

Pregnancy and Lactation Research *Activities, Collaborations, and Opportunities*

21st Century Cures Act Section 2041, PRGLAC Task Force

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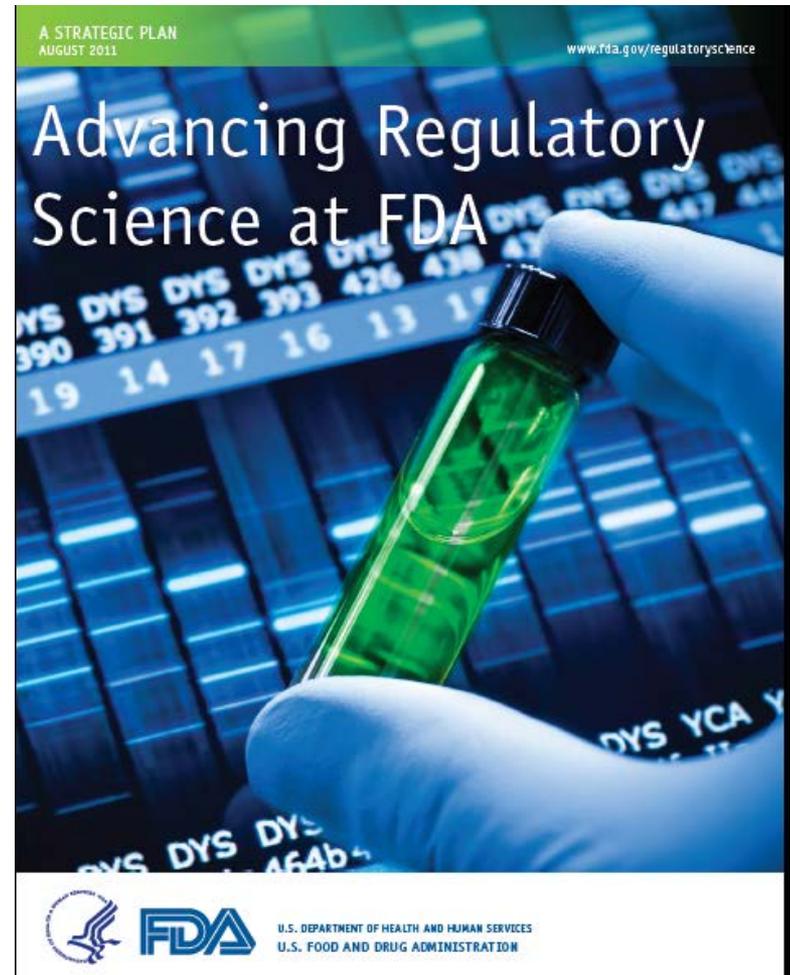
Research Collaborations

FDA collaborates internally and externally with federal, academic and other organizations to develop a variety of programs to benefit pregnant and lactating women

FDA Regulatory Science

What is Regulatory Science?

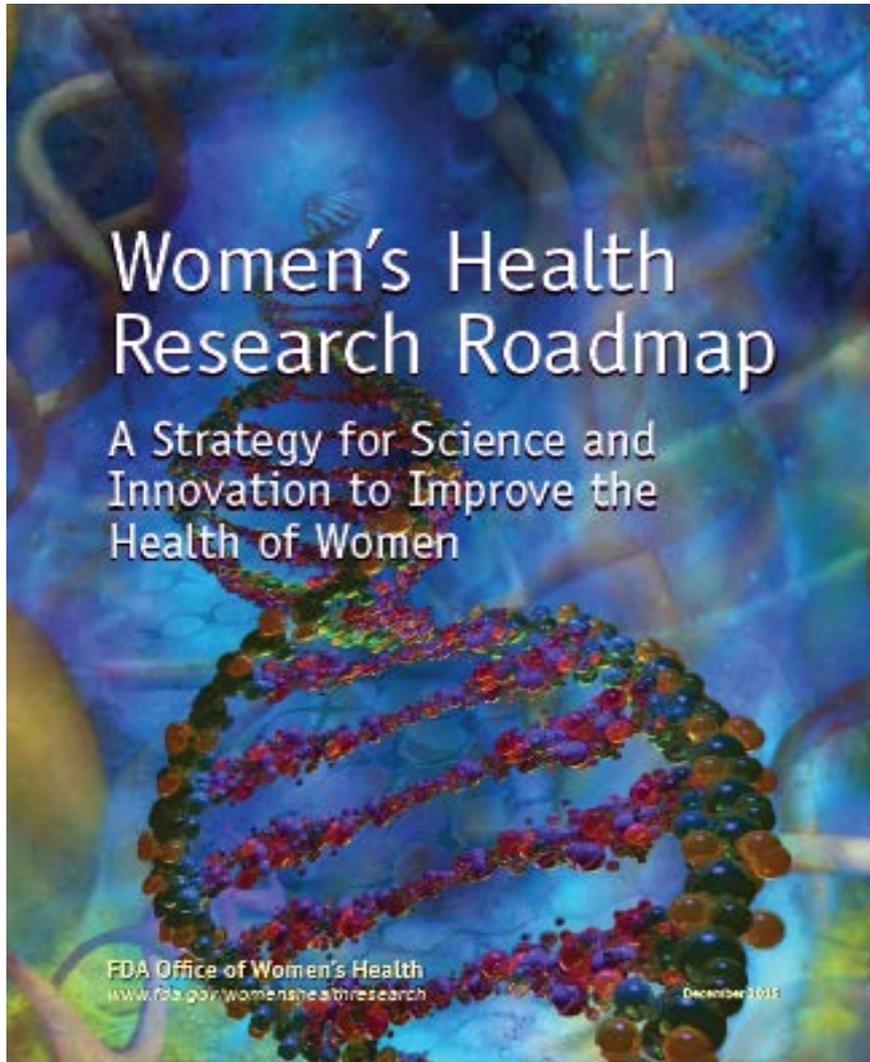
The science of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of FDA regulated products.



