

# PRIVATE ENVIRONMENTAL GOVERNANCE TO ADDRESS MANUFACTURING RELEASES OF ANTIBIOTICS

by Michael G. Mahoney

Michael G. Mahoney is a Visiting Scholar at the Environmental Law Institute, and previously was Vice President and Assistant General Counsel and Chief Environment, Health, and Safety Compliance Counsel for Pfizer.

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## SUMMARY

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Demand for generic pharmaceuticals has resulted in China and India becoming the largest producers of these products in the world. Pollution from pharmaceutical manufacturing in both of these countries is a recognized environmental and public health problem, and the release of residual antibiotics is a contributor to antimicrobial resistance, which is projected to result in 10 million deaths per year by 2050 unless significant action is taken. This Article argues that implementation of voluntary sustainability standards is needed to address pharmaceutical manufacturing wastewater pollution, that this approach would drive market demand for pharmaceuticals produced in this way, and that this market response should also drive other manufacturers to improve their operations.

The Lancet Commission on Pollution and Health concluded that pollution is the largest environmental cause of disease and premature death in the world today.<sup>1</sup> Diseases caused by pollution were responsible for an estimated nine million premature deaths in 2015 (16% of all deaths worldwide).<sup>2</sup> Rapid industrialization and urbanization have intensified pollution and resulting environmental health risks, especially in developing countries. Pollution stunts economic growth and exacerbates poverty and inequality in both urban and rural areas; and poor people, who cannot afford to protect themselves from the negative impacts of pollution, are suffering the most.<sup>3</sup>

A significant portion of the pollution in developing countries such as China and India results from the manufacturing of goods for export to developed countries, including in the petrochemical, chemical, and pharmaceutical sectors.<sup>4</sup> Industrial growth is fueled, in large part, by developed countries' consumer demand for lower-cost products. This industrial growth, coupled with the lack of environmental regulations or poor enforcement of regula-

tions (collectively, gaps in the environmental rule of law (EROL)), are the key reasons for these serious pollution problems in developing countries.<sup>5</sup>

Consumers' demand for lower-cost generic pharmaceuticals has resulted in China and India becoming the largest producers of these products in the world. Pollution from pharmaceutical manufacturing in both of these countries is a recognized environmental and public health problem.<sup>6</sup> The release of residual antibiotics<sup>7</sup> from pharmaceutical manufacturing has been identified by the World Health Organization (WHO) as a contributor to antimicrobial resistance (AMR),<sup>8</sup> which is projected to result in 10 million deaths per year by 2050 unless significant action is taken to address this global health issue.<sup>9</sup>

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1. Philip J. Landrigan et al., *The Lancet Commission on Pollution and Health*, 391 LANCET 462 (2018), available at [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(17\)32345-0.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(17)32345-0.pdf).  
2. *Id.*  
3. World Bank, *Pollution*, <https://www.worldbank.org/en/topic/pollution> (last visited May 26, 2021).  
4. International Trade Administration, *India—Country Commercial Guide: Environmental Technology*, <https://www.trade.gov/knowledge-product/india-environmental-technology> (last published Aug. 25, 2020).

5. Steven Bernard & Amy Kazmin, *Dirty Air: How India Became the Most Polluted Country on Earth*, FIN. TIMES, Dec. 11, 2018.  
6. D.G. Joakim Larsson, *Pollution From Drug Manufacturing: Review and Perspectives*, 369 PHIL. TRANSACTIONS ROYAL SOC'Y B 20130571 (2014), <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4213584/>.  
7. The primary cause of antimicrobial resistance (AMR) is the mismanagement of antibiotics; however, the mismanagement of other anti-infectives, including antifungal and antiviral products, also contributes to the issue. The private environmental governance approach discussed in this Article to address residuals in manufacturing wastewaters can and should be applied for other anti-infectives.  
8. Ana Mulero, *WHO Stresses Role of GMP in Combatting Antimicrobial Resistance*, REGUL. AFFS. PROS. SOC'Y, May 16, 2019, <https://www.raps.org/news-and-articles/news-articles/2019/5/who-stresses-role-of-gmp-in-combatting-antimicrobi>.  
9. JIM O'NEILL ET AL., REVIEW ON ANTIMICROBIAL RESISTANCE, TACKLING DRUG-RESISTANT INFECTIONS GLOBALLY: FINAL REPORT AND RECOM-

Although not limited to pharmaceutical manufacturing in China and India, the high-production volumes of antibiotics in these countries to satisfy consumers in developed countries, coupled with the lack of pharmaceutical industry-specific regulations and poor environmental regulatory enforcement, is an example of a significant gap in EROL that has resulted in large volumes of residual antibiotics being released to the environment largely unchecked. This is resulting in significant environmental and public health impacts.<sup>10</sup>

The use of private environmental governance approaches in China and India and in other markets, either in advance of effective government regulation or to strengthen ineffective regulation, including the use of third-party certification systems to augment or replace regulatory action and to provide market incentives to establish a culture of compliance, holds great promise to address a gap in EROL such as the lack of regulation of antibiotics in manufacturing waste streams.<sup>11</sup>

The implementation of private environmental governance approaches, primarily through voluntary sustainability standards (VSS), is achieving meaningful environmental improvements to address challenges in several areas, including in advancement of sustainable palm oil production, sustainable fisheries, and sustainable forestry practices. If such a private environmental governance approach can be successfully implemented to address pharmaceutical manufacturing wastewater pollution, it would hold promise as a potential model to address other manufacturing pollution issues related to industrial activity in China and India, and other countries with similar pollution problems.

Several multinational pharmaceutical companies have begun to work together to develop a VSS to limit the discharge of antibiotics from manufacturing sites to safe levels that would eventually be audited against by an independent and credible environmental engineering firm. This work is in the early stages of development, and to make a meaningful environmental impact the effort will need support from key stakeholders, including input from large government buyers of generic antibiotics, to

help create a market response that rewards responsible antibiotic manufacturing.<sup>12</sup>

The primary purpose of this Article is to review the critical public health need for a stringent VSS for antibiotic manufacturing and to demonstrate that a private environmental governance approach, if properly designed and implemented, could address this significant environmental and public health issue and provide buyers and consumers of antibiotics the needed confidence that the antibiotics that they purchase are manufactured responsibly.

The growth of pharmaceutical manufacturing in India and the resulting pollution is a focus here because of the large numbers of studies that have been conducted in India documenting pollution from antibiotics released in manufacturing wastewaters; however, this is a global environmental and public health issue, and a well-designed VSS to address this issue is needed worldwide.

The Article provides examples of several VSS that are being implemented and that are resulting in environmental benefits as well as increased market share for products that meet the standard. A similar approach that provides buyers and consumers with confidence in how the generic antibiotic was manufactured should drive market demand for the product, and this market response should drive other manufacturers of antibiotics to improve their operations so they can also benefit in the market. A market preference for antibiotics manufactured in an environmentally responsible manner should provide an important catalyst to improve environmental aspects of the pharmaceutical manufacturing supply chain in the near term. Few other issues impact public health so acutely that, without significant improvements in the near term across a large and complex manufacturing supply chain, tens of thousands of people will remain at risk of adverse health impacts.<sup>13</sup>

## I. Overview of AMR Public Health Concerns and Public Policy Responses

AMR is a serious global health risk that is estimated to be responsible for 700,000 deaths per year globally, including 35,000 deaths per year in the United States,<sup>14</sup> 25,000 deaths in the European Union (EU),<sup>15</sup> and 58,000 infant

MENDATIONS (2016), [https://amr-review.org/sites/default/files/160518\\_Final%20paper\\_with%20cover.pdf](https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf).

10. UNITED NATIONS ENVIRONMENT PROGRAMME, ENVIRONMENTAL RULE OF LAW: FIRST GLOBAL REPORT 31 (2019):

Weak environmental institutions foster noncompliance. If institutions are unable to effectively inspect, prosecute, and adjudicate environmental violations, the regulated community may reasonably believe that violations will not be punished. Weak environmental institutions can have more pernicious effects. A failure to have robust environmental institutions can create 'a system of broader institutional weakness which can result in corruption' that not just threatens the institutions implicated but undermines confidence in the state generally. Corruption and weak environmental institutions create an uncertain investment climate. (citations omitted).

11. *Id.* at 32 ("Recognizing this, governments increasingly utilize different strategies to target the various groups. There may be awards, priority in bidding on procurement, and tax benefits to those who always comply or go beyond compliance.").

12. The AMR Industry Alliance's announcement of a voluntary environmental standard and certification scheme for antibiotic manufacturing and call for stakeholder involvement at the 2020 World Health Summit is available at Video: Antimicrobial Resistance—World Health Summit (World Health Summit 2020) (at the 30-minute mark), <https://www.youtube.com/watch?v=GgB1vjR8BZw&t=1312s>. The Environmental Law Institute was subsequently invited to be a stakeholder, and has been represented by the author who has participated in several initial stakeholder steering team meetings on the development of a VSS.

