FDA Updates

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Teratology Society Meeting
Clearwater, Florida 6-24-2018

Disclaimer

- I do not have any financial disclosures to report
- This presentation represents the views of the speaker, and not the official position of the FDA

Objectives

- Pregnancy Registry Guidance
- Recent Risk Communication Advisory Committee meeting
- Clinical Trials in Pregnant Women Guidance
- Task Force on Research in Pregnant and Lactating Women
- Recent Dolutegravir Drug Safety Communication

Pregnancy Registry Guidance

- FDA is working on a revised guidance
- Based on input received at 2014 FDA public meeting
- Includes other types of postmarketing data collection methods


communication
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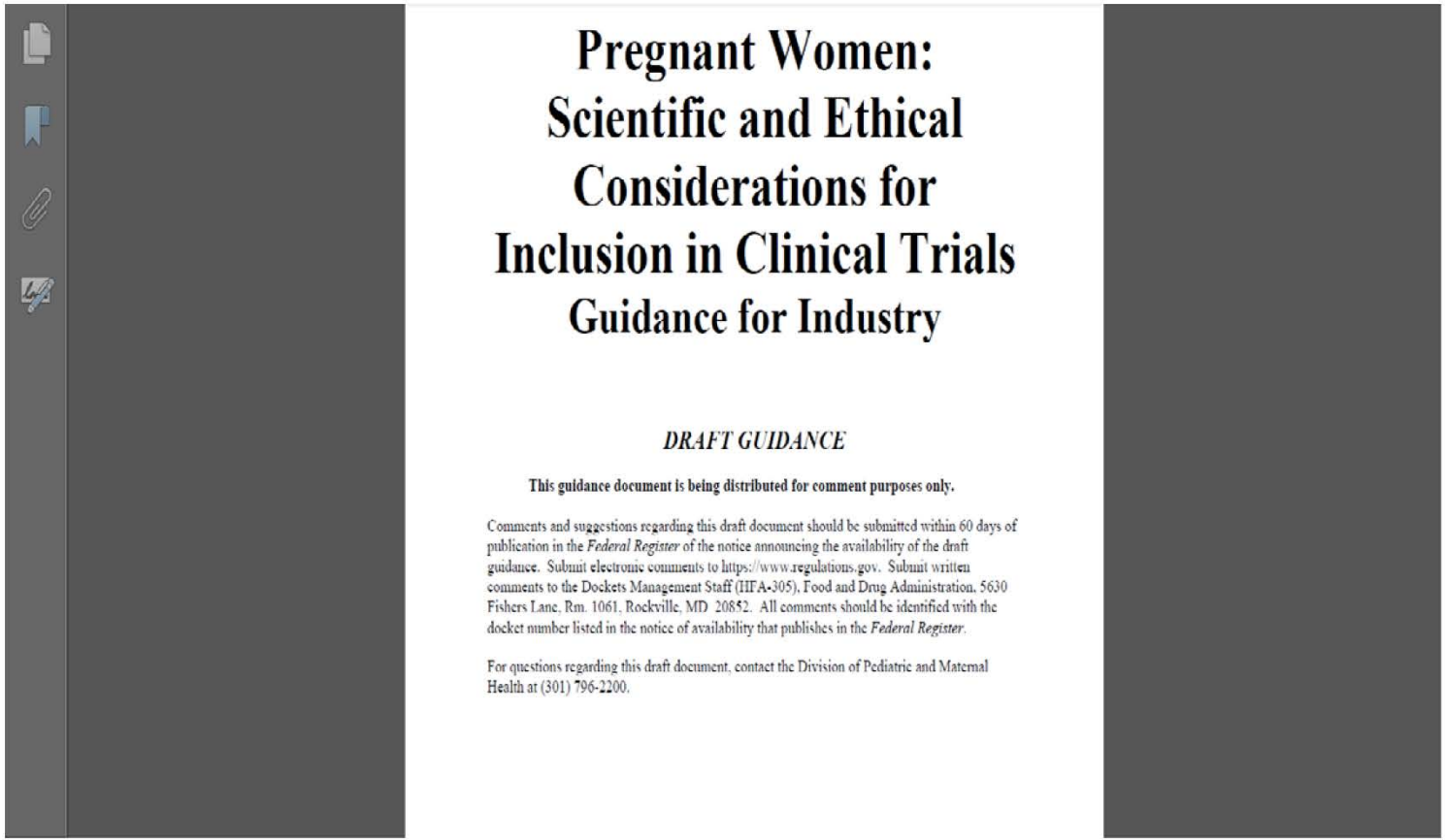
ship; young people
letter or messag

Risk Communication Advisory Committee (RCAC) Meeting

- Held on March 5-6, 2018
- Impact of Pregnancy and Lactation Labeling Rule (PLLR)
  - How information in PLLR labeling is being perceived and used by healthcare providers (HCPs)
  - Factors that are critical to HCPs' interpretation of the data and counseling of pregnant women on the risks and benefits of a medication
  - How to convey risk information to health care providers to inform risk-benefit considerations

Key Messages from PLLR RCAC

- Use plain language; avoid confusing terms
- Present concise messaging for busy clinicians
- Consider a visual tool to present information
- Provide clarity on quality of data
- Perform message testing
- Education needed regarding use of medication in pregnancy not being off-label use



Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact the Division of Pediatric and Maternal Health at (301) 796-2200.

Clinical Trials Draft Guidance

- Ethical and scientific considerations
  - For when it would be appropriate to include pregnant women in clinical trials
  - Follows HHS framework of human subject protection regulations
  - Considerations for premarket vs. postmarket setting
  - Women who become pregnant during a trial
- Effort to advance scientific research in pregnant women
- Public comment period April 9-June 8, 2018

U.S. Department of Health and Human Services

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Regulatory Information

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21st Century Cures Act

21st Century Cures Act Deliverables

Resources for You

- 21st Century Cures Act (Congress.gov)

21st Century Cures Act

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The 21st Century Cures Act (Cures Act), signed into law on December 13, 2016, is designed to help accelerate medical product development and bring new innovations and advances to patients who need them faster and more efficiently.

The law builds on FDA's ongoing work to incorporate the perspectives of patients into the development of drugs, biological products, and devices in FDA's decision-making process. Cures enhances our ability to modernize clinical trial designs and clinical outcome assessments, which will speed the development and review of novel medical products, including medical countermeasures.

It also provides new authority to help FDA improve our ability to recruit and retain scientific, technical, and professional experts and it establishes new expedited product development programs, including:

- The Regenerative Medicine Advanced Therapy, or RMAT, that offers a new expedited option for certain eligible biologics products.
- The Breakthrough Devices program, designed to speed the review of certain innovative medical devices.

Task Force on Research Specific to Pregnant and Lactating Women (PRGLAC)

- Required under the 21st Century Cures Act of 2016
- Objectives: Identify and address gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women
- Prepare a report and recommendations to the Secretary of the Department of Health and Human Services (due September 2018)

May 15, 2018 Meeting Recommendations

- Central focus is aimed at changing the culture
- Create a presumption of inclusion
- Research is needed in multiple areas
  - Epidemiologic (pregnancy registries, etc.)
  - Clinical Pharmacology
  - Basic science (understanding mechanisms such as preterm labor, low milk supply, etc.)
- Collect long term outcome data
- Reduce liability

Meeting Recommendations-Registries

- Optimize Pregnancy Registries
- Create a user-friendly website for registry listing
- Develop standards and common data elements
  - Include maternal, obstetric, and child outcomes in addition to birth defects
- Facilitate access to data and transparency of information
- Develop disease focused registries
- Move toward a single registry for all therapeutic products

New Drug Safety Information

FDA Drug Safety Communication

FDA to evaluate potential risk of neural tube birth defects with HIV medicine dolutegravir (Juluca, Tivicay, Triumeq)

Safety Announcement

[05-18-2018] The U.S. Food and Drug Administration (FDA) is alerting the public that serious cases of neural tube birth defects involving the brain, spine, and spinal cord have been reported in babies born to women treated with dolutegravir used to treat human immunodeficiency virus (HIV). Preliminary results from an ongoing observational study in Botswana found that women who received dolutegravir at the time of becoming pregnant or early in the first trimester appear to be at higher risk for these defects.

Neural tube defects are birth defects that can occur early in pregnancy when the spinal cord, brain, and related structures do not form properly. To date, in this observational study there are no reported cases of babies born with neural tube defects to women starting dolutegravir later in pregnancy. We are investigating this new safety issue and will update the public when we have more information.

Dolutegravir is an FDA-approved antiretroviral medicine used in combination with other antiretroviral medicines to treat HIV, the virus that can cause acquired immunodeficiency syndrome (AIDS). Dolutegravir works by blocking integrase, an HIV enzyme, to prevent the virus from multiplying and can reduce the amount of HIV in the body. Stopping dolutegravir without first talking to a prescriber can cause the HIV infection to become worse. Approved in 2013, dolutegravir has been on the market for 5 years, and is available as a single ingredient product under the brand name Tivicay and as a fixed dose combination tablet with other HIV medicines under the brand names Juluca and Triumeq.

Patients should not stop taking dolutegravir without first talking to your health care professional because stopping your medicine can cause the HIV infection to worsen. In addition:

- If you are already pregnant, stopping your dolutegravir-containing regimen without switching to alternative HIV medicines could cause the amount of virus to increase and spread HIV to your baby.
- If you take a dolutegravir-containing regimen at the time of becoming pregnant and

Dolutegravir Drug Safety Communication

Health care professionals should inform women of childbearing age about the potential risk of neural tube defects when a dolutegravir-containing regimen is used at the time of conception and early in pregnancy. In addition:

- Health care professionals should weigh the benefits and the risks of dolutegravir when prescribing antiretroviral medicines to women of childbearing age. Alternative antiretroviral medicines should be considered. Discuss the relative risks and benefits of appropriate alternative antiretroviral therapies.
- If the decision is made to use dolutegravir in women of childbearing age, health care professionals should reinforce the consistent use of effective birth control.
- Perform pregnancy testing before initiating a dolutegravir-containing regimen in women of childbearing age to exclude pregnancy.

Ongoing monitoring will continue as part of the observational study in Botswana. Additional birth outcomes are projected from pregnant women who were exposed to dolutegravir at the time of becoming pregnant. We will conduct a comprehensive review of the results and any other data that becomes available. We will update the public with any new information. To monitor birth outcomes of pregnant women, report pregnancy exposures to the Antiretroviral Pregnancy Registry at 1-800-258-4263.

Questions

Useful Links

- Clinical Trials in Pregnant Women Draft Guidance https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM603873.pdf
- PLLR Risk Communication Advisory Committee Meeting transcript and other materials https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/RiskCommunicationAdvisoryCommittee/ucm594576.htm
- PRGLAC https://www.nichd.nih.gov/About/Advisory/PRGLAC
- Dolutegravir Drug Safety Communication https://www.fda.gov/Drugs/DrugSafety/ucm608112.htm