Enhancing Trial Populations –Pediatric and Pregnant Patients

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Disclosures and Acknowledgements

- I have no financial relationships to disclose relating to this presentation

- The views expressed in this talk represent my opinions and do not necessarily represent the views of FDA

Objectives

- Provide a brief overview of the historical perspectives related to inclusion of children and pregnant women in clinical trials

- Provide current FDA thinking about inclusion of children and pregnant women in clinical trials

Pediatric Drug Development
General Principles

- Pediatric patients should have access to products that have been appropriately evaluated
- Product development programs should include pediatric studies when pediatric use is anticipated
- Incorporation of regulatory standards into pediatric clinical research strengthens the quality of the research

From FDA guidance to industry titled *E11(R1)- Clinical Investigation of Medicinal Products in the Pediatric Population,* December 2017

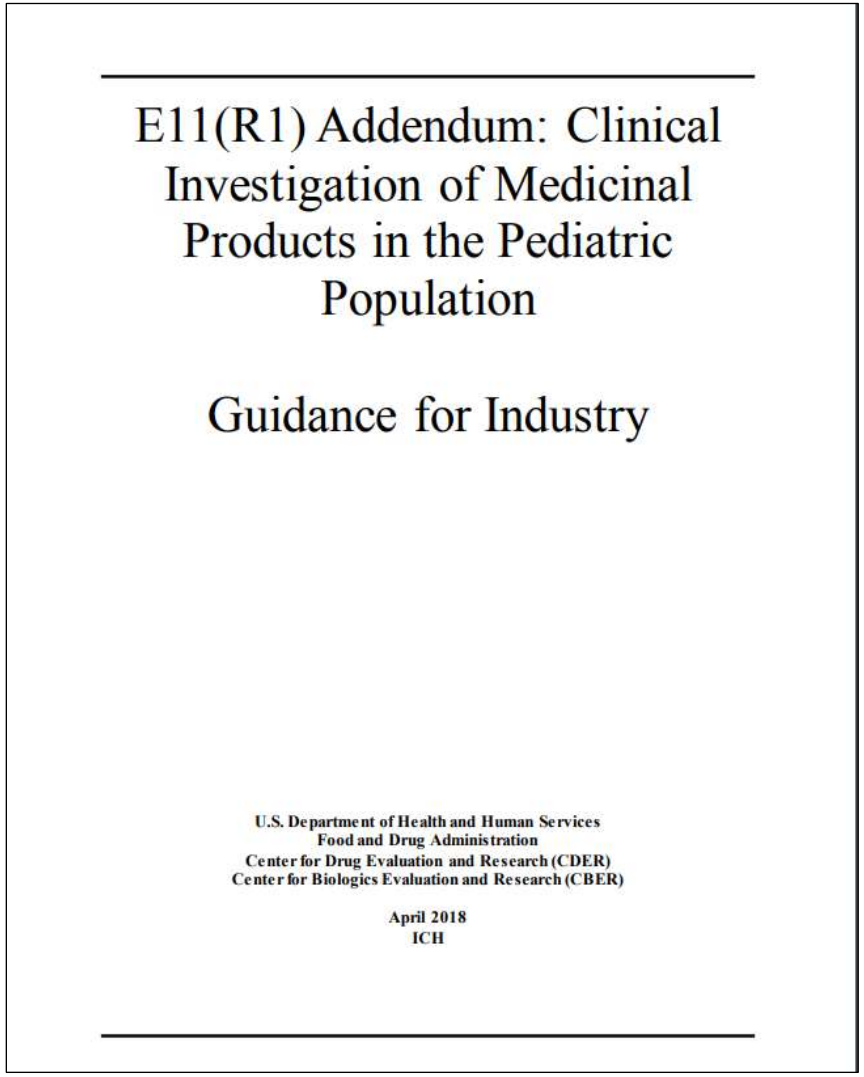
Special Considerations for Pediatric Product Development

- Ethical considerations
  - Children should only be enrolled in a clinical trial if the scientific and/or public health objectives cannot be met through enrolling subjects who can provide informed consent personally (i.e., adults)
  - Absent a prospect of direct therapeutic benefit, the risks to which a child would be exposed in a clinical trial must be “low”
  - Children should not be placed at a disadvantage after being enrolled in a clinical trial, either through exposure to excessive risks or by failing to get necessary health care
- Feasibility considerations
  - The prevalence and/or incidence of a condition is generally much lower compared to adult populations

21 CFR Part 50 Subpart D--Additional Safeguards for Children in Clinical Investigations

ICH E11(R1) (April 2018)

- Describes use of pediatric extrapolation to improve efficiency and feasibility of pediatric product development
- Describes age-related safety and risk consideration for enrollment
  - Strategies such as staggered enrollment based on age should be justified



E11(R1) Addendum: Clinical Investigation of Medicinal Products in the Pediatric Population

Guidance for Industry

U.S. Department of Health and Human Services
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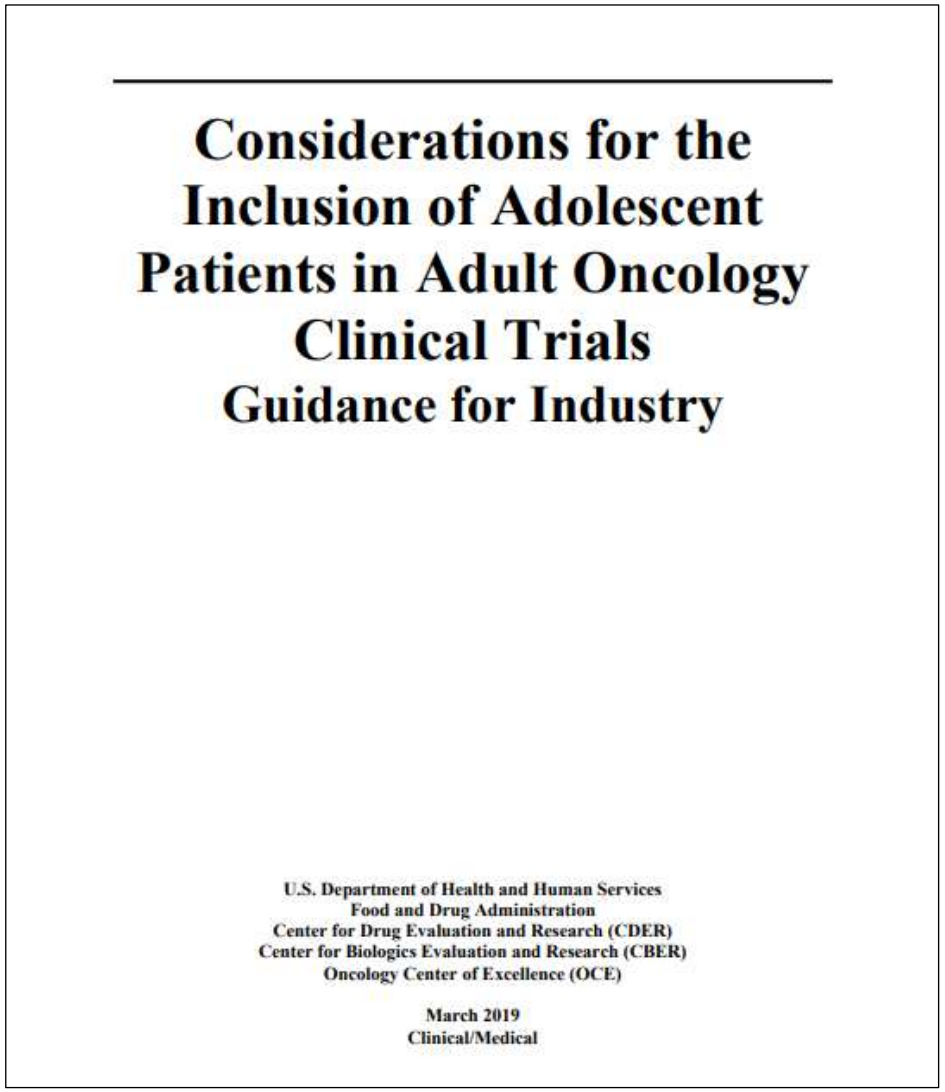
April 2018
ICH

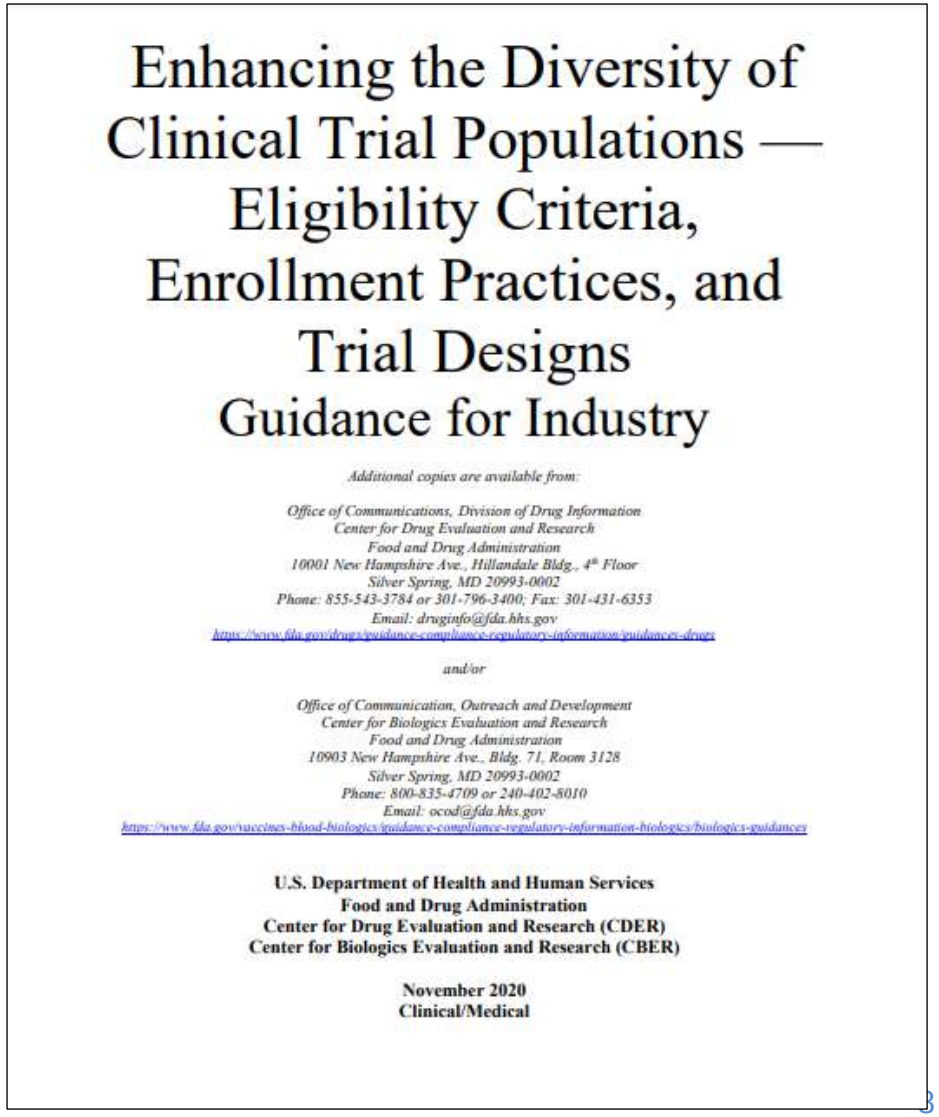
Inclusion of Adolescent Patients in Adult Oncology Trials (March 2019)

- Adolescent oncology patients, have historically been ineligible for enrollment in adult oncology clinical trials.
  - As a result, adolescent oncology patients may have delayed access to potentially effective therapies.
- Adolescent oncology patients should be eligible for enrollment in adult oncology clinical trials at all stages of drug development when the histology and biologic behavior of the cancer under investigation is the same in, or the molecular target of the drug is relevant to, cancers in both adult and adolescent patients



Enhancing Diversity of Clinical Trial Populations (November 2020)

- Includes pediatric enrollment considerations incorporated in other guidances
  - Inclusion of Adolescent Patients in Adult Oncology Trials
  - ICH E11(R1)
- Early planning important
- Justification of staggering of enrollment by pediatric age groups is necessary



Enhancing the Diversity of Clinical Trial Populations — Eligibility Criteria, Enrollment Practices, and Trial Designs

Guidance for Industry

Additional copies are available from:

Office of Communications, Division of Drug Information
Center for Drug Evaluation and Research
Food and Drug Administration
10001 New Hampshire Ave., Hillandale Bldg., 4th Floor
Silver Spring, MD 20993-0002
Phone: 855-543-3784 or 301-796-3400; Fax: 301-431-6353
Email: druginfo@fda.hhs.gov
https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs

and/or

Office of Communication, Outreach and Development
Center for Biologics Evaluation and Research
Food and Drug Administration
10903 New Hampshire Ave., Bldg. 71, Room 3128
Silver Spring, MD 20993-0002
Phone: 800-835-4709 or 240-402-8010
Email: ocod@fda.hhs.gov
https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances

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Inclusion of Pregnant Patients in Clinical Trials

Pregnancy and Lactation Labeling Rule (PLLR)

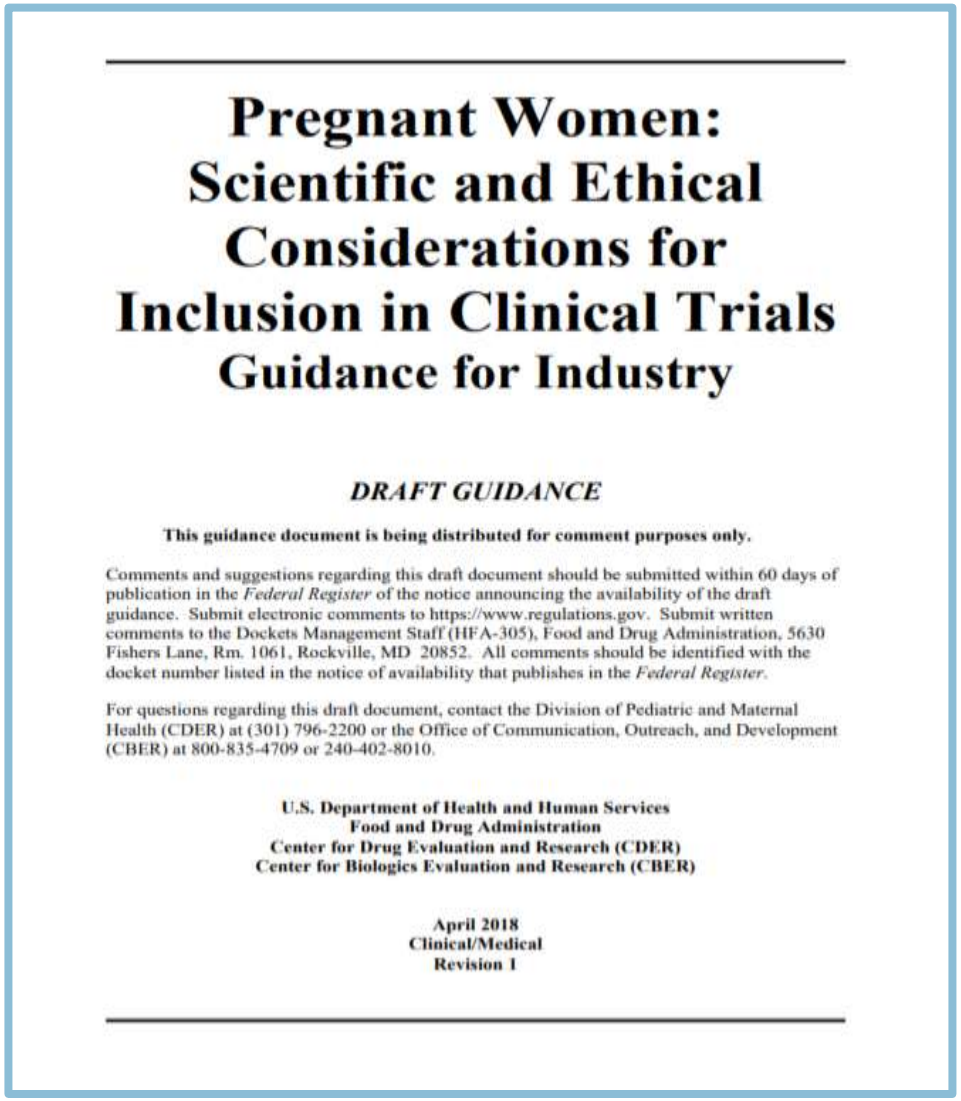
- ALL prescription drugs are required to remove pregnancy letter categories
- Revise content and format of Sections 8.1, 8.2, and 8.3
- Intended to improve communication of risk information