13. Compare projected 2050 AMR deaths to COVID-19 deaths. Statista, *Projected Number of Coronavirus (COVID-19) Deaths Worldwide From Dec. 1, 2020 to Mar. 31, 2021, by Scenario*, <https://www.statista.com/statistics/1176553/covid-projected-deaths-by-scenario/> (last visited May 26, 2021).

14. Centers for Disease Control and Prevention, *Antibiotic/Antimicrobial Resistance (AR/AMR)*, <https://www.cdc.gov/drugresistance/index.html> (last reviewed July 20, 2020).

15. EUROPEAN COMMISSION, A EUROPEAN ONE HEALTH ACTION PLAN AGAINST ANTIMICROBIAL RESISTANCE (AMR) (2017) [hereinafter ONE HEALTH AC-

deaths in India.<sup>16</sup> AMR typically presents when a patient develops either an infection from a pathogenic bacteria, fungus, or virus, and antimicrobial medicines that normally are effective in treating the infection are ineffective because the microbial agent has become resistant through mutation to the medicine.

AMR has always occurred in the environment through natural selection, but the overuse of antibiotics and other anti-infectives over the past few decades has accelerated its occurrence. Without effective policies to prevent the spread of AMR, it has been estimated that the global death toll would reach 10 million per year by 2050, more people than currently die from cancer<sup>17</sup> and significantly more than the staggering 2.6 million deaths worldwide from COVID-19 that occurred in the first year of the pandemic.<sup>18</sup> In addition to the human toll, AMR increases health care costs and decreases economic productivity due to illness. The urgency of this issue was highlighted in 2015 with the WHO's Global Action Plan on AMR.<sup>19</sup> In 2016, the United Nations General Assembly (UNGA) adopted an AMR declaration—at that time, only the fourth public health issue to reach the UNGA agenda in its history.<sup>20</sup>

The overuse of antibiotics in patients and animals has for some time been recognized as the primary contributor to the increased emergence and spread of drug-resistant microbes.<sup>21</sup> More recently, the development and spread of AMR in the environment has been identified as a contributing source of the problem. Antimicrobial compounds can be released to the environment through patient use (e.g., disposal of unused medicines, unmetabolized medicines released in wastewater treatment effluent, etc.), animal use (e.g., livestock, aquaculture, companion animals, etc.), and as residues in pharmaceutical manufacturing effluent and other wastes.<sup>22</sup>

The environmental contribution to AMR has received significant attention in the United States, the EU, other developed countries, and major developing countries including China and India, and policy responses have been proposed to address the problem. In 2011, the EU identified the need for “substantially reinforced action” and promoted a more holistic approach, known as the One Health approach, to address AMR in both humans and animals. This plan calls for “cooperation on reduction of

the environmental pollution by antimicrobial medicines particularly from production facilities.”<sup>23</sup> The EU's One Health approach includes support for the development of technologies that enable efficient and rapid degradation of antibiotics in wastewater and the environment and reduce the spread of AMR.<sup>24</sup>

Individual EU Member States have also expressed concerns that pharmaceutical manufacturing wastewater is a significant potential source of AMR. In May 2016, the O'Neill report on AMR, sanctioned by the U.K. government, recommended the establishment of targets for maximum levels of antimicrobial active pharmaceutical ingredient (API) discharges associated with the manufacture of pharmaceutical products and urged pharmaceutical companies to improve monitoring of API discharges from owned manufacturing facilities and third-party suppliers.<sup>25</sup> The report also called for pharmaceutical companies to support the installation of proper waste processing facilities to reduce or eliminate discharge of API residuals.

As a result of this focus on the contribution from antibiotic manufacturing, several EU Member States that purchase significant quantities of antibiotics from China and India to supply their state-administered health care systems have expressed concerns about antibiotics being purchased from companies that are not producing them in an environmentally responsible manner.<sup>26</sup> These EU Member States and other stakeholders have identified the lack of transparency in the pharmaceutical manufacturing supply chain as a significant obstacle to efforts to incentivize environmentally responsible pharmaceutical manufacturing.<sup>27</sup>

The United States has developed a National Strategy and accompanying National Action Plan (NAP) for Combating Antibiotic-Resistant Bacteria, which provides a road map for the federal government to work domestically and internationally to detect, prevent, and control illness and death related to antibiotic-resistant infections over five years (2015-2020). Although the NAP adopted a One Health approach, it does not address the potential contribution of pharmaceutical manufacturing waste to AMR. In September 2018, the Secretary of Health and Human Services tasked the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria with providing recom-

TION PLAN], [https://ec.europa.eu/health/sites/default/files/antimicrobial-resistance/docs/amr\\_2017\\_action-plan.pdf](https://ec.europa.eu/health/sites/default/files/antimicrobial-resistance/docs/amr_2017_action-plan.pdf).

16. Madlen Davies, *Babies Hit the Hardest by India's Antibiotic Resistance Crisis*, BUREAU INVESTIGATIVE JOURNALISM, Nov. 14, 2018, <https://www.thebureauinvestigates.com/stories/2018-11-14/babies-hit-the-hardest-by-indias-antibiotic-resistance-crisis>.

17. O'NEILL ET AL., *supra* note 9.

18. Bruce Y. Lee, *One Year After Coronavirus Declared, How Many Deaths From Covid 19?*, FORBES, Mar. 13, 2021.

19. WHO, GLOBAL ACTION PLAN ON ANTIMICROBIAL RESISTANCE (2015), [https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763\\_eng.pdf](https://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf).

20. *Political Declaration of the High-Level Meeting of the General Assembly on Antimicrobial Resistance*, U.N. GAOR, 71st Sess., Doc. A/71/L.2 (2016), <https://digitallibrary.un.org/record/842813?ln=en>.

21. WHO, *About AMR*, <https://www.euro.who.int/en/health-topics/disease-prevention/antimicrobial-resistance/about-amr> (last visited May 26, 2021).

22. O'NEILL ET AL., *supra* note 9.

23. ONE HEALTH ACTION PLAN, *supra* note 15.

24. *Id.*

25. O'NEILL ET AL., *supra* note 9.

26. NICOLAI SCHAAP ET AL., STOCKHOLM INTERNATIONAL WATER INSTITUTE, REDUCING EMISSIONS FROM ANTIBIOTIC PRODUCTION 10 (2020) [hereinafter SIWI WHITEPAPER]:

Although different in detail and how the information is applied . . . both countries [Norway and Sweden] follow the logic of some level of disclosure of the supply chain and environmental strategies preventing emissions of APIs to the environment. Stakeholder dialogues indicate that procurers in other countries, including Denmark, Germany and the Netherlands, are looking at these pioneers and investigate options to apply comparable methods.

See also D.G. Joakim Larsson & Jerker Fick, *Transparency Throughout the Production Chain—A Way to Reduce Pollution From the Manufacturing of Pharmaceuticals?*, 53 REGUL. TOXICOLOGY & PHARMACOLOGY 161 (2009).

27. ACCESS TO MEDICINE FOUNDATION, ANTIMICROBIAL RESISTANCE BENCHMARK 2020, [https://accesstomedicinefoundation.org/media/uploads/downloads/5f3f76733efaa\\_Antimicrobial\\_Resistance\\_Benchmark\\_2020.pdf](https://accesstomedicinefoundation.org/media/uploads/downloads/5f3f76733efaa_Antimicrobial_Resistance_Benchmark_2020.pdf).

mendations on key priority areas for the next iteration of the NAP from 2020 to 2025. In July 2019, the Advisory Council issued its report of recommendations for combating antibiotic-resistant bacteria.

Although there are general recommendations to expand focus on a One Health approach, the report does not identify or address the potential contribution of pharmaceutical manufacturing to AMR. To date, the U.S. Environmental Protection Agency has not identified or considered pharmaceutical residuals in manufacturing wastewater as part of its regulatory agenda. However, scientific support for limiting pharmaceutical manufacturing wastewater discharges of pharmaceutical products is increasing, and in 2019, the U.S. Geological Survey (USGS) published a study showing that concentrations of certain pharmaceuticals were significantly higher in effluents from publicly owned treatment works (POTWs) that received wastewaters from pharmaceutical manufacturing facilities than those that did not.<sup>28</sup>

The Chinese government issued an NAP to contain AMR in August 2016.<sup>29</sup> The plan called for the environmental protection authorities to strengthen the prevention and governance of environmental pollution from antibiotics, but, to date, no legislation specific to limiting antibiotics in manufacturing wastewater has been promulgated.<sup>30</sup>

India has also adopted a One Health approach and established an NAP in 2017. The NAP specifically included an intent to create policies that regulate antibiotic residues in industrial effluents.<sup>31</sup> In early 2020, India proposed regulations that, if enacted, would impose stringent manufacturing discharge limits on antibiotics. The Indian pharmaceutical trade association submitted extensive comments on the proposed regulations that stated that they believe the proposed regulations were overly stringent and technically flawed, and they recommended that the voluntary approach developed by the AMR Industry Alliance provided a more practical approach to reducing the discharge of antibiotics in wastewater discharges.<sup>32</sup>

In summary, despite the attention to the environmental contribution to AMR since 2011, no jurisdiction has established laws or regulations that limit the discharge of anti-infectives from pharmaceutical manufacturing, and this gap in EROL and the lack of transparency in the supply chain results in buyers of antibiotics having little or no ability to determine if the antimicrobials they purchase were manufactured in an environmentally responsible manner.

