine in the group of advanced candidates relies on a different type of vaccine R&D, virus inactivation; this is the ZPIV vaccine, developed by the Army in collaboration with NIAID and Biomedical Advanced Research and Development Authority (BARDA).

DNA vaccines and inactivated vaccines are at opposite sides of the spectrum in vaccine development.<sup>253</sup> Vaccine inactivation relies on a well-understood process that has been used for many decades.<sup>254</sup> DNA vaccines, in contrast, are considered a less traditional vaccine platform.<sup>255</sup> In the early

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249. *Id.*

250. Press Release, Inovio, Inovio Launches Zika Vaccine Trial in Midst of Puerto Rico Epidemic to Explore Early Signals of Vaccine Efficacy (Aug. 29, 2016), <http://ir.inovio.com/default.aspx?SectionId=5cc5ecae-6c48-4521-a1ad-480e593e4835&LanguageId=1&PressReleaseId=96eefbb4-9716-431e-b4b2-67f58281eb5e> [<https://perma.cc/VSA5-URJM>].

251. Jennifer Abbasi, *Zika Vaccine Enters Clinical Trials*, 316 JAMA 1249 (2016). A second group of vaccines is currently in the late stages of preclinical development, with phase I clinical trials expected to have begun in the second half of 2017: the live dengue vaccine that Brazil's Butantan Institute licensed from NIAID; the Moderna/BARDA mRNA vaccine; and the inactivated vaccine developed by Indian pharmaceutical giant Bharat. GLOPID-R, *supra* note 248, at 1–2. At least eight other vaccine candidates currently in late preclinical development were expected to begin phase I trials in late 2017. *Id.* at 2.

252. Since the early stages of the Zika vaccine race, the NIH has also funded the development of two other non-DNA vaccines, in partnership with the National Institute of Allergy and Infectious Diseases, *see* Table 2. The NIH has also been part of a second Zika vaccine partnership, the one led by the Walter Reed Army Institute of Research. *Id.*

253. Inactivated vaccines use killed viruses or bacteria to stimulate weakened immune responses from the organism. Examples include the vaccines for hepatitis A, influenza, polio, cholera, and rabies. For other examples, *see* CENTERS FOR DISEASE CONTROL & PREVENTION, U.S. VACCINES (2017), <https://www.cdc.gov/vaccines/pubs/pinkbook/downloads/appendices/B/us-vaccines.pdf> [<https://perma.cc/9JAR-THEY>].

254. *See Different Types of Vaccines*, THE HISTORY OF VACCINES, <https://www.historyofvaccines.org/content/articles/different-types-vaccines> [<https://perma.cc/K9X5-63AZ>].

255. *See, e.g.*, Richard Harris, *Testing Begins on an Experimental Zika Vaccine With Inactivated Virus*, NPR (Nov. 7, 2016, 12:15 PM), <https://www.npr.org/sections/health-shots/2016/11/07/501015866/testing-begins-on-an-experimental-zika-vaccine-with-inactivated-virus>. DNA vaccines rely on technology that is much more recent than vaccine inactivation, which dates to the early 1990s. An injection of DNA plasmid is used to trigger a strong immune response from an organism. *See* De-chu Tang et al., *Genetic Immunization Is a Simple Method for Eliciting an Immune Response*, 356 NATURE 152 (1992); Jeffrey B. Ulmer et al.,

2000s, the NIH funded R&D on DNA vaccines, including one that targeted West Nile, a flavivirus like Zika.<sup>256</sup> Early results were promising, but no pharmaceutical company showed interest in the vaccine.<sup>257</sup> Adding to this—a feature inherent to non-mainstream diseases, as discussed in Part I—further research has also raised questions surrounding the efficacy of DNA vaccines.<sup>258</sup> For this reason, although there are DNA vaccines for animals on the market,<sup>259</sup> no DNA vaccine for use in humans has ever been approved by the Food and Drug Administration (FDA).<sup>260</sup>

Yet the results from early clinical trials of the NIH-sponsored Zika DNA vaccine appear promising.<sup>261</sup> Regardless of final outcomes concerning this particular vaccine, the race prompted by the 2015–16 outbreak has not only contributed to Zika-specific R&D, but it has also increased knowledge of DNA vaccine platforms in a significant way.

While there is great buzz surrounding Zika DNA vaccines, inactivated vaccines remain the prevalent approach in the global race. The Army's frontrunner (ZPIV vaccine) is perhaps the best embodiment of how a change in the incentives landscape impacts R&D timelines. The Army decided to develop

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*Heterologous Protection Against Influenza by Injection of DNA Encoding a Viral Protein*, 259 SCIENCE 1745 (1993); see also John J. Donnelly et al., *DNA Vaccines: Progress and Challenges*, 175 J. IMMUNOLOGY 633 (2005); Bernadette Ferraro et al., *Clinical Applications of DNA Vaccines: Current Progress*, 53 CLINICAL INFECTIOUS DISEASES 296 (2011) (describing current research on how plasmid DNA triggers immune responses). In addition to DNA plasmid, ongoing research also suggests that RNA and other molecules might be used in future vaccines. See *DNA Vaccines*, WORLD HEALTH ORG., <http://www.who.int/biologicals/areas/vaccines/dna/en> [<https://perma.cc/2NMP-AF5G>].

256. See Julie E. Martin et al., *A West Nile Virus DNA Vaccine Induces Neutralizing Antibody in Healthy Adults During a Phase 1 Clinical Trial*, 196 J. INFECTIOUS DISEASES 1732 (2007); see also Kendall Powell, *DNA Vaccines—Back in the Saddle Again?*, 22 NATURE BIOTECH. 799 (2004) (describing current challenges surrounding DNA-based vaccines).
257. Katie Thomas, *The Race for a Zika Vaccine*, N.Y. TIMES (Nov. 19, 2016), <https://www.nytimes.com/2016/11/20/business/testing-the-limits-of-biotech-in-the-race-for-a-zika-vaccine.html>.
258. See, e.g., Tom-Ole Løvås et al., *DNA Vaccines: MHC II-Targeted Vaccine Protein Produced by Transfected Muscle Fibres Induces a Local Inflammatory Cell Infiltrate in Mice*, 9 PLOS ONE 1 (2014).
259. See Michele A. Kutzler & David B. Weiner, *DNA Vaccines: Ready for Prime Time?*, 9 NATURE REV. GENETICS 776 (2008).
260. See *Guidance for Industry: Considerations for Plasmid DNA Vaccines for Infectious Disease Indications*, FDA, <https://www.fda.gov/biologicsbloodvaccines/guidancecomplianceregulatoryinformation/guidances/vaccines/ucm074770.htm> [<https://perma.cc/XT2L-QTP3>] (last updated June 17, 2015).
261. Jennifer Govero et al., *Zika Virus Infection Damages the Testes in Mice*, 540 NATURE 438, 438 (2016).

a Zika vaccine in January 2016.<sup>262</sup> Scientists resorted to cell-based technology that had already been used by the Army to develop a vaccine for Japanese encephalitis (also a flavivirus) in 2009.<sup>263</sup> The first experiments began in April, with results submitted to *Nature* magazine in May and published in June.<sup>264</sup> Clinical trials for ZPIV began in November 2016, less than a year after the Army entered the Zika race.<sup>265</sup>

With vaccine development taking an average of eight to twelve years, the timeline of ZPIV illustrates how certain catalytic events (in this case, a transnational outbreak) override the market-based dynamics that IP introduces into scientific R&D. Adding to that, the borrowing of existing technology to speed up R&D in the flavivirus family contributes to other R&D areas—for instance, intra-genus R&D through reuse and adaptation of existing vaccine platforms or similar technology. This approach constitutes a relatively inexpensive way of increasing vaccine R&D in general and may result in the unearthing of potential vaccine candidates for use in future, unpredictable outbreaks.

But the technology-borrowing that took place at the Army also reinforces the idea that the perverse effects of IP incentives have delayed the existence of the first Zika vaccine. If it is indeed possible to develop a safe and effective vaccine in such a short span of time and by resorting to known technology, then before the outbreak, Zika must already have been low-hanging fruit. That no one bridged that gap—in the same way that the West Nile vaccine candidate failed to attract commercial attention a few years before Zika—underscores the idea of a general lack of “R&D preparedness” for outbreak diseases.<sup>266</sup>

From a public health perspective, the WHO now considers Zika to be a “chronic threat,” framing the disease in a similar way it frames malaria.<sup>267</sup> As

262. Annette M. Boyle, *Army Research Produces Zika Vaccine Candidate in Record Time*, U.S. MED. (Aug. 2016), <http://www.usmedicine.com/agencies/departments-of-defense-dod/army-research-produces-zika-vaccine-candidate-in-record-time> [https://perma.cc/SM8K-25Q5].

