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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm.1061
Rockville, MD 20852

April 7, 2005

Attention: Jeffrey Shuren, Assistant Commissioner for Policy

Re: Use of Color of Pharmaceutical Product Labels; Labeling and Packaging; Public Hearing (70 Fed. Reg. 5687, February 3, 2005)

Dear Mr. Shuren:

The American Society of Anesthesiologists would like to offer comments for the record on the above-captioned hearing. The practice of anesthesiology requires the administration of a wide variety of potent medications that are often given in high acuity situations and in environments with poor visibility and multiple distractions. Our member physicians have a strong interest in methods to reduce the incidence of perioperative medication errors.

In October 2004, ASA adopted a formal "Statement on the Labeling of Pharmaceuticals for Use in Anesthesiology," supporting the use of five cumulative methods of enhancing the impact of labeling on patient safety, consistent with standards established by the American Society for Testing and Materials International (ASTM). The ASA Statement is attached to this letter as Appendix A. The Commission will note that the fourth method described is the use of standard background color as with user-applied syringe labels established by ASTM in International Standard D4774, *Standard Specifications for User Applied Drug Labels in Anesthesiology*.

The ASTM color-coding system for syringes containing medications used during an anesthetic serves to identify the *class* of drug (induction agents, muscle relaxants, vasopressors, etc.). It should be seen as a complement to the other standards supported in our Statement: label content, font, contrasting background and bar coding. Color-coding can help with drug classification but prominently printing the drug's name, concentration and volume or total contents is the most important method of ensuring that users will accurately identify the specific medications.

ASA would like to share our views on the issues raised in the four questions in the Federal Register notice.

1. *How and under what circumstances has the use of color on pharmaceutical packaging and/or labeling demonstrated an improvement in patient care? If there is no discernible improvement, please describe what you consider to be the deficiencies in the program.*

   Many anesthesiologists believe that color-coding on anesthesia syringes and ampoules lowers the likelihood of errors, but empirical studies are inconclusive. A noteworthy study published in 2004 (Fasting S, Gisvold SE. Adverse drug errors in anesthesia, and the impact of coloured syringe labels. *Can J Anesth.* 2000;47:1060-1067) and including 55,426 procedures showed a reduction in total drug errors from 40 to 23, a reduction in syringe swaps from 16 to 12, and a statistically significant (p=0.04) reduction in ampoule swaps with the use of color coded labels only. The authors suggest that color alone may not be a sufficient visual cue to eliminate errors. Relative syringe size may also play a part.

   Fasting and Gisvold noted that most errors occurred during anesthesia induction, at a time when the anesthesiologists were giving multiple drugs in quick order and were performing multiple other tasks as well. Despite the lack of evidence for color-coding as a safety strategy, if it were part of a multi-factorial system for preventing errors there could be an improvement in the error rate. One of those other factors might be consistency of color-coding between a given manufacturer's labels for ampoules and syringes and the caps on the bottles or vials in the anesthesia medication drawer. Most vials are arranged in the anesthesia medication drawer so that only their tops are visible. There was no attempt in the Fasting and Gisvold study to standardize colors for the containers and the syringes.

2. *Are there specific classes of drugs where use of color has demonstrated value? Are there classes where use of color is a hindrance to public safety?*

   Drugs used in situations where the anesthesiologist is administering multiple drugs rapidly while performing additional activities would be the most likely to benefit from the use of color-coding, although the studies to date have not demonstrated this benefit. These multi-drug rapid-response situations include the induction of anesthesia, particularly muscle relaxants, and emergencies in which the anesthesiologist is using epinephrine, ephedrine, phenylephrine, resuscitation agents, and other drugs.

3. *Are there drug products currently marketed that do not use color but should use color to aid in identification of the drug? If so, how should color be used?*

   A good starting point in identifying drugs that would benefit from the use of color-coding would be the survey of hospitals conducted by the Institute for Safe Medical Practice (www.ismp.org). Most hospitals in the survey consider the following classes and individual drugs commonly used in anesthesiology practice to be "high alert" medications:

- IV adrenergic agonists – epinephrine
- IV conscious sedation agents – midazolam, diazepam
- Neuromuscular blocking agents – succinylcholine, pancuronium, vercuronium, rocuronium, mivacurium, cis-atracurium
- IV narcotics and opiates – morphine, meperedine, fentanyl, sufentanil, remifentanil, hydromorphone
- IV general anesthetics – propofol, thiopental, etomidate
- IV inotropic agents – digoxin, milrinone, dopamine, dobutamine, etc.
- Electrolytes – potassium, magnesium, calcium
- Anticoagulants – heparin

As we have stated above, color-coding would be best used as part of a multi-factorial strategy for improving the effect of medication labels and packaging on patient safety.

4. *How should the effectiveness of application of color on drug products be scientifically validated?*

ASA believes that the best means of evaluating the effectiveness of color-coding would be a multi-centered prospective analysis of the effect of color-coding ampoules and syringes consistently with each other, or possibly of coloring the liquid medication itself. Simulator trials could be used effectively as well to analyze, in detail, the effect of color-coding on the accuracy of medication selection and administration in the operating room

We hope that our comments are useful. Please contact Karin Bierstein, JD, MPH in our Washington office (k.bierstein@asawash.org, 202-289-2222) if the Commission has questions with which ASA might be able to help you.

Sincerely,

Eugene P. Sinclair, MD
President

Attachment

STATEMENT ON THE LABELING OF PHARMACEUTICALS FOR USE IN ANESTHESIOLOGY

(Approved by ASA House of Delegates on October 27, 2004)

Rationale:
The practice of anesthesiology requires the administration of a wide variety of potent medications. These medications are often given in high acuity situations and in environments with poor visibility and multiple distractions. Medications with widely differing actions, such as muscle relaxants, vasopressors, and vasodