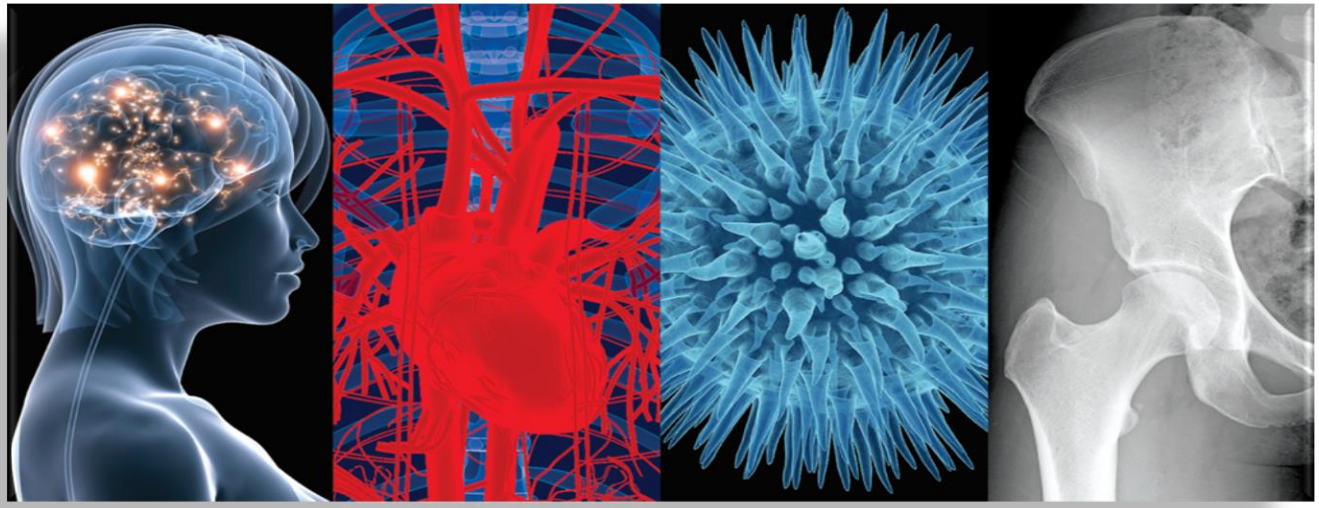


Sex Differences in Brain Disorders: Emerging Transcriptomic Evidence and Implications for Therapeutic Development

The National Academies of Sciences, Engineering, and Medicine

Kaveeta Parikh Vasisht, MD PharmD

Associate Commissioner for Women's Health

Director, Office of Women's Health

U.S Food and Drug Administration

September 23, 2020

Disclaimer

The views expressed are those of the speaker and do not necessarily reflect official policy of the US FDA. No official endorsement by the US FDA is intended or should be inferred. No Conflicts of Interest.

