



December 16, 2019

The Honorable Diana DeGette
2111 Rayburn House Office Building
United States House of Representatives
Washington, DC 20515

The Honorable Fred Upton
2183 Rayburn House Office Building
United States House of Representatives
Washington, DC 20515

Re: Cures 2.0 Call to Action

Dear Representatives DeGette and Upton,

On behalf of Treatment Action Group (TAG), we thank you for opening the opportunity to comment on a prospective update to the 21st Century Cures Act (Cures 2.0) legislation. TAG is an independent, activist and community-based research and policy think tank fighting for better treatment, prevention, a vaccine, and a cure for HIV, tuberculosis (TB), and hepatitis C virus (HCV).

HIV, TB, and HCV collectively represent the most formidable infectious disease epidemics, both globally and in the United States, that continue to need new treatments and high-quality biomedical interventions to save lives. Specific provisions within Cures 2.0 can help make significant advances in the science-based agenda seeking to end these epidemics through the U.S. Food and Drug Administration (FDA), by bolstering the evidence base needed to ensure high-quality biomedical interventions for those communities who need them most, to implementing policy solutions that support affordable downstream access to medical innovations and meet the resounding call from the American public to lower drug prices. We are dedicated to advancing the science and innovation necessary to see an end to these epidemics, and welcome the invitation to provide our input to this proposed legislation.

Maintaining Stringent Regulatory Authority (SRA) to Safeguard Public Health

First and foremost, the FDA must be able to maintain, and even further strengthen, its premier stringent regulatory authority in the approval of new medicines and devices. The FDA is our nation's frontline agency charged with promoting high-quality science as a prerequisite for the approval of new medicines and technologies, which in turn ensures rigorous ethical standards for clinical trials and conducting research. Without the FDA enforcing these requirements and protections, patients are left with greater uncertainty regarding the safety and efficacy of their medications, and trial participants are at risk of being subject to less thorough ethical standards. With its regulatory authority, FDA can demand that pharmaceutical developers produce better quality data and science to ensure that prospective

medicines reflect the needs of priority populations that are in need of the intervention.

Contrary to the viewpoint that strengthening the FDA's regulatory authority would slow the pipeline of public health innovations by impeding access or market entry, studies have shown the opposite. Between 2011-2015 the FDA has approved more medicines than its counterpart SRA agency in Europe.ⁱ In fact, they can help ensure access to reviewed medicines by creating such access requirements and amplifying the Right to Science as enshrined in the Universal Declaration of Human Rights.ⁱⁱ While public and Congressional pressure continues to urge the FDA to accelerate the approval process, we caution that any proposals should not undermine FDA's world-renowned regulatory role or circumvent requirements on conducting rigorous, ethical clinical trials. Therefore, as you consider many policy proposals for the prospective 21st Century Cures Act 2.0 legislation, we strongly urge you to maintain the important regulatory function of the FDA, and reject any proposals that seek to weaken scientific standards or deregulate the agency.

Rather, stringency is the strength of the FDA, and we should consider implementing measures that capitalize on this key role of the FDA to further safeguard public health through Cures 2.0. In order to ensure goals of safety and access are met, the FDA must hold developers accountable for post-approval research requirements. Previous reports have found that a large portion of such research requirements were never completed, as the agency does not have the resources necessary to enforce them.ⁱⁱⁱ Other requirements for existing pathways must be closely monitored as well, including the Limited Population Pathway for Antibacterial and Antifungal Drugs. This pathway was used in the approval of the TB drug pretomanid, allowing for significantly lowered trial standards despite the fact that it did not meet the requirement of treating a disease so rare it would be extremely difficult to enroll a clinical trial.^{iv}

Patients' confidentiality must also be strictly protected in clinical trials and healthcare, as exciting health data technologies need to be sufficiently balanced with patient rights to informed consent and privacy. This need for confidentiality is especially urgent in the context of pervasive HIV, TB, and HCV stigma. For example, some recent mergers of prominent health data companies have provided further insight into the troublesome and opaque standards for patient data privacy. As part of Project Nightingale, Google quietly acquired the medical history data (including names) of millions of Americans from Ascension, one of the largest healthcare providers in the country—and these data were accessible to staff at Google.^v Due to outdated health privacy laws, this transfer was completely legal.

Cures 2.0 is in the position to strengthen the FDA's role to regulate and protect private patient data against misuse in the rapidly emerging health data sector. Examples to consider include the World Health Organization's (WHO) Good Governance for Medicines (GGM) program, which seeks to prevent corruption in the pharmaceutical industry through increased regulatory transparency and country-level enforcement.^{vi} A recent report titled "Big Data and Artificial Intelligence for Achieving Universal Health Coverage" outlined guidelines for establishing regulatory frameworks that protect such rights as consent, privacy, and benefit-sharing.^{vii} If authorized by Cures 2.0, the FDA should issue similar guidance targeted at the private sector that similarly outlays regulatory frameworks to shield patient consent, rights and

confidentiality in an era of big data.

Requiring the Inclusion of Key Populations in Research

To ensure that prospective treatments, diagnostics, vaccines, and preventative technologies reflect the needs of impacted communities, Cures 2.0 must require biomedical developers to prioritize key populations in clinical research, especially for populations that have routinely and historically been excluded from participation in clinical trials.

This has particularly been the case for HIV and HCV, for which research has not included participants who inject drugs in studying the efficacy of regimens containing tenofovir alafenamide (TAF) or direct-acting antivirals. These represent two of the most important innovations in recent history, yet there exists no clinical guidance on their efficacy among the people most directly impacted by the viruses they treat. Similarly, despite the fact that escalating opioid use disorder and overdose crises and TB affect some of the same populations in the U.S., they still lack sufficient information about how opioid substitution therapy interacts with drugs for TB treatment.

Moreover, there is insufficient research on direct-acting antivirals as evidence of hepatitis C treatment-as-prevention (TasP) among men who have sex with men and who use drugs, and PrEP to prevent HIV in people who use and inject drugs. In addition, Gilead's clinical trials for the HIV prevention drug Descovy were permitted to continue despite the fact that they would not include any cisgender women – a population deeply impacted by risk of HIV exposure in many countries and some communities in the US. As a result, Descovy is not approved as a prevention intervention for cisgender women. Exclusion of these key populations lowers the quality of data used in the approval of medicines, and produces blindspots on potential side-effects or how to properly implement prospective public health interventions in communities.

To help stop this kind of exclusion, FDA should be compelled through Cures 2.0 to formulate and release a guidance document that formalizes Good Participatory Practice (GPP) Guidelines, such as [those developed by UNAIDS and AVAC](#). In order to lend further authority to these guidelines, FDA should require drug developers to provide written justification for the exclusion of key populations from clinical trials. This would help shift the paradigm from one of presumed exclusion of key populations to one of presumed inclusion, with exclusion justified and in writing. Though these actions alone would not stop all forms of unjustifiable exclusion from research, they would go a long way towards providing the necessary data to address some of the country's most pressing public health concerns and generate transparency on why developers choose to exclude certain populations by providing a rigorous, scientific justification.

Recognizing the research blindspot of key populations such as pregnant and lactating women, the previous iteration of the 21st Century Cures Act commendably established the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC). As a direct result of this legislation, recent PRGLAC recommendations have outlined how the government can facilitate adequate inclusion and monitoring of pregnant and lactating people

in clinical trials, thereby protecting the health of parents and future generations of infants. Some recommendations include:

- Providing adequate resources to develop new tools and models for research in pregnant and lactating people;
- Changing regulations to recognize maternal consent to research as sufficient;
- Improving knowledge among providers about research needs and increasing the number of qualified clinicians;
- Creating new systems to support necessary research and leveraging existing networks;
- Increasing public awareness about the need for a research base on pregnant and lactating people.

These recommendations also included specific guidance for FDA action, including removing pregnant women as a designated vulnerable population.^{viii} The next version of the 21st Century Cures Act should act upon implementing these recommendations, and work with community stakeholders on how these recommendations can impact diseases like TB, where exclusion of pregnant women and lactating women remains a significant issue. Furthermore, the establishment of PRGLAC, and the recommendations that have been written as a result, offer a model for how Cures 2.0 could address similar paucity of data for other key populations that are historically excluded, especially those impacted by HIV, TB, and HCV.

Promoting Access and Innovation

The first iteration of the 21st Century Cures Act contained many important provisions, but can still be improved to address issues of access to medicines as public health goods. The most urgent public health needs are not always the most profitable to address, and often aren't prioritized by biomedical developers at all. This is why Cures 2.0 must be bold in its steps to strengthen FDA's ability to make biomedical innovation accessible, while bolstering the agency's ability to ensure accountability and transparency of the biomedical manufacturing sector, writ large.

