

Via Electronic Submission

November 17, 2017

Scott Gottlieb, MD
Commissioner
United States Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Re: FDA-2017-N-3615: Administering the Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access; Public Meeting; Request for Comments; Extension of Comment Period

Dear Commissioner Gottlieb:

The EveryLife Foundation for Rare Diseases (“EveryLife”) is an organization dedicated to improving the science and predictability of the development of rare disease therapies. Currently, there are fewer than 400 FDA approved treatments for the 7,000 rare diseases which affect more than 30 million Americans. The science exists for many of these diseases to be treated but treatments may never be developed for rare disease patients because of roadblocks in the development process, such as a lack of investment and a challenging regulatory environment.

The EveryLife Foundation works with patient organizations, industry, academia, the FDA and the National Institutes of Health (“NIH”) to improve the clinical development process through our Community Congress, annual Rare Disease Scientific Workshop, and legislation at the state and federal levels.

EveryLife thanks the FDA for the opportunity to provide comments on the public meeting entitled “The Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access” published in the Federal Register on September 19, 2017.¹

Striking an appropriate balance between the incentive to innovate and access to affordable therapies is essential to strengthening the American health care system and securing patient access to new and innovative therapies. Policymaking in this area should place special emphasis on promoting the development of and access to new therapies for rare disease patients where the need for innovative and lifesaving treatments is not being met. Congress and the FDA should work to promote patient access to new products by promoting efforts to repurpose products already approved by the FDA to treat rare disease indications.

¹ <https://www.federalregister.gov/documents/2017/09/19/2017-19904/administering-the-hatch-waxman-amendments-ensuring-a-balance-between-innovation-and-access-public>

Congress and FDA should focus on promoting the development of new therapies for rare disease treatment by providing incentives to repurpose existing scientific knowledge and economic investments. This approach would bring additional therapies that are proven safe and effective to patients suffering from rare disease or disorders with lower upfront costs and a faster development time.

Rare disease patients remain an underserved population by the pharmaceutical industry and face harsh economic and clinical realities. There are approximately 30 million Americans that suffer from over 7,000 known rare diseases; while the overall population of people affected by rare disease is large, individual diseases have small patient populations. Thus, the usual market incentives for pharmaceutical companies to invest in disease therapies do not work for rare diseases. The purpose of the Orphan Drug Act of 1983 was to ameliorate this well-known disconnect. The incentives offered by the Orphan Drug Act, plus scientific and technological advancements have led to a recent increase in the development of treatments for rare diseases. But while this trajectory is promising, the work is far from done.

Developing new therapies is an expensive venture. Recent estimates place the average cost of developing a new drug as high as 2.6 billion dollars.² Absent appropriate financial incentives, pharmaceutical companies would be less likely to invest in developing therapies to treat rare diseases because development costs far outweigh the commercial potential for rare disease products. Moreover, new technologies, like next-generation genomic sequencing, are enabling better diagnosis of specific conditions, which is expanding the gap between the number of known rare diseases and the dearth of dedicated treatments. These new economic and clinical realities require new solutions to foster innovation. By leveraging existing knowledge, rare disease patients could have faster access to more affordable therapies that are proven to be safe and effective for their conditions.

Today, for many rare disease patients the only medications available are those that are prescribed off-label. One study estimates that 90% of all patients with rare diseases have been prescribed off-label treatments.³ Such high reliance on off-label use has significant consequences for patients and the health care system. First, off-label use of clinical therapies is often not supported by scientific or clinical evidence.⁴ This leads to an inefficient use of health care resources at a time when drug costs and other health care costs are closely scrutinized. Further, without clinical evidence demonstrating quality and safety, there is non-trivial risk associated with off-label use. For example, a 2016 study demonstrated that off-label use that is not supported by adequate

² “Cost to Develop and Win Marketing Approval for a New Drug is \$2.6 Billion,” Tufts Center for the Study of Drug Development website, http://csdd.tufts.edu/news/complete_story/pr_tufts_csdd_2014_cost_study

³ Bryan Liang & Tim Mackey, *Reforming Off-Label Promotion to Enhance Orphan Disease Treatment*, SCIENCE Jan. 15, 2010 at 273.

⁴ Health Affairs, *Off-Label Drug Promotion*, HEALTH AFFAIRS, June 30, 2016 available at <http://www.healthaffairs.org/doi/10.1377/hpb20160630.920075/full/>.

evidence is associated with significantly higher rates of adverse drug events.⁵ Moreover, off-label use of prescription drugs is often not covered by insurance companies, leaving patients responsible for the typically high cost of off-label medicine.