FDA

Office of the Commissioner

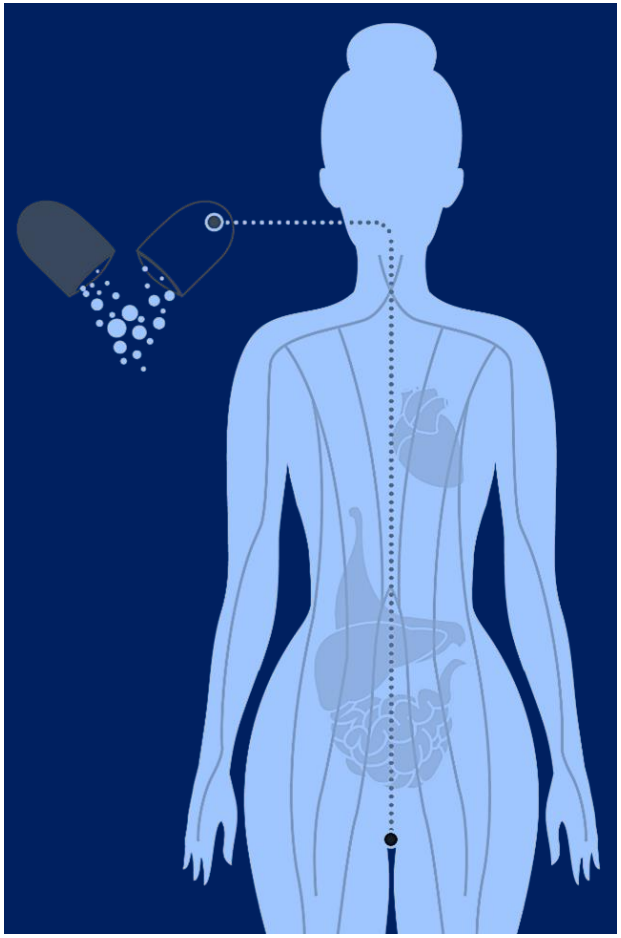
OFFICE OF WOMEN'S HEALTH

Working Across FDA to Advance the Health of Women

Research/Funding Training Sex Diff. Consults Consumer Information

- Center for Drug Evaluation and Research
- Center for Biologics Evaluation and Research
- Center for Devices and Radiologic Health
- National Center for Toxicology Research
- Center for Tobacco Products
- Center for Food Safety and Nutrition

Our Mission



- **Promote the inclusion of women in clinical trials** and the implementation of guidelines concerning the representation of women in clinical trials and the completion of sex/gender analysis

- **Identify** and monitor the progress of **crosscutting** and multidisciplinary women's health initiatives including **changing needs, areas that require study, and new challenges** to the health of women as they relate to FDA's mission

- **Serve** as the **principal advisor to the Commissioner** and other key Agency officials on **scientific, ethical, and policy** issues relating to women's health

Office of Women's Health

SCIENCE

EDUCATION

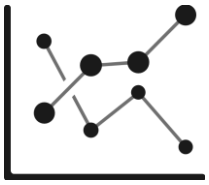
ENGAGEMENT

OWH achieves its mission through the foundational principle that Sex is a Biological Variable (SABV)

SEX DIFFERENCES

PRE-CLINICAL STUDIES
Using Both Male and Female Animals

POST-MARKETING MONITORING AND SAFETY ALERTS



DATA ON SAFETY AND EFFECTIVENESS

SEX ANALYSES

1998 "Demographic Rule"

