

Pregnancy & Lactation Labeling Rule (PLLR)

Industry Perspective and Learnings

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Agenda



- One sponsor's approach
- Labeling role
- FDA feedback
- Challenges sponsors may face
- Learnings



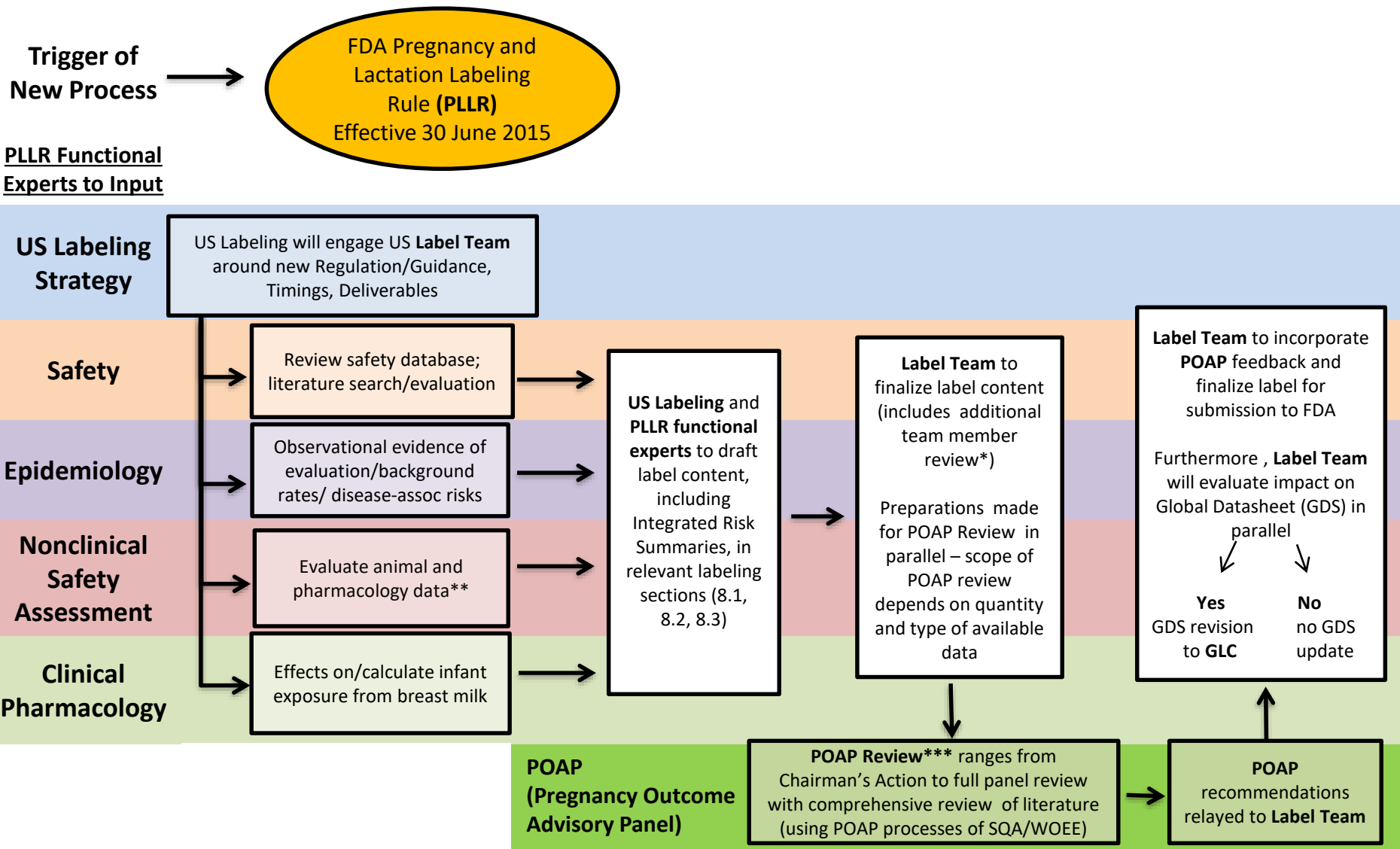
Sponsor Approach



- Established PLLR subteam
- Crossfunctional
 - Labeling
 - Nonclinical
 - Safety
 - Epidemiology
- Created materials for training, e.g. Process Flow Graphic
- Broad awareness to relevant groups
 - Emails
 - Presentations



Schematic of Process



* Regulatory, Clinical, Commercial, Legal.

** Engage Nonclinical Regulatory to assist with identification of non-clinical study reports.

***Time for POAP review needs to be incorporated into submission timings.

Global Labeling Committee (GLC); Study Quality Assessment (SQA); Weight of Evidence Evaluation (WOEE).

Sponsor Approach



- Proposed plan to meet Regulation presented to management
- Gained Safety Board approval
- Identified required timelines for the 80+ US labels needing converting
- Assigned alternative staggered timelines for extensive mature product portfolio
 - Quarterly assignments over 3+ years



Sponsor Approach



- Established internal review process
 - Aid consistency
 - Share experiences across therapy areas
 - Track learnings
- Review of all new and converted labels
 - 2 members of Labeling group pre-review
 - Internal Pregnancy Advisory panel review



Labeling Role



- Identify relevant functional experts
- Kickoff meetings to explain process
 - Initiate well in advance of regulatory timings
 - Provide timings
 - Outline of team support needed
- Educate and then educate some more
- Ensure compliance with new regulation and guidance
- Collate GSK experiences and share learnings



Review of Other Approved Labels



In the U.S. general population, the estimated background risk of major birth defects and of miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The reported rate of major birth defects among deliveries to women with migraine ranged from 2.2% to 2.9% and of miscarriage was 17%, which were similar to rates reported in women without migraine.

DAILYMED

ALL DRUGS HUMAN DRUGS ANIMAL DRUGS MORE WAYS TO SEARCH ▼

Enter drug, NDC code, drug class, or Set ID

HOME + NEWS FDA GUIDANCES & INFO + HLM SPL RESOURCES + APPLICATION DEVELOPMENT SUPPORT HELP

BROWSE DRUG CLASSES

PRINT SHARE

Note: As FDA indexes SPL, only VA NDF-RT Classifications that the FDA considers scientifically valid and clinically meaningful are used. Therefore, the drug classes that are available for a DailyMed query represent a subset of all VA NDF-RT classifications.

To find drugs that belong to a specific drug class, type in the drug class in the search box or select from the [list of drug classes](#).

This archive allows the user to retrieve the label current for a given date.

Drug Classes Search

Enter drug class

REFINE SEARCH BY ☒ ALL ☐ FDA Established Pharmacologic Classes ☐ VA NDF-RT Classifications All Categories ▼

Clinical Considerations

Disease-Associated Maternal and/or Embryofetal Risk: In women with poorly or moderately controlled asthma, there is an increased risk of several perinatal adverse outcomes such as pre-eclampsia in the mother and prematurity, low birth weight, and small for gestational age in the neonate. Pregnant women with asthma should be closely monitored and medication adjusted as necessary to maintain optimal asthma control.

Submissions



- Standardized template aligned to PLLR sections
- Includes reference to all data supporting changes

Additional Information to Support Changes to Pregnancy, Lactation, and Nonclinical Toxicology Data in the US Label for TRADENAME

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Gather FDA Feedback



Insights from FDA Feedback



- Clinical

- All published data not appropriate for labeling
- Data needs to be robust
 - Qualitative > Quantitative
- Limited information in Clinical Considerations accepted
- Able to align with “class” PLLR labels in some cases

- Nonclinical

- Requests for original nonclinical presentation of data
 - Exposure multiples updated based on AUC changed back to based on BSA
 - Maternal toxicity information removed
-

Insights from FDA Feedback



- Lactation
 - Required PLLR risk/benefit statement removed
 - Animal lactation data removed
 - Terminology changes, e.g. “child” to “infant” in risk/benefit statement
- Miscellaneous
 - Original study reports requested
 - Comments received on other sections of label



Challenges



- Education and training needed
- Time-consuming work
 - Searches/review of internal data, published literature
 - Mapping out historical content
- Differing interpretations of data
 - Internally
 - Sponsor vs. FDA
- Lack of resource assigned to projects
 - Adequate resource needed from multiple disciplines
 - Some sponsors outsourced work



Sponsor Learnings



- Timeline development for portfolio is key
 - Spread out submission timings across quarters
 - Not all in June



- Internal discussions should start well before target submission
- Re-evaluation of older data may generate additional questions
- Company core safety information may be impacted

- Appears thinking still evolving with experience gained
- Changes to Final Guidance should help clarify some feedback
- We have gotten better doing PLLR over time
 - Better evaluating data
 - Better supporting documents
 - “Progress, not perfection”





Thank You

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PLLR Resources for Sponsors



FDA PLLR Website

<https://www.fda.gov/drugs/developmentapprovalprocess/developmentresources/labeling/ucm093307.htm>

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>

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>

DailyMed

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

LactMed

<http://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm>

List of Pregnancy Exposure Registries

<https://www.fda.gov/ScienceResearch/SpecialTopics/WomensHealthResearch/ucm134848.htm>