ONE HEALTH MICROBIOME RESEARCH ACROSS FDA CENTERS

Contributed by the Microbiome Working Group (MWG)

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* Not pictured

What is a Microbiome? The term microbiome/microbiota refers to the community of microbial species connected by physical location, inter-relationships of function, and collective genomic potential. There is extensive data-based evidence that human, animal and environmental microbiota play highly significant and varied roles in states of health and disease.

Who is the Microbiome Working Group (MWG) and what do they do? MWG Members are representatives from FDA Centers and Offices spanning the agency (above). The mission of the Food and Drug Administration's Microbiome Working Group (MWG) is to gather FDA scientists from a wide breath of subject matter expertise (SME), to foster an improved understanding of the role of human and environmental microbiomes** in health and disease, and to identify areas of scientific and regulatory challenges that may be significantly impacted by this advancing science. The MWG works to identify research needs, data gaps, and opportunities of collaboration between the Centers to advance regulatory science in this field and support regulatory decisions of FDA-regulated products.

MICROBIOME SCIENCES AT FDA

In response to the rapid advancement of science and technology and corresponding implications for FDA-regulated products, FDA Regulatory Science Strategic priorities now include microbiome research sciences.

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As FDA regulates a broad range of products and devices that interact either directly or indirectly with human and animal microbiota, multiple Centers and Offices are involved in research that spans microbiology, toxicology, nutrition, immunology, antimicrobial resistance and a wide range of additional categories. Food, antibiotics, drug and chemical residues may shape gastrointestinal microbiota, cosmetics may alter skin microbiota, and metabolites of all of these may influence complex microbiome mediated processes highly significant to human health.

Additionally, FDA regulates and evaluates products that are comprised intentionally or unintentionally of microbes and/or microbial communities such as fecal microbiota transplants, live microbes in foods, dietary supplements, tobacco products, and live biotherapeutic products. Microbiome research provides insight into the mechanistic action of such products to lead to data based evaluation of potential toxic or beneficial effects and correlated recommendations and regulatory policy. Here, representatives of the Microbiome Working Group (MWG) (which spans 9 Centers and Offices) provide a comprehensive portfolio of FDA microbiome research in their respective Centers and Offices, as well as a snapshot of intra and interagency collaborative efforts. Details of some of these research components are highlighted here and additionally presented as individual posters

Examples of Microbiome Research Across FDA Centers

Microbiome based One Health antimicrobial resistance monitoring

The National Antimicrobial Resistance Monitoring Systems (NARMS) directs a portfolio of microbiome-based resistome research to capture the full complement of antimicrobial resistance in animals, food, feed and the environment to better understand the movement of pathogens and resistant genes across the domains of One Health.

Fecal Microbiota Transplantation (FMT)

FDA has been studying recurrent *Clostridioides difficile* infections, including assessment of methods for ensuring safety, understanding how manufacturing procedures alter the microbial composition of FMT products, and working to identify biomarkers of an effective microbial community to assess product potency.

Impact of drug residues on the human intestinal microbiome of consumers of animal-derived foods from treated animals

This topic is evaluated through one of the assessments needed during the approval process of drugs for food producing animals. Research collaborations between CVM and NCTR, focuses on methodological aspects and experimental conditions to be used while addressing this human food safety endpoint of concern, some of which were included as part of the harmonized guidance (GFI#159/VICH GL#36). Currently, further collaborations between CVM and NCTR, as well as other research efforts in CVM, will help to address some of the questions to support regulatory decisions of CVM-regulated products, such as the determination of relivable methods to determine the NOEC/NOEL (No Observable Effect Level/Concentration) to ultimately calculate the ADI (Acceptable Daily Intake) for a food animal drug product.

Biologic therapeutics, including nanodrugs in animal models

Research is ongoing in animal models to characterize the impact of biologic therapeutics on gut microbiota and innate immune response to highlight mechanistic variation mediated by gut microbiota. Differences have been observed between genders and ages. Deciphering the response to a therapeutic agent mediated by the gut microbiome may identify populations more likely to respond to therapeutic interventions, thus informing regulatory recommendations for biologic therapies and small molecule drugs. Similar approaches are currently used to evaluate the safety of nanodrug formulation in animal and non-animal models.

Development of "intestine-on-a-chip" model, as alternative to animal models to evaluate the impact of drug residues on the human intestinal microbiome

Animal models are not a perfect surrogate for studying how the human microbiome responds to antimicrobial drug resides. Existing animal models have limitations mimicking human intestinal physiology and microbiome complexity, thereby limiting evaluation accuracy and interpretation. Efforts are ongoing to develop an "intestine- on-a-chip" model as an alternative to animal models to study the effect

Phenotypic characterization of bacteria associated with antibiotic-coated catheters

Studies are ongoing to examine the phenotypic characteristics of bacteria grown with antibiotic-coated catheters in a biofilm reactor and to identify antimicrobial resistance markers using transcriptomic and proteomic profiles of representative bacteria following continuous exposure to the antibiotic-coated catheters in a biofilm reactor.

Baseline profiling and pathogen detection from foods, feeds, pre and probiotics and associated production environments

Laboratory and bioinformatic method evaluation is ongoing for use with targeted and target independent characterization of specific bacteria, viral, and fungal species from complex microbiome samples. Targeted gene sequencing offers speed, sensitivity, and scalability and target independent approaches provide a comprehensive total microbial landscape of food, feeds, pre and probiotics and associated built (indoor) and agricultural production environments. Programs like GenomeTrakr, MetagenomeTrakr and ResistomeTrakr use NGS data to efficiently track pathogens and AMR through complex ecologies.

Impact of xenobiotics on microbiomes

Laboratory and bioinformatic methods evaluation is ongoing to develop standard operation procedures (SOPS) to investigate changes in composition and functionality of gut microbiota in response to exposure to xenobiotics, food contaminants, supplements or food ingredients (i.e., artificial sweeteners, dietary fibers, nutrition). In some studies, the impact of xenobiotics is also assessed during fetal, lactational and transgenerational exposure.