



# Industry Perspective

Christina Bucci-Rechtweg, MD

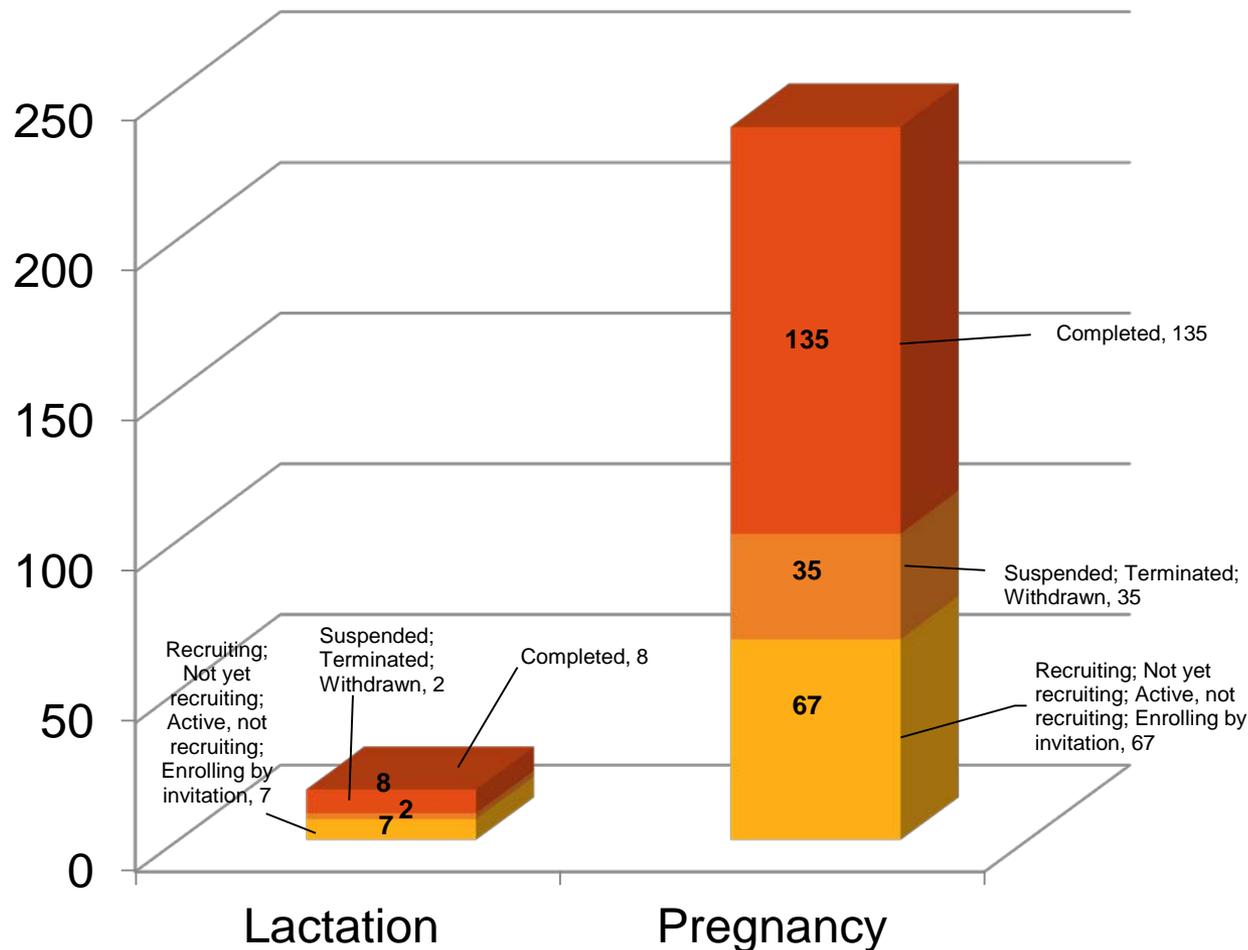
Global Head, Pediatric & Maternal Health Policy, Novartis

Federal Task Force on Research for Pregnant and Lactating Women

21 & 22 August 2017

# Interventional trial status in the US

## Industry sponsored



### Search terms include

Study type: "interventional"  
Study phase: "Early Phase 1; Phase 1; Phase 2; Phase 3; Phase 4"  
Funder type: "industry"

- Completed
- Suspended; Terminated; Withdrawn
- Recruiting; Not yet recruiting; Active, not recruiting; Enrolling by invitation

# Trades

## ➤ Biotechnology Innovation Organization Preclinical Safety Committee (BioSafe)



- BIO members are involved in the research and development of innovative healthcare, agricultural, industrial and environmental biotechnology products
- BioSafe serves as a resource for BIO staff and member companies by identifying and responding to key scientific and regulatory issues related to the preclinical safety evaluation of biopharmaceutical products
  - Over 30 companies
  - Develop white papers, responses to regulatory guidance, and expert topic meetings

- International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH)
  - Brings together regulatory authorities and the pharmaceutical industry to discuss and achieve consensus on scientific and technical aspects of drug registration
  - Mission: To achieve greater harmonization worldwide to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner
    - S5(R2): Detection of Toxicity to Reproduction for Medicinal Products & Toxicity to Male Fertility
    - S5(R3): Revision of S5 Guideline on Detection of Toxicity to Reproduction for Human Pharmaceuticals
    - S6(R1): Preclinical Safety Evaluation of Biotechnology-Derived Pharmaceuticals
    - S9: Nonclinical Evaluation for Anticancer Pharmaceuticals
    - M3(R2) & M3(R2) Q&As: Guidance on Nonclinical Safety studies for the Conduct of Human Clinical Trials and Marketing Authorization for Pharmaceuticals

# Public-Private partnerships (1)



- ILSI Health and Environmental Sciences Institute (HESI) Developmental and Reproductive Toxicology (DaRT)
  - Provides a forum where scientists from industry, government and academia can exchange information and initiate activities to:
    - Advance science related to DART
    - Develop consensus on the appropriate use of experimental data for human health risk assessment
    - Areas of scientific focus include:
      - Developmental toxicology
      - Male fertility
      - Female fertility
      - Juvenile toxicology
      - Multi-disciplinary guidance as it relates to DART issues

# Public-Private partnerships (2)



## ➤ Impactful publications

(<http://hesiglobal.org/developmental-and-reproductive-toxicology-dart/>) include:

- Theunissen P et al. Comparing rat and rabbit embryo-fetal developmental toxicity data for 379 pharmaceuticals: on systemic dose and developmental effects. *Critical Reviews in Toxicology*. 2016.
- Stewart J et al. Birth Control in Clinical Trials: Industry Survey of Current Use Practices, Governance, and Monitoring. *TIRS*. 2016.
- Scialli AR et al. Potential Seminal Transport of Pharmaceuticals to the Conceptus. *Reproductive Toxicology*. 2015.

## Public-Private partnerships (3)



- Planned and held US- and EU-focused workshops that provided practical training on the requirements related to the FDAs Pregnancy and Lactation Labeling Rule
- Satellite meeting of the European Teratology Society
  - Best Practices in Interpreting Developmental Toxicity Data for Classification and Labeling (<http://hesiglobal.org/wp-content/uploads/sites/11/2017/08/HESI-ETS-CMR-Best-Practices-Workshop.pdf>)
    - To achieve a consistent and accurate classification in regard to developmental toxicity, in particular within the REACH, biocides or pesticide regulations
    - Topics
      - The interpretation of developmental toxicity studies (developmental effects in the presence of maternal toxicity)
      - The weight of evidence in determining a classification

# Public-Private partnerships



## PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium)

<https://www.imi.europa.eu/content/protect>

Consortium of 34 public and private participants (2009)

- To address limitations of current methods in the field of pharmacoepidemiology and pharmacovigilance
- To enhance the monitoring of the safety of medicinal products
- To better evaluate and communicate benefit-risk profiles throughout lifecycle
- Assessed modern means of collecting data on medication, lifestyle and risk factors directly from consumers in 4 countries (2066 pregnant women)
- ❖ Dreyer et al. PROTECT Pregnancy Study- An Exploratory Study of Self-Reported Medication Use in Pregnant Women, ICPE Boston, 25 August 2015 ([http://www.imi-protect.eu/documents/Dreyeretel.PROTECTPregnancyStudy-AnExploratoryStudyofSelf-ReportedMedicationUseinPregnan\\_000.pdf](http://www.imi-protect.eu/documents/Dreyeretel.PROTECTPregnancyStudy-AnExploratoryStudyofSelf-ReportedMedicationUseinPregnan_000.pdf))

*“Direct to consumer studies offer important benefits in obtaining data not found in prescription drug registries and electronic health records, and these type of studies will be most informative when combined with selected data from other sources to validate clinical outcomes of interest, and to corroborate most important exposures.”*

## ConcePTION (Continuum of Evidence from Pregnancy Exposures, Reproductive Toxicology & Breastfeeding to Improve Outcomes Now)

### ➤ IMI Consultative Workshop

- 15 Dec 2016 (Brussels) Safe use of medicines during pregnancy/lactation
- In response to the European Institute of Women's Health (EIWH) Call to Action on 'Safe Use of Medicines During Pregnancy and Lactation' (<https://eurohealth.ie/safe-use-of-medicines-during-pregnancy-lactation/>)
- Opportunity for collaboration stemming from:
  - Expectations of the public and regulators for better information on risks associated with disease and medication are rising (new pregnancy and lactation labeling guidelines in EU are anticipated)
  - New data analytic approaches and data sources allow efficient access to and learning from much larger pregnant populations
  - Growing consensus across stakeholders that collaboration is the way forward to address the issue

- The ConcePTION project proposal addresses
  - The unmet need for a science and data driven approach to define the standards for generating data on medicines used during pregnancy and breastfeeding
  - To provide better information to both the HCP and the women who are or want to become pregnant or breastfeed
  - 15 EFPIA member companies
  - Call launch anticipated in October 2017

## European Forum for Good Clinical Practice (EFGCP)

- Non-profit organization established by and for individuals with a professional involvement in the conduct of biomedical research
  - Purpose: To promote good clinical practice and encourage the practice of common, high-quality standards in all stages of biomedical research
  - Position statement (Mar 2014)

*“As part of the responsible transition for a woman who falls pregnant during a study, the EFGCP strongly recommends:*

*That she meets the researchers responsible for her care in the study, along with an appropriate counsellor to discuss:*

- *Implications for her and her baby,*
- *Whether or not she should remain in the study,*
- *What further data collection will be done,*
- *and future therapeutic management and prenatal care.*

*That her study medication is unblinded and shared with her, unless she takes an informed position not to unblind.”*

## DIA Medicines in Pregnancy Forum (2014)

- To gain multi-stakeholder alignment on key ethical questions related to research in pregnant women, and to provide insight on how best to facilitate discussion and action
  - *When is it ethically appropriate to include or unethical not to include pregnant patients in clinical studies, and how can ethical barriers be addressed?*
  - *What are the most appropriate methods to collect and share data on medication use in pregnancy, and what is the best process for sharing such information?*

# Multi-stakeholder forums

---

## Resulting publications

1. Dewulf L. Medicines in pregnancy: women and children first? *TIRS*. 2013. 47:528–532.
2. European Forum for Good Clinical Practice (EFCGP) annual conference report. Benefit and risks of research: how do we redress the current imbalance? Brussels, Belgium. 2014.  
<http://www.efgcp.eu/Downloads/confDocuments/EFGCP%20Annual%20Conference%202014%20Report%20F.pdf>
3. Clemow D et al. Clinical data for informed medication use in pregnancy: strengths, limitations, gaps, and a need to continue moving forward. *TIRS*. 2014. 48:145-154.
4. Clemow D et al. A proposed framework to address needs of clinical data for informed medication use in pregnancy. *TIRS*. 2014. 48:145–154
5. Clemow D et al. Medicines in Pregnancy Forum: Proceedings on Ethical and Legal Considerations. *TIRS*. 2015. 49(3):326-332.



Thank You!

Christina Bucci-Rechtweg

Global Head, Pediatric & Maternal Health Policy

Novartis Pharmaceuticals

*Christina.buccirechtweg@novartis.com*