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The Efficiency of Bringing Drugs to Market Versus the Fairness of Making Drugs Accessible

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As the 2014 Ebola outbreak continues to spread in West Africa, drug companies, national governments, and public health entities as a whole are coming under increasing criticism for failing to offer what many would view as equitable approaches to addressing public health epidemics, particularly those occurring in poor or developing nations. Indeed, public health threats like the Ebola virus challenge drug companies to find the right balance between making unproven treatments available to desperate populations and ensuring the safety and efficacy of treatments that have yet to undergo comprehensive clinical testing. Furthermore, striking such a balance highlights a medical ethics issue that has haunted some of these drug companies in the past: conducting clinical trials on foreign populations with few of the ethical and safety protections required by western cultures, yet then pricing drugs out of the market for these same populations once they are FDA approved.

Foreign Data to Support U.S. Drug Marketing Approval

The Federal Food, Drug, and Cosmetic Act (FFDCA), which gives the FDA legal authority to oversee the safety and efficacy of drugs in the U.S., requires that several conditions be met before marketing approval can be granted. Among other requirements, 21 U.S.C. § 355(d) requires data showing that a new drug is safe for use under prescribed conditions and substantial evidence of efficacy as demonstrated through controlled clinical trials on human subjects. Clinical trials are normally conducted for multiple research phases that generally progress according to dosage and number of subjects (anywhere from a few participants to a few thousand participants) and are carried out at a large expense to the drug sponsor.

While legally conducting clinical trials on human subjects in the U.S. requires a drug maker to first obtain an Investigational New Drug (IND) designation from the FDA, 21 U.S.C. § 312.120(a) stipulates that the FDA can also "accept as support for an … application for marketing approval … a well-designed and well-conducted foreign clinical study not conducted under and IND," provided that the "study was conducted in accordance with good clinical practice (GCP)," and that the "FDA is able to validate the data from the study through onsite inspection if the agency deems it necessary." Drug companies may realize significant benefits from conducting clinical trials abroad, such as lower costs and faster study results. In fact, a report issued by the Department of Health and Human Services in 2010 indicated that approximately 40 – 65% of all clinical trials investigating FDA-regulated products are conducted outside of the U.S. One significant factor that has contributed to a shift of clinical trials to foreign countries is a loophole in FDA regulations that allows foreign clinical trial data to be considered for U.S. marketing approval even if U.S. clinical trials suggest that a drug has no benefit. In some cases, clinical trials may be carried out in countries where regulatory laws or weak or non-existent.

Not surprisingly, critics have expressed concerns about the shift to such foreign clinical trials (especially in developing countries) as related to rights and welfare of study participants, data integrity, and the applicability of study results to the U.S. population. In one example, Pfizer settled charges and lawsuits brought by Nigerian clinical trial participants in *Abdullahi v. Pfizer, Inc.*

following an additional lawsuit brought the Nigerian government, which accused Pfizer of improprieties in testing an experimental antibiotic in a clinical trial during which 11 children died in a 1996 Meningitis outbreak in northern Nigeria. While Pfizer denied any wrongdoing and insisted that the deaths resulted from the disease and not from its drug, such a case highlights the concern that critics have about participant welfare in clinical trials conducted abroad.

The 2014 Ebola Outbreak as a Case Study in Experimental Drug Accessibility

Now, juxtapose the ability of U.S. drug companies to perform clinical trials on participants in underdeveloped countries with a lack of access to experimental treatments for populations within such countries during times of urgent medical need—the 2014 Ebola outbreak has spotlighted this issue. In August, 2014, the experimental drug ZMapp targeting the Ebola virus was provided to two American medical workers who contracted the virus while providing aid to infected patients in West Africa under an expanded access program, in which the FDA allows use of an investigational drug outside of a clinical trial by patients with serious or life-threatening conditions who do not meet enrollment criteria for clinical trials. One hurdle that currently prevents larger-scale dissemination of ZMapp is the fact that the drug has yet to undergo clinical trials proving its safety and efficacy. For example, while the American medical workers have shown significant improvement following treatment with the drug, two other individuals that received the drug abroad in August 2014 did not survive the infection. Furthermore, the FDA has yet to approve any drugs for the treatment or prevention of the Ebola virus.

With the unavailability of experimental treatments in affected regions, several health practitioners in Africa and other countries have called for the release of the drug to African doctors treating affected patients as a matter of both morality and practical course. However, some warn that making unapproved experimental drugs more widely available would be unethical, especially in light of past clinical trials that have been conducted in developing countries by Western sponsors. In an August 2014 summary of an Ebola Virus Disease panel discussion, the World Health Organization stated that “it is ethical to offer unproven interventions with as yet unknown efficacy and adverse effects, as potential treatment or prevention” in certain situations.

Ultimately, making treatments accessible to populations most in need of medical care, while ensuring the safety and effectiveness of those treatments in an ethical manner will require continued vigilance by national regulatory bodies and a commitment to a coordination of international efforts.