The FDA can play a larger role in ensuring downstream access and affordability for medicines, especially those supported by publicly funded research and development (R&D). Recent studies have found that publicly funded research was involved in every single FDA-approved medicine from 2010-2016, and that one-quarter of all new medicines relied upon public funding even into late-stage clinical trials.^{ix} Technologies underwritten by the taxpayer should be broadly available. The FDA has authority to grant market exclusivity to products; Cures 2.0 could include provisions to ensure exclusivity is only granted for products not financed by public investment, to ensure that medicines are affordable and accessible to the taxpayers who initially funded the R&D.

Even a "sunshine" requirement to promote transparency by requiring the sources and amount of public funding and other incentives that have underwritten the development of new medicines and other health technologies to be included in regulatory submissions would be

helpful in making prospective medicines and biomedical technologies more accessible; this would establish parameters for making fair and affordable pricing because it would take into account the full range of incentives and government investment received by a developer that led to a medicine's approval.

There are, ultimately, many ways to incentivize health innovation that do not encourage or extend pharmaceutical monopolies that have been subject to fierce American public discourse in the context of reigning in drug pricing. FDA has risen to the challenge of incentivizing research already by offering such useful incentives as funding grants, waived application fees, and tax credits that help to facilitate drug development and approval. In this way, researchers receive a financial incentive that does not jeopardize public access to the medicines derived from their research.

Other existing FDA incentives on patents and marketing exclusivity extensions may incentivize companies, but often at the expense of access. This legislation should avoid proposals for any incentives that extend the duration of patent-protected monopolies beyond current limits, as well as improve problematic incentives like priority review vouchers (PRV). PRVs are problematic as there is no requirement for medicines rewarded by PRVs to be new or accessible; PRVs can, in fact, be awarded even when a treatment has been developed exclusively using public funding. Cures 2.0 should direct FDA to close these loopholes by requiring that medicines rewarded by PRVs be novel therapies, not ones already developed, and be registered and affordable in countries where the neglected disease it treats is most common.

Ensuring Transparency

Cures 2.0 must also ensure that researchers provide full and transparent access to clinical trials data. Transparency on clinical trial data is crucial to an informed public and patient community, and helps to prevent misinterpretation of trial data which could lead to inappropriate prescribing. Requiring that clinical trial data be publicly available would not compromise researchers' merited intellectual property rights or infringe on their ability to be remunerated and to generate profits from true innovations, and would instead ensure that the medicines they develop are used in the safest, most tolerable, and most effective way possible. Access to data is often a crucial first step towards further research on medicines.

There have recently been many troubling trends in litigation brought by pharmaceutical companies to protect clinical trial data as "trade secrets"—often in cases with dubious claims, and in attempts at extending a monopoly.^x Such litigation can also inhibit the entry of generics into the marketplace, which must be strengthened to make medicines accessible and affordable to the American public, in keeping with the American value of free competition as the basis of our economic system.

One promising policy solution to trade secrets protections is the "fair use" doctrine. Similar to its use in copyright law that can circumvent dubious trade secret claims, fair use can allow intellectual property to be made available for the purposes of research.^{xi} In one recent example, Pfizer licensed tuberculosis (TB) drug candidate sutezolid exclusively to Sequella,

a small biotechnology company without the resources necessary to advance further development. The exclusive nature of the license prevented other companies and research institutions interested in advancing the development of sutezolid from accessing pre-clinical and early clinical data, leaving sutezolid stuck in the same phase of development for almost a decade. A recent licensing agreement between Pfizer and the Medicines Patent Pool has finally made these data publicly accessible, renewing hope that development of sutezolid may finally advance. Strengthening Cures 2.0 to provide for upfront clinical trial data transparency could have spared years of lost progress on sutezolid.

Addressing Market Failure for Small Volume, High Need Public Health Products

In order to facilitate necessary public health innovation, Cures 2.0 can take steps to correct market failings for urgent, if rare or not lucrative, public health conditions. For example, some urgent health threats such as drug-resistant TB (DR-TB) currently affect a relatively small number of people and thus represent the potential for a small profit margin. In other cases, a disease that might afflict a large number of people globally is somewhat rare (though still urgent) inside the United States.

Such an example is TB, when combined with the small market like the U.S., discourages biomedical developers from pursuing FDA registration for optimized formulations due to user-fees that outpace expected return in sales. This leaves TB patients in the U.S. without access to many medicines that are available on the global market, some of which have been developed with U.S. public funding. For example, 3HP regimen—a game changing intervention that combines two drugs (rifapentine and isoniazid) to drastically shorten the time to treat TB infection and prevent active, transmissible disease— was developed in large part by the U.S. Centers for Disease Control and Prevention, but a combination formulation of 3HP has not been submitted for approval inside the U.S. Similarly, American children lack access to pediatric formulations of lifesaving TB medication that are widely available globally, leaving physicians and parents to estimate and split adult doses of TB medicines, and putting children at risk of suboptimal treatment. Cures 2.0 should consider measures to provide the FDA with fiscal assistance to cover application fees to catalyze global product sponsors to register with the FDA, and undergo review to expand the market of these needed medications for Americans.

