Enhancing Drug and Device Safety and Effectiveness

Presentation by Sarah Sorscher, JD/MPH Researcher, Public Citizen's Health Research Group before the bipartisan HELP Innovation Working Group April 14, 2015



CLINICAL TRIAL DATA TRANSPARENCY



Benefits of FDA Data Transparency

- Find new information on safety and effectiveness
- Bring to light problems not detected during rapid FDA reviews
- Combine data sets to learn how rare sub-groups respond, advancing personalized medicine
- Avoid unnecessary clinical trials, saving costs and protecting human subjects from potentially harmful experiments



Data Transparency Momentum

- The Institute of Medicine recommended that the FDA share full CSRs (redacted for commercial or personal info) for all drugs, after approval or final abandonment.
- The European Medicines Agency (EMA) already shares clinical trial data on drugs approved in Europe.
- A White House memorandum urges agencies to maximize the public availability of information arising from federally funded research.
- The National Institutes of Health requests data sharing from recipients of federal grants.
- Recent legislation to promote greater data sharing includes: HR 2031 (2013) and HR 617 (2015).



Our Proposal

We support enhancing existing data sharing mechanisms through legislation to mandate publication of all CSRs and related electronic data sets (with personal info and trade secrets redacted) after drug is finally approved or rejected by the FDA.



SPEED VERSUS SAFETY



Breakthrough Therapy 2012 Drugs earning the breakthrough designation, which may be based on surrogate endpoints, receive 2010 greater FDA resources to expedite their development and approval. **Accelerated Approval** Accelerated Approval is available for drugs treating serious or life-threatening diseases and permits approval based on surrogate endpoints (e.g. regression of tumor) in place of clinical 2000 endpoints (e.g. mortality). **Priority Review** "Standard review" requires FDA action within 12 months (shortened to 10 months in 2002). "Priority review," applied to drugs appearing to represent therapeutic advances, requires FDA action 1992 within 6 months. 1990 Fast Track Drugs intended for serious or life-threatening diseases, 1988 permitting approval after phase II. **Orphan Drug** For drugs treating rare diseases, defined as drugs 'for which there is no reasonable expectation' of 1983 profitability or (as of 1984) conditions affecting fewer than 200,000 people in the U.S. 1980

Figure 1 Timeline of formal enactment of special FDA designations for drugs. Description and chronology of five special regulatory designations for prescription drugs that can lead to expedited approval or accelerated testing.

Speed vs. Safety

Five Existing Pathways

- Breakthrough Therapy
- Accelerated Approval
- Priority Review
- Fast Track
- Orphan Drug

Source: AS Kesselheim and JJ Darrow, "FDA Designations for Therapeutics and Their Impact on Drug Development and Regulatory Review Outcomes," *Clinical Pharmacology & Therapeutics* January 2015; 97(1): 29-36
Slide credit: Anthony D. So, MD, MPA, Program on Global Health and Technology Access, Sanford School of Public Policy, Duke University

Current Reality: Faster Cures

- 56% of new chemical entities approved 2002-2013 benefited from at least one accelerated pathway.
- From 2001-2010 the FDA approved 63.7% and 85.7% of novel therapeutic agents earlier than did their European and Canadian drug regulators, respectively.

Source: AS Kesselheim and JJ Darrow, "FDA Designations for Therapeutics and Their Impact on Drug Development and Regulatory Review Outcomes," *Clinical Pharmacology & Therapeutics* January 2015; 97(1): 29-36



Case Study: Bedaquiline (Sirturo)

- Approved based on a single, small, phase II randomized, placebo-controlled trial in patients with MDR-TB
- Surrogate endpoint: time until sputum free of TB
- standard combination of antibiotics for MDR-TB versus standard combo + bedaquiline.
- Drug killed more TB
- Drug also killed more patients (9 versus 2)
- Post-market study submission deadline— 03/2022



FDA Commissioner Margaret Hamburg Remarks on 21st Century Cures Bill

"There's a misperception that you might be able to speed up innovation by lowering the standards for safety and efficacy, and I think that would be a terrible mistake that would not only just damage patients, but industry as well."

Source: Virgil Dickson, "FDA's Hamburg, on her way out, blasts bill aimed speeding innovation," Modern Healthcare, March 27, 2015.