28. Tia-Marie Scott et al., *Pharmaceutical Manufacturing Facility Discharges Can Substantially Increase the Pharmaceutical Load to U.S. Wastewaters*, 636 SCI. TOTAL ENV'T 69 (2018), available at <https://www.sciencedirect.com/science/article/pii/S0048969718313354?via%3Dihub>.

29. YONGHONG XIAO, A NATIONAL ACTION PLAN TO CONTAIN ANTIMICROBIAL RESISTANCE IN CHINA: CONTENTS, ACTIONS, AND EXPECTATIONS.

30. *Id.*

31. Susanne A. Kraemer et al., *Antibiotic Pollution in the Environment: From Microbial Ecology to Public Policy*, 7 MICROORGANISMS 180 (2019), available at <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6616856/>.

32. In January 2020, the Indian government announced proposed regulations to reduce antibiotics in manufacturing wastewaters.

## II. The Magnitude of Environmental Pollution From Antibiotics

The environment is a significant contributor to antibiotic resistance. Bacteria in soil, rivers, and seawater can develop resistance through contact with resistant bacteria (transfer of resistance genes), antibiotics, disinfectant agents released by human activity, as well as heavy metals that may propagate AMR in the environment.<sup>33</sup> People and livestock are then potentially exposed to more resistant bacteria through food, water, and air. Many studies document high levels of antibiotics in natural waters in the proximity of pharmaceutical production facilities in many countries, including China, India, EU Member States, and the United States.<sup>34</sup>

Antibiotic concentrations in some effluents are too low to be lethal to exposed bacteria but are high enough to induce AMR. Scientific studies document a correlation between the type and number of highly resistant bacteria and the level of antibiotic pollution.<sup>35</sup> Poor control of waste and wastewater, such as that encountered in China and India, which are both major global producers of antibiotics, lead to the entry of residual antibiotics into waters that are contaminated with pathogenic bacteria from untreated sewage. This increases the risk of the development of AMR.<sup>36</sup> Further, a vast array of contaminants in municipal and industrial wastewater also increases pressure on bacteria to become resistant.

Concentrations in rivers and other natural waters are also influenced by wastewater treatment facilities as well as antibiotic use in the populations they serve. Wastewater treatment plants that serve communities and municipalities generally use either aerobic or anaerobic biological systems to reduce or remove conventional pollutants, such as nutrients, organic matter, suspended solids, and pathogens, but this technology generally does not effectively remove or reduce APIs such as antibiotics. In most cases, pharmaceutical manufacturing facilities employ similarly designed biological wastewater systems and, as a result, these systems provide little or no treatment of APIs from pharmaceutical manufacturing processes. The activated sludge (biological material) found in these wastewater treatment plants can absorb some of the antibiotics, increasing the susceptibility of bacteria and other organisms in the activated sludge to becoming resistant to antibiotics. This increases the risk for

33. WHO, DRAFT DOCUMENT FOR COMMENTS: ENVIRONMENTAL ASPECTS OF GOOD MANUFACTURING PRACTICES: POINTS TO CONSIDER FOR MANUFACTURERS AND INSPECTORS IN THE PREVENTION OF ANTIMICROBIAL RESISTANCE (2019), [https://www.who.int/medicines/areas/quality\\_safety/quality\\_assurance/qas19\\_802\\_environmental\\_aspects\\_of\\_GMP.pdf?ua=1](https://www.who.int/medicines/areas/quality_safety/quality_assurance/qas19_802_environmental_aspects_of_GMP.pdf?ua=1).

34. Alejandra Borunda, *First Global Look Finds Most Rivers Awash With Antibiotics*, NAT'L GEOGRAPHIC, May 29, 2019, <https://www.nationalgeographic.com/environment/2019/05/hundreds-of-worlds-rivers-contain-dangerous-levels-antibiotics/>.

35. Bhagwana Ram & Manish Kumar, *Correlation Appraisal of Antibiotic Resistance With Fecal, Metal, and Microplastic Contamination in a Tropical Indian River, Lakes, and Sewage*, 3 NPJ CLEAN WATER (2020), <https://doi.org/10.1038/s41545-020-0050-1>.

36. Andrew C. Singer et al., *Review of Antimicrobial Resistance in the Environment and Its Relevance to Environmental Regulators*, FRONTIERS MICROBIOLOGY, Nov. 1, 2016, <https://www.frontiersin.org/articles/10.3389/fmicb.2016.01728/full>.

AMR in the areas where the sludge is applied (e.g., as fertilizer on farms) and in receiving water bodies where effluents containing residual activated sludge are discharged.

In 2019, the largest global study of antibiotic levels in rivers measured elevated antibiotic concentrations in 200 rivers in 90 countries in North America (including the United States), South America, Europe, Asia, and Africa. The study concluded that pharmaceutical manufacturing pollution was clearly detected as the source of elevated antibiotics in a number of rivers in Africa and Asia and also in some European rivers.<sup>37</sup>

Although the global study did not identify pharmaceutical manufacturing facilities as a source of elevated antibiotics in rivers studied in the United States, in 2018 the USGS published a study that evaluated a national network of 13 POTWs, and compared the levels of pharmaceuticals in the effluent of the treatment plants from six POTWs receiving discharges from pharmaceutical manufacturing facilities with seven treatment plants that did not receive discharges from pharmaceutical manufacturing. Effluent samples were analyzed for 120 pharmaceuticals and pharmaceutical metabolites. Of these, 33 pharmaceuticals had concentrations substantially higher in pharmaceutical manufacturing facility-influenced effluent (maximum 555 parts per billion) compared to effluent from control sites (maximum 0.175 parts per billion). The study concluded that pharmaceutical manufacturing facilities are a significant source of pharmaceuticals to the environment.<sup>38</sup>

### III. Environmental Pollution Issues in India

India is a significant global producer of pharmaceuticals, and has played an important role in making affordable medicines widely accessible through the production of very low-cost generic pharmaceuticals. This much lower cost of manufacturing has driven many large multinational pharmaceutical companies both to establish their own manufacturing plants in India and to create large supplier networks within the country. The resulting significant increase in accessibility of low-cost pharmaceuticals has saved millions of lives globally, but has also come with environmental and public health impacts.

India is the largest provider of generic drugs globally, with a pharmaceutical market valued at \$33 billion in 2017 that was expected to reach \$55 billion in 2020.<sup>39</sup> India's pharmaceutical exports were valued at \$17.3 billion in 2018, and 31% of India's total drug exports went to the United States.<sup>40</sup> The country accounts for approximately 30% in terms of volume and 10% in value of the U.S. generic market. The Indian biotechnology industry is

expected to grow at an average rate of about 30% per year and to reach \$100 billion by 2025.<sup>41</sup>

The industry is mainly divided into two segments, API and formulation (finished dosage form products). The export percentage of formulation drugs has increased over the past decade and in 2017 formulation drugs accounted for almost 65% of the total pharmaceutical export from India, while API accounted for 33% of the total pharmaceutical export from India.<sup>42</sup> The majority of APIs used in the formulated products are imported from China and represent nearly \$3.5 billion worth of APIs every year. These APIs, which are manufactured at extremely low cost, are formulated by Indian companies and many are then sold to foreign markets as finished dosage products.<sup>43</sup> The COVID-19 pandemic has created shortages in the supply of API from China and, as a result, the Indian government announced in May 2020 a government program to help fund the construction of three new bulk drug zones in India to increase the production of APIs.<sup>44</sup>

Both API and formulation manufacturing of antibiotics result in the potential loss of residual antibiotics from the production process to the environment. API manufacturing, because of its scale, complexity, and production volumes, has the potential to release more significant quantities of antibiotics to the environment than formulation manufacturing. However, the tremendous growth of antimicrobial formulation manufacturing in the past decade and projected growth of API manufacturing has and will continue, if not managed properly, to result in significant environmental pollution. The lack of transparency in pharmaceutical supply chains makes it almost impossible to map the journey of a pharmaceutical product from API manufacturing to product formulation to the pharmacy shelf. Food and Drug Administration (FDA) regulations do not require that manufacturers indicate on the final product label where the final product was formulated and, as a result, measuring a drug's environmental impact is particularly challenging where various stages of production are outsourced to suppliers.

The Indian pharmaceutical industry is highly fragmented, with more than 20,000 registered manufacturing units nationwide, and is also geographically dispersed, as manufacturing hubs are now in multiple locations across the country, with the states of Maharashtra, Gujarat, Telangana, Andhra Pradesh, West Bengal, and Tamil Nadu all registering a sizeable API and formulation manufacturing presence.<sup>45</sup> Over the past two decades, Hyderabad and Bangalore have become the largest hubs of pharmaceutical

37. Borunda, *supra* note 34.

38. Scott et al., *supra* note 28.

39. *Indian Pharmaceutical Market, Strong the Weight of Generics*, PHARMA WORLD MAG., Nov. 21, 2018, <https://www.pharmaworldmagazine.com/indian-pharmaceutical-market-strong-the-weight-of-generics>.

40. *Id.*

41. *Id.*

42. *Id.*

43. CHANGING MARKETS & ECOSTORM, IMPACTS OF PHARMACEUTICAL POLLUTION ON COMMUNITIES AND ENVIRONMENT IN INDIA (2016), [https://insights.nordea.com/wp-content/uploads/2019/02/Impacts-of-Pharmaceutical-Pollution-on-Communities-and-Environment-in-India\\_2016\\_com\\_0.pdf](https://insights.nordea.com/wp-content/uploads/2019/02/Impacts-of-Pharmaceutical-Pollution-on-Communities-and-Environment-in-India_2016_com_0.pdf) [hereinafter NORDEA REPORT] (researched and prepared for Nordea Asset Management).

44. Avishek Majumder & Priya Chetty, *An Overview of the Pharmaceutical Industry of India*, PROJECT GURU, Nov. 19, 2018, <https://www.projectguru.in/pharmaceutical-industry-india/>.

45. NORDEA REPORT, *supra* note 43, at 10.

manufacturing, with hundreds of both domestic and foreign-owned pharmaceutical plants located in and around these areas.

The city of Hyderabad has become the center for bulk API drug manufacturing,<sup>46</sup> and studies conducted in 2007 and 2008 revealed very high concentrations of APIs in streams, lakes, and effluent from local wastewater treatment plants in the region.<sup>47</sup> The concentrations in the effluent from a treatment plant receiving wastewater from about 90 manufacturing units were, for some pharmaceuticals, greater than those found in the blood of patients taking medicine. The concentration of ciprofloxacin, a broad-spectrum antibiotic, was as high as 31 milligrams per liter, which is approximately one million times greater than the levels that are regularly found in treated municipal sewage effluents, and is toxic to a range of organisms. The estimated total release of ciprofloxacin for one day was 44 kilograms, which is equivalent to Sweden's entire consumption over five days, or, expressed in another manner, sufficient to treat everyone in a city with 44,000 inhabitants.<sup>48</sup>

Hyderabad is now known as the "bulk drug capital" of India and accounts for nearly one-fifth of India's pharmaceutical exports.<sup>49</sup> The city's Patancheru-Bollaram industrial cluster, which is part of the Medak District, is home to a variety of industries including more than 100 drug manufacturing facilities. It is the source of severe water pollution, and has on two separate occasions, in 2010 and in 2013, been subject to a ban on further expansion by the Indian Ministry of Environment and Forests (Indian Environmental Ministry) owing to its status as a critically polluted area.<sup>50</sup> Several studies, including a detailed survey by Greenpeace in 2004, have highlighted how people, animals, crops, and land in the Medak District and other industrial zones surrounding Hyderabad have been afflicted by the pollution.<sup>51</sup>

In the past decade, Visakhapatnam, on the coast of the state of Andhra Pradesh, has emerged as a rival to Hyderabad's dominance of the bulk drug industry in the region. While its pharmaceutical industry is less developed compared to Hyderabad's, the Andhra Pradesh state government has ambitious future plans, and environmental sampling shows that waste from existing plants has already taken a significant toll on local villages and fish stocks.<sup>52</sup>

Pollution in areas surrounding these manufacturing plants is so extensive that it is easily evident through visual and olfactory observation.<sup>53</sup> Recent studies suggest that India, as well as China, are hotbeds for the spread of AMR because of the high levels of antibiotics and antibiotic-resistant microbes in soils and water bodies in the immediate

and surrounding areas of pharmaceutical manufacturing plants.<sup>54</sup> This presents not only a significant local public health concern but, because of globalization and international travel, localized contamination and the creation of antibiotic-resistance has global consequences.

#### IV. Government Response in India

The social and environmental costs of the development of Hyderabad's and other hubs of manufacturing are plain to see in the neighborhoods and villages surrounding the industrial areas, and have been well-documented over a period of decades.<sup>55</sup> However, the response from both the central government and the state authorities has been largely inadequate, and, over the years, irresponsible drug manufacturers have continued pumping large quantities of untreated or inadequately treated pharmaceutical waste into the environment. Inhabitants living and working in the vicinity of drug manufacturing units in Hyderabad, Visakhapatnam, and other locations have been impacted by the pollution. It has affected their livelihoods in the form of livestock deaths and decreased agricultural yields, and there have been many reports of serious impacts on the health of members of the surrounding community.<sup>56</sup>

In 1997, in response to these significant localized pollution impacts, the Supreme Court of India banned the establishment or expansion of bulk API drug manufacturing plants in the Patancheru-Bollaram region and mandated that these API manufacturers install zero liquid discharge (ZLD) wastewater treatment units, meaning that wastewater from these sites had to be treated and then reused on-site.<sup>57</sup> It is widely accepted that this requirement has been poorly enforced and that, even though most API facilities in this area have installed ZLD treatment, these units are not operated in a responsible manner.<sup>58</sup> Further, the ruling did not address wastewater from formulation manufacturing facilities, which have continued to proliferate in this region and other regions of India.

Since 2016, a number of EU Member States, in large part because of the volume of antibiotics that they import from India, called for the Indian government to impose stringent environmental limits on wastewater discharges from all manufactures of antibiotics. They have also called for drug regulatory agencies, including FDA, to expand good manufacturing practice (GMP) requirements to include antimicrobial waste management. In response, in 2018, the WHO's executive board provided technical

46. *Id.*

47. Larsson, *supra* note 6.

48. *Id.*

49. NORDEA REPORT, *supra* note 43, at 10.

50. *Id.*

51. *Id.*

52. *Id.*

53. *Id.* See the photos at <https://www.nordea.com/Images/35-107206/impacts%201-20.pdf>, taken by the consultant in the vicinity of pharmaceutical manufacturers in and around the city of Hyderabad.

54. CHANGING MARKETS & ECOSTORM, SUPERBUGS IN THE SUPPLY CHAIN: HOW POLLUTION FROM ANTIBIOTICS FACTORIES IN INDIA AND CHINA IS FUELING THE GLOBAL RISE OF DRUG-RESISTANT INFECTIONS (2016), [https://epha.org/wp-content/uploads/2016/10/Superbugsinthesupplychain\\_CMreport.pdf](https://epha.org/wp-content/uploads/2016/10/Superbugsinthesupplychain_CMreport.pdf).

55. Joakim Larsson et al., *Effluent From Drug Manufactures Contains Extremely High Levels of Pharmaceuticals*, 148 J. HAZARDOUS MATERIALS 751 (2007), available at [https://www.researchgate.net/publication/6134174\\_Effluent\\_From\\_Drug\\_Manufactures\\_Contains\\_Extremely\\_High\\_Levels\\_of\\_Pharmaceutical](https://www.researchgate.net/publication/6134174_Effluent_From_Drug_Manufactures_Contains_Extremely_High_Levels_of_Pharmaceutical).