263. NAT'L INST. HEALTH, *supra* note 155.

264. Rafael A. Larocca et al., *Vaccine Protection Against Zika Virus From Brazil*, 536 NATURE 474 (2016).

265. *Zika Virus Purified Inactivated Vaccine (ZPIV) Accelerated Vaccination Schedule Study (Z001)*, U.S. NAT'L LIBR. OF MED., <https://clinicaltrials.gov/ct2/show/NCT02937233> [https://perma.cc/5VU7-AP2M] (last updated Sept. 29, 2017); see also Kathleen Curthoys, *Human Testing Begins on Zika Virus Vaccine Developed by the Army*, ARMYTIMES (Nov. 8, 2016), <https://www.armytimes.com/news/your-army/2016/11/08/human-testing-begins-on-zika-virus-vaccine-developed-by-the-army> [https://perma.cc/EVN4-RGXX].

266. R&D BLUEPRINT, *supra* note 7, at 6.

267. See Fifth Meeting of the Emergency Regarding Zika Virus, WORLD HEALTH ORG. (Nov. 18, 2016), <http://www.who.int/mediacentre/news/statements/2016/zika-fifth-ec/en> [https://perma.cc/VNY3-H68G].

the Organization points out, “[m]any aspects of this disease and associated consequences still remain to be understood, but this can best be done through sustained research.”<sup>268</sup> Yet, even now that the association between Zika and severe neurological and congenital defects is known, the virus will likely continue to be perceived as less harmful than Ebola.<sup>269</sup> Zika is also unlikely to benefit from the extra layer of R&D incentives that attach to Ebola by virtue of its having been deemed a material threat to national security.<sup>270</sup>

Even with Zika R&D making remarkable progress, there are further problems to consider. Of course, expedited Zika R&D (as is the case with Ebola) is of no avail to patients affected by the 2015–16 outbreak, or until a safe and effective vaccine enters the market. But the availability of a Zika vaccine is still not enough to ensure that future patients will be able to benefit from it.<sup>271</sup> In exchange for an R&D challenge that is met, the patent bargain rewards the innovator with market exclusivity, opening the door for commercialization of the invention in monopoly-like conditions. IP that emerges from outbreak-induced R&D is subject to the same rules that apply to other inventions. In the case of Zika—even though the vaccine-race timeline indicates that IP alone failed to incentivize R&D—currently emerging post-outbreak vaccine technology is patent-protected. In at least one case,<sup>272</sup> the initial developer of a Zika vaccine considered licensing it to a private-sector pharmaceutical company under an exclusive agreement,<sup>273</sup> a decision that raises questions about the affordability of vaccines for future target populations. I address these issues, which embody a different type of IP-related inefficiency,<sup>274</sup> in Part II.

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268. *Id.*

269. See Daniel R. Lucey & Lawrence O. Gostin, *The Emerging Zika Pandemic: Enhancing Preparedness*, 315 JAMA 865, 866 (2016) (contrasting the transregional magnitude of the 2015 Zika outbreak with previous outbreaks); Barrett, *supra* note 224 (noting that the smaller scale and impact of pre-2015 outbreaks caused the Zika virus not to be perceived as a major pathogen).

270. PHEMCE, *supra* note 123.

271. *Infra* Subpart II.C.

272. The Army’s ZPIV vaccine, described in Subpart I.C.2.a.

273. The Army is in the process of licensing ZPIV to French pharmaceutical company Sanofi. *Infra* Subpart II.C.

274. For purposes of this Article, IP inefficiencies arising after an outbreak and spikes in R&D incentives are grouped together under what I have called “transactional IP inefficiencies.” *Infra* Subpart II.A.

## II. INEFFICIENCIES AND LACK OF IP PREPAREDNESS AFTER AN OUTBREAK STARTS

### A. Transactional IP Inefficiencies

So far, the Article has addressed the problem of IP qua incentives to R&D in the context of outbreak diseases. As the cases of Ebola and Zika illustrate, large-scale outbreaks temporarily heighten incentives to R&D, igniting a race for the development of vaccines funded through a realignment of private, public, and public-private players to support the development of new vaccines.

However, the overall impact of IP on outbreak diseases is broader than the domain of incentives. For pathogens on which there has been a modicum of pre-outbreak R&D, it is likely that technology protectable by IP rights will have emerged before the start of an outbreak. Recall for instance the Ebola vaccine developed in Canada (rVSV-ZEBOV), which was protected by patent rights a full decade before the beginning of the 2014–16 outbreak.<sup>275</sup> While a significant amount of pre-outbreak R&D is conducted at government level—as was the case for several Ebola and Zika vaccine candidates—it is not uncommon to see the resulting IP migrate elsewhere (or be shared with additional partners) as soon as enhanced funding streams open up. Governmental research institutions remain the default locus for R&D in under-incentivized areas, but private entities often appear during the phases of clinical trials, large-scale vaccine manufacturing, and obtainment of regulatory approval. When transfers of preexisting IP occur—and especially in cases where a private company takes over the R&D process rather than partnering with a research institution—it is desirable that IP rights change hands as quickly as possible. With outbreak-spiked funding being necessarily short-lived, a delay in transfers of IP rights after an outbreak starts constitutes another form of inefficiency that impacts not only R&D timelines, but also preparedness for future outbreaks.

Even in the case of pathogens for which there are virtually no pre-outbreak R&D, like Zika, transfers of IP rights during the final stages of vaccine R&D may still produce detrimental effects at yet another level. Consider now the vaccine developed by the Army in the wake of the 2015–16 Zika outbreak. In 2017, the Army licensed its vaccine candidate (ZPIV) to a French pharmaceutical company, a process that drew much criticism due to its opacity and to the lack of provisions dealing with affordability issues, as described in

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275. Can. Patent No. WO 2004/011488 A2, *supra* note 132.

greater detail below.<sup>276</sup> If IP that emerges from new R&D is licensed in a way that exacerbates the monopoly-like qualities of the patent bargain, it is possible that vaccines end up being made available at higher costs than needed, thus pricing out<sup>277</sup> certain segments of the population who cannot afford them.<sup>278</sup> IP preparedness entails anticipating this scenario and making sure *ex ante* that licensing agreements contain provisions guaranteeing affordability of vaccines.

These types of IP inefficiencies, termed here “transactional” for descriptive purposes, are distinguishable from the ones covered in Part I. Transactional inefficiencies embody a malfunction that occurs during the transfer of IP rights. From a temporal viewpoint, these inefficiencies occur after an outbreak erupts, as opposed to incentives inefficiencies, which characterize the pre-outbreak phase.

However, even though transactional inefficiencies impact transfers of IP that take place after an outbreak begins, they also differ among themselves. The first group of transactional inefficiencies—illustrated below through an Ebola case study—encompasses problems with the transfer of preexisting IP rights during the early stages of an outbreak.<sup>279</sup> In contrast, the second group—illustrated below through a Zika case study—refers to the transfer of emerging IP rights after an outbreak is over (or possibly during its very late stages). The following Parts address these subtypes of transactional inefficiencies in turn.

## **B. Lack of IP Preparedness in the Early Stages of an Outbreak**

As discussed with respect to the role of IP as an incentives mechanism, some degree of inefficiency is expected as a byproduct of the patent bargain, which gives patent holders strong control over their exclusive rights.<sup>280</sup> While

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276. *Infra* Subpart II.C.

277. This is an embodiment of the phenomenon of deadweight loss described in Part I. See Shavell & van Ypersele, *supra* note 90 and accompanying text.

278. As further detailed below, an additional concern arises in the case of vaccines developed by government research institutions and then licensed to private companies, as happened with ZPIV. In this scenario, if the pharmaceutical company licensed to sell the vaccine is left unchecked and charges profit-maximizing prices, consumers, who have already funded governmental R&D through taxes, will now pay a second time for the same good—now subsidizing a private company. See *infra* Subpart II.B.

279. *Infra* Subpart III.A.

280. *Supra* notes 90–91 and accompanying text.

not unlimited,<sup>281</sup> this control may be exerted in ways that disproportionately lower social welfare.

During the early stages of an outbreak, lack of IP preparedness is tied to transactional inefficiencies affecting the transfer of preexisting technology. With funding streams opening up once the outbreak begins, preexisting technology might be needed to expedite the R&D of vaccine candidates. The transfer of this technology, however, might not occur as speedily as necessary. The following case study on the transfer of patented Ebola technology shortly after the beginning of the Ebola outbreak illustrates this scenario. The case study focuses on the leading Ebola vaccine candidate (rVSV-ZEBOV), which was mapped in greater detail in Part I.<sup>282</sup>

Broadly speaking, negotiations surrounding the preexisting IP needed for outbreak-induced R&D on Ebola vaccine candidates proceeded at an unusually fast pace. In fact, more than one vaccine candidate was pushed through the R&D pipeline before all IP licensing provisions were agreed upon (as well as some other contractual provisions).<sup>283</sup> But there was one significant exception to the expedited model. This case involved NewLink Genetics, the small<sup>284</sup> Iowa-based pharmaceutical company that had acquired the IP of the rVSV-ZEBOV vaccine from the Canadian government in 2011.<sup>285</sup>

Even before the outbreak, rVSV-ZEBOV was considered one of the “most-promising strategies” in Ebola R&D.<sup>286</sup> NewLink, however, did not move the vaccine through its pipeline for years.<sup>287</sup> When the 2014–16 outbreak began and incentives for Ebola R&D spiked, the company finally turned its attention to rVSV-ZEBOV.<sup>288</sup> However, it soon became apparent that NewLink lacked the resources to manufacture the vaccine.<sup>289</sup> Even in the face of mounting scrutiny and a growing public health crisis, NewLink delayed

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281. See, e.g., 35 U.S.C. § 209(a) (2012) (subjecting the licensing of federally owned inventions to certain criteria that take into account the public interest).

282. *Supra* Figure 1.

283. See Julia Barnes-Weise & Ana Santos Rutschman, *Ebola and the Accidental Consortia*, HUFFINGTON POST (Apr. 7, 2015, 2:01 PM), [http://www.huffingtonpost.com/julia-barnesweise/post\\_9271\\_b\\_7019058.html](http://www.huffingtonpost.com/julia-barnesweise/post_9271_b_7019058.html) [https://perma.cc/2KQU-EJEW].

284. To this day, NewLink’s footprint remains discreet. See NEWLINK GENETICS, *supra* note 139 and accompanying text.

285. *Id.*

286. Andrea Marzi et al., *Vesicular Stomatitis Virus-Based Ebola Vaccines With Improved Cross-Protective Efficacy*, 204 J. INFECTIOUS DISEASES 1066, 1067 (2011).

287. See *supra* note 142 and accompanying text.

288. From the beginning of the licensing agreement, it took seventeen quarters for the vaccine to enter clinical trials. See Amir Attaran & Jason W. Nickerson, *Is Canada Patent Deal Obstructing Ebola Vaccine Development?*, 384 LANCET S61, S61 (2014).

289. *Id.*

licensing of rVSV-ZEBOV.<sup>290</sup> Although back-traced to late 2013, by March 2014 the outbreak was a matter of international concern.<sup>291</sup> A Public Health Emergency was declared in August.<sup>292</sup> It was not until November—at this point under pressure from the WHO, among others—that NewLink entered into its licensing agreement with one of the world’s largest pharmaceutical companies, Merck.<sup>293</sup> The latter rushed manufacturing of the vaccine, and started clinical trials for rVSV-ZEBOV shortly thereafter.<sup>294</sup>

Having originally acquired the rights to rVSV-ZEBOV for U.S. \$205,000, NewLink received U.S. \$30 million for transferring IP rights to Merck, with an additional U.S. \$20 million due at the beginning of clinical trials.<sup>295</sup> If rVSV-ZEBOV gains regulatory approval and is commercialized, NewLink will also be entitled to additional royalties. These amounts constitute a patent-enabled windfall, as NewLink did not contribute to innovative R&D—or to any type of R&D, for that matter. By taking advantage of its position as the rights holder of a happenstance portfolio, it circumvented the patent bargain through parasitic exploitation of IP rights on technology developed by the public sector.<sup>296</sup> Moreover, Merck succeeded in starting clinical trials in under two months after obtaining a license for rVSV-ZEBOV. In this context, NewLink’s nonworking of the patent, coupled with the refusal to license the vaccine for a period of over three months, is likely to have delayed the beginning of clinical trials for the leading vaccine candidate during a severe public health crisis.

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290. *Id.*

291. The Institut Pasteur in Lyon was the first entity to identify the virus as belonging to the Ebola family, on March 21, 2014. See WORLD HEALTH ORG., Origins of the 2014 Ebola Epidemic, <http://www.who.int/csr/disease/ebola/one-year-report/virus-origin/en>.

292. See WORLD HEALTH ORG., *supra* note 159 and accompanying text.

293. See Helen Braswell, *Canadian-Made Ebola Vaccine Gets Help From Merck*, TORONTO STAR (Nov. 24, 2014), [https://www.thestar.com/business/2014/11/24/canadianmade\\_ebola\\_vaccine\\_gets\\_help\\_from\\_merck.html](https://www.thestar.com/business/2014/11/24/canadianmade_ebola_vaccine_gets_help_from_merck.html) [<https://perma.cc/T6VY-X7TB>]; Elizabeth Payne, *The Story of ‘the Canadian Vaccine’ That Beat Back Ebola*, OTTAWA CITIZEN (Sept. 2, 2016, 5:11 PM), <http://ottawacitizen.com/news/national/the-canadian-vaccine-how-scientists-in-a-country-without-a-single-case-of-ebola-wrestle-the-deadly-disease-to-the-ground>.

294. See J.A. Regules et al., *A Recombinant Vesicular Stomatitis Virus Ebola Vaccine*, 376 NEW ENG. J. MED. 330, 333 (2017).

295. Lisa Schnirring, *NewLink, Merck Deal Boosts Prospects for Ebola Vaccine*, CIDRAP (Nov. 24, 2014), <http://www.cidrap.umn.edu/news-perspective/2014/11/newlink-merck-deal-boosts-prospects-ebola-vaccine> [<https://perma.cc/4U9R-C3V6>].

296. It can be argued that NewLink acquired the rights at market value before the outbreak altered the incentives landscape (and consequentially altered the market value for the technology in question). Nonetheless, the patent bargain rewards innovation and, in this case, the one entity that did not contribute any innovative R&D was (1) over-rewarded and (2) used the patent in a way that hindered expedited R&D during a period of public health crisis.



NewLink's behavior illustrates a different type of IP-related inefficiency, now in the form of a hold-up in the transfer of technology during the early stages of an outbreak. To be sure, this was the only case in which an entity hindered the transfer of IP during this outbreak (and in its immediate aftermath). However, what happened with NewLink fits squarely into the general mold of outbreak-disease R&D and is therefore replicable. As seen above, basic R&D is very often conducted by the public sector during the pre-outbreak period. The resulting IP is relatively cheap due to the underlying market failure, making it affordable to small private-sector companies. While many small biopharmaceutical companies do engage in innovative R&D (for example, as Okairos did before the outbreak),<sup>297</sup> others might either lack the capacity to develop the technology or choose to wait for a catalyst that will raise the value of the corresponding IP. A scenario in which the NewLink hold-up repeats itself is not only possible, it is also logical from the perspective of an agent seeking to maximize the economic efficiency of a patent portfolio.

In Part III, I propose a novel mechanism to counter this type of transactional inefficiency in future outbreaks—a dormant license (enabling transfer of IP) that becomes active as soon as a formal declaration of public health emergency or crisis is issued. Part III also explores the positive dimensions of IP negotiations that effectively sped up Ebola R&D during the early stages of the outbreak. Namely, it proposes the creation of streamlined agreement frameworks that could be used to expedite the negotiation of provisions governing transfers of IP rights in situations of public health emergency.<sup>298</sup>

### C. Lack of IP Preparedness in Post-Outbreak Period

During the early stages of an outbreak, the most significant issue with rights transfers is the potential for IP hold-up involving preexisting technology, but in the late- and post-outbreak periods, the problem shifts altogether. Now, the concern centers around IP transfers of late-stage technology emerging from outbreak R&D. In this situation, the problem is not one of timing or maximization of funding, but rather of impact of IP licensing on public health. The commercialization of biopharmaceutical innovation in conditions that over-reward the rights holder, allowable up to a certain point under domestic patent law,<sup>299</sup> may lead to socially undesirable deadweight loss.<sup>300</sup>

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297. See GLAXOSMITHKLINE, *supra* note 208 and accompanying text.

298. *Infra*, Subpart III.C.

299. However, as further detailed below, 35 U.S.C. § 201(f) (2012) and 35 U.S.C. § 209(a)–(e) (2012) pose some limits to the scope of patent rights in this context.