In addition, even when medicines are developed and approved for use in the U.S., small markets can create problems for downstream access. National TB programs contend with difficulties in procuring medicines for TB patients in the U.S. due to a fragmented market that's prone to price spikes and supply disruptions with too few suppliers. Each drug in complex drug resistant TB treatment regimens have their own procurement process, which saddle the public health system with additional work. The FDA through Cures 2.0 can implement solutions to stabilize this routine problem of TB drug supply that complicates public health efforts in the elimination of this disease.

Proposed solutions involve engaging with existing global resources. In the case of allowing Americans to benefit from medicines already available in foreign markets, the U.S. could tap the existing U.S. taxpayer-funded procurement mechanism, the Global Drug Facility (GDF),

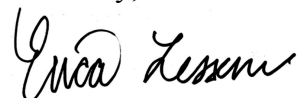
to allow importation of medicines in the GDF catalogue that have met other reputable quality assurance requirements, such as the European Medicines Agency (EMA), World Health Organization (WHO) Prequalification, or the Global Fund Expert Review Panel.

Conclusion

The proposed Cures 2.0 legislation has the potential to increase the volume, quality, and accessibility of biomedical R&D to the benefit of those most in need of innovative medicines. However, this can only happen with improvements in FDA's regulatory authority and enforcement capabilities to ensure that treatments are safe, affordable, and effective for all key populations.

We thank you for the opportunity to submit comments on Cures 2.0, and we look forward to continued engagement on this legislation. We also look forward to the opportunity to engage with your respective offices on these recommendations. Please do not hesitate to contact Erica Lessem, Deputy Executive Director for Programs, at Erica.Lessem@treatmentactiongroup.org with any questions.

Sincerely,



Erica Lessem, MPH
Deputy Executive Director of Programs
Treatment Action Group

ⁱ Downing NS, Zhang AD, Ross JS. Letter to the Editor. The New England Journal of Medicine, 2017 April 6. <https://www.nejm.org/doi/10.1056/NEJMc1700103>

ⁱⁱ United Nations Educational, Scientific, and Cultural Organization. Science as a human right: the need of a unified concept. 2018 November 30. <https://en.unesco.org/news/science-human-right-need-unified-concept>

ⁱⁱⁱ McKenna L, Lessem E. The FDA's Concession Conundrum. TAGline. 2015 Fall.

<http://www.treatmentactiongroup.org/tagline/2015/fall/fdas-concession-conundrum>

^{iv} Treatment Action Group. Statement from Treatment Action Group on U.S. FDA Approval of Pretomanid. 2019 August 14. <http://www.treatmentactiongroup.org/content/statement-treatment-action-group-us-fda-approval-pretomanid>

^v Pilkington E. "Google's secret cache of medical data includes names and full details of millions – whistleblower." The Guardian. 2019 November 12.

<https://www.theguardian.com/technology/2019/nov/12/google-medical-data-project-nightingale-secret-transfer-us-health-information>

^{vi} World Health Organization. Good Governance for Medicines (GGM) Overview.

<https://www.who.int/medicines/areas/policy/goodgovernance/en/>

^{vii} World Health Organization. Big data and artificial intelligence for achieving universal health coverage: an international consultation on ethics. Meeting Report, 12-13 October 2017, Miami, Florida, USA.

<https://apps.who.int/iris/bitstream/handle/10665/275417/WHO-HMM-IER-REK-2018.2-eng.pdf?ua=1>

^{viii} National Institutes of Health (U.S.). List of Recommendations from the Task Force on Research Specific to Pregnant Women and Lactating Women (PRGLAC). 2018 September.

<https://www.nichd.nih.gov/about/advisory/PRGLAC/recommendations>

^{ix} Nayak RK, Avorn J, Kesselheim AS. Public sector financial support for late stage discovery of new drugs in the United States: cohort study. *BMJ*, 2019 September 23; 367:l5766.

<https://www.bmj.com/content/367/bmj.l5766>

^x Global Health Justice Partnership. Trade secrets as barriers to access to medicines. New Haven: Yale Law School; 2019 July.

^{xi} U.S. Copyright Office. More Information on Fair Use. 2019 September. <https://www.copyright.gov/fair-use/more-info.html>