Even though the rare disease patient population is underserved, there is great promise to improve access by leveraging existing scientific and clinical knowledge through a process known as repurposing. Repurposing takes an existing FDA-approved therapy and studies whether alternative uses may support a novel FDA indication. Providing an incentive to repurpose FDA approved therapies through an extended period of market exclusivity will reward the development of new evidence and aid in alleviating the critical access gap facing rare disease patients today. Repurposing is less expensive than new development, can get approved drugs to patients more quickly, and improves safety and efficacy for people with rare diseases. But it still costs companies money, and needs to be incentivized.

The proposed incentive to repurpose approved drugs by rewarding new FDA labeling indications builds on the lessons learned from previous efforts to drive innovation for underserved populations. Both the Orphan Drug Act (ODA) and the Best Pharmaceuticals for Children Act (BPCA) provide successful frameworks for approaching the innovation gap for underserved populations.

The ODA offers several incentives to support the development of new drugs for rare diseases. The most successful in promoting innovation was the availability of 7 years of market exclusivity for products that are designated by the Secretary for the treatment of a rare disease or condition.⁶ This spurred research that would not have taken place without the exclusivity provision. One study found that only 10 percent of clinical trials on orphan drugs would have been conducted in the absence of financial incentives.⁷

Similarly, the BPCA was enacted in 2002 to promote clinical investigation of the safety and efficacy of existing drugs in children.⁸ The BPCA provides a 6 month extension in marketing exclusivity in exchange for studying the effects of on-patent and off-patent drugs in children. The BPCA does not require a sponsor to successfully obtain a labeling change as a result of the incentivized research. The BPCA has resulted in over 600 labeling changes, substantial clinical

⁵ Tewodros Eguale, David Buckeridge, Amam Verma, et al, *Association of Off-label Drug Use and Adverse Events in an Adult Population*, JAMA INTERNAL MEDICINE, available at <https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2467782>

⁶ Orphan Drug Act, Pub. L. 97-414, 96 Stat. 2049 (creating § 525 - §528 of the Federal Food, Drug, and Cosmetic Act as amended).

⁷ CR Blankart, T Stargardt, J Schreyogg, *Availability of and access to orphan drugs: an international comparison of pharmaceutical treatments for pulmonary arterial hypertension, Fabry disease, hereditary angioedema and chronic myeloid leukaemia*, PHARMACOECONOMICS, Jan. 29, 2011 available at <https://www.ncbi.nlm.nih.gov/pubmed/21073206>.

⁸ Best Pharmaceuticals for Children Act, Pub. L. 107-109, 115 Stat. 1408.

data on drug safety and efficacy in pediatric populations, and a reduction in adverse drug reactions.⁹

There is a growing body of evidence that shows repurposing FDA approved drugs is a faster and less expensive development route than traditional drug development. Leveraging these advantages will increase patient access to drugs that are proven to be safe and effective rare disease treatments. EveryLife supports a solution that builds upon the lessons learned from the ODA and BPCA. Congress and FDA should support a solution that provides an additional 6 months of marketing exclusivity to drugs that are repurposed and approved for an orphan indication. Through this approach, the resources that companies invest in researching and validating additional indications for existing therapies will result in meaningful studies that have a high probability of success and are targeted toward serving an underserved population. This approach rewards significant innovation and the judicious use of resources, which lead to appreciable public health benefits through access to therapies that are proven to be safe and effective for the treatment of rare diseases and disorders.

The Everylife Foundation opposes efforts to extend monopolies on branded drug products in ways that “game the system” without providing appreciable public health benefits. Policymakers should discourage efforts that extend monopolies without any meaningful innovation or additional research and encourage efforts to speed the approval of generics.

There has been significant public debate over the rising costs of drugs and strategies to lower prices for consumers. Congress and the FDA should take steps to limit the strategies that manufacturers may exploit to prolong their monopolies without producing meaningful public health benefits or conducting novel research.

Specifically, the Everylife Foundation believes that policymakers should act to limit conduct that may evergreen exclusivity and act to stop abuses of the Risk Evaluation and Mitigation Strategies to prevent generic drugs from coming to market in a timely and expedient fashion.

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Thank you for the opportunity to provide comments on the public meeting entitled “The Hatch-Waxman Amendments: Ensuring a Balance Between Innovation and Access.” Please contact Rachel Klein at rklein@everylifefoundation.org with any questions.

Sincerely,

Rachel Klein
Senior Director of Advocacy and Strategy
EveryLife Foundation

⁹ Data on pediatric label changes from *FDA Access Data, New Pediatric Labeling Database*