The most up-to-date case in point—and perhaps the most significant case in the history of vaccine licensing—has recently emerged in the context of the Zika vaccine race. Throughout 2018 and 2019, several vaccine candidates are expected to approach the later stages of R&D.<sup>301</sup> As seen above, the initial leading candidate was ZPIV, the vaccine developed by the U.S. Army.<sup>302</sup> In December 2016, the Army announced the intent to license the vaccine, on which two patent applications were pending, to French pharmaceutical company Sanofi.<sup>303</sup> The full notice of intent reads as follows:

The Department of the Army hereby gives notice of its intent to grant an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/343,315, entitled, “Zika Virus Vaccine and Methods of Production” filed May 31, 2016 and an exclusive, royalty-bearing, revocable license to pending United States Provisional Patent Application 62/370,260, entitled, “Zika Vaccine and Methods of Preparation” filed August 3, 2016 to Sanofi Pasteur, Inc., having its principal place of business at 1 Discovery Drive, Swiftwater, PA 18370.<sup>304</sup>

The notice presents two problems. The first is the opacity: It does not disclose a single term of the licensing agreement beyond exclusivity. The second is exclusivity itself.

As far as opacity is concerned, the notice formally complies with the requirements set forth in the Patent Act for the licensing of federally funded inventions.<sup>305</sup> But the lack of substantive information regarding the terms of the license is troubling from a public policy perspective, especially given the nature of the invention that is being licensed. This has prompted nongovernmental organization Knowledge Ecology International (KEI) to file comments asking the Army: “Whose interests are served by the lack of transparency: the large French drug and vaccine manufacturer Sanofi, or the

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300. This deadweight loss takes the form of would-be consumers who cannot afford the vaccine.

301. *Supra* Table 2. See also Helen Branswell, *As Foreign Powers Approve Ebola Vaccines, U.S. Drug Makers Lag in Development Pipeline*, STAT (Dec. 8, 2017), <https://www.statnews.com/2017/12/08/ebola-vaccine-development> [<https://perma.cc/65F5-W4X4>].

302. See Pellerin, *supra* note 229.

303. Intent to Grant an Exclusive License of U.S. Government-Owned Patents Notice, 81 FED. REG. 89,087 (Dec. 9, 2016).

304. *Id.*

305. 35 U.S.C. § 209(e) (2012).

U.S. taxpayers and residents who pay for the Army's research budget, and will have to pay if the vaccine is approved by the FDA?"<sup>306</sup>

The second half of the question raised by KEI ties into the problems raised by the exclusivity of the license. To better understand these, it is helpful to take a closer look at the development of the vaccine as it approached phase II clinical trials in mid-2016. While most of the development of the vaccine was carried out by the Army,<sup>307</sup> Sanofi was brought onboard in July 2016 to help with manufacturing and to push the vaccine into phase II development.<sup>308</sup> That September, BARDA awarded Sanofi a U.S. \$43 million contract to fund the manufacture of the vaccine, to which U.S. \$130 million would be added if phase II results are promising.<sup>309</sup> Federal funding has therefore supported early R&D on the vaccine (through the Army) and mid-stage R&D (through Sanofi).

Federally funded inventions, which since 1980 are eligible for patent protection under the regime established by the Bayh-Dole Act,<sup>310</sup> raise nuanced questions when it comes to reaping the economic benefits associated with patent exclusivity. On the one hand, public-sector funding puts taxpayers' money to use in curing a market failure, which in cases like vaccine development can negatively impact public health. On the other hand, while the public sector plays a crucial role in jumpstarting early-stage R&D on underfunded goods, it often lacks the capacity to transform those goods into end-products. At this stage, the entrance of a private-sector party into the R&D process is common, especially in the biopharmaceutical arena. This is not an undesirable prospect if it ensures that the invention will enter the market and consumers will be able to benefit from it.

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306. KEI Comments RE Army Intent to Grant Exclusive License, KNOWLEDGE ECOLOGY INT'L (Mar. 10, 2017), [http://keionline.org/sites/default/files/KEI-March\\_10\\_2017-3rd-Comments-Zika.pdf](http://keionline.org/sites/default/files/KEI-March_10_2017-3rd-Comments-Zika.pdf) [<https://perma.cc/EU3W-BEB2>] (noting that the Army was unresponsive to requests for additional information concerning the terms of the proposed license).

307. In partnership with NIAID. See *supra* Table 2.

308. Press Release, Sanofi Pasteur, BARDA Grants \$43.2 Million USD to Sanofi Pasteur for Zika (Sept. 26, 2016), <http://www.news.sanofi.us/press-releases?item=137143> [<https://perma.cc/H9XG-Y4YL>].

309. See *Timeline of U.S. Army & Sanofi Zika Vaccine Collaboration*, KNOWLEDGE ECOLOGY INT'L, <https://www.keionline.org/book/government-funded-inventions/zika-resources-on-2016-2017-army-exclusive-patent-license-to-sanofi/timeline-of-u-s-army-sanofi-zika-vaccine-collaboration> [<https://perma.cc/2U8U-8S33>].

310. Pub. L. No. 96-517, § 6(a), 94 Stat. 3018, 3019–28 (1980) (codified as amended at 35 U.S.C. §§ 200–212 (1994)). While allowing for the patentability of research supported by federal funding, the Act established a limited number of accountability mechanisms. See Arti K. Rai & Bhaven N. Sampat, *Accountability in Patenting of Federally Funded Research*, 30 NATURE BIOTECH. 953, 954–56 (2012). See also text accompanying notes 312–15.

In the case of the Army's Zika vaccine candidate, federal funds were used to support both the work done by the Army and the complementary work done by a large pharmaceutical company. Sanofi has therefore received a financial incentive in exchange for its participation in the R&D process. When patent exclusivity is added to that set of incentives, it might lead to a situation of over-rewarding. In the context of transfer of rights, an exclusive license constitutes the strongest form of control over the market for the protected good. It prevents competition, which in turn is likely to drive prices up and cause deadweight loss. When these inefficiencies affect goods like vaccines (which many have argued should be considered global public goods for health),<sup>311</sup> an especially careful assessment of the impact of exclusivity must be made. If exclusivity is granted, but not needed, at the very least we are in a scenario of bad innovation policy. Senator Sanders, writing in a *New York Times* editorial, colorfully summarized the situation:

A Zika vaccine would be a tremendous scientific advancement and could prevent birth defects, including severe congenital brain damage, in countless children around the world. American soldiers serving in Zika-prone areas need it. American consumers should not be forced to pay the highest price in the world for a vaccine we paid to help develop. A failure by the government to demand fair prices from Sanofi in exchange for giving the company a monopoly would be only one more example of the broader insanity around American drug prices.<sup>312</sup>

Though per Bayh-Dole rules the Army is entitled to apply for a patent on a federally funded vaccine, the terms under which it can license the corresponding patent(s) are not unrestricted. Federal law establishes that a federally funded invention can only be licensed if exclusivity constitutes a "reasonable and necessary incentive" to fund late-stage R&D and bring the invention to the market, or promote public access to the invention in a similar form.<sup>313</sup> If a license is granted on an exclusive basis, then the public-sector entity has to make sure that "the proposed scope of exclusivity is not greater than reasonably necessary to provide the incentive for bringing the invention to practical application"<sup>314</sup> and that "granting the license will not tend to

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311. See generally WORKING GROUP 2 OF THE COMM'N ON MACROECONOMICS AND HEALTH, WORLD HEALTH ORG., GLOBAL PUBLIC GOODS FOR HEALTH (2002).

312. See Sanders, *supra* note 31.

313. 35 U.S.C. § 209(a)(1) (2012).

314. *Id.* § 209(a)(2).

substantially lessen competition.”<sup>315</sup> Additional conditions, like first preference for small businesses, apply to both exclusive and nonexclusive licenses.<sup>316</sup>

Due to the opacity of the notice given by the Army, it is obviously impossible to make concrete determinations as to whether the exclusive license over the ZPIV vaccine satisfies these requirements. However, the cumulative financial incentives that Sanofi stands to gain from obtaining an exclusive license, in addition to the BARDA funding, raise significant doubts on at least two points: the need for an exclusive license (*vis-à-vis* a nonexclusive license) to incentivize late-stage R&D and bring the vaccine to market; and the impact of the exclusivity on the affordability of the vaccine. Overall, the Patent Act mandates that federally funded goods be available to the public “on reasonable terms”<sup>317</sup> and it is at least questionable whether putting Sanofi in a monopoly-like position achieves this goal.

