The FDA Modernization Act 3.0

H.R. 2821, S.355

The FDA Modernization Act 2.0 (FDAMA 2.0) was enacted into law as Sec. 3209 of the Consolidated Appropriations Act, 2023, which President Biden signed on Dec. 29, 2022. FDAMA 2.0 lifted a mandate in the Federal Food, Drug, and Cosmetic Act (FDCA) that required animal testing of investigational new drugs (INDs) to establish safety and efficacy prior to clinical trials in humans.

FDAMA 2.0 did not ban animal testing, but it offered drug sponsors the option to use 21st century alternatives such as cell-based assays, organ chips, computer modeling, and bioprinting. The goal was not only to make drug testing more humane, speed drug development by reducing the attrition rate, since non-animal methods are typically superior predictors of human responses to drugs. An astonishing 90-95% of drugs that pass animal tests go on to fail in human clinical trials, wasting precious time for patients.[1]

Over 7,000 rare diseases affect between 25-35 million Americans — and 95% of those diseases have no cure. Rare-disease patients stand to benefit substantially by the acceptance of non-animal methods because the poor reliability of animal models compounds high R&D costs to disincentivize investment in this area. The innovative 21st century methods outlined in FDAMA 2.0 are among the most promising frontiers in understanding rare diseases: organ chips for Barth Syndrome, 3D models (organoids) of the midbrain for NGLY1 deficiency (a rare neurological disease), and artificial intelligence (AI) in developing treatments for Fragile-X syndrome. As a 2022 article noted of Fragile-X, "[t]his is a disease for which there were no mouse models. A different approach was needed, and the patients-on-a-chip model, combined with AI, seemed to be the best solution."[2]

The Problem

To date, the FDA has not updated its regulations to conform with the law Congress passed in 2022. Dozens of FDA regulations continue to call for animal tests without offering drug sponsors any other option. FDA programs that qualify non-animal test methods are cursory, ineffective, and lack transparency.

The Solution

To effectuate the will of Congress, the FDA Modernization Act 3.0 would:

- Require the FDA to publish a final rule to fully implement FDAMA 2.0.[3]

[1] National Institutes of Health, National Center for Advancing Translational Sciences (NCATS), "New Therapeutic Uses": https://ncats.nih.gov/research/research-activities/ntu. Accessed 28 Jan. 2024. Additionally, federal regulations already recognize that "animal reproduction studies are not always predictive of human response." See 21 C.F.R. §201.80(f)(6)(i)(b).

[2] Ed Miseta, "Needed: An AI Revolution in the Rare Disease Space," Clinical Leader, 11 Nov. 2022: https://www.clinicalleader.com/doc/needed-an-ai-revolution-in-the-rare-disease-space-0001

[3] To amend the sections of title 21, Code of Federal Regulations, to replace any references to "animal" tests, data, studies, models, and research with a reference to nonclinical tests, data, studies, models, and research: See 21 C.F.R. §§ 312.22(c), 312.23(a)(3)(iv), 312.23(a)(5)(ii), 312.23(a)(5)(iii), 312.23(a)(8), 312.23(a)(8)(i), 312.23(a)(8)(ii), 312.23(a)(10)(i), 312.23(a)(10)(ii), 312.33(a)(6), 312.82(a), 312.88, 314.50(d)(2),314.50(d)(2)(iv), 314.50(d)(5)(i), 314.50(d)(5)(vi)(a), 314.50(d)(5)(vi)(b), 314.93(e)(2), 315.6(d), 330.10(a)(2), 610.35(d). Definitions: to add the definition of "nonclinical test" in section 505(z) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(z)) to sections 312.3, 314.3, 315.2, and 601.31 of title 21, Code of Federal Regulations.