Comparison of state of pediatrics prior to BPCA/PREA and current state of Ob/Lactation

Components necessary for successful trials/collection of data	Pediatrics before enactment of BPCA/PREA	Obstetrics – current state	Lactation – current state
	BPCA (2002), PREA (2003)		
Adequately trained researchers	Suboptimal # developmental and pediatric pharmacologists prior to BPCA PPRU started in 1994 supporting 8-9 years of training prior to passage of BPCA Increasing numbers (54) trained using BPCA funds (T32) Industry has also trained pediatric trialists (unknown number)	Only about 15-20 OB PI pharmacologists in US; 1 T32 training program plus 6 academic institutions (OPRU) Solid foundation of obstetrician physician scientists and clinical trialists, but few pharmacologists	Limited experts cross-trained in lactation and pharmacology, however often lactation is discussed and investigated by pediatricians, opportunity to tap into the richness of the pediatrician expertise post BPCA
Infrastructure to conduct needed studies/clinical trials	PPRU provided proof of concept – feasibility of including children in clinical trials; PTN established mid-2000s. Industry has also invested and improved clinical trials in pediatrics to support regulatory decision making	OPRU Network structure in place at 6 institutions (2004-present) Strong infrastructure for studies/trials in obstetrics and high-risk pregnancy in the MFMU Network since 1985 Global network since 2001 Very few individual RO1s- issues with lack of expertise by applicants and reviewers	OPRU could perform these studies, has done few in the past. Focus has been on pregnancy for medical and logistic reasons

Components necessary for successful trials/collection of data	Pediatrics before enactment of BPCA/PREA	Obstetrics – current state	Lactation – current state
Legal requirement to include target population	No requirement for inclusion of children until BPCA passed in 2002 and PREA in 2003[1]	No requirement to include pregnant women in drug studies	No requirement to include lactating women in drug studies
Industry involvement	Very little involvement until BPCA and PREA enacted; studies can be done under BPCA and/or PREA; most studies are done under PREA; when a written request under BPCA is declined (off-patent), it can be referred to NIH	Industry largely involved in post-marketing safety studies and data collection in pregnancy. Differential approach to drugs used by pregnant women compared to drugs used to treat diseases of pregnancy	Little industry involvement

[1] The first incentive provisions for pediatric studies were included under the Food and Drug Administration Modernization Act (FDAMA) in 1997; and the Pediatric Rule (1998) which was struck

Components necessary for successful trials/collection of data	Pediatrics before enactment of BPCA/PREA	Obstetrics – current state	Lactation – current state
Basic science	Suboptimal - multiple gaps in developmental pharmacology affecting safety, efficacy, dosing	Poor - fundamental lack of knowledge of teratogenicity/overlap of pathways of drug action and teratogenicity; disease mechanism of pregnancy-specific conditions; understanding of drug safety in pregnancy- how to know if teratogenicity from drug or other mechanism in order to de-risk drug development Unknown appropriate dosing of common medications in pregnancy based on ADME characteristics in pregnant women Model informed drug development	Lack of knowledge about transfer of drug into human breastmilk, and transfer of drugs from human milk to infants. Current state includes data in animal studies and transfer of drugs to animal milk. Field could be advanced by developing PBPK models and in obtaining more robust human data.
Adequate # reviewers (FDA)	FDA has the Office of Pediatric Therapeutics and the CDER Division of Maternal and Child Health	Limited	
Adequate # reviewers/program (NIH)	May be adequate - however many of them came from the PPRU there is often conflict of interest	Limited	
Legislative support	AAP critical to getting BPCA/PREA passed	SMFM/ACOG coalition of organizations responsible for TF legislation	SMFM/ACOG coalition of organizations responsible for TF legislation
Stakeholder Engagement	AAP	SMFM/ACOG/AAP	SMFM/ACOG/AAP

Components necessary for successful trials/collection of data	Pediatrics before enactment of BPCA/PREA	Obstetrics – current state	Lactation – current state
FDA *(The information reflected here is very brief and the topic will be more fully explored during the February 26 PRGLAC Panel 1 presentation and moderated Q&A.)*	After BPCA and PREA were enacted, Written Requests issued under BPCA and Pediatric Study Plans required under PREA.	As noted in discussions during the previous PRGLAC public meetings, many drugs utilized in the obstetrics population are off patent	As noted in discussions during the previous PRGLAC public meetings, many drugs utilized in the obstetrics population are off patent
NIH	PPRU preceded BPCA; PTN implements BPCA; coordination across ICs	OPRU preceded TF mandate. Uncertain commitment from other ICs	No formal structure in place