

Draft Guidance on the Drug Abuse and Dependence Section of Labeling

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- The labeling examples in this presentation are provided only to demonstrate current labeling development challenges and should not be considered FDA recommended templates.
- Reference to any marketed products is for illustrative purposes only and does not constitute endorsement by the FDA.

Learning objectives

- Describe recommendations for prescription drug labeling outlined in draft guidance on the Drug Abuse and Dependence section
- Identify labeling information discussed today that is relevant for your organization



Draft Guidance on the Drug Abuse and Dependence (DAD) Section of Labeling

Drug Abuse and Dependence Section of Labeling for Human Prescription Drug and Biological Products — Content and Format

Guidance for Industry

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

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For questions regarding this draft document, contact (CDER) Iris Masucci, 301-796-2500, or (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010.

U.S. Department of Health and Human Services
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Labeling

DAD guidance applies to:

- Prescription drugs controlled under the Controlled Substances Act (CSA)
- Certain prescription drugs not controlled under the CSA for which there is important information to convey to health care providers related to abuse and dependence

Distribution of information

- Detailed information about drug abuse and dependence is included in the DAD section of labeling
- Other relevant sections should:
 - Discuss only those aspects of the information that are pertinent to those sections' scopes and purposes
 - Not repeat the identical content or level of detail found in the DAD section

Distribution example

For products that have abuse or dependence information in both the Warnings and Precautions and DAD sections:

- DAD section will have the detailed abuse or dependence information (e.g., description of study designs and results of abuse liability studies)
- Warnings and Precautions section will have the succinct description of the adverse reaction or risk, the clinical implications, and recommendations for managing risks related to abuse or dependence

Drug Abuse and Dependence section

Composed of three subsections:

- 9.1 Controlled Substance
- 9.2 Abuse
- 9.3 Dependence

9.1 Controlled Substance subsection

- If a drug is scheduled under the CSA, the subsection must state that the drug is a controlled substance and identify the schedule under which the drug is controlled (§ 201.57(c)(10)(i))
- Should identify the proprietary name (if a proprietary name exists) and the active ingredient(s) or drug substance(s) that is (are) controlled

Guidance examples

- DRUG-X contains xxxxxx, a Schedule II controlled substance.
[typical presentation]
- Active ingredient-Y is a Schedule II controlled substance.
[for product without a proprietary name]
- DRUG-Z contains zzzzzzz. (Controlled substance schedule to be determined after review by the Drug Enforcement Administration.)
[when scheduling is pending]

Non-scheduled drugs with information in 9.2 or 9.3



Examples:

- A demonstrated lack of abuse potential for a new drug in a therapeutic category in which most other products are controlled substances may be relevant information to include in subsection 9.2
- Non-controlled drug may include information on physical dependence in subsection 9.3 when discontinuation of the drug has been shown to cause a withdrawal syndrome

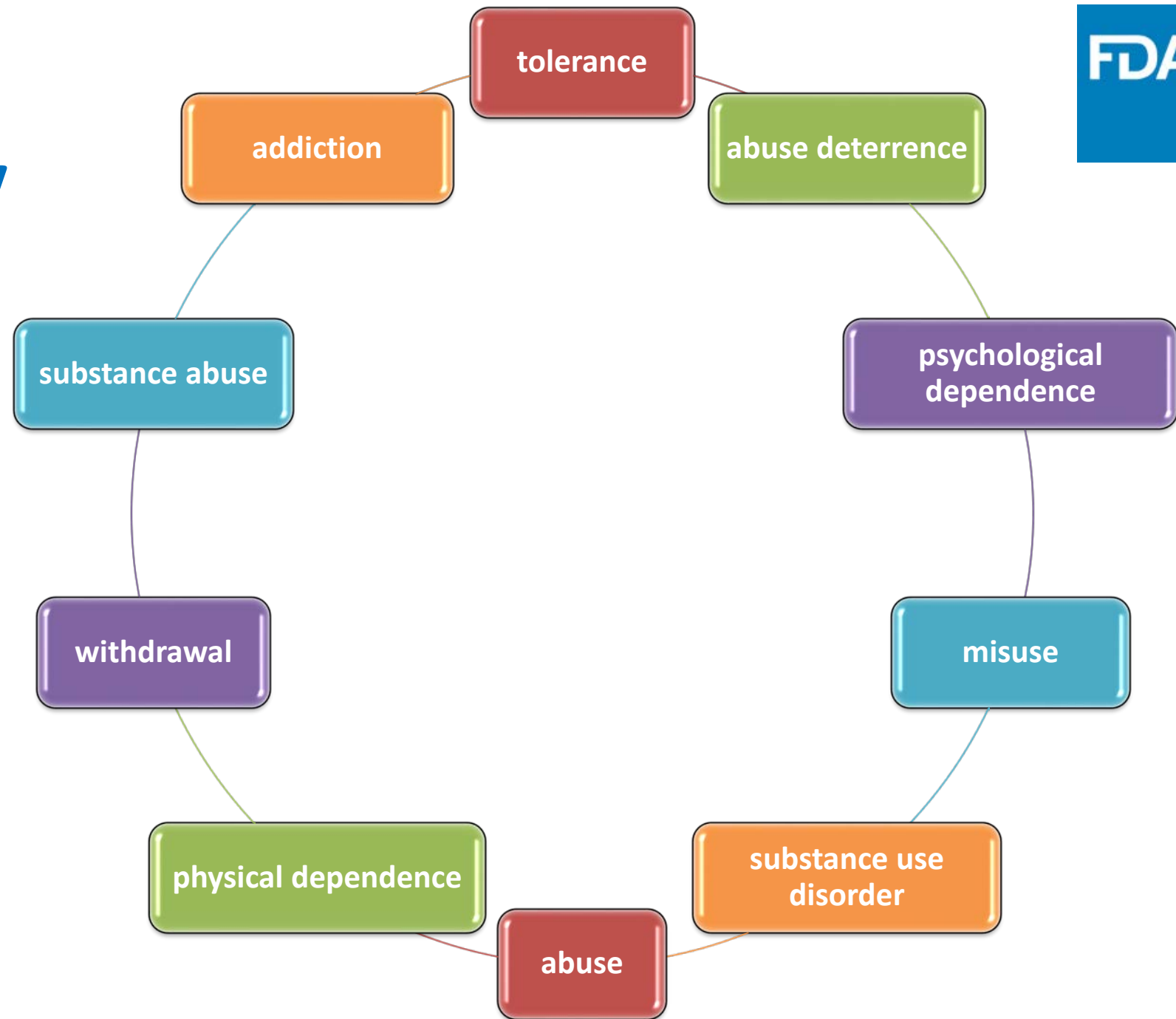
Non-scheduled drugs with information in 9.2 or 9.3



