FDA's Medical Countermeasures Initiative: Strengthening Regulatory Science to Further the Development of Medical Countermeasures

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Abstract

In 2010, the U.S. Food and Drug Administration (FDA) established the Medical Countermeasures Initiative (MCMi) focusing increased resources on promoting the development of medical countermeasures (MCMs) by establishing clear regulatory pathways for MCMs, instituting effective regulatory policies and mechanisms to facilitate timely access to available MCMs, and advancing MCM regulatory science to create the tools, standards, and approaches that support regulatory decision-making.

As such the FDA plays a vital and active role protecting the United States from chemical, biological, radiological, nuclear (CBRN), and emerging infectious disease threats (such as SARS-CoV-2, Zika, and Ebola viruses, and pandemic influenza). The FDA is responsible for assessing the safety and effectiveness of MCMs – including diagnostic tests, drugs, and vaccines – that are needed to counter these threats. In addition, The FDA works closely with public and private sector partners to advance the development and availability of investigational MCMs.

The MCMi Regulatory Science Program has supported over 200 intra- and extramural regulatory science projects that have resulted in the development of innovative regulatory science tools and capabilities. Examples include support of SARS-CoV-2 and Zika virus reference reagents for diagnostic developers, FDA-ARGOS (a publicly available microbial genomic sequence reference database for diagnostic tests based on next generation sequencing technology), the cross-species immune reference database, and development of microphysiological systems (MPS) models of COVID-19 and acute radiation syndrome to support MCM evaluation.

Introduction

The MCMi Regulatory Science Program supports a robust intra- and extramural research portfolio focused on helping to translate cutting-edge science and technology into innovative, safe, and effective MCMs. The mission of the MCM regulatory science program is to foster MCM regulatory science initiatives to:

1. Develop solutions to complex regulatory science problems
2. Facilitate incorporation of cutting-edge science into the regulatory review process
3. Make product development more efficient and predictable

This program is being implemented through partnerships, and support of intra- and extramural research projects. The intramural research program, which began in 2011, has enhanced and expanded existing MCM research efforts at FDA. In 2012, the extramural program was initiated using the FDA Broad Agency Announcement (BAA) for Advanced Research and Development of Regulatory Science: FDABAA-21-00123N (FY21); Area #7.

MCMi Regulatory Science Priority Research Areas

- Identifying, developing, and qualifying drug development tools, such as animal models and immune biomarkers, to assess safety and efficacy of MCMs
- Advancing broadly applicable, commercially ready tools, technologies, and platforms that can improve the manufacturing efficiency, consistency, and quality of MCMs
- Developing reference materials related to CBRN threat agents and emerging infectious diseases to facilitate development of MCMs
- Validating next-generation *in vitro* diagnostics platforms
- Developing and qualifying *in silico* predictive models (e.g., MPS) and *in vitro* assays to complement the use of *in vivo* animal models to assess safety and efficacy of MCMs
- Assessing the performance, design, and reuse of emergency medical equipment including personal protective equipment

Medical Countermeasure Regulatory Science Research

Fostering innovation, including the use of novel technologies, to support MCM development and evaluation

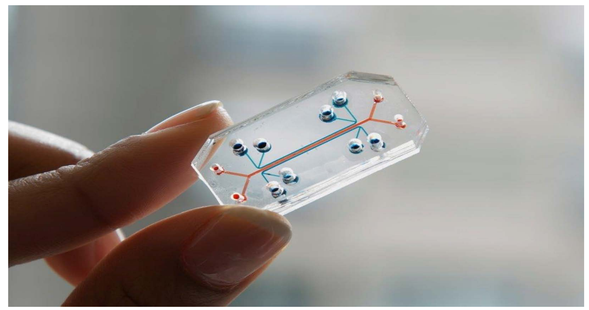
Project Area	Project Title	Principal Investigator(s)	Program
Therapeutics	Artificial Intelligence Powering Precision-Medicine Based Drug Repurposing Against COVID-19	Dr. Zhichao Liu National Center for Toxicological Research, FDA	Intramural
Diagnostics	FDA-ARGOS (FDA Database for Regulatory Grade Microbial Sequences)	Dr. Yi Yan Center for Devices and Radiological Health, FDA Dr. Maria Rios Center for Biologics Evaluation and Research, FDA	Intramural
Reagents	Zika virus reference materials for diagnostic developers	Dr. Mayra Garcia and Dr. Stephen Lovell Center for Devices and Radiological Health, FDA Dr. Maria Rios Center for Biologics Evaluation and Research, FDA	Intramural
	FDA SARS-CoV-2 Reference Panel	Dr. Mayra Garcia Center for Devices and Radiological Health, FDA Dr. David McGivern and Dr. Tony Wang Center for Biologics Evaluation and Research, FDA	Intramural
Vaccines	Correlates of protection against Ebola virus predictive of vaccine efficacy	Dr. Surender Khurana Center for Biologics Evaluation and Research, FDA	Intramural
	Characterizing immunity to Ebola and Marburg to support medical countermeasure development	Dr. Anne Rimoin University of California, Los Angeles (UCLA) School of Public Health	Extramural
In silico predictive models	Human organ chips for radiation countermeasure development	Dr. Donald Ingber Wyss Institute, Harvard University	Extramural
	Development of MPS model of Zika virus disease	Dr. Dayton Petibone National Center for Toxicological Research, FDA	Intramural
Biomarkers (Immunity and Pathogenicity)	FDA and global partners to analyze coronavirus samples*	Dr. Julian Hiscox University of Liverpool	Extramural
	Comparison of Host Responses to Ebola Virus Disease	Dr. Miles Caroll Public Health England (PHE)	Extramural
	Cellular signaling and immune correlates for SARS-CoV-2 infection*	Dr. Garry Nolan Stanford University	Extramural
	A new approach for understanding Ebola virus pathogenesis	Dr. Pardis Sabeti The Broad Institute	Extramural
Sampling/pathogenesis	U.S. Department of Defense and FDA collaborate to help speed potential countermeasures for Ebola and other viruses	COL David Saunders US Army Medical Research Institute for Infectious Diseases	Extramural (Interagency)

*Supported in partnership with the Office of Biodefense Research Resources, and Translational Research, DMID, NIAID, NIH

Summary

To date the MCMi Regulatory Science Program has supported 200+ intra- and extramural regulatory science projects to accelerate FDA's ability to perform science-based review of MCMs. Program accomplishments include:

- Developed reference materials for SARS-CoV-2 and Zika in vitro diagnostic devices (IVDs) and Zika serological tests
- Expanded FDA-ARGOS database to support IVD development
- Characterized host-pathogen responses and identification of biomarkers and correlates of protection
- Developed radiation and Zika virus microphysiological system (MPS) models to enhance MCM assessment
- Applied the cross-species immune system reference database to better understand Ebola, Zika, and SARS-CoV-2 infection to facilitate MCM development



Under an MCMi project, Wyss Institute scientists are developing MPS models of radiation damage in lung, gut, and bone marrow (Image: Wyss Institute)

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