An Anesthesiologist's Perspective on Labeling

The ASA Statement, USP Involvement, and ASTM Standards

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Disclosures

Committee Memberships

- **ASA Committee on Equipment & Facilities**
- **ASA Ad Hoc Committee on Physical Demands of Anesthesiologists**
- **USP Nomenclature and Labeling Expert Committee (NLEC) and NLEC Labeling Subcommittee**
- **ASTM Committee F02 (Primary Barrier Packaging) and Subcommittee F02.50 (Package Design and Development), as APSF representative**
- **APSF Medication Safety Patient Safety Priority Advisory Group (PSPAG)**
- **AAMI Human Factors Engineering and Health Information Technology Committees**
- **No Financial Disclosures**

Outline

- **A brief look back**
- **Why do we label medications?**
- **Terminology**
- **The role of standards, guidelines, and statements**
- **ASA Statement on Pharmaceuticals Used in Anesthesiology**
- **USP Chapter <7>**
- **ASTM Standards**
- **Final messages**

A Brief Look Back

- Death of Hannah Greener (1848)
- Death after strychnine was given instead of bismuth (1867)
  - "the appearance of the bismuth is very like that of strychnine."
  - Two possibilities: strychnine was given by mistake, or by gross negligence, because the doctor "might have kept his ordinary drugs and his poisons in such a way that he could not tell which he was using."
- Medication errors first specifically mentioned (1953)
  - Considered to be a nursing problem.
- Beecher and Todd: death rate attributable to anesthesia (1954)
  - "...whether due to agent or technic, or to their misapplications."
  - Medication errors: "Error in choice of anesthetic agent" and "Error in administration of agent"
  - Deaths with muscle relaxant use: "...incidence of clearly recognized gross misuse of these agents is so low that it can hardly be called an important factor."
- Cooper et al (1984)
  - Medication errors are common
  - Administration errors and syringe swaps were most common
- 1990s: Adverse Drug Event study (Harvard)
  - Lucian Leape, David Cullen, David Bates
- Summary paper at study's conclusion
  - Cullen DJ, Bates DW, Leape LL. Prevention of Adverse Drug Events: A Decade of Progress in Patient Safety. J Clin Anesthesia 2000; 12:600-614.
  - "Medication safety was not a topic of interest to our colleagues," but soon after, began to appear in ASA programs, and publications on the subject became more frequent (D. Cullen, personal communication).
- ASA Statement on the Labeling of Pharmaceuticals for use in Anesthesiology approved (2004)

Why Medications Are Labeled

- Reduces medication errors
  - Quick and accurate medication identification
    - Syringes
    - Vials and Ampules
    - Infusions
- Correct drug
  - Medication name
    - Look-alike errors
  - Select correct medication
    - Syringe swaps
- Correct patient
- Correct dosing
  - Concentration
- Correct route of administration
- Date and Time
  - Medication has not expired

Terminology

- **Labeling[1]**
  - **All written, printed, or graphic matter accompanying an article (drug) at any time while in interstate commerce or held for sale after shipment or delivery in interstate commerce**
- **Labels[1]**
  - **Any display of written, printed, or graphic matter on the immediate container of any article**
- **Principle Display Panel[2]**
  - **The part of the label most likely to be displayed, presented, or shown to, or examined by the end user**
  - **Usually the label on a vial or ampule**

[1] US Food and Drug Administration. Requirements on content and format of labeling for human prescription drug and biological products. Final rule. Fed Regist. 2006 Jan 24;71(15):3921-97

[2] US Food and Drug Administration. Safety considerations for container labels and carton labeling design to minimize medication errors: Guidance for industry. Silver Spring, MD; May 2022

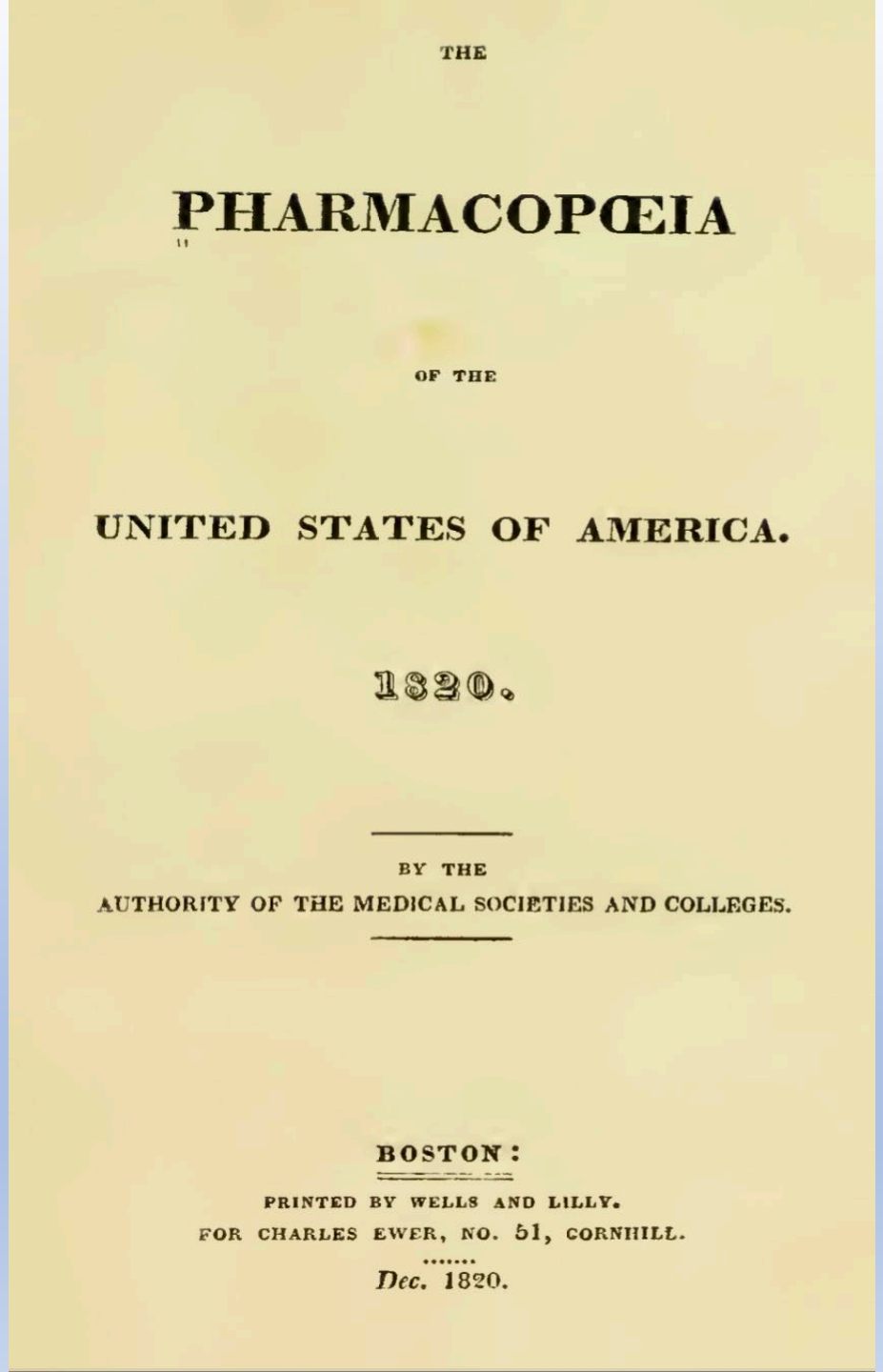
The role of standards, guidelines, and statements

- **Standards provide a reliable basis for expectations about the quantity, weight, extent, value, or quality**
  - **Expectation that measurement or production will be the same**
  - **Example: USP ensures that drugs are produced to a given level of quality, no matter who makes them, so that the public can be assured of the safety and efficacy of the drug supply**
  - **Often are viewed as requirements, typically enforceable**
- **Guidelines have a similar purpose but lack the authority of standards**
  - **Example: WHO guidelines serve as recommendations for clinical practice**
- **Statements**
  - **Provide recommendations or information to improve practices**
  - **Do not typically carry any authority**
  - **Example: ASA Statement on Labeling of Pharmaceuticals for use in Anesthesiology**

ASA Statement on the Labeling of Pharmaceuticals For Use in Anesthesiology

- **First approved by HOD October, 2004**
  - **"The primary consideration in the design of labels for pharmaceutical containers should be patient safety and the reduction of medication errors."**
  - **ASA supports manufacture and use of pharmaceuticals with labels meeting standards c/w ASTM[1]: Label content, font, background contrast, color; Bar coding (vials, ampules).**
- **Last revision December, 2020**
  - **"The primary consideration for the design and use of labels for syringes, drug infusion bags, and medication containers should be the reduction of medication errors and thus safer patient care."**
  - **ASA supports manufacture and use of pharmaceuticals with labels meeting standards c/w ASTM[2] and ISO[3], plus recommendations from FDA and ISMP: Label content, font and print characteristics, text/background contrast, reserved colors, label material, label enhancements (bar coding), lettering (Tall Man), regulatory requirements (NPSG 03.04.01), label placement, readability and color recognition.**

[1]ASTM D4774-94 [2]ASTM D4774-11R17 [3]ISO 26825-08



THE

PHARMACOPŒIA

OF THE

UNITED STATES OF AMERICA.

1820.

BY THE
AUTHORITY OF THE MEDICAL SOCIETIES AND COLLEGES.

BOSTON:
PRINTED BY WELLS AND LILLY.
FOR CHARLES EWER, NO. 51, CORNHILL.
Dec. 1820.

The United States Pharmacopeia, as shown here, was established and first published in 1820

United States Pharmacopeia (USP)

- **From the preface of the original publication:**
  - **Select from substances which possess medicinal power those for which the utility is most fully established and best understood;**
  - **Form from them preparations and compositions in which their powers may be exerted to the greatest advantage;**
  - **Distinguish those articles by convenient and definite names, to prevent trouble or uncertainty by physicians and apothecaries;**
  - **Its value depends on the fidelity with which it conforms to the best state of medical knowledge of the day;**
  - **Its usefulness depends on the sanction it receives from the medical community and the public, and the extent to which it governs the language and practice of those whose use it is intended;**
  - **Contains the formulae for the preparations and compositions of those articles which have received the sanction of the faculty in this country;**
  - **The essential properties of names ought to be expressiveness, brevity, and dissimilarity.**
- **USP develops quality standards that help protect people's public health**
  - **Standards for medicines are in the USP and the National Formulary (NF);**
  - **USP and NF are two official compendia recognized in the FD&C Act and enforced by FDA as mandatory;**
  - **USP has no role in enforcement of these standards; it is the responsibility of the FDA and other government authorities.**

USP General Chapter <7>: Labeling

- **"Provides definitions and standards for labeling of official articles."**
  - **All articles in USP or NF are subject to the requirements in this chapter.**
- **Specifies label content for injectable products.**
- **Specifies labeling formats for the following items:**
  - **Quantity per total volume is the primary expression of strength.**
    - **Exceptions: When not effective in preventing medication errors, e.g., insulin; For local anesthetics (use of percentage).**
    - **Ratio expressions are no longer permitted.**
  - **Potassium, neuromuscular blocking agents.**
  - **Expression of expiration and beyond use dates.**
  - **Compounded preparations.**
  - **Use of leading and terminal zeroes.**
  - **Electrolyte concentrations.**
  - **Abbreviations for the terms "Units" and "International Units" are not permitted.**

ASTM International

- Formerly American Society for Testing and Materials
  - Established 1898 to address frequent rail breaks
  - Developed a standard for the steel used to make the rails
  - Renamed 2001
- Develops and publishes voluntary consensus standards
  - Has no role in requiring or enforcing compliance
  - Standards may become mandatory if referenced by government, corporation, or by external contract
  - Standards are developed by member contributions
    - Over 30,000 technical experts and professionals from over 140 countries
    - Creates test methods, specifications, classifications, guides, and practices

ASTM Standards of Interest

- D4774-11 (reapproved 2017)
  - Standard Specification for User Applied Drug Labels in Anesthesiology
  - Withdrawn 2022
    - Decline in industry support?
    - No individual at ASTM to champion continued use
    - APSF now a member of ASTM
  - Currently in ballot for reinstatement, with multiple revisions
- D4775/D4775M-09 (reapproved 2014)
  - Standard Specification for Identification and Configuration of Prefilled Syringes and Delivery Systems for Drugs
  - Withdrawn 2022
    - Will be submitted for reinstatement
- D4267-07 (reapproved 2015)
  - Standard Specification for Labels for Small-Volume (100 mL or Less) Parenteral Drug Containers
  - Withdrawn 2022
    - Will be submitted for reinstatement
- D6398-08 (reapproved 2014)
  - Standard Practice to Enhance Identification of Drug Names on Labels
  - Withdrawn 2022
    - Will be submitted for reinstatement

Significant differences: ASTM D4774 vs. ISO 26825:2020

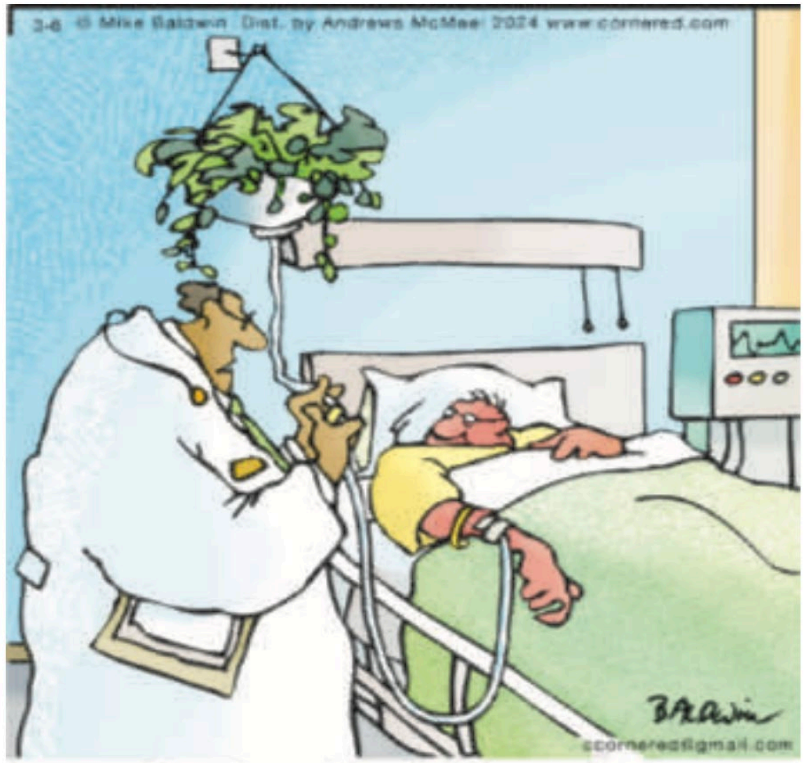
	ASTM D4774 (being revised and reinstated)	ISO 6825:2020
When first approved and/or published	Approved 1988, initial publication 1994	Initial publication 2008
Where standard's use is preferred	Intended for US market	Intended for non-US markets
Medication naming and use of Tall Man Lettering	Uses accepted US terminology (e.g., succinylcholine) Generic names, with optional use of proprietary name Describes and provides examples for use of Tall Man Lettering, when it is indicated, and cites several references for its use	Uses British/International terminology, (e.g., suxamethonium) Naming defers to pharmacopeia of country used Only provides a single reference and one example for Tall Man Lettering, but omits several other examples (e.g., ePHEDrine, droPERidol, EPINEPHrine)
Objective of the standard	Facilitate correct identification of drugs in syringes	Identify syringe contents "just before use during anaesthesia"
Hazard the standard addresses	Risk of medication errors and wrong drug administration	Does not state
Use of background color	Aids identification of drug classes, but user must still read label	Aids identification of drug classes, but user must still read label
Labels with Black text on White background	May be used as an alternative to colored labels	Does not state
Drug classes addressed by standard	Nine classes, each with a separate and distinct color Ninth class is beta-blockers, with unique copper color	Eight classes, each with a separate and distinct color Does not include beta-blockers as a separate class
Drugs without a pre-existing label color	Includes template for "Other drugs" without pre-existing labels, using black text on white background	Includes labels for "Miscellaneous drugs" using black text on white background
Local anesthetics	Strength can be indicated as either % or mg/mL	Does not specify
Use of Reverse Plate Lettering for Sux, Epi, and Beta-blocker labels	Uses background color for lettering (red for sux, violet for epi), and white lettering for beta-blocker reverse plate label	Uses white color for lettering for the reverse plate drug labels, as well as white lettering for benzodiazepine labels (not reverse plate lettering)
Presentation of information	Seems more organized and easier to read	Seems less well-organized and perhaps harder to read

Final Messages

- **Labels are important to medication safety**
- **Label design matters**
- **Standards are important guides to label design**

Drabble

Cornered



"I ordered an IV, not an ivy."