In August 2017, BARDA suspended funding for Zika R&D, choosing to focus its resources exclusively on surveillance of the disease.<sup>318</sup> Shortly thereafter, Sanofi announced that it would stop developing the vaccine.<sup>319</sup> Now that the Army’s only private-sector partner in this venture has pulled out due to funding cuts, R&D on the most promising Zika vaccine candidate has stopped. Had the Army chosen to work with multiple licensees, there would be a possibility that one of them would be able to carry on the work, albeit at slower speed. With a considerable amount of innovation today taking place outside big pharma, within small or specialized startup companies, this prospect is not far-fetched.

If it turns out that the Army-Sanofi deal would have violated the statutory restrictions on licensing of federally funded inventions, then the patent system—which failed to provide pre-outbreak incentives to Zika R&D—would have failed again in over-rewarding the rights holder in a way that is detrimental to public health.

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315. *Id.* § 209(a)(4).

316. *Id.* § 209(c).

317. 35 U.S.C. § 201(f) (1994).

318. See Press Release, Sanofi Pasteur, Sanofi Statement on Zika Vaccine License (Sept. 1, 2017), <http://www.news.sanofi.us/Sanofi-Statement-on-Zika-Vaccine-License> [<https://perma.cc/XC4Z-L7QR>].

319. *Id.*

### III. IMPROVING IP PREPAREDNESS FOR FUTURE OUTBREAKS

#### A. IP Preparedness for Future Outbreak Diseases

There is broad consensus that we are not prepared for future outbreaks.<sup>320</sup> Although the global health community expects certain pathogens to emerge in the near future, others lurk dormant, or even undiscovered.

The back-to-back outbreaks of 2014–16 improved scientific knowledge of Ebola and Zika. R&D strides in both fields are expected to translate into the first commercially available vaccines for both diseases.<sup>321</sup> New diagnostics, therapies, and vector-control methods are also under development and may contribute to preventing or minimizing future outbreaks.<sup>322</sup> Nevertheless, even in these fields—which attracted substantial amounts of attention and funding—experts believe that we are ill-prepared to deal with resurgences of the viruses. Most prominently, this argument has been made with reference to Ebola, where sustained R&D is needed for years to come but has already begun to decrease noticeably.<sup>323</sup> As one expert<sup>324</sup> put it in January 2017, shortly after the publication of promising clinical-trial results on Ebola vaccines candidates, “I can’t say that all the momentum has been lost. But it’s pretty hard to run a semi-truck on a lawnmower motor. There’s not enough push and pull right now. Things are happening in more of what I’d call a routine matter of trying to follow through on this.”<sup>325</sup>

Zika R&D is also beginning to contend with post-outbreak challenges, including the lack of patient populations in which to test vaccine candidates,<sup>326</sup>

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320. See *Fail to Prepare No More*, 2 NATURE MICROBIOLOGY 1 (2017) (noting some strides in increasing preparedness for upcoming outbreaks); Bill Gates, *The Next Outbreak? We’re Not Ready* (Mar. 2015), [https://www.ted.com/talks/bill\\_gates\\_the\\_next\\_disaster\\_we\\_re\\_not\\_ready](https://www.ted.com/talks/bill_gates_the_next_disaster_we_re_not_ready) [<https://perma.cc/E9UJ-QD5V>].

321. See, e.g., Jamey Keaten, *Final Test Results Confirm Ebola Vaccine Highly Effective*, AP NEWS (Dec. 23, 2016), <https://apnews.com/4c64ebfd92a8411a9390633d156bd36c> [<https://perma.cc/W52J-KAMG>].

322. WORLD HEALTH ORG., *supra* note 227.

323. See CIDRAP, *supra* note 9; Branswell, *supra* note 9.

324. Michael Osterholm is the director of the Center for Infectious Diseases Research and Policy (CIDRAP) at the University of Minnesota, which has funded research about successes and failures surrounding the development of the Ebola vaccine candidates.

325. See Branswell, *supra* note 9.

326. See Carmen Heredia Rodriguez, *To Test Zika Vaccines, Scientists Need a New Outbreak*, NPR (Feb. 23, 2017, 12:43 PM), <https://www.npr.org/sections/health-shots/2017/02/23/516822252/to-test-zika-vaccines-scientists-need-a-new-outbreak>.

while licensing of some of these candidates raises questions about the affordability of approved vaccines.<sup>327</sup>

Creating better networks around Ebola, Zika, and outbreak diseases in general depends on combined efforts from many disciplines, among which IP plays an important part. Drawing on lessons from different aspects of two case studies, this Article makes the case for a comprehensive understanding of the multidimensional effects of IP on the way we address outbreak diseases. Moving toward a comprehensive framework entails considering all forms of IP inefficiencies as interconnected aspects of a large-scale problem.

The premise of IP preparedness is that dissociating incentives from other aspects of the IP cycle not only leads to an incomplete view of outbreak-disease R&D, but it is also fundamentally detrimental to our innovation policy. If we focus solely on correcting incentives-based market failures, we may be able to generate higher levels of R&D—and in that sense cure or mitigate the market failure. But access to any emerging innovation may be undermined if the patent bargain runs its course in a way that over-rewards IP-rights holders. If innovators or their licensees are able to commercialize drugs and vaccines in a way that generates significant deadweight loss, they create a new market failure—by using the means devised to respond to the initial market failure. Both scenarios are detrimental to innovation policy for outbreak diseases. Similarly, we should not miss the opportunity to leverage successful natural experiments—such as the negotiation model for preexisting IP adopted by most parties during the early stages of Ebola R&D—and test their adaptability to future outbreaks.

Applying this idea of IP preparedness, the following Subparts survey existing mechanisms that can be employed to address the different types of inefficiencies faced by outbreak diseases, building on the positive lessons from Ebola and Zika (particularly at the level of transactional IP). Additionally, they propose a new mechanism to deal with an inefficiency (hold-up of preexisting IP) that is especially detrimental in the context of outbreak diseases.

## **B. IP Preparedness in Pre- and Inter-Outbreak Periods**

Incentives to outbreak-disease R&D are not entirely lacking. As seen in Part I, top-tier diseases benefit from small-scale networks of support that result in sustained (albeit suboptimal) levels of funding. An example already mentioned is malaria, for which funding ranged consistently from just shy of

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327. See generally *supra* Subpart II.C.

U.S. \$500 million in 2007 to U.S. \$565 million in 2015,<sup>328</sup> amounts that represent a four-fold increase from 1993 levels.<sup>329</sup> Funding for malaria R&D was largely bolstered by three funders: the Bill & Melinda Gates Foundation (the largest funder) and the public sectors in the United States and the European Union.<sup>330</sup> In addition to, and benefiting from, these funding streams, several partnerships have populated R&D in this field. Some are ad hoc product-development partnerships or nonprofits, like the Medicines for Malaria Venture<sup>331</sup> and the Roll Back Malaria Partnership.<sup>332</sup> Others are subprojects within larger organizations engaged in small-scale product development, like the nonprofit Foundation for Innovative New Diagnostics (FIND), which focuses on six different types of underfunded diseases;<sup>333</sup> the Innovative Vector Control Consortium (IVCC), a product-development partnership that focuses a significant amount of its resources on malaria;<sup>334</sup> the Drugs for Neglected Diseases Initiative (DNDi), a nonprofit specializing on neglected disease R&D, including malaria;<sup>335</sup> and the Malaria Initiative, a program within the Gates-funded nonprofit PATH.<sup>336</sup>

Most outbreak diseases, however, do not attract this breadth of R&D support. Absent a major catalyst like the 2014–16 outbreaks, most diseases are permanently affected by severe market failures in the pre- and inter-outbreak periods. In the aftermath of the Ebola outbreak, the United Nations (UN) proposed the creation of an international fund to support R&D for priority infectious outbreak diseases, setting the minimum threshold for the fund at U.S. \$1 billion per year.<sup>337</sup> While this amount pales in comparison to the overall yearly funding needs of the diseases identified by the WHO as priorities for probable outbreaks,<sup>338</sup> it should be noted that only HIV/AIDS commands more

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328. See POLICY CURES RESEARCH, *supra* note 49, at 28.

329. See PATH, STAYING THE COURSE? MALARIA RESEARCH AND DEVELOPMENT IN A TIME OF ECONOMIC UNCERTAINTY 13 (2011).

330. See *Higher Research Funding Leads to 4x Rise in New Anti-Malaria Product Pipeline*, MALARIA.COM (June 29, 2011), <http://www.malaria.com/news/malaria-research-fundin> [<https://perma.cc/5LSF-Z37D>].