Lessons from PLLR Implementation

- New format provide excellent framework to discuss data and provide risks statements when data are sufficient
- The data in many cases are absent
- When some data are available the quality and quantity of data are often limited
- Data to support definitive risk statements are usually lacking

Inclusion of Pregnant Patients in Clinical Trials (April 2018)

- When to include pregnant women in clinical trials
- Follows HHS framework of human subject protection regulations
- Considerations for postmarket vs. premarket setting
- Women who become pregnant during a trial



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 (CDER) at (301) 796-2200 or the Office of Communication, Outreach, and Development (CBER) at 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
Food and Drug Administration
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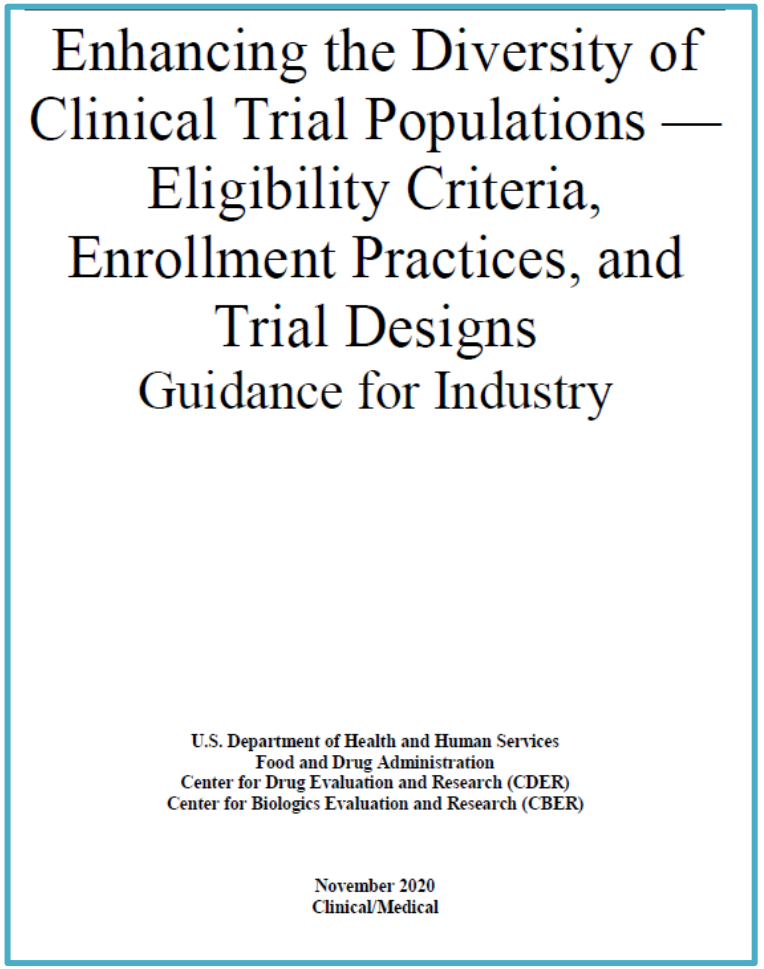
April 2018
Clinical/Medical
Revision 1

Enhancing Diversity of Clinical Trial Populations (November 2020)

- Provides links to other relevant guidances
  - Pregnant Women: Scientific and Ethical Considerations for Inclusion in Clinical Trials
  - Postapproval Pregnancy Safety Studies
- Women who become pregnant during a trial
  - Includes consideration for obtaining pharmacokinetic sampling when possible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Summary

- Enrollment of pediatric patients into clinical trials requires special considerations
  - Moving away from arbitrary staggering of enrollment based on age subsets
- Enrollment of Pregnant patients into clinical trials
  - Moving away from the paradigm of “automatic exclusion”
- Both has unique ethical considerations
- Both require early planning (e.g., nonclinical studies)
- Both deserve to have drugs with information to support their safe and effective use

Challenge Question

- True or False: Children should only be enrolled in clinical trials after the drug has been approved in adults.

- False: Pediatric patients may be enrolled in clinical trials if there is prospect of direct benefit and the trial does not pose undue risk to the child