Include a subsection 9.1 with a single sentence stating that the active ingredient(s) or drug substance(s) is (are) not controlled

- DRUG-X contains xxxxxx, which is not a controlled substance.
- Active ingredient-Y is not a controlled substance.

Terminology



Terminology

Five major concepts for the DAD section:

- Abuse
- Misuse
- Addiction
- Physical dependence
- Tolerance

Terminology – What goes where?

9.2 Abuse

Abuse

Misuse

Addiction

9.3 Dependence

Physical dependence

Tolerance

Terminology

- These terms are commonly confused and misinterpreted
- Guidance recommends that definitions of these terms be included in the DAD section
 - To ensure common understanding
 - To facilitate the diagnosis and management of substance use disorders

9.2 Abuse subsection



- Contains information related to **abuse, misuse, and addiction** that is important for prescribers to consider
- Must state the types of abuse that can occur with the drug and the adverse reactions pertinent to them and must identify particularly susceptible patient populations, if known (§201.57(c)(10)(ii))

9.2 Abuse subsection



- Should summarize information that supports recommendations on how to prevent or mitigate risks associated with abuse
- Should include risks specific to abuse of the product, such as those related to a product's particular formulation
- May include information on risks resulting from inappropriate routes or methods of administration

9.2 Abuse subsection



- Should summarize results from human abuse potential studies that adequately characterize the abuse potential of the drug product
- Should summarize studies conducted to evaluate the abuse-deterrent properties of a drug product

9.2 Abuse subsection



- For drugs with a risk of abuse, include the following definition:

Abuse is the intentional, non-therapeutic use of a drug, even once, for its desirable psychological or physiological effects.

9.2 Abuse subsection

- For drugs with a risk of misuse that would negatively impact health or functioning, include the following definition:

Misuse is the intentional use, for therapeutic purposes, of a drug by an individual in a way other than prescribed by a health care provider or for whom it was not prescribed.

9.2 Abuse subsection



- For drugs with a risk of addiction, include the following definition:

Drug addiction is a cluster of behavioral, cognitive, and physiological phenomena that may include a strong desire to take the drug, difficulties in controlling drug use (e.g., continuing drug use despite harmful consequences, giving a higher priority to drug use than other activities and obligations), and possible tolerance or physical dependence.

9.3 Dependence subsection

- Must contain information about the drug related to **physical dependence**, withdrawal, and **tolerance**
- Must describe characteristic effects resulting from the psychological and physical dependence that occurs with the drug and must identify, if known, the quantity of the drug over a period of time that may lead to tolerance or dependence, or both

§ 201.57(c)(10)(iii)

9.3 Dependence subsection

- Should summarize signs and symptoms of withdrawal after chronic use or abuse of the drug
- Should summarize the information that supports recommendations to health care providers on how to prevent or mitigate risks associated with physical dependence, withdrawal, and tolerance

9.3 Dependence subsection

- For drugs to which patients may develop physical dependence, include the following definition:

Physical dependence is a state that develops as a result of physiological adaptation in response to repeated drug use, manifested by withdrawal signs and symptoms after abrupt discontinuation or a significant dose reduction of a drug.

9.3 Dependence subsection

- For drugs to which patients may develop tolerance, include the following definition:

Tolerance is a physiological state characterized by a reduced response to a drug after repeated administration (i.e., a higher dose of a drug is required to produce the same effect that was once obtained at a lower dose).

What not to include in DAD section

- Speculative or promotional language
- Detailed information on disposal of controlled substances, which typically appears elsewhere in labeling (e.g., in the Patient Counseling Information section)
- Lengthy definitions — other than those recommended for inclusion in labeling in this guidance — or discussions related to abuse and dependence

Challenge question

True or false: For drugs that are not controlled substances, the Drug Abuse and Dependence section should always be omitted from labeling.

- a) True
- b) False

Questions?