331. See MEDS. FOR MALARIA VENTURE, *supra* note 51.

332. RBM PARTNERSHIP, <http://www.rollbackmalaria.org> [<https://perma.cc/5W3Q-QZGK>].

333. FIND's malaria portfolio is available at <https://www.finddx.org/malaria>.

334. IVCC, <http://www.ivcc.com> [<https://perma.cc/RJA7-JR4S>].

335. DRUGS FOR NEGLECTED DISEASES INITIATIVE, <https://www.dndi.org> [<https://perma.cc/BTV8-SF8U>].

336. MALARIA VACCINE INITIATIVE, <http://www.malariavaccine.org> [<http://perma.cc/VC6J-2ZKX>].

337. See HIGH-LEVEL PANEL ON THE GLOBAL RESPONSE TO HEALTH CRISES, PROTECTING HUMANITY FROM FUTURE HEALTH CRISES 18 (2016), [http://www.un.org/News/dh/infocus/HLP/2016-02-05\\_Final\\_Report\\_Global\\_Response\\_to\\_Health\\_Crises.pdf](http://www.un.org/News/dh/infocus/HLP/2016-02-05_Final_Report_Global_Response_to_Health_Crises.pdf) [<https://perma.cc/LC2W-FRB4>].

338. See R&D BLUEPRINT, *supra* note 7.



than U.S. \$1 billion per year in funding.<sup>339</sup> This suggests that, if implemented, the fund would have the potential to have an actual impact on R&D on some of the most severely underfunded diseases.

The UN approach is also indicative of the type of proposals that have been put forth to counter IP market failures at the incentives level. Since the patent bargain is incapable of attracting R&D attention, or sufficient levels thereof, other models seek to supplement IP incentives by rewarding risk and investment in different ways. The same UN report recommended the adoption of “direct public or private grants, tax breaks for organizations undertaking R&D, prizes for successful achievement of research goals, advance market commitments, or subsidization of basic research efforts.”<sup>340</sup> While a full treatment of each individual mechanism is beyond the scope of the Article, it should be noted that these mechanisms have long been endorsed<sup>341</sup> by literature analyzing market failures in general (and not just in the context of severely underfunded diseases).<sup>342</sup> Biopharmaceutical R&D has long been considered one of the leading areas where patent incentives alone are in general suboptimal, and many of the alternative models listed above were not devised as specific instruments to incentivize R&D on areas with especially acute market failures. Nevertheless, many of these options are already being explored—episodically—in the context of outbreak-disease R&D, and especially in the field of vaccines. For instance, as described in previous Parts, vaccine procurement is a major component of the work developed by BARDA in the United States and Gavi in Switzerland.<sup>343</sup>

In the early 2010s, an unusual form of incentive lodged at the FDA in the United States emerged and appears to have regained momentum during the Ebola and Zika outbreaks. Entitled the priority review voucher, it mandates that the FDA award a voucher to sponsors that gain approval for drugs treating certain underfunded diseases.<sup>344</sup> The award voucher is to be used at a later time to speed up approval of another, unrelated drug. The second drug—the drug on which the voucher is used—does not necessarily have to treat an

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339. See POLICY CURES RESEARCH, *supra* note 49, at 19.

340. See HIGH-LEVEL PANEL ON THE GLOBAL RESPONSE TO HEALTH CRISES, *supra* note 337, at 59.

341. As well as criticized. See generally Roin, *supra* note 79; Hemel & Ouellette, *supra* note 94.

342. See generally Roin, *supra* note 79; Hemel & Ouellette, *supra* note 92.

343. FDA, *supra* note 193; see also *Supply and Procurement of Immunisation Products*, GAVI: THE VACCINE ALLIANCE, <http://www.gavi.org/about/gavis-business-model/vaccine-supply-and-procurement> [https://perma.cc/5HWB-2AQK] (describing Gavi’s business model).

344. The voucher system was first proposed by Ridley et al. in 2006. See David B. Ridley et al., *Developing Drugs for Developing Countries*, 25 HEALTH AFF. 313, 313 (2006).

underfunded disease.<sup>345</sup> The basic idea is that there is a sizable economic advantage associated with having the second drug enter the market sooner. Early approval of the second drug would then constitute an incentive for the private sector to invest in R&D for traditionally neglected diseases.<sup>346</sup> Because the vouchers are transferable, sale of an award voucher (which other companies would then be entitled to use to quicken approval of any drug of their choice) is another form of monetizing the incentive.<sup>347</sup>

Both Ebola and Zika were added to the list of underfunded diseases that are eligible for a voucher during the outbreaks.<sup>348</sup> The 21<sup>st</sup> Century Cures Act,<sup>349</sup> passed in December 2016, extended the voucher program to medical countermeasures,<sup>350</sup> a category that includes vaccines for chemical, biological, radiological, and nuclear defense—and hence for which R&D on diseases like Ebola will potentially qualify.

Nominally, these vouchers are industry-subsidized, which would constitute an original approach to solving the private-sector market failure in biopharmaceutical R&D. In practice, however, the vouchers are being used as a means to expedite the approval of blockbuster drugs (such as cholesterol drugs, in which little to no market failure exists) with no evidence of the corresponding economic return actually being directed toward R&D on any type of neglected disease.<sup>351</sup>

The adoption of one or more mechanisms listed above constitutes a form of enhancing IP preparedness by addressing the incentives side of the problem. The following Subparts turn to proposals dealing with inefficiencies arising from transfers of IP rights.

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345. *Id.* at 315.

346. *Id.* at 313.

347. *Id.*

348. See S. 2917, 113th Cong. (2014); see also Pub. L. No. 113-233, 128 Stat. 2127 (2014).

349. 21st Century Cures Act, Pub. L. No. 114-255, § 2036 (2016).

350. The FDA defines medical countermeasures as “products (biologics, drugs, devices) that may be used in the event of a potential public health emergency stemming from a terrorist attack with a biological, chemical, or radiological/nuclear material, a naturally occurring emerging disease, or a natural disaster.” FDA, *supra* note 193.

351. See Ana Santos Rutschman, *The Priority Review Voucher Program at the FDA: From Neglected Tropical Diseases to the 21st Century Cures Act*, 26 ANNALS OF HEALTH L. 71, 83 (2017) (describing the voucher program and showing that the political goodwill associated with the Ebola and Zika vouchers is misaligned with the goal of incentivizing innovation).

### C. IP Preparedness in Early-Stage Outbreaks

The WHO pointed out that the 2014–16 Ebola outbreak demonstrated that “it is possible to compress R&D timelines from a decade or longer to less than a single year.”<sup>352</sup> While it is debatable whether this proposition is universally applicable to R&D in future outbreaks, the development of the Ebola vaccine can be regarded as a success story from the point of view of expediting complex R&D against the outbreak clock.

However, this success coexisted with inefficiencies in transactional IP, and they are likely to have affected the pace of R&D surrounding a vaccine that was, and remains to this day, the leading candidate in the Ebola vaccine race. Drawing on the positive aspects of IP negotiations—how multiple players came together and agreed on IP terms much more quickly than usual—I propose a mechanism that would (1) leverage these aspects to maximize efficiency in IP negotiations during an outbreak and (2) counteract potential inefficiencies arising from hold-up situations.

This solution is based on the creation of a streamlined IP framework governing certain transfers of IP related to outbreak-disease technology (for example, vaccines). The idea behind the IP framework is to replicate the expedited licensing model that several companies and institutions informally adopted during the early stages of the Ebola outbreak. One factor that enabled the unusually swift transfer of IP for the Ebola vaccines was the fact that not all licensing agreements were completed by the time multiparty R&D began.<sup>353</sup> Nevertheless, incomplete licensing packages are not a replicable, or desirable, process. Instead, this proposal is applicable in a conditioned scenario, and only to outbreak-disease technology developed by public-sector institutions (such as the National Institutes of Health in the U.S.).

A *streamlined IP framework*, which in this particular case can be described as a dormant licensing agreement, would work according to the following model. A public-sector institution develops outbreak-disease technology. When that technology is transferred to a private-sector company, the *streamlined IP framework* attaches to the transfer, but only becomes applicable if the rights are retransferred during a formal outbreak. The *framework* is a basic IP licensing agreement developed or adopted by the public-sector institution and previously agreed to by the initial licensee. When an outbreak occurs, if the licensee does not work the technology within a certain period of

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352. See R&D BLUEPRINT, *supra* note 7, at 6.

353. Note that these agreements included IP provisions and other contractual arrangements.

time<sup>354</sup> and refuses to license it, then any entity ready to meet the terms of the *framework* would become the new licensee through notification to the public-sector institution—and payment, set in the *framework* by reference to the original licensing agreement, to the first licensee.