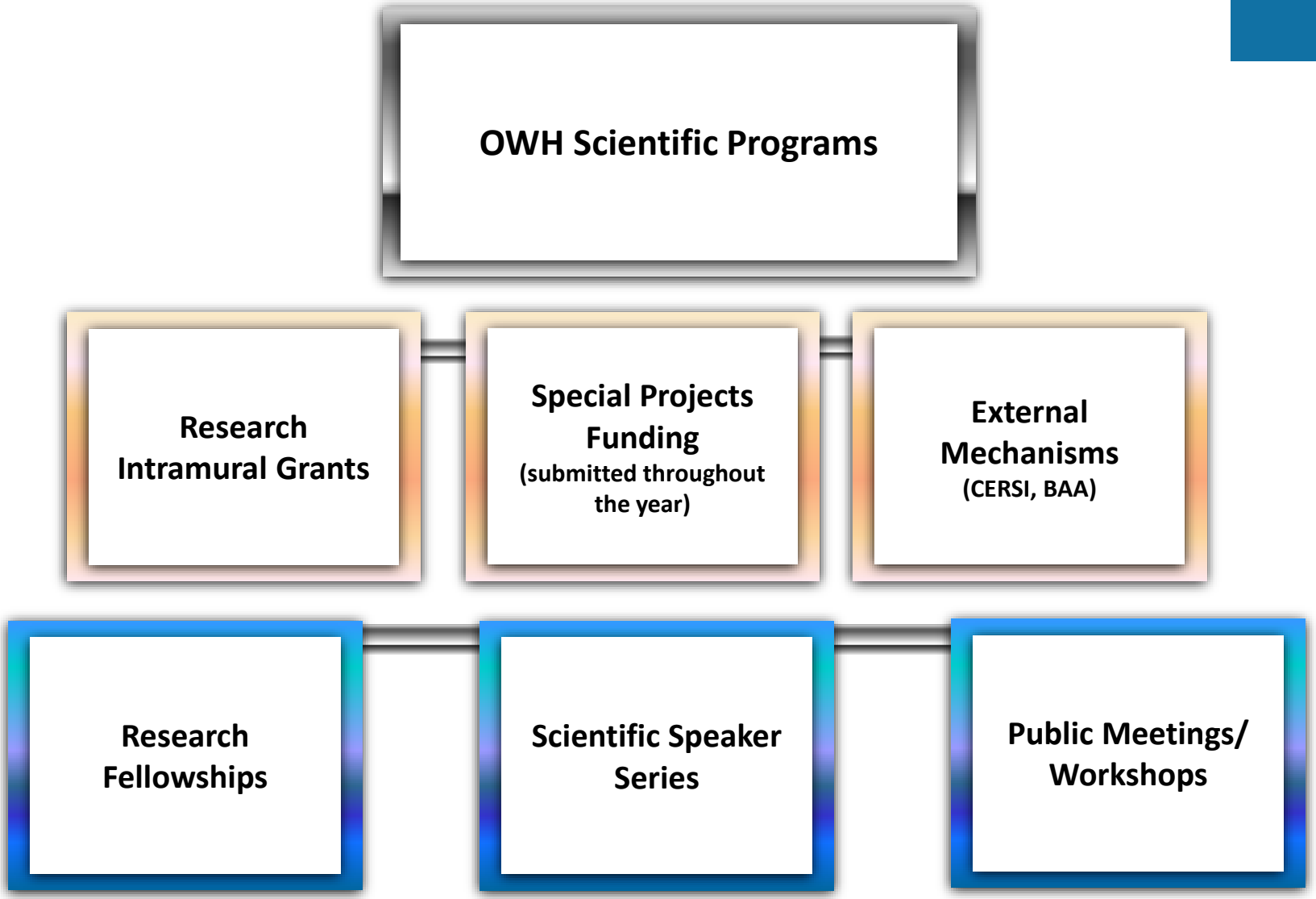
IND regulations (21 CFR 312.33(a)(2)):

- Require that IND data regarding subjects' participation in clinical trials be presented in annual reports by gender, age, and race.

NDA regulations, at 21 CFR 314.50(d)(5)(v), (vi)(a):

- Require sponsors of NDAs to include summaries of effectiveness and safety data presented by gender, age, and race.


FDA U.S. FOOD & DRUG ADMINISTRATION
2019
DRUG TRIALS SNAPSHOTS
SUMMARY REPORT
Clinical Trials
40 Novel Drugs
Women 63%
January 2020
www.fda.gov


OWH Scientific Programs
Research Intramural Grants
Special Projects Funding (submitted throughout the year)
External Mechanisms (CERSI, BAA)
Research Fellowships
Scientific Speaker Series
Public Meetings/ Workshops

OWH Created the First FDA Women's Health Research Roadmap

http://inside.fda.gov:9003/downloads/scienceresearch/specialtopics/womenshealthresearch/ucm479681.pdf

Priority Areas Outlined in OWH *Women's Health Research Roadmap*

Read the Women's Health Research Roadmap

https://www.fda.gov/science-research/womens-health-research/womens-health-research-roadmap

Research Funded by OWH

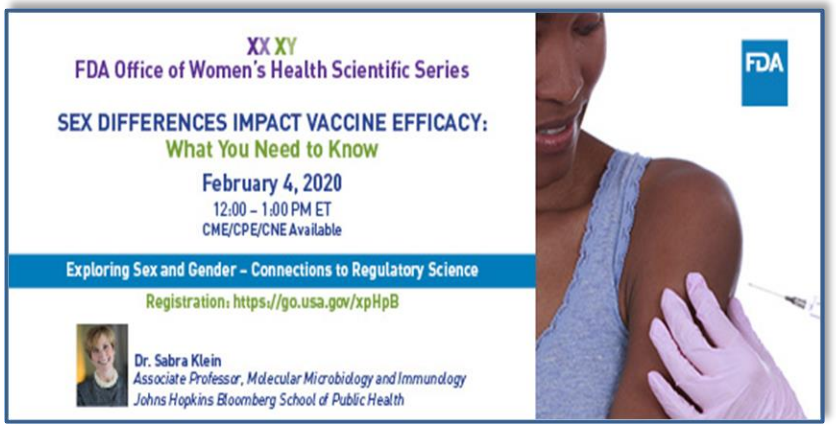
- Identifying **genetic mechanisms** of **doxorubicin-Induced cardiotoxicity (DIC)**
- Comprehensive assessment of **sex-differential smoking-related effects** in publicly available **gene expression data**
- Impact of sex-based differences in the expression of host **non-coding RNA biomarkers** that can **diagnose early HIV-1 infection**
- Sex differences related to **Alzheimer's disease** as revealed by **Exome sequencing and RNA Seq**
- Evaluation of **transcriptomics-based** predictions of sex- and age-related susceptibilities to **treatment-induced adverse effects** in F344 rats
- The role of **epigenetic mechanisms** in re-expression of ER, PR, and HER receptors in **triple negative breast cancer**: effects of FDA approved epigenetic drugs and dietary agents

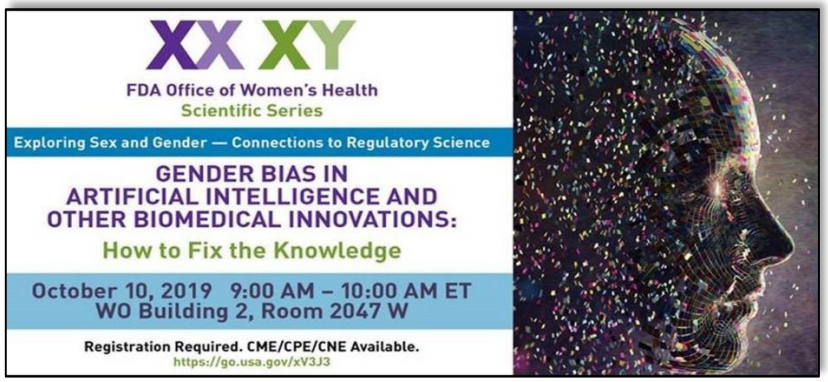
Bench to Bedside:

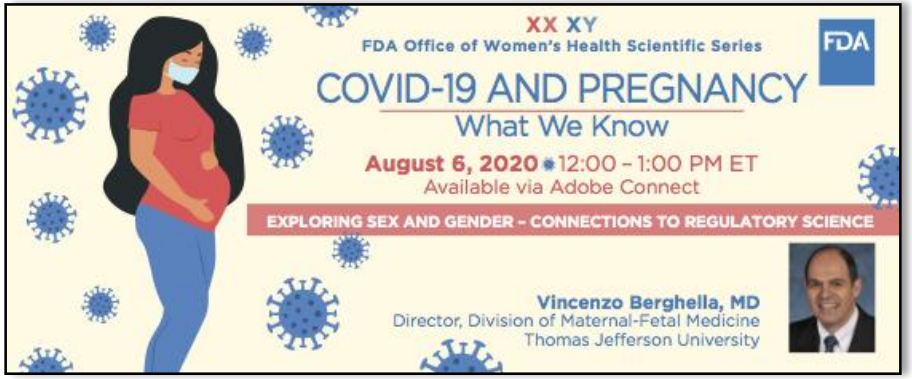
Integrating Sex and Gender to Improve Human Health Course

