# Product Labeling Relevant to Safety

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# Outline

- Purpose of FDA-approved product labeling
- Key sections relevant to safety
  - Definition: Adverse Reaction
  - Warnings and Precautions
  - Boxed Warning
  - Specific Population/ Pregnancy
  - Abuse and Dependence/ Dependence

# Purpose of the FDA-approved product labeling

- A prescription drug product's FDA-approved labeling is a compilation of information about the product
- This labeling contains information necessary for safe and effective use of the product.
- It is written for the health care practitioner audience, because prescription drugs require "professional supervision of a practitioner licensed by law to administer such drug".

FR Notice 1/24/2006: Requirements on Content and Format of Labeing for Human Prescription Drugs and Biological Products

# FDA-approved product labeling

- Contains a summary of essential scientific information needed for safe and effective use of drug
- Is informative and accurate and neither promotional in tone nor false or misleading
- Is updated when new information becomes available that causes labeling to become inaccurate, false, or misleading

See 21 CFR 201.56(a)

# Full Prescribing Information – Table of Contents

**FULL PRESCRIBING INFORMATION**

Boxed Warning
1 Indications and Usage
2 Dosage and Administration
3 Dosage Forms and Strengths
4 Contraindications
5 Warnings and Precautions
6 Adverse Reactions
7 Drug Interactions
8 Use in Specific Populations
9 Drug Abuse and Dependence
10 Overdosage
11 Description
12 Clinical Pharmacology
13 Nonclinical Toxicology
14 Clinical Studies
15 References
16 How Supplied/Storage and Handling
17 Patient Counseling Information

# Definition of Adverse Reaction

- "For the purposes of prescription drug labeling, an adverse reaction is an undesirable effect reasonably associated with the use of the drug, that may occur as part of the pharmacological action of the drug or may be unpredictable in its occurrence.

- This definition does not include all adverse events observed during use of a drug, only those for which there is some basis to believe there is a causal relationship between the drug and the occurrence of the adverse event."

21 CFR 201.57(c)(7).

# Warnings and Precautions section

- Should describe serious or clinically significant adverse reactions that occurred with the drug or risks that are expected to occur
- Each Warnings and Precautions section should include a succinct description of a topic and should include (if known):
  - Known risk factors for adverse reaction
  - Outcome
  - Numerical estimate of risk or adverse reaction rate
  - Steps to take to prevent, monitor, or manage an adverse reaction

See 21 CFR 201.57(c)(6) and
Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling guidance

# Factors used in determining if an adverse reaction warrants inclusion in the Warnings and Precautions section

- The relative seriousness of the disease or condition being treated.
- A high absolute risk or rate of AR occurrence
- An AR that may lead to a potentially serious outcome unless an action is taken to prevent a serious outcome (e.g., dosage reduction or discontinuation)
- An AR that could be prevented or managed with appropriate patient selection, monitoring, or avoidance of concomitant therapy.
- An AR that can significantly affect patient compliance particularly when non-compliance has potentially serious consequences.

# Boxed Warning

- Ordinarily used in the following situations:
  - Adverse reactions that are so serious in proportion to potential benefit that it is essential it be considered in assessing risks and benefits of using a drug,

    OR
  - There is a serious adverse reaction that can be prevented or reduced in frequency or severity by appropriate use of drug,

    OR
  - Drug is approved with restrictions to assure safe use because drug can be safely used only if distribution or use is restricted
- Can also be used in other situations:
  - To highlight a warning that is especially important to prescriber
  - For a drug that poses risk-benefit considerations that are unique among drugs in a drug class

See Warnings and Precautions, Contraindications, and Boxed Warning Sections of Labeling guidance

# Boxed Warning

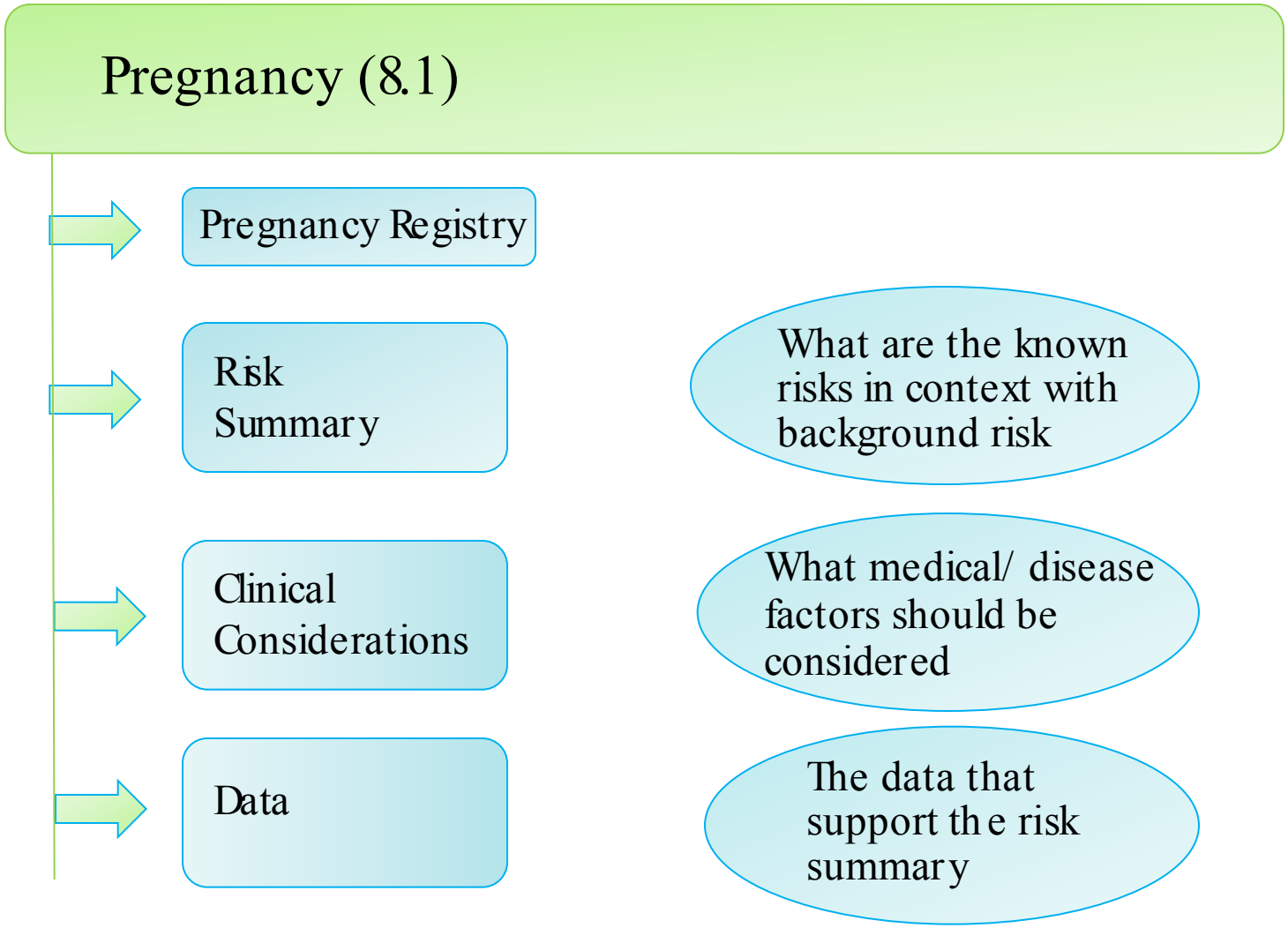
- Must:
  - Contain "contraindications or serious warnings, particularly those that may lead to death or serious injury"
  - Be the first section in Full Prescribing Information
  - Be surrounded by a "box" (i.e., single black line)

See 21 CFR 201.57(c)(1)

# Specific Populations: Pregnancy subsection

- All prescription drugs approved on or after June 30, 2001 must revise content and format of the Pregnancy and Nursing Mothers (Lactation) subsections of labeling
  - Pregnancy letter categories are replaced with an integrated Risk Summary
- ALL prescription drugs are required to remove pregnancy letter categories

# Revised Format



# Abuse and Dependence: Dependence subsection

- Characteristic effects resulting from psychological and physical dependence with the drug.
- Adverse effects of abrupt withdrawal.
  - Procedures necessary to diagnose dependence and principles of treating the effects of abrupt withdrawal.
- If withdrawal effects are serious or clinically significant because they have implications for prescribing decisions or patient management, there may be a related warning in the WARNINGS AND PRECAUTIONS section.

# Summary

- FDA-approved product labeling is FDA's key tool for communicating information necessary for the safe and effective use of a product.
- Safety information can be included in a variety of sections depending on the seriousness of the adverse reaction