## 1. The Need for Streamlined IP Frameworks

The possibility of a hold-up of IP rights during the early stages of an outbreak is arguably the most detrimental of the inefficiencies identified in Parts I and II. Outbreak diseases are among the most severely underfunded diseases, with very limited support for R&D, if any. An outbreak opens up a unique and short-lived window for R&D resource maximization. This was evidenced by the 258 percent increase in Ebola funding during the first year of the outbreak, a number that has since declined.<sup>355</sup> Similarly, the 2015 outbreak jumpstarted Zika R&D, with one of the major funders suspending funding for the development of a vaccine less than a year after the outbreak ended.<sup>356</sup>

The importance of capitalizing on the narrow period in which an outbreak disease becomes a source of concern stretches across many domains. For instance, initial clinical trials for Ebola vaccine candidates were hampered by a declining number of Ebola-related infections as the outbreak began to wind up,<sup>357</sup> a problem that affects the pace of outbreak-spiked R&D. But perhaps no domain is as crucial as the transfer of intellectual property covering existing vaccine technologies. Companies with not-fully-developed vaccine candidates in their portfolios may struggle to muster the resources needed to quickly produce and test the vaccine, as illustrated by the Ebola case study presented in Part II. They may also engage in a strategy of immediate profit maximization,

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354. The exact amount of time would be based on the characteristics of the technology in question. (For example, for the type of vaccine or proximity to preexisting vaccine technology as the case studies on Ebola and Zika illustrated, in some situations there will be preexisting vaccines that can be adapted to respond to new outbreaks, whereas in others we will face a vaccine vacuum.)

355. See POLICY CURES RESEARCH, *supra* note 49, at 6.

356. Pasteur, *supra* note 319 and accompanying text. Residual financial support for the monitoring of Zika mosquitos and disease transmission is still ongoing.

357. See Alexandra Sifferlin, *Lack of Ebola Cases Shifts Vaccine Trials Away From Liberia*, TIME (Mar. 13, 2015), <http://time.com/3743945/ebola-vaccine-trials> [<http://perma.cc/MZ6N-YN3X>] (describing the decision of the National Institutes of Health to relocate the clinical trials of an Ebola vaccine candidate from Liberia to Guinea due to the impossibility of enrolling volunteers who were at risk for Ebola infection after the outbreak in Liberia was contained).

electing to wait to license their vaccine technology to the highest bidder once an outbreak sparks demand.<sup>358</sup>

The inability to push incipient vaccine candidates through the R&D pipeline as soon as an outbreak begins—or the strategic choice to delay the licensing of vaccine technology—is at odds with the extraordinary funding suddenly made available for research on otherwise overlooked diseases. Delayed transfers of IP at this stage are especially problematic, as funding might start to shrink by the time the licensee finally begins testing and developing the vaccine technology. IP hold-up, either due to lack of R&D capacity or rent-seeking behavior, squanders the opportunity of maximizing R&D at peak funding. Consider again the case of NewLink’s Ebola vaccine. Emergency status for Ebola began in August 2014 and ended in March 2016.<sup>359</sup> In this context, the three-month period in which the vaccine was not developed (August to November 2014) is much more significant than a similar delay in R&D for mainstream diseases, where funding is unlikely to decline.

As outbreaks swiftly alter the funding landscape for certain diseases, the need to ensure efficient transfers of IP rights over much-needed technology—in particular, vaccines—is paramount. Against this backdrop, a streamlined mechanism to operate these transfers is especially well-suited to address the specific dynamics introduced by outbreaks. A streamlined framework individuates *ex ante* the core IP provisions that must be agreed upon for a transfer to occur. This feature reduces transaction costs once an outbreak begins, hence speeding IP negotiations and, as a consequence, the development of technologies for which funding is temporary.

A streamlined IP framework may take different forms, ranging from a set of narrowly defined rights and conditions that parties include in their licensing agreements, to more generic provisions (akin to guiding principles). The former has the advantage of being a more efficient tool for speeding up the licensing process: The more densely populated a framework, the less bargaining remains once the technology is needed. The latter still requires some degree of filling in activity by negotiating parties. But while a more specific IP framework is better to hasten negotiations during a public health crisis, it also

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358. NewLink acquired rights over rVSV-ZEBOV from the Canadian government for U.S. \$205,000 and later transferred them to Merck for U.S. \$30 million (to which an extra U.S. \$20 million could be added under certain conditions). See *supra* note 295 and accompanying text. The profit made by the company was made solely on the basis of having acquired a technology for which there was sudden demand, with no development on NewLink’s part. This fact will not be lost on smaller companies unable or unwilling to innovate in traditionally competitive areas.

359. See WORLD HEALTH ORG., *supra* note 159; Branswell, *supra* note 161.

poses the risk of low adherence, as companies might be reluctant to agree ex ante to a broad set of provisions. Conversely, a more loosely delineated framework may be more attractive ex ante.

## 2. Benefits of a Dormant License

A dormant license, as proposed in this Article, is an embodiment of a more stringent IP framework. It therefore has the advantage of being a more efficient tool for accelerating IP negotiations, and the drawback of being possibly unattractive to parties unwilling to commit ex ante (for example, private-sector companies with some degree of bargaining power).

Yet, given the specificities of outbreak-disease R&D, such a stringent mechanism is also the most appropriate. A porous framework is of little to no use in the context of outbreaks. If crucial provisions have not been agreed upon, gains in negotiation speed will likely be minimal. The potential for disagreement is still considerable among companies interested in the transfer of IP. Moreover, a looser framework is unlikely to solve the problem posed by companies engaging in profit maximization by waiting for the highest bidder to enter the negotiation process. Even more critically, inaction from such a company—by not developing the technology—has to be explicitly addressed ex ante, which is the main function of a dormant license.

As described above, a license that is negotiated ex ante is the most efficient way of avoiding delays once an outbreak begins and funding streams open. Such a license shifts the bulk of transaction costs pre-outbreak. A powerful argument in favor of a dormant license is that R&D on outbreak diseases will remain very low during pre-outbreak periods, and hence unattractive to major private-sector companies. As seen with Ebola and Zika, existing pre-outbreak vaccine technology, if any, is likely to be developed by the public sector. When existing technology is transferred to the private sector before an outbreak, the licensee will likely be a smaller pharmaceutical company, as illustrated by the case of the Ebola vaccine candidate licensed to a small Iowa-based company.<sup>360</sup> Smaller companies that cannot compete in mainstream drug R&D are natural candidates for government-developed technologies approaching the clinical-trial stage.<sup>361</sup> As outbreaks increase in periodicity and

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360. See NEWLINK GENETICS, *supra* note 139 and accompanying text.

361. Typically, the government turns over the later stages of R&D to private sector companies, large and small. Having borne the risk of initial development of a drug, as well as associated costs, government research institutions lack the funding to manufacture most drugs and see them through clinical trials. An example of this was the attempted licensing

scale, acquisition of vaccine technology before an outbreak constitutes an increasingly viable business strategy. In a playing field in which smaller players abound, the likelihood of adoption of a stringent licensing mechanism increases: These players have less bargaining power vis-à-vis government institutions than large pharmaceutical companies, and comparatively more to gain from the development of outbreak-related technology.

In the context of outbreak-disease R&D, another benefit of a dormant license is that it puts pressure on companies to develop the technology through a catalytic event that coincides with a spike in funding. Even if a smaller company that has licensed a vaccine from the government is unable to work it pre-outbreak, a dormant license becomes a Sword of Damocles only once an outbreak starts. At this point, funders are exceptionally quick to mobilize. And because a dormant license only springs to life with the formal declaration of an emergency, even smaller pharmaceutical companies have time to mobilize resources and attract additional funding before the license clock starts ticking.

In addition to the informal stages of the outbreak, in which the license is still dormant, there is also a period of time after the trigger event during which companies can start the development of the technology, before having to license it to others. For purposes of starting the license clock, the triggering event can be a declaration from the WHO or the NIH, or a standard developed by the public-sector institution licensing the invention in the first place. Because formal outbreak declarations tend to lag,<sup>362</sup> this gives companies a reasonable timeline for moving vaccines through the R&D pipeline.

The fact that the license is dormant also assuages concerns of companies that intend to develop technology licensed pre-outbreak, even if prospectively. In a scenario in which a company diligently begins R&D once an outbreak occurs, the license does not spring to life. Moreover, it is reasonable to expect most companies, however small, to be legitimately interested in the development of vaccines and drugs in general as opposed to pursuing rent-seeking strategies. In fact, there is an increasing number of small biotechnology

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deal between the Army and private-sector company Sanofi regarding the Zika vaccine. WORLD HEALTH ORG., *supra* note 226 and accompanying text. Government partnerships with private-sector companies also occur outside the sphere of outbreak diseases, or even underfunded ones, encompassing most mainstream drugs. Take the case of oncologic drugs, for which the National Institutes of Health routinely partner with different pharmaceutical companies. See *NIH Partners With 11 Leading Biopharmaceutical Companies to Accelerate the Development of New Cancer Immunotherapy Strategies for More Patients*, NAT'L INSTS. OF HEALTH (Oct. 12, 2017), <https://www.nih.gov/news-events/news-releases/nih-partners-11-leading-biopharmaceutical-companies-accelerate-development-new-cancer-immunotherapy-strategies-more-patients> [https://perma.cc/7N3F-YS9X].

362. See Roland, *supra* note 57 and accompanying text.

startups that are considered more innovative than traditional, large pharmaceutical companies.<sup>363</sup> In this sense, a dormant license does not constitute a deterrent to companies negotiating vaccine technology with public-sector institutions.

However, one advantage of a dormant license embedded in a larger licensing agreement is that it serves as a deterrent to companies focused on immediate profit maximization through retransfer of IP. In this case, it is more efficient for this type of company to look for technologies that are not subject to dormant licensing provisions, a move that gives them more time to seek out the licensing deal that generates the most revenue. And in the event that a rent-seeking company agrees to a dormant license (or switches its business model after acquiring the technology), it then has a limited period of time in which to transfer the technology. This minimizes the impact of IP hold-up and provides companies interested in licensing the technology with a timeframe in which to prepare to compete in the R&D arena.

Because licensees under a dormant license model develop the technology on a nonexclusive basis, this proposal promotes competition. However, competition-enhancing measures may generate *too much* competition, to the point at which no companies have incentives to license the technology in the first place. This may of course happen if a plethora of nonexclusive licenses are granted through the dormant license regime. Nevertheless, there are two factors that attenuate this possibility. On the one hand, there are additional funding streams available, combined with the uncertainty inherent to outbreaks of infectious diseases. At the time the decision to license on a nonexclusive basis is made, the outcome of the outbreak is unknown; it may end soon or last for years, creating a very large market for new drugs and vaccines. The flipside of the risk posed by increased competition is that forgoing the opportunity to enter an R&D race might also entail missing out on a blockbuster market.

On the other hand, outbreak-spiked R&D is uber-competitive, even in the absence of nonexclusive licenses. As illustrated by the case of Zika R&D, shortly after the outbreak began, there were around forty entities involved in the Zika vaccine race.<sup>364</sup> Among these entities, there were twenty-seven different vaccine candidates in development in mid-2017, as detailed in Table 2. A closer look at these candidates shows that several candidates were

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363. See Jennifer Alsever, *Big Pharma Innovation in Small Places*, FORTUNE (May 13, 2016), <http://fortune.com/2016/05/13/big-pharma-biotech-startups> [<https://perma.cc/PQ5Z-HJXN>].

364. See *supra* Table 2.



based on exactly the same technology (for example, inactivated purified virus or DNA vaccines). The history of vaccine development is marked by simultaneous R&D on similar technologies, with outbreaks accentuating the race-like aspects of vaccine development.<sup>365</sup> Against this backdrop, the potential drawback of unrestrained competition triggered by a dormant license becomes less significant. In addition to this, the Patent Act already establishes that public-sector technology transferred to private companies should be preferentially licensed on a nonexclusive basis,<sup>366</sup> which further dilutes concerns posed by excessive competition.

Lastly, it is worth noting that this proposal is designed as a response to the idiosyncratic problems posed by R&D on outbreak diseases. It can be applied to any kind of outbreak-funded technology, including diagnostics, therapeutics, and vector-control methods.<sup>367</sup> The most relevant field of application is nonetheless vaccine technology, not only because the field of vaccine R&D is the primary recipient of outbreak funding, but also because of the preventive role of vaccines on outbreak outcomes and their positive impact on health systems.<sup>368</sup>

#### D. IP Preparedness in the Post-Outbreak

As seen above, the successful development of an Ebola or Zika vaccine does not necessarily mean that it will be widely available or affordable. As costly R&D for outbreak diseases faces an uncertain market in which to recoup costs, exploitation of patent rights in monopoly-like conditions often leads to a scenario in which those most in need of a therapy or vaccine cannot access it.<sup>369</sup>

Several institutions, especially in the nonprofit arena, are increasingly adopting IP policies to ensure widespread availability and affordability of health technologies. One of the most prominent examples is the policy pursued by the Drugs for Neglected Diseases Initiative (DNDi).<sup>370</sup> While DNDi

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365. See generally MEREDITH WADMAN, *THE VACCINE RACE: SCIENCE, POLITICS, AND THE HUMAN COSTS OF DEFEATING DISEASE* (2017) (providing an in-depth account of the race surrounding the first polio vaccine).

366. 35 U.S.C. §§ 207–209 (2012).

367. See *supra* Table 2.

368. See Nathalie Legeron et al., *Role of Vaccination in the Sustainability of Healthcare Systems*, 3 J. Mkt. Access Health Pol'y 1 (2015).

369. See *supra* note 79 and accompanying text.

370. INNOVATIVE VECTOR CONTROL CONSORTIUM, *supra* note 335 and accompanying text. DNDi's IP policy, as stated in the organization's business plan, is guided by the "need to ensure that drugs are affordable to and access is equitable for patients who need them" and "the desire to develop drugs as public goods when possible." See *DNDi's Intellectual*

recognizes that it will have to enter into contractual relationships that include acquisition, management, or enforcement of IP, the institution's default strategy "does not seek to finance its research and operations through IP rent revenues."<sup>371</sup> Although an exhaustive description of DNDi's business model is beyond the scope of this Part of the Article, a few examples illustrate the overarching concept: The organization does not support R&D projects requiring the use of preexisting IP at a cost that does not (financially) allow for follow-up R&D to be performed in-house or out-contracted by DNDi;<sup>372</sup> it develops and licenses health technologies according to principles of maximization of availability and affordability of drugs instead of "restrictive IP strategies that maximize patent revenue;"<sup>373</sup> and it uses model agreements "to enable alternative forms of dispute resolution" as a way to avoid litigation.<sup>374</sup>

This is not to say that the approach taken by DNDi is scalable.<sup>375</sup> But these are principles that should inform IP and health innovation policies in other sectors. To provide but one practical example—and drawing from the case study on the attempted licensure of the Army's Zika vaccine—several of DNDi's principles (or adaptations thereof) could be read as best practices for the licensing of health innovations funded by the public-sector. Drawing further from the example of the case study on Zika, a modest but meaningful improvement would be to require public-sector entities to fully disclose terms of proposed licenses when complying with the notice requirement set forth in 35 U.S.C. § 209(e). This provision requires federal agencies to give a simple notice of intent to license and also to consider comments received in response to the note, but it is silent on the disclosure of substantive information about the license beyond the exclusivity. § 209(e) could be amended to require disclosure of at least some elements, like the term of the license, termination, and pricing provisions.

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*Property Policy*, DRUGS FOR NEGLECTED DISEASES INITIATIVE, <https://www.dndi.org/wp-content/uploads/2009/03/ip%20policy.pdf> [<https://perma.cc/X6LN-86L5>].

371. *Id.* at III and IV.

372. *Id.* at V.

373. *Id.* at III.

374. *Id.* at VI.

375. Small institutions like DNDi operate on limited budgets, which do not allow for R&D in certain areas to be conducted. See *Funding*, DRUGS FOR NEGLECTED DISEASES INITIATIVE, <https://www.dndi.org/achievements/asq/partnership-overview-2/funding> [<https://perma.cc/C7JW-7YR4>].

## CONCLUSION

Outbreak diseases place an enormous burden on public health. Yet they fit poorly into the patent-based incentives mold, which causes R&D on outbreak pathogens to be grossly underfunded. Moreover, even when large-scale outbreaks cause a spike in funding, outbreak-induced R&D can be plagued by different types of IP inefficiencies that affect the ongoing development of health technologies, as well as the future availability and affordability of vaccines, therapies, and diagnostics for outbreak diseases. Through case studies on the Ebola and Zika vaccine races, I have taken the first steps in identifying, characterizing and analyzing the manifold interactions between IP and vaccine development in the context of outbreak diseases. It has also sought to survey legal and policy mechanisms that mitigate the shortcomings and amplify the successes of the IP of Ebola and Zika, making the lessons from the case studies applicable to other outbreak diseases. Further, it has put forth a new solution—a dormant license—that has the potential to greatly reduce an especially problematic type of transactional IP inefficiency in the early stages of an outbreak. As new and old pathogens erupt in increasingly complex ways, increasing our IP preparedness by lessening the impact of these inefficiencies will remain a critical task.