https://orwh.od.nih.gov/career-development-education/e-learning/bench-bedside

Scientific Speaker Series







SCIENTIFIC ENGAGEMENT

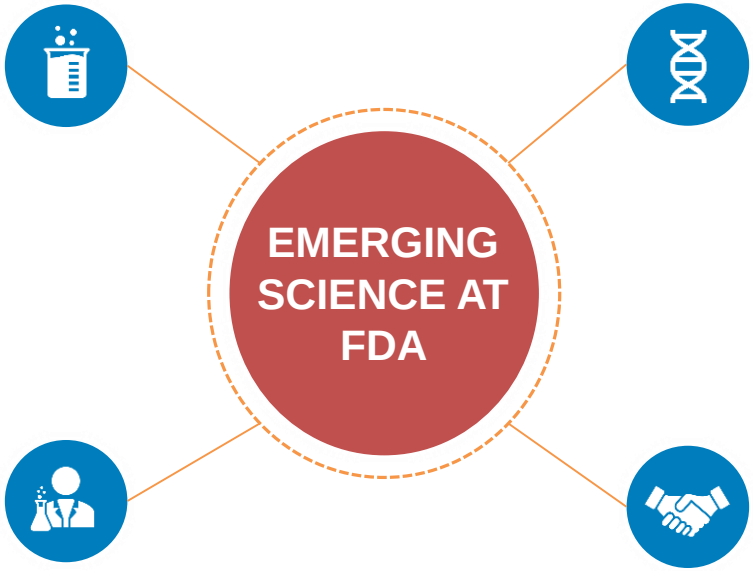
Scientific Partnership Mechanisms

FDA BAA

FDA solicits proposals for innovative ideas and approaches in developing and evaluating FDA-regulated products. This is a competitive contract mechanism.

CERSI Program

Under cooperative agreement grants, the Program supports collaborations between FDA and academic institutions to advance regulatory science through innovative research, training, and scientific exchanges.



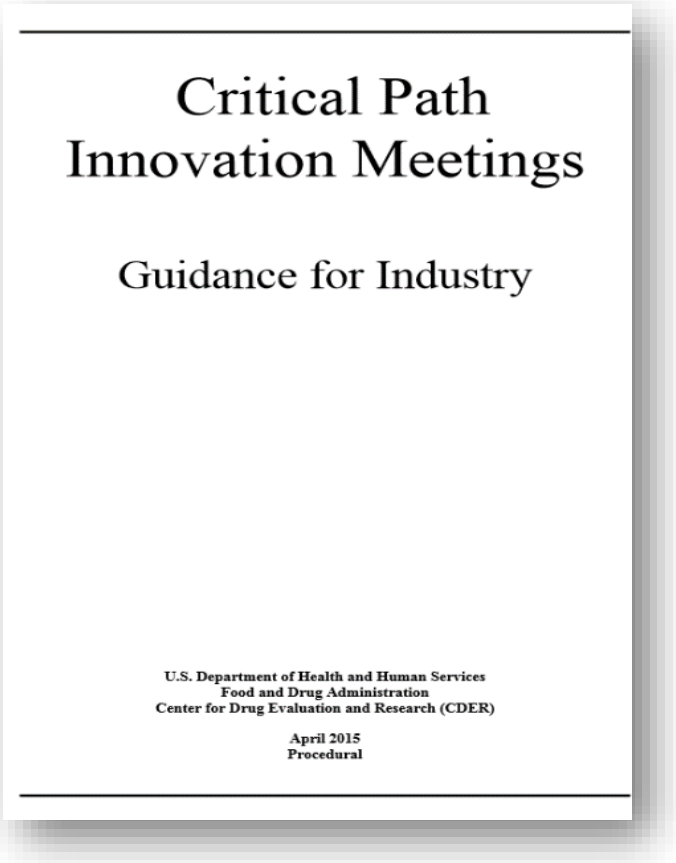
CRADAs

Collaborative engagement to advance innovations in regulatory science. This mechanism is authorized under the Federal Technology Transfer Act.

MOUs

Declaration of shared initiatives and partnership goals between FDA and external academic or non-profit organization, or federal agency. This is not a legally binding mechanism.

Critical Path Innovation Meeting


Critical Path Innovation Meetings

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

April 2015
Procedural

- Discussion of the science, medicine, and regulatory aspects of innovation in drug development
- Non-binding meeting
- Not a meeting about a specific approval pathway

Office of Translational Sciences
Critical Path Innovation Meeting

http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformion/Guidances/UCM417627.pdf

CPIM Topics

- Clinical Trial Endpoints
- Biomarker Development
- Drug Development Tools
- Innovative Trial Designs
- Clinical Trial Networks
- Natural History Studies
- COA Development
- Rare Diseases
- Databases
- Registries

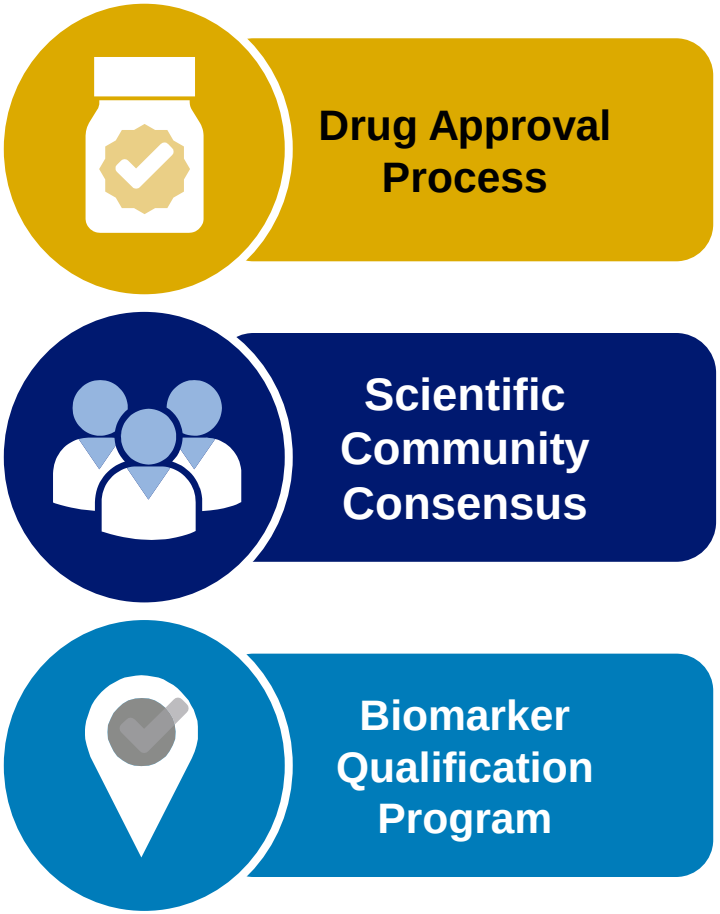
If you have questions, please send any inquiries to: CPIMInquiries@fda.hhs.gov

Drug Development Tools | DDTs

DDTs are methods, materials, or measures that can potentially facilitate drug development. FDA established qualification programs to support DDT development.

Office of Women's Health
Source: https://www.fda.gov/drugs/development-approval-process-drugs/drug-development-tools-ddts

BIOMARKER INTEGRATION INTO DRUG DEVELOPMENT



Note: These pathways do not exist in isolation and many times parallel efforts are underway within or between pathways. All share common core concepts, are data-driven, and involve regulatory assessment and outcomes based on the available data.

Facilitating Biomarker Development: Strategies for Scientific Communication, Pathway Prioritization, Data-Sharing, and Stakeholder Collaboration; Published June 2016, Duke-Margolis Center for Health Policy

INitial **T**argeted **E**ngagement for **R**egulatory **A**dvice on **C**BER produc**T**s **(INTERACT)**

INTERACT Meetings

Meeting is an informal non-binding consultation with the Center for Biologics Evaluation and Research (CBER) at FDA.

An INTERACT meeting enables sponsors to obtain preliminary informal consultation for innovative investigational products at an early stage of development on issues that are not yet at the pre-IND meeting phase.

Office of Women's Health
https://www.fda.gov/vaccines-blood-biologics/industry-biologics/interact-meetings

Advancing Alternative Methods at FDA

Alternative Methods Working Group (AMWG)

- Strengthen FDA's long commitment to promoting the development and use of new technologies and to reduce animal testing
- Discuss new alternative *in vitro/in silico/in vivo methods* across FDA
- Interact with U.S. Federal partners and other global stakeholders to facilitate discussion and development of draft performance criteria for such assays.

https://www.fda.gov/science-research/about-science-research-fda/advancing-alternative-methods-fda

How do we bring the science forward?

- Research
- Education
- Meetings
  - CPIMS, INTERACT, AMWG
- Drug Development Tools
- Sponsor Meetings with FDA as appropriate

www.fda.gov/womens

www.fda.gov/womenshealthresearch

@FDAWomen on Twitter