Pregnancy & Lactation Research



FDA Office of Women's Health



- **Represents**
Collective commitment across FDA
- **Resource**
Leverage OWH scientific resources
- **Recognize**
7 Priority Areas

Examples of Pregnancy and Lactation Research Conducted Through Intramural Grant Funding

- **Population-based computational framework for assessing xenobiotic disposition and interaction effects in pregnant women**, Annie Lumen, PhD/NCTR (2017)
- **Assessment of Placental Transmission of Zika Virus Glycoprotein E Immunogen**-Evi Struble, PhD/CBER (2016)
- **Bayesian demographic subgroup analyses for pregnant women**- Judy X. Li, PhD/CBER (2015)
- **Evaluation of pharmacokinetics of thrombogenic impurity following different routes of immune globulin administration during pregnancy** - Mikhail Ovanesov, PhD, CBER (2014)
- **Applications of Clinical Pharmacology Principles in Pharmacotherapy of Diseases in Pregnancy** - Srikanth Nallani, Ph.D CDER (2012)
- **MRI in pregnant patients: A systematic analysis of Radio-frequency heating with multi-transmit technology** - Leonardo Angelone, PhD, CDRH (2012)

Public/Private Collaborations

- Internal Exposure to Drugs and Chemicals¹¹ (NCTR, CDER, CFSAN, NICHD, Risk Sciences International, Duke University, Proctor and Gamble, University of Rhode Island)
- Medication Exposure Pregnancy Risk Evaluation Program¹² (CDER, HMO Research Network, Kaiser Permanente, Vanderbilt)
- Electromagnetic Exposure Studies¹³ (University of Houston, IT'IS Foundation)
- Lactation Studies (CDER, NICHD, Duke)

Interagency Collaborations

- Treating for Two^{1,2} (OWH, CDER, DPMH, CDC)
- Oxybenzone Studies^{3,4,5} (NTP/NIEHS, CDER, NCTR)
- BPA Metabolism⁶ (NCTR, CDRH, CFSAN, NTP/NIEHS)
- National Health and Nutrition Examination Survey^{7,8} (CFSAN, CDC)
- Dietary Patterns during preconception/pregnancy and Related Disorders and Birth outcomes^{9,10} (FDA, USDA)

Medication Exposure Pregnancy Risk Evaluation Program¹²

(CDER, HMO Research Network, Kaiser Permanente, Vanderbilt)

- A collaborative effort intended to provide a large, ethnically and geographically diverse population with which to address a variety of important and timely issues surrounding medication use in pregnancy, and to provide an avenue for ongoing research
- Brings together the clinical and research expertise and population-based databases from 9 study sites which conduct post marketing surveillance studies
- Data resources include information on maternal and infant characteristics and medical care from automated databases



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Medication Exposure in Pregnancy Risk Evaluation Program

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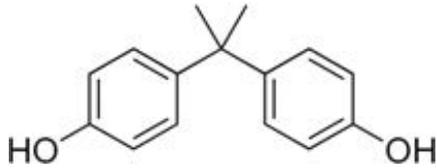
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Medication Exposure in Pregnancy Risk Evaluation Program (MEPREP)

- Studies completed using MEPREP, include
 - Birth certificate linkage¹⁴, elective induction¹⁵, linkage algorithms¹⁶, risks of sulfonamide use¹⁷
 - Evaluation of the prevalence of asthma medications¹⁸, anticonvulsants¹⁹, antidiabetics²⁰, antipsychotics²¹, and antivirals²²
 - Validity studies to evaluate data elements within the databases and gestational age assumptions based upon administrative data^{23,24}
- Ongoing studies using MEPREP, include
 - A 3-year FDA-funded epidemiologic study beginning in 2016, to evaluate the association between neural tube defects and maternal exposure to prescription opioids during early pregnancy



BISPHENOL A (BPA)

- Industrial chemical used in the manufacture of polycarbonate plastic and epoxy resins, possesses weak estrogenic activity
- Found in food and drink packaging, medical devices, dental sealants, digital media (CDs, DVDs), thermal paper products
- Widespread human exposure; detected in ~95% urine samples of US population (NHANES)
- Estimated human daily intake is $< 1 \mu\text{g BPA/kg body weight (bw)}$
- Major route of human exposure is dietary

CLARITY-BPA

- Consortium Linking Academic and Regulatory Insights on the Toxicity of BPA
- Research consortium involving scientists from:
 - FDA/NCTR and FDA/Center for Food Safety and Applied Nutrition (CFSAN)
 - NIEHS/NTP and DERT (Division of Extramural Research/Training)
 - 13 NIEHS/DERT-funded university-based grantees
- Concept was suggested by NIEHS given on-going disagreement on the conclusions on BPA safety of the preponderance of international regulatory agencies, including FDA, and some academic investigators
- Intention was to integrate data from university-based grantee studies with those of a guideline-compliant study to contribute to the safety assessment of BPA

NCTR'S 2-YEAR CHRONIC (CLARITY-BPA "CORE") STUDY

- **Modified guideline, GLP-compliant study**
- **Prior 90-day toxicology study using same model showed clear adverse effects only at 100 and 300 mg/kg body weight/day (Delclos *et al.*, Toxicol Sci 139:174-197, 2014)**
 - **High dose for the 2 year study is 25 mg/kg body weight/day, selected relative to human exposures (i.e. adequate safety margin) rather than 90-study results**
- **All CLARITY-BPA participants were involved in and agreed upon the final design of the core study**
- **Detailed descriptions of study concept and design have been published:**
 - **Schug *et al.*, A new approach to synergize academic and guideline-compliant research: the CLARITY-BPA research program. Reprod Toxicol 40: 25-30, 2013**
 - **Heindel *et al.*, NIEHS/FDA CLARITY-BPA research program update. Reprod Toxicol 58: 33-44, 2015**

Biomarkers, Endpoints and Other Tools BEST (FDA, NIH)

- Clarifies terminology related to biomarkers and surrogate endpoints
- Examples
 - Monitoring Biomarker
 - Serial fundal height during pregnancy (pg 7)
 - Predictive Biomarker
 - Serum protein levels during pregnancy (pg 18)



<https://www.ncbi.nlm.nih.gov/books/NBK326791/?report=reader>

<https://blogs.fda.gov/fdavoice/index.php/tag/biomarkers-endpoints-and-other-tools-best/>

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Women's Health Research

- OWH Research and Development Program
- OWH Research Initiatives
- OWH Presentations and Publications
- Understanding Sex Differences
- Women in Clinical Trials
- Pregnancy Registries**

Pregnancy Registries

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Many women need to take medicine while they are pregnant. Some women take medicines for health problems, like diabetes or high blood pressure, that can start or get worse when a woman is pregnant. Some women use medicine before they find out they are pregnant.

A pregnancy exposure registry is a study that collects health information from women who take prescription medicines or vaccines when they are pregnant. Information is also collected on the newborn baby. This information is compared with women who have not taken medicine during pregnancy.

Enrolling in a pregnancy exposure registry can help improve safety information on medicines used during pregnancy and can be used to update drug labeling, more about how you can help.

[Pregnant Women](#)
[Health Professionals](#)
[Find a Registry](#)

Resources for You

- List of Pregnancy Exposure Registries
- Tips for Pregnant Women
- Women's Health Topics
- Free Publications for Women

FCIC Order Page For Women Free Pubs Google homepage Inside.FDA Patient Network Web Slice Gallery

List of Pregnancy Exposure Registries

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Pregnancy exposure registries are studies that collect health information on medical product exposures such as drugs and vaccines during pregnancy. The registries on this page are posted based on a sponsor or investigator's request to list their registry. The registries listed on the webpage may not represent a comprehensive list of pregnancy exposure registries. FDA does not conduct any of these studies. FDA does not endorse any registry and is not responsible for the content of registries listed on this webpage. This webpage is open to the public and intended for informational purposes only.

Search by Medicine or Medical Condition:

(Search results update automatically as you type)

Spotlight

- [Pregnancy Registry Homepage](#)
- [Other Pregnancy Resources](#)
- [Report a Problem with a Medicine](#)

Show 10 entries

Medicine	Medical Condition	Registry	How to contact	Status
Multiple Drugs	Autoimmune Diseases: Crohn's Disease, Rheumatoid Arthritis, Psoriasis, Psoriatic Arthritis, Multiple Sclerosis (MS)	OTIS Autoimmune Diseases Study	MotherToBaby Pregnancy Studies conducted by the Organization of Teratology Information Specialists (OTIS) Website: http://www.pregnancystudies.org/ongoing-pregnancy-studies/autoimmune-studies/ Phone: 1-877-311-8972	Ongoing
Multiple Drugs	Asthma	OTIS Pregnancy Outcomes and Asthma	MotherToBaby Pregnancy Studies conducted by the Organization of Teratology Information Specialists	Ongoing

www.fda.gov/pregnancyregistries

PREGNANCY REGISTRIES

Pregnancy and Lactation

FDA GUIDANCES

FDA Guidances: Pregnancy and Lactation

Submission of Premarket Notifications for Magnetic Resonance Diagnostic Devices²⁵

Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components²⁶

Considerations for Developmental Toxicity Studies for Preventive and Therapeutic Vaccines for Infectious Disease Indications²⁷

Reproductive and Developmental Toxicities — Integrating Study Results to Assess Concerns²⁸

Evaluating the risks of drug exposure in human pregnancies²⁹

Establishing Pregnancy Exposure Registries³⁰

Draft Guidances



Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products-Content and Format³¹



Pharmacokinetics in Pregnancy - Study Design, Data Analysis, and Impact on Dosing and Labeling³²



Clinical Lactation Studies - Study Design, Data Analysis and Recommendations for Labeling³³

Opportunities

FDA MECHANISMS FOR EXTERNAL RESEARCH ENGAGEMENT

FDA Centers of Excellence in Regulatory Science and Innovation (CERSI)

Mission & Goals:

To facilitate cooperative relationships and build strategic alliances among FDA and leading **academic institutions** to provide the Agency ready access to research capabilities, training and education and a platform for communication and dialogue with stakeholders in support of FDA's regulatory science needs, scientific workforce development, and its regulatory mission that includes speeding innovations to advance public health.

For more information, visit CERSI web site:

<https://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm301667.htm>

<https://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/ucm493022.htm>

CERSI Framework

Research

- Research Collaborations with FDA
- Pilot Projects

Training

- Certificate & Masters Programs
- Scientific Exchange

Administration

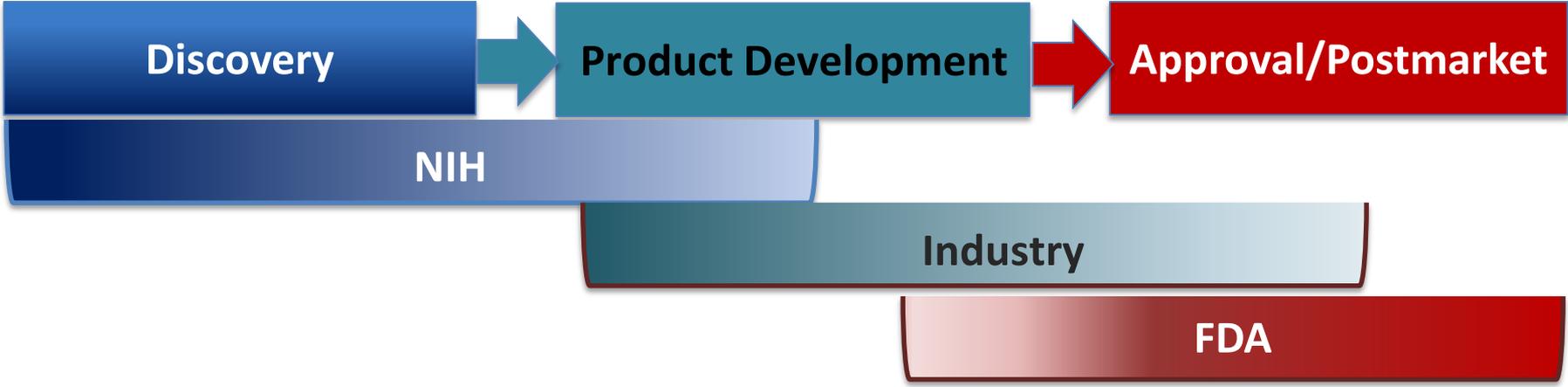
- Workshops, Lectures and Visits
- Core Facilities and program supports

Extramural Research Funded Through the Broad Agency Announcement (BAA)

- Solicitation encourages science and tech-based participation & academia to meet FDA goals for regulatory science
- Focus on FDA Scientific Priority Areas in *Advancing Regulatory Science*

Research Environments

Knowledge Transfer and Application Occurs Across Environments



Opportunities to Strengthen Research Collaboration

- **Awareness**
 - Communication
- **Engagement**
 - Relationships
- **Collaboration**
 - Actively working together
- **Dissemination**
 - Strategic outreach
- **Endurance**
 - Continued Collaboration



THANK YOU

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