56. NORDEA REPORT, *supra* note 43, at 15.

57. *Id.*

58. *Id.*

input on GMP guidance on waste and wastewater management from the production of critically important antibiotics.<sup>59</sup> FDA and other regulatory agencies would likely need to seek revisions in relevant regulations and/or underlying law to expand GMP requirements to antimicrobial waste management.<sup>60</sup> Despite the calls for the incorporation of environmental criteria into GMP regulations, publicly, FDA has not considered revising GMP requirements.<sup>61</sup>

In January 2020, the Indian Environmental Ministry published proposed regulations to limit the level of antibiotic residues in wastewater that pharmaceutical manufacturing facilities would be permitted to discharge into receiving water bodies. The regulations would also apply to treated effluent from common effluent treatment plants that are used by multiple API bulk drug and formulation manufacturing facilities.<sup>62</sup> The proposed regulations, if implemented, will apply to all drug manufacturing companies in India and will have specific wastewater discharge limits for 121 common antibiotics.<sup>63</sup>

The proposed rules established a 60-day public comment period. The India Drug Manufacturers' Association provided extensive comments that essentially claimed that the proposed regulations were unnecessarily stringent, that the limits were not supported by science, and that the ministry should consider following the approach of the AMR Industry Alliance.<sup>64</sup>

Even if the Indian Environmental Ministry moves quickly to finalize its proposed rules establishing discharge limits for APIs, stakeholders will likely continue to have significant concerns with the ability of the government to enforce these requirements, because of a lack of experienced inspectors needed to conduct highly technical assessments of a significant number of manufacturing facilities.<sup>65</sup> The poor enforcement of the Supreme Court's 1997 ruling that mandated for API facilities in the Hyderabad region the installation of a ZLD wastewater unit, is an example of the current significant issues with enforcement. Even certain stakeholders that support the proposed regulations

have serious concerns about the ability of the Indian Environmental Ministry and local environmental agencies to enforce the requirements because of the lack of experienced inspectors and because of corruption concerns.<sup>66</sup>

## V. Pharmaceutical Industry Response to Pollution

Many large multinational pharmaceutical companies have been working with their suppliers over the past decade to minimize the release of antibiotics and other pharmaceuticals to the environment. Most of these companies employ a risk-based approach at owned sites, and work with their suppliers using the same approach as the primary way of demonstrating that trace levels of antibiotics released in manufacturing wastewater discharges do not result in a risk to the environment or public health. The risk-based approach involves the manufacturing site estimating the loss of an antibiotic product from its manufacturing process to the site's wastewater. The mass of the antibiotic lost to the wastewater and, subsequently, the environment is then calculated to determine the predicted environmental concentration (PEC) of the antibiotic. The PEC is then compared to the predicted no-effect concentration (PNEC) of the antibiotic and if the PEC is less than the PNEC, then the amount of the antibiotic released is deemed acceptable.

In 2016, a number of pharmaceutical companies announced, at the 2016 World Economic Forum in Davos, the Declaration by the Pharmaceutical, Biotechnology, and Diagnostics Industries on Combating Antimicrobial Resistance. Following this declaration, 13 pharmaceutical companies announced specific commitments, as part of its industry road map, that they would take to address AMR. The commitments are to reduce the environmental impact from the production of antibiotics; help ensure antibiotics are used only by patients who need them; improve access to current and future antibiotics, vaccines, and diagnostics; and explore new research opportunities for open collaborations between industry and the public sector.

The AMR Industry Alliance (Alliance) was formed in 2017 to implement those commitments. The industry's commitment to addressing manufacturing-related concerns states that measures will be supported to reduce the environmental impact from the production of antibiotics, and that the following four goals will be completed by the Alliance's Manufacturing Working Group:

1. Review manufacturing and supply chains to assess good practice in controlling releases of antibiotics into the environment.
2. Establish a common framework for managing antibiotic discharge and start to apply it across manufacturing and supply chains by 2018.

59. WHO, *supra* note 33.

60. FDA and drug regulatory agencies in other countries have jurisdiction to inspect manufacturers abroad if they supply products into their country. Currently, the manufacturing requirements regulated by FDA and other drug regulatory agencies relate to product quality management and not environmental management.

61. The author conducted multiple Internet searches using various combinations of keywords—"AMR," "antibiotics," "manufacturing waste," "FDA," "environmental," "GMP"—and found no FDA documents or articles suggesting FDA is considering revising GMP to include environmental waste management.

62. Victoria Rees, *Limiting Antibiotic Manufacturing Discharge in Indian Wastewater*, EUR. PHARMACEUTICAL REV., Mar. 12, 2020, <https://www.europeanpharmaceuticalreview.com/article/115074/limiting-antibiotic-manufacturing-discharge-in-indian-wastewater/>.

63. *Id.*

64. Andrew Wasley et al., *Indian Drug Companies Try to Gut Antibiotic Pollution Controls*, BUREAU INVESTIGATIVE JOURNALISM, Mar. 31, 2020, <https://www.thebureauinvestigates.com/stories/2020-03-31/indian-drug-companies-try-to-gut-antibiotic-pollution-controls>.

65. UNITED NATIONS ENVIRONMENT PROGRAMME, *supra* note 10, at 28. A key reason for limited traction of environmental law in India is that the laws generally do not give the government civil enforcement authority or a range of enforcement sanctions short of shutting down pollution sources, which is often politically untenable. This gap in the law inhibits effective enforcement.

66. T.T. Ram Mohan, *Good Laws Exist—But Laws Alone Won't Fix India's Pharmaceutical Pollution*, SCI.: THE WIRE, Mar. 25, 2020, <https://science.thewire.in/environment/pharma-pollution-tuberculosis-antimicrobial-resistance-patancheru-bollaram-ngt/>. See also *A System in Shambles*, DOWN TO EARTH, July 31, 2001, <https://www.downtoearth.org.in/coverage/a-system-in-shambles-16636>.

3. Work with stakeholders to develop a practical mechanism to transparently demonstrate that supply chains meet the standards in the framework.
4. Work with independent technical experts to establish science-driven, risk-based targets for discharge concentrations for antibiotics and good practice methods to reduce the environmental impact of manufacturing discharges by 2020.

In 2018, the Alliance published the Antibiotic Manufacturing Framework, which sets minimum requirements for water and solid waste management, as well as guidance for conducting audits of antibiotic manufacturing operations. In 2019, the Alliance published a list of science-driven, risk-based target concentrations for wastewater discharges from antibiotic manufacturing operations. The Alliance approach is enforced through voluntary annual member reporting and it is likely that this approach will become a component of the industry's Pharmaceutical Supply Chain Initiative (PSCI). PSCI was established more than a decade ago by several large multinational companies and created principles for responsible environmental, health and safety, labor, and ethical practices that member companies expect of their suppliers.

In 2019, the Alliance developed a unified approach to establishing discharge targets for antibiotic manufacturing, based on PNECs, for use in environmental risk assessments of antibiotics. The discharge target can be derived using these PNECs and site-specific parameters. The Alliance's publication of the PNEC table fulfills its commitment to publish science-driven, risk-based targets for discharge concentrations of antibiotics.

Despite these significant recent actions by many of the large multinational pharmaceutical companies to better assure more responsible production in its supply chain,<sup>67</sup> the view of some governmental and nongovernmental (NGO) stakeholders is that the Alliance approach may not be protective enough. In their view, manufacturing sites are not moving fast enough to address pollution, and the Alliance and its members are still not as transparent as needed relative to which manufacturing sites are achieving the antibiotic discharge targets established by the Alliance.

Access to Medicine, a well-respected NGO, has for many years monitored and rated pharmaceutical companies on their efforts to provide medicines to populations that do not have the financial resources to pay for needed medicines. Since 2018, it has evaluated and graded companies on their efforts to address the AMR issue. In its

2020 benchmark report, it concluded that no companies published: (1) the levels of antibiotics in wastewaters discharged from their sites; (2) the full results of audits conducted at these sites; and (3) the results of audits to suppliers sites or the suppliers' identities.<sup>68</sup> The report noted that none of the 18 companies that have signed on to the Alliance's manufacturing commitments report monitoring antibacterial levels discharged by external, privately owned wastewater treatment plants, nor report requiring wastewater treatment plants to set limits for antibacterial discharge or monitor discharge levels.<sup>69</sup>

One important disincentive for the action of smaller manufacturers is the complexity and non-transparency of the pharmaceutical supply chain—for example, simple information on what company produces the API in a given product and where that production takes place is considered confidential by most companies, and is usually only available to the authorizing agencies to facilitate quality control inspections. This makes it a complicated task for governments and institutions to create effective systems for pollution control, or for third parties (including consumers and media) to exert pressure by linking sometimes apparently polluting production sites abroad to the companies selling the final products in consumer states.<sup>70</sup>

Dr. Joakim Larsson, an environmental pharmacologist at the University of Gothenburg, who is viewed by most stakeholders, including industry, as the leading scientist on the contribution of manufacturing wastewaters to AMR, has been supportive of the Alliance's voluntary approach to reducing antibiotics in manufacturing discharges, but more recently has suggested that the Alliance's technical approach for preventing AMR in water bodies may not be protective enough. In an article published shortly after the Indian Environmental Ministry proposed antibiotic discharge regulations, Dr. Larsson stated that the Alliance's voluntary PNEC targets are a very good starting point, but he raised some concerns about the Alliance's approach of setting antibiotic discharge targets in surface waters such as rivers and streams, rather than imposing the limits on manufacturers' discharges of the wastewater.<sup>71</sup> He stated that "bacteria are already present in wastewater, which can carry high levels of antibiotics. That means the bacteria can start to develop resistance before the waste reaches surface waters, where dilution can reduce drug concentrations."<sup>72</sup>

Dr. Larsson, Access to Medicine, and others have also expressed concerns about a "lack of transparency" in production supply chains, because the locations where antibiotic drugs are manufactured by suppliers are generally not

67. The AMR Industry Alliance has brought together more than 100 generic and research-based pharmaceutical companies that are committed to efforts in fighting AMR across four key areas: research, appropriate use, access, and manufacturing and the environment. However, as of January 2020, only 18 Alliance members have committed to work together to support specific measures to reduce environmental pollution from antibiotics. One measure included the establishment of science-driven, risk-based targets for discharge concentrations for antibiotics and good practice methods to reduce the environmental impact of manufacturing discharges. Since these measures are voluntary and self-regulated, and only 18 members have committed to them, there remain significant concerns that industry efforts will not adequately address the manufacturing discharge issue.

68. ACCESS TO MEDICINE FOUNDATION, *supra* note 27.

69. *Id.*

70. Niels Nijsingh et al., *Managing Pollution From Antibiotics Manufacturing: Charting Actors, Incentives, and Disincentives*, 18 ENV'T HEALTH 1 (2019), available at <https://ehjournal.biomedcentral.com/track/pdf/10.1186/s12940-019-0531-1>.

71. Natasha Gilbert, *Industry Says Voluntary Plan to Curb Antibiotic Pollution Is Working, but Critics Want Regulation*, SCIENCE, Jan. 24, 2020, <https://www.sciencemag.org/news/2020/01/industry-says-voluntary-plan-curb-antibiotic-pollution-working-critics-want-regulation>.

72. *Id.*

made public by pharmaceutical companies.<sup>73</sup> Health Care Without Harm, an international group that advocates for environmentally responsible health care, does not believe the Alliance's voluntary approach goes far enough, and believes that there is an urgent need to establish a strong legislative framework to increase transparency and improve consistency throughout the supply chain.<sup>74</sup>

In addition to several stakeholder concerns with the Alliance's approach to addressing antibiotics in manufacturing wastewater, the Alliance's voluntary approach could also disadvantage large multinational companies relative to the smaller companies operating in India that provide drug products to the EU and the United States, because these multinational companies are more likely to require their suppliers to comply with the voluntary scheme. The actions required of multinational suppliers in many cases could require the suppliers to spend capital to install advanced wastewater controls, which would add to their cost of goods. Smaller manufacturing companies that are not suppliers for multinational companies and that have not signed on to the Alliance's manufacturing commitments will likely not expend capital to voluntarily control antibiotic product residues in wastewater discharges, allowing them to produce antibiotics at a lower cost than companies adding controls. This could lead to lost market share for generic products sold by multinational companies.

The Alliance, perhaps in response to stakeholder concerns and in recognition that their suppliers could be disadvantaged if they implement the Alliance's approach, is now developing a private sustainability standard that would be audited against by an independent, credible third-party technical engineering organization.<sup>75</sup> This approach holds the potential to address stakeholders' concerns about transparency and stringency of the voluntary Alliance standard because its development would involve input from key stakeholders.<sup>76</sup> The approach could potentially level the playing field, and ultimately raise environmental performance across the entire pharmaceutical supply chain. This type of certification could be provided to governmental and large institutional buyers to demonstrate that the drug product has been manufactured in a manner that is not expected to contribute to AMR. There are strong signals that markets in the EU might provide a buying preference to products with such a third-party certification.<sup>77</sup>

Because of the complexity of the pharmaceutical supply chain, with bulk API manufactured typically by one company and then sold to another company for formulation of the final drug product by mixing the API with excipients, there is a need to track the API and its manufacturing through the supply chain. This could potentially be accomplished using blockchain technology, and the use of

a QR code on the product label that could be scanned and linked to the blockchain to retrieve data related to where the antibiotic was initially produced and where it was formulated with excipients to make the final drug product. The blockchain would include the key environmental data related to manufacturing, including whether the antibiotic was manufactured in an environmentally responsible manner through the supply chain steps and the certification status of the production process at the different supply chain steps.

As described in detail below, a number of VSS that were developed, implemented, and assessed in a credible manner have resulted in significant improvements in a number of areas facing significant environmental challenges.

## VI. Private Governance Approaches to Address Gaps in EROL

Over the past few decades, VSS have emerged as a new governance approach to address significant environmental, fair trade, labor, human rights, and other social issues in product supply chains.<sup>78</sup> In the 1990s, the first VSS with global reach were launched in the areas of agriculture, forestry, and fair trade. The rapid growth of these standards is part of a broader trend in a governance shift from a system of state-centered or public governance toward a private governance system. These establish a new regulatory system, as VSS set social and environmental standards for transnational production, and they often operate certification programs to verify compliance in global value chains.<sup>79</sup> The Sustainability Map<sup>80</sup> of the International Trade Centre is an inventory of VSS, and now counts more than 240 programs that are active in a wide range of countries and product fields.

Many VSS have been successful in reducing the negative environmental impacts of commodity production, while also bringing benefits for communities, workers, and businesses. A growing body of evidence demonstrates that positive changes occur when products from fisheries, farms, forests, industry, and other enterprises are certified against credible standards. Documented positive impacts from certified operations or products include reduced environmental pollution, lessened impacts on biodiversity, and increased product quality, higher incomes, and improved labor conditions.<sup>81</sup>

In addition, the impact of standards goes beyond the individual certified operations and can also affect whole systems, in both large and small ways, by shaping govern-

73. ACCESS TO MEDICINE FOUNDATION, *supra* note 27, at 61.

74. Press Release, Health Care Without Harm, Time to Clean Up the Pharmaceutical Industry (Sept. 15, 2020), <https://noharm-europe.org/articles/press-release/europe/time-clean-pharmaceutical-industry>.

75. Video: Antimicrobial Resistance—World Health Summit, *supra* note 12 (at the 30-minute mark).

76. *Id.* (invitation to stakeholders at the 31-minute mark).

77. SIWI WHITEPAPER, *supra* note 26.

78. KATHARINA BISSINGER ET AL., INTERNATIONAL TRADE CENTRE, LINKING VOLUNTARY STANDARDS TO SUSTAINABLE DEVELOPMENT GOALS (2020).

79. UNITED NATIONS FORUM ON SUSTAINABILITY STANDARDS, VOLUNTARY SUSTAINABILITY STANDARDS, TRADE, AND SUSTAINABLE DEVELOPMENT: 3RD FLAGSHIP REPORT OF THE UNITED NATIONS SUSTAINABILITY STANDARDS (UNFSS) (2018).

80. Sustainability Map, *Home Page*, <https://www.sustainabilitymap.org> (last visited May 26, 2021).

81. WWF ET AL., VOLUNTARY SUSTAINABILITY STANDARDS 2018, [https://www.isealliance.org/sites/default/files/resource/2019-05/WWF\\_ISEAL\\_VSS\\_Systemic\\_Impacts\\_2018\\_4pager.pdf](https://www.isealliance.org/sites/default/files/resource/2019-05/WWF_ISEAL_VSS_Systemic_Impacts_2018_4pager.pdf).

ment and private-sector policies, sharing knowledge and training, and raising consumer awareness. In doing so, they help to create an enabling environment for sustainable production and consumption practices across complex supply chains that can significantly benefit the public and the environment.<sup>82</sup> These systemic impacts can play a significant role in tackling the root causes of unsustainable practices and extending, deepening, and sustaining the positive effects of certification.

Importantly, these standards can result in significant sustainability improvements in operations or products that pose serious global environmental challenges. Examples include the Roundtable on Sustainable Palm Oil, Marine Stewardship Council, Aluminum Stewardship Initiative, Global Organic Textile Standard, and Rainforest Alliance. These standards have been successful because consumers of products, in the respective sectors, create a market demand for products that meet the environmental and/or sustainability standard. In the agriculture sector, commodities with a significant share of global production certified by a sustainability standard include cocoa (25%), coffee (23%), cotton (16%), tea (16%), and palm oil (12%).<sup>83</sup>

Increasingly popular as a governance approach for sustainable supply chain management, reputational risk mitigation, and the promotion of competitiveness, more and more leading companies in global value chains are adopting VSS for their products and making buying decisions dependent on suppliers' compliance with voluntary standards or requirements.

Given the growing salience of sustainability issues on the international policy agenda, VSS are now also being discussed as a key instrument to help multinational corporations and governments contribute toward achieving the United Nations' Sustainable Development Goals and its 2030 targets.<sup>84</sup>

#### A. Growing Market Demand for Antibiotics Manufactured in an Environmentally Responsible Manner

The United Nations launched the Sustainable Procurement in the Health Sector Initiative (SPHS) in 2012. Representing a cumulative purchasing power of \$5 billion, SPHS aims to lower the environmental and social impacts of its procurement and to act as a driver for change by engaging with suppliers, awareness-raising, and promoting capacity-building.<sup>85</sup> The initiative runs the Sustainable Health in Procurement Project (SHiPP), which aims to develop universally applicable criteria for sustainable procurement in the health sector and to strengthen the

capacity for sustainable production, procurement, supply, and disposal of health care products in low- and middle-income countries.<sup>86</sup>

The most recent national initiative for sustainable pharmaceutical procurement practices is in Norway, where the Hospital Procurement Trust manages the procurement of pharmaceutical products for all health authorities in the country. It has launched a new antibiotic procurement policy in which suppliers that can document good environmental efforts during the manufacturing process will have an advantage in the selection process, based on the "supplier's environmental policy, environmental strategy, and control system for environmental issues."<sup>87</sup> Under the new system, "environmentally friendly production will be weighted by 30 percent as allocation criteria."<sup>88</sup>

In Sweden, the sustainability criteria for public procurement of medicines were updated in 2019.<sup>89</sup> Beyond the availability of basic supply chain information and environmental risk information of the API, contract clauses require the suppliers to have systems in place to map and prevent emissions of APIs to the environment. One specific clause requires that a supplier of a pharmaceutical drug adopt a publicly available environmental policy, decided by senior management, which includes a commitment to reduce the risks of API emissions to the environment in the manufacture of the contracted medicinal products.<sup>90</sup> Although different in detail and how the information is applied, both countries require some level of disclosure of the supply chain and environmental strategies to prevent APIs from being released to the environment.

#### B. The Importance of Credibility, Relevance, and Legitimacy in VSS

Despite the growth in VSS to address environmental and other social challenges, there is no universally agreed-to criteria for the establishment of a VSS, and many have been developed without key stakeholder input and/or are not effective. As a result, many VSS lack credibility. VSS that are not credible can erode trust in those that are credible, and many stakeholders, including governmental environmental regulators and the public, are skeptical of the ability of VSS to effectively address important environmental challenges.<sup>91</sup>

82. Media Release, Research Institute of Organic Agriculture, New Report Finds Voluntary Sustainability Standards on the Rise (Oct. 1, 2018), <https://www.fibl.org/en/info-centre/news/new-report-finds-voluntary-sustainability-standards-on-the-rise.html>.

83. *Id.*

84. BISSINGER ET AL., *supra* note 78.

85. SIWI WHITEPAPER, *supra* note 26.

86. SPHS, *Sustainable Health in Procurement Project (SHiPP)*, <https://savingslivesustainably.org/knowledge-practice/contribution/sustainable-health-in-procurement-project-shipp/530> (last updated July 2, 2018).

87. Sykehusinnkjøp HF, *New Environmental Criteria for the Procurement of Pharmaceuticals*, <https://sykehusinnkjop.no/nyheter/new-environmental-criteria-for-the-procurement-of-pharmaceuticals> (last updated Feb. 24, 2021).

88. *Id.*

89. Swedish National Agency for Public Procurement, *Home Page*, <https://www.upphandlingsmyndigheten.se/en/> (last visited May 26, 2021).

90. *Id.*

91. Lucia Gatti et al., *Grey Zone In—Greenwash Out. A Review of Greenwashing Research and Implications for the Voluntary-Mandatory Transition of CSR*, 4 INT'L J. CORP. SOC. RESP. (2019), <https://doi.org/10.1186/s40991-019-0044-9>.

Credibility, relevance, and legitimacy are often cited as determinants of how to convert what science has identified as a need into environmental policy and serve as criteria for their evaluation.<sup>92</sup> In general, credibility can be understood as the quality or power of inspiring belief, relevance as the degree of relation to the matter at hand, and legitimacy as conformity to recognized principles or accepted rules and standards.<sup>93</sup> When applied to environmental or public health challenges, relevance can be thought of in terms of effectiveness—in other words, is the VSS effective in addressing the environmental or public health challenge?

Organizations and scholars have identified criteria for determining whether these key attributes have been achieved in a VSS. The International Social and Environmental Accreditation and Labelling (ISEAL) Alliance is a London-based umbrella organization of leading VSS programs, and uses the term “standard system” to describe “the collective of organizations responsible for the activities involved in the implementation of a voluntary sustainability standard, including standard-setting, capacity-building, assurance, labeling, and monitoring and evaluation.” ISEAL has established a set of principles that identify the attributes of a credible VSS. ISEAL has also developed three codes of good practice that provide a globally recognized framework used by credible sustainability standards.

The good practices focus on the core elements of a credible sustainability standard. The standard-setting good practice defines how a standard should be developed, structured, and revised. It requires multi-stakeholder consultation and decisionmaking, and ensures clear and auditable conditions in the standard itself. The good practice on assurance provides a framework for assessing compliance with standards. It encourages assurance that is rigorous and accessible, ensuring accurate and transparent results. The good practice on impacts outlines robust monitoring and evaluation systems. It provides standards with a road map to measure progress against sustainability goals and to improve practices over time.<sup>94</sup>

A number of academic experts have also researched and identified what attributes are needed for a VSS to be credible, effective, and legitimate in terms of determining whether the private governance approach is an adequate substitute for a robust public governance approach.<sup>95</sup> Informed by these experts, Louis Leonard distilled a two-

part governance inquiry for private governance approaches to address climate change—built upon concepts of effectiveness and legitimacy. Leonard identified the following inquiries to frame the analysis of whether a private climate governance approach is an appropriate substitute for a public governance approach<sup>96</sup>:

1. *Is the private environmental governance system effective?*  
Does the collective body of private climate activity measure up against key operational functions expected of public policy? How can we be confident that particular private initiatives are likely to achieve their goals?
2. *Is a private environmental governance system legitimate?*  
Do private climate initiatives meet considerations of legitimacy by addressing three core safeguards: procedural fairness, transparency, and justice?

The inquiries appear to be readily adaptable to most private environmental governance approaches, and the analysis of the effectiveness and legitimacy of a private environmental approach is discussed with this view.

### C. Considerations to Help Assure an Effective Antibiotic Manufacturing Process VSS Scheme

Leonard recommended that effectiveness calls for examination at both the systems and initiative levels. First, if a private system seeks to advance public priorities, effectiveness suggests that it drive behaviors and results that, in some meaningful way, are comparable to those of a “good” public system. Recognizing the risks of comparing real-world actions to hypothetical public policy, Leonard suggested a systemwide effectiveness framework based upon core “operational functions” that might be expected under public environmental law. These are identified below, and examples of how they might inform a VSS for the reduction of antibiotics in manufacturing wastewater effluents are described.

#### 1. Motivating Participation

In a public law system, entities are compelled to participate by the threat of negative sanctions or the benefit of positive incentives. In the absence of legal coercion, other mechanisms are needed to drive private-sector actors to enter the system.

Certain EU Member States have expressed concerns about buying generic antibiotics to supply their health care systems from manufacturers that are not producing the

actors involved in climate governance against considerations of justice, legitimacy, and effectiveness.

96. Although Leonard’s inquiry focused on private climate governance, it provides a framework for analysis of private governance approaches to other environmental challenges.

92. Ulrich Heink et al., *Conceptualizing Credibility, Relevance, and Legitimacy for Evaluating the Effectiveness of Science-Policy Interfaces: Challenges and Opportunities*, 42 *SCI. & PUB. POL’Y* 676 (2015).

93. *Id.*

94. ISEAL, *ISEAL Credibility Principles*, <https://www.isealalliance.org/credible-sustainability-standards/iseal-credibility-principles> (last visited May 26, 2021).

95. Louis G. Leonard III, *Under the Radar: A Coherent System of Climate Governance, Driven by Business*, 50 *ELR* 10546, 10550 (July 2020). Business administration scholars Eric Orts and Sarah Light suggest 10 normative criteria to inform comparisons of private and public environmental governance. Michael Vandenbergh and Jonathan Gilligan analyze private climate action against questions of accountability, environmental justice, adequacy, and effectiveness. Christopher May explores traditional notions of governance powers and the extent to which companies effectively and legitimately exercise those powers. Political scientists, like Liliana Andonova et al. and Jonathan Kuyper et al., examine the broader set of non-state

antibiotics in an environmentally responsible manner. A credible VSS would allow a manufacturer to demonstrate that its generic antibiotic was produced in an environmentally responsible manner, resulting in providing the buyer a choice in purchasing a responsibly made antibiotic over one that does not demonstrate responsible production. This type of market reward system could drive additional private actors to enter the system.

## 2. Setting Standards

Effective public policy standards include emissions targets, technology-based performance standards, and other tools to align policy with science-informed goals. An effective private system also needs standards that promote alignment with societal, science-based benchmarks.

The VSS for antibiotic manufacturing processes would need to establish a scientifically based safe wastewater emission level, and could do this by applying the PNEC established for antibiotics by leading scientific experts in the field and which has been adopted by the AMR Industry Alliance. Whether this concentration is applied at the facility fence line or in the receiving water body should be informed by external, independent technical experts that participate in the development of the VSS.

## 3. Assessing and Disclosing Emissions Data

An environmental governance system requires information on emissions attributed to specific actors to facilitate allocation of responsibility. Particularly in a decentralized private system, these data should be as transparently accessible as possible.

A VSS that establishes a discharge concentration limit on an antibiotic will help determine the antibiotic emissions of the participating manufacturer and help identify the sources of manufacturers of the same generic antibiotics that are not participating in the scheme through sampling in receiving water bodies. But this only comes with transparency relative to where specific generic antibiotics are manufactured in the region.

## 4. Driving Implementation

Public law uses various tools to foster performance against standards and goals, including subsidies, market-based instruments, and capacity-building programs. A private system needs to create tools and initiatives specifically focused on helping address implementation challenges within and across companies and sectors.

An antibiotic market that rewards responsible manufacturers and punishes irresponsible manufacturers should drive the implementation of the VSS. Smaller manufacturers would also greatly benefit from capacity-building due to the technical challenges of wastewater treatment of antibiotics, so the VSS scheme that is being developed by the AMR Industry Alliance should consider funding for capacity-building for smaller manufacturers. Other VSS

schemes have funded capacity-building for nonparticipating entities.<sup>97</sup>

## 5. Fostering Cooperation With the Government and Other Partners

Any good public environmental policy addressing global environmental challenges would recognize that achieving global goals requires action across systems (e.g., geographic, political, social, economic), and would include elements to foster such engagement. A private system also should not operate in a vacuum, and must promote connections and cooperation with other systems advancing protection of the environment and public health, particularly around public policy.

The focus of this Article is to demonstrate the need for, and to gain support for, a VSS designed and implemented to address the very significant environmental and public health challenges in India caused by poorly treated manufacturing wastewaters containing antibiotic residuals. The need is most urgent in India because India has more pharmaceutical manufacturers than any other country (although China leads the world in API manufacturing sites), and because the vast majority of its water bodies where effluents are discharged are used for household bathing, fishing, and recreation, so the risk of AMR from direct environmental contact is very high.

That said, according to the USGS and academic research, high levels of antibiotics from pharmaceutical manufacturing are present in many rivers in China, the United States, and many countries in Europe, Africa, and South America. The WHO and United Nations have concluded that antibiotics in water bodies from manufacturing is a global public health challenge, and since there are no environmental laws limiting antibiotics in wastewater anywhere in the world, a VSS should drive cooperation, engagement, and action across geographic and political systems.

## 6. Tracking Progress

Mechanisms to measure and publicly report progress against goals are fundamental to any governance system. In a distributed, bottom-up private system, accurate and accessible tracking systems are vital.

The AMR Industry Alliance is already publicly reporting progress against goals it has established for implementing the measures it has adopted for reducing antibiotics from manufacturing. Stakeholders have commented that although progress is being made, more transparency is needed in progress reporting. Since the VSS would be developed on a product-specific basis and require the manufacturing process to be assessed to certify the product, this would drive transparency in public reporting of progress against industry goals.

97. WWF ET AL., *supra* note 81.

## 7. Promoting Accountability

Most public environmental law systems have robust mechanisms to hold to account those who do not comply, but some form of accountability is fundamental to the function of governance, including private governance.

An independent third-party verification of compliance with the VSS could be the primary mechanism to promote accountability of compliance since significant noncompliance should result in loss of a product's certification. If the system is designed properly, a product lacking certification should result in less market preference.

## 8. Coordinating the System

The scope of a global environmental challenge demands governance that can manage complexity. Although government bureaucracies implementing complex policies raise their own issues, coordination strategies are a common attribute of public governance. An inherently decentralized private governance system needs to efficiently engage targeted participants, limit overlapping initiatives, ensure scaling of impactful initiatives, and fill critical gaps, all while maintaining agility and a culture of innovation.

Many final products manufacturers (formulation facilities) purchase the antibiotic API from other manufacturers, many of which are located in China. A mature VSS certification scheme would need to consider limiting a product's certification to those that use API material that meet the VSS standard—in other words, both the API manufacturing process and the final formulation process would need to meet the VSS standard. This will require coordination across companies and in many cases across regions of the world.

### D. Considerations to Assure a Legitimate Antibiotic Manufacturing Process VSS

In addition to a VSS scheme being effective, it is important that the VSS is a “legitimate” form of governance. Leonard concluded that what defines a legitimate form of private environmental governance warrants additional research, but identified the following important considerations: (1) fair decisionmaking process; (2) transparency around information and outcomes; and (3) equity and justice. Since in public environmental governance these attributes are widely accepted as being essential for robust governance, the antibiotic manufacturing process VSS scheme should consider these and others that help assure the legitimacy of the governance approach.

#### 1. Fair Decisionmaking

As Leonard observed, the groups implicated by decisions are (1) targeted participants in the initiatives (often companies or other private actors) and (2) the public at large, whose interests these initiatives serve. As such, key decisionmaking should be fair to both groups.

In light of this, in developing the antibiotic manufacturing process VSS scheme, the following should be considered: initiatives have clear, consistent, transparent decisionmaking processes that provide notice of key decisions; input is solicited from the public and targeted participants; and initiatives are responsive to public comments, including complaints about decisions made.

#### 2. Transparency of Decisions and Data

Transparency of decisions and data is important for targeted participants in private initiatives, for fostering public participation, and, in many respects, for the effectiveness of the system as a whole. Maximizing transparency of decisions and data can build public confidence and legitimacy in the private system.

#### 3. Equity and Justice

Although antibiotics released in manufacturing wastewater discharges pose global public health risks because of how pathogens with resistant genes can spread due to global travel and other mechanisms, the most acute impacts of antibiotics in wastewater discharges are on the communities in the vicinity of poorly managed pharmaceutical manufacturing plants. In India, for example, these communities are typically made up of poor individuals that use the local environment to grow their food, for drinking water, and for hygiene needs (bathing and laundering in local water bodies). An equitable and just antibiotic manufacturing process VSS scheme needs to consider an implementation plan that addresses, on a priority basis, the special needs of these communities.

An antibiotic manufacturing process VSS that is developed and implemented in a manner that meets the widely recognized criteria for credibility, effectiveness, and legitimacy can fill a void or complement a public regulatory standard. Robust compliance with an antibiotic manufacturing process VSS could be achievable through a strong signal in the marketplace that antibiotic products that are certified against the VSS will gain market preference over antibiotic products that do not comply with the VSS.<sup>98</sup>

This is not to suggest that public actors play no role in the field of voluntary standard-setting; to the contrary, many VSS have benefited from public engagement in one way or another. In this regard, governments and international organizations sometimes provide direct and indirect support to VSS (e.g., funding, technical assistance, or endorsement). There are several publicly sponsored voluntary programs and prominent examples include the U.S. Department of Agriculture's National Organic Program and EU organic farming.

98. See Sykehusinnkjøp HF, *supra* note 87 (“When preparing a new procurement of antibiotics, suppliers that can document good environmental efforts during the manufacturing process will, for the first time, be rewarded in the procurement process.”).

## **VII. Conclusion: A VSS for Antibiotic Manufacturing Processes Should Be Supported by Stakeholders Because of the Significant Benefits to Public Health**

The significant pollution challenges in India and elsewhere stemming from pharmaceutical manufacturing are due in large part to gaps in EROL. This public health challenge presents an opportunity to develop and implement a private environmental governance approach as a stand-alone approach or to complement a government regulatory program. The development and implementation of a VSS that appropriately limits the release of antibiotic residues to the environment and that uses an independent, credible assessment of the manufacturing operations to certify that production of a particular antibiotic product fully complies with the standard would likely lead to significant improvements, because there is a large market composed of EU Member States that are seeking to purchase antibiotic products that are manufactured responsibly.

A VSS, developed in a transparent manner and with the input of technical and governance experts, has the potential to be more quickly and widely implemented than an approach that employs only a public governance approach. An approach that provides buyers and consumers the con-

fidence (i.e., designed to be effective and is legitimate) in how the generic antibiotic was manufactured should drive the market demand for the product, and this market response should drive other manufacturers of antibiotics to improve their operations so that they can also benefit in the market. A market preference for antibiotics manufactured in an environmentally responsible manner should provide an important catalyst to improve environmental aspects of the pharmaceutical manufacturing supply chain in the near term.

This VSS approach would level the playing field between responsible actors that spend money on environmental controls that could increase their cost of goods, potentially making them less competitive in the marketplace, and irresponsible actors that do not spend money on environmental controls, because the market approach should reward actors that produce antibiotics in an environmentally responsible manner. There are few other issues that impact public health so significantly, that without significant improvements in the near term across a large and complex supply chain, tens of thousands of individuals will remain at risk of adverse health impacts.<sup>99</sup>

For the reasons articulated here, government actors, buyers of antibiotics, and public health officials should consider working closely as stakeholders in support of the AMR Industry Alliance effort to develop a VSS to address this very significant public health challenge.

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99. Statista, *supra* note 13.