The Pregnancy and Lactation Labeling Rule (PLLR)

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Overview

- Introduction-Pregnancy and Medication Use
- History of Pregnancy Labeling
- Overview of PLLR Labeling Changes
- PLLR Summary and Resources
- Discussion/Q&A

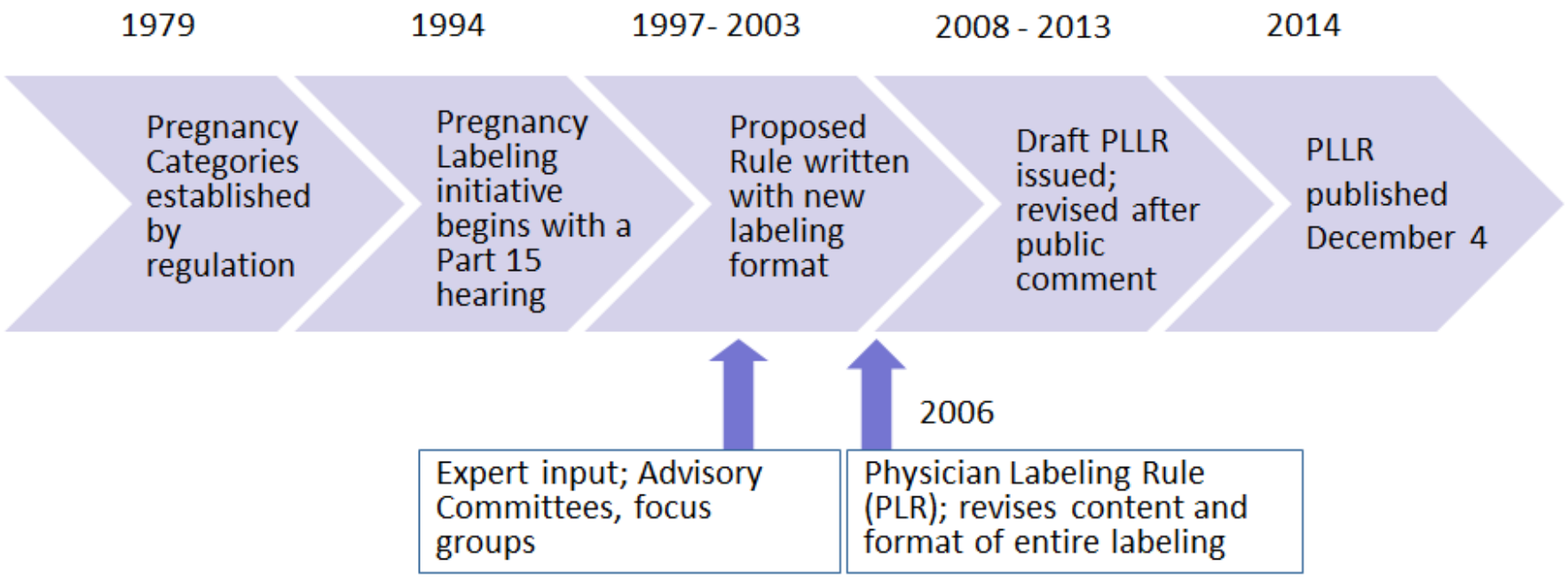
Introduction-Pregnancy and Medication Use

- Estimated six million pregnancies in US every year
- 50% of pregnant women reported taking at least one medication
- Pregnant women take an average of 2.6 medications at any time during pregnancy
- First trimester use of prescription medications has increased by more than 60%
- Use of 4 or more medications in the first trimester has tripled

Ventura SJ, Curtin SC, Abma JC, Henshaw SK. Estimated pregnancy rates and outcomes for the United States 1990-2008. National vital statistics report; vol 60 no 7. 2012.

Mitchell AA, Gilboa SM, Werler MM, et al., Medication use during pregnancy, with particular focus on prescription drugs: 1976-2008. Am J Obstet Gynecol. 2011;205(1):51.e1-8.

PLLR: Historical Overview



Why PLLR

- Pregnancy categories (A, B, C, D, and X) were often confusing and did not accurately or consistently communicate differences in degrees of fetal risk

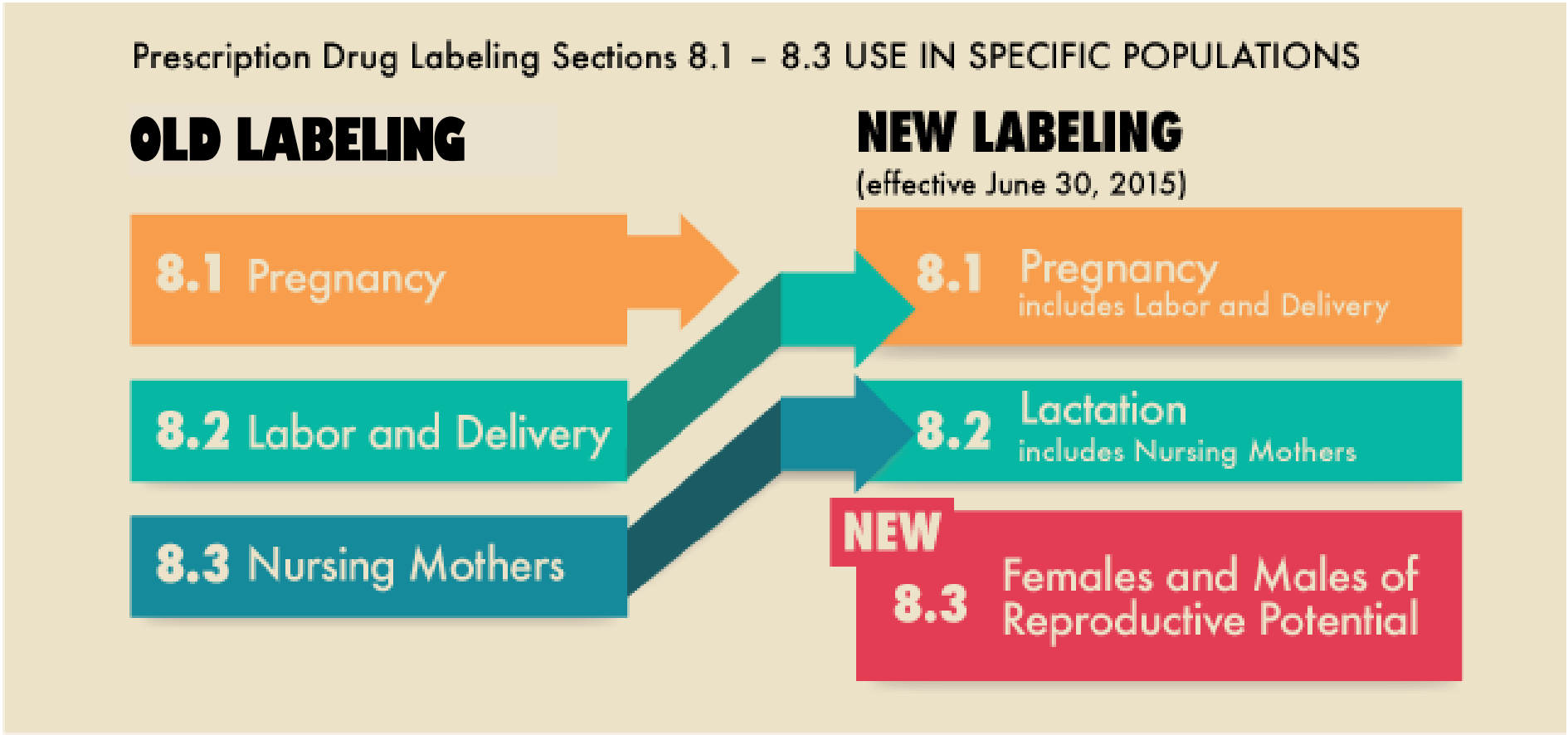
Intent of PLLR

- Provide the prescriber with relevant information for critical decision-making when treating pregnant or lactating women
- More complete assessment of the known risks based on the available data
- Considerations of medical/disease factors

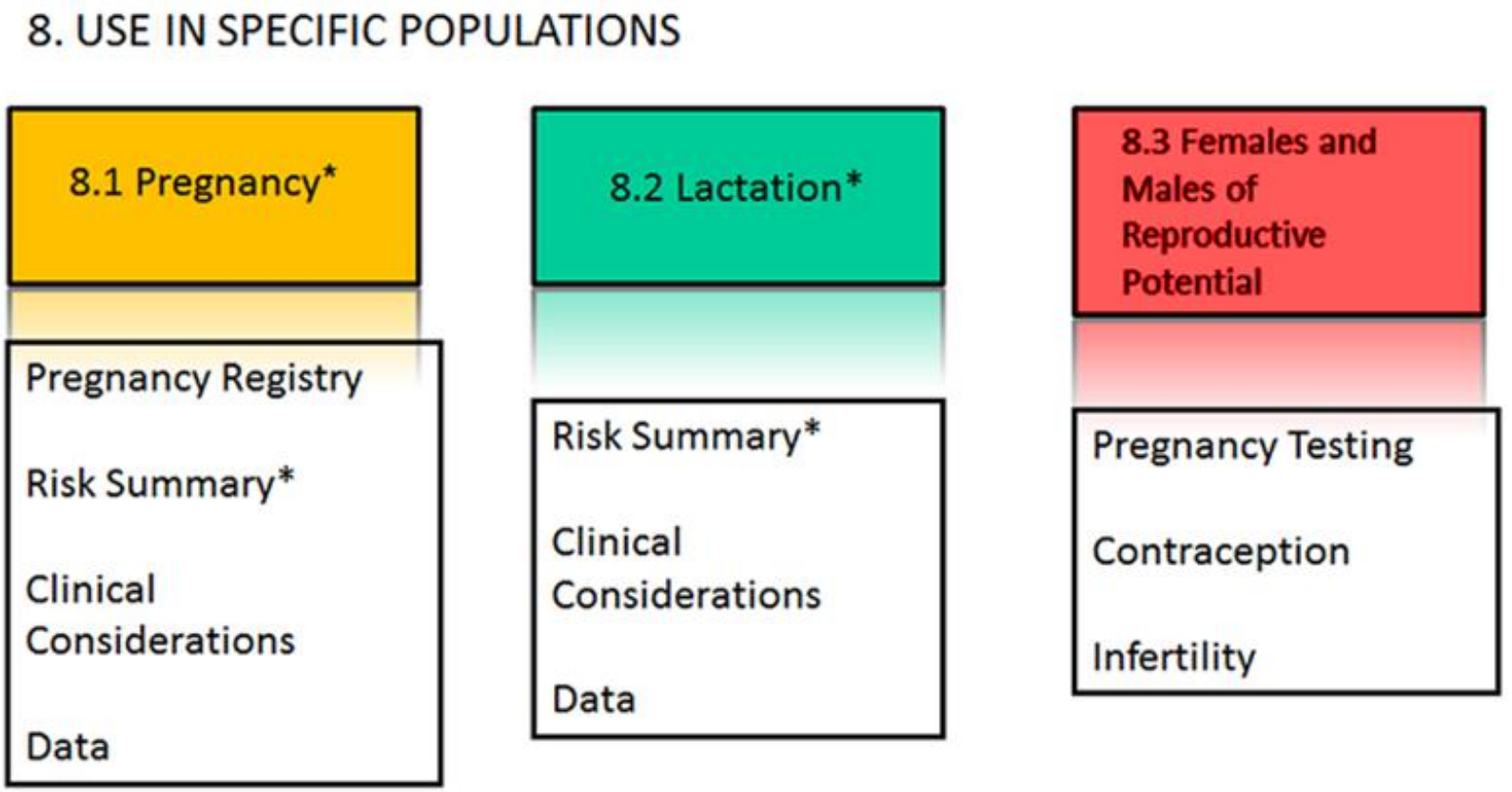
PLLR Implementation

- Effective date **June 30, 2015**
- PLLR implementation is a gradual process that will occur 3 to 5 years from the effective date
- **ALL** prescription drug labeling will be required to remove pregnancy letter categories
- Prescription drugs approved on or after June 30, 2001 have additional content and formatting requirements
- Reorganizes information in prescription drug labeling to more clearly describe available data to aid decisions and counseling of patients using prescription drugs

Overview of PLLR Labeling Changes



PLLR – Changes to Labeling



*Required

See draft guidance: Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format.

8.1 Pregnancy-Pregnancy Exposure Registry

- Pregnancy Exposure Registry
  - "There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to TRADENAME during pregnancy."
- Includes specific contact information
  - Phone
  - Website

8.1 Pregnancy- Risk Summary*

- Drugs without systemic absorption
  - "[TRADENAME] is not absorbed systemically following (route of administration) and maternal use is not expected to result in fetal exposure to the drug."
- Drugs with systemic absorption
  - When use of a drug is contraindicated during pregnancy, that information must be stated first in the Risk Summary
  - Risk statement based on human data*
  - Risk statement based on animal data*
  - Risk statement based on pharmacology
  - Background risk information in general population*
  - Background risk information in disease population

*Required

8.1 Pregnancy- Clinical Considerations

- Clinical Considerations (five optional subheadings)
  - Disease-Associated Maternal and/or Embryo/Fetal Risk
  - Dose Adjustments During Pregnancy and the Post-Partum Period
  - Maternal Adverse Reactions
  - Fetal/Neonatal Adverse Reactions
  - Labor or Delivery

8.1 Pregnancy- Data

- Data
  - Detailed description of the data that provide the scientific basis for the summary information presented in the Risk Summary and Clinical Considerations headings
    - Human Data
    - Animal Data

8.2 Lactation- Risk Summary*

- Drugs without systemic absorption

"[TRADENAME] is not absorbed systemically by the mother following (route of administration) and breastfeeding is not expected to result in exposure of the infant to [drugname]."

- Drugs with systemic absorption
  - Presence of drug in human milk*
    - Concentration in milk
    - Actual or estimated infant daily dose
  - Effects of drug on the breastfed infant*
  - Effects of drug on milk production*
  - Risk and benefit statement

*Required

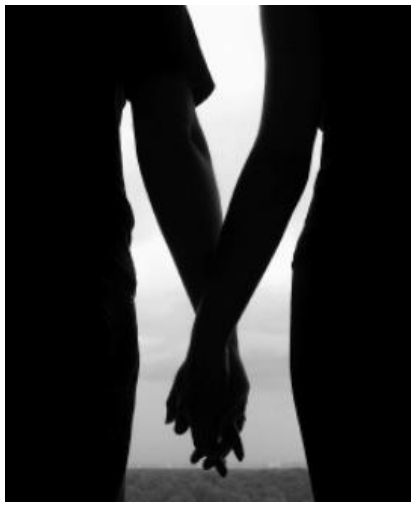
8.2 Lactation- Clinical Considerations and Data

- Clinical Considerations
  - Minimizing exposure to the breastfed infant
  - Monitoring the breastfed infant for Adverse Reactions

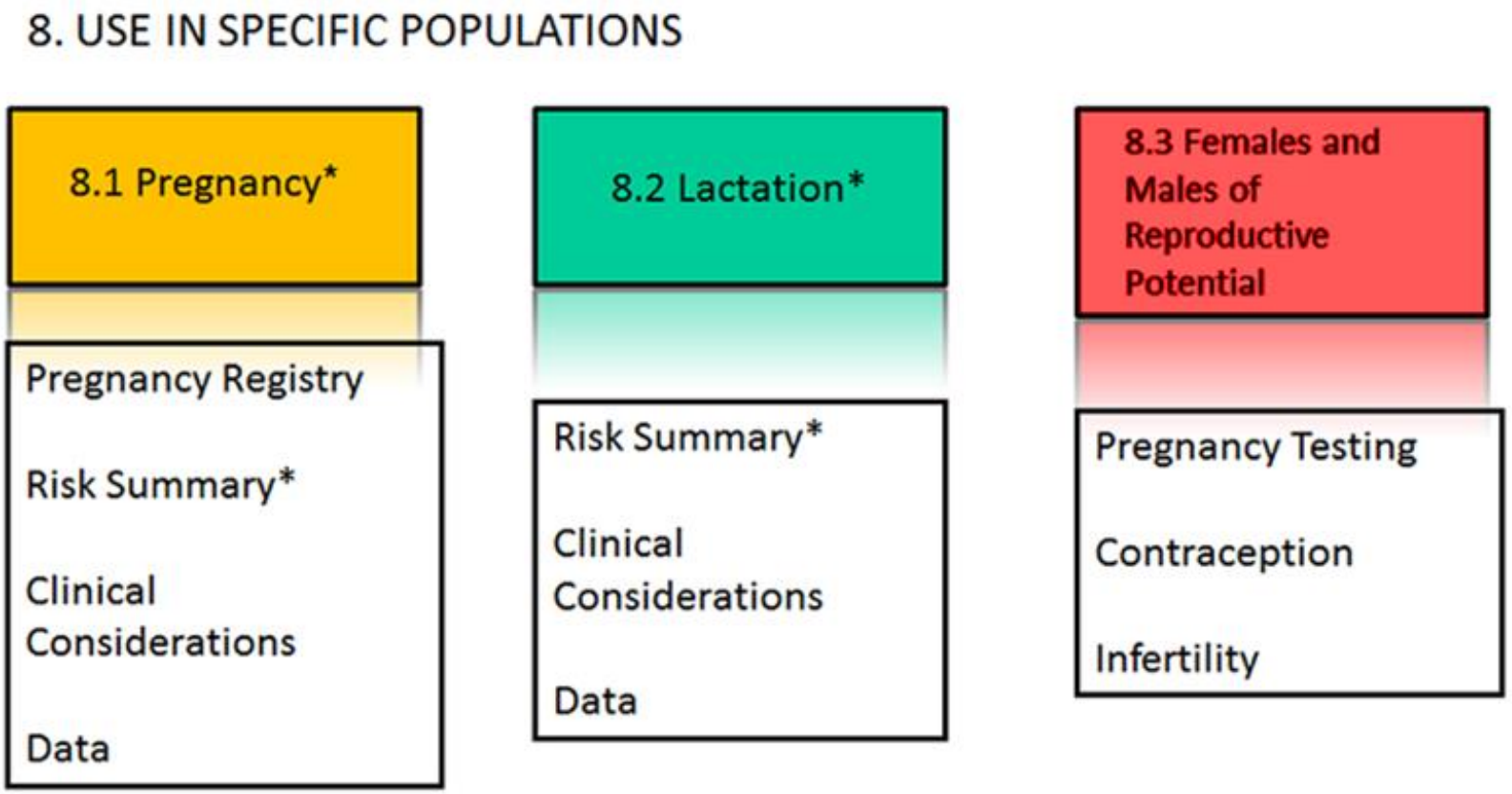
- Data - Include only when information are available
  - Description of clinical lactation study/data
  - Description of animal lactation study (only if there are no human data)

8.3 Females and Males of Reproductive Potential

- Include when there are requirements or recommendations for pregnancy testing and/or contraception and/or when human and/or animal data suggest drug effects on fertility (three optional headings)
  - Pregnancy Testing
  - Contraception
  - Infertility



PLLR – Changes to Labeling



*Required

See draft guidance: Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products – Content and Format.

PLLR Resources

- Webpage for PLLR
  https://www.fda.gov/Drugs/DevelopmentApprovalProcess/DevelopmentResources/Labeling/ucm093307.htm

- Draft Guidance for Industry: *Pregnancy, Lactation, and Reproductive Potential: Labeling for Human Prescription Drug and Biological Products — Content and Format*
  http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/ guidances/ucm425398.pdf

- Pregnancy and Lactation Labeling Final Rule
  https://www.federalregister.gov/documents/2014/12/04/2014-28241/content-and-format-of-labeling-for-human-prescription-drug-and-biological-products-requirements-for

PLLR Resources

- PLR Requirements for Prescribing Information http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm

For Current labeling:

- Drugs @FDA http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
- Daily Med (National Library of Medicine)

  http://dailymed.nlm.nih.gov/dailymed/about.cfm

Conclusion

- The PLLR provides a more structured approach to labeling
- The intent of PLLR is to provide **clearer communication of available data** to aid in complex risk/benefit discussions between prescribers and their patients

FEEDBACK/DISCUSSION

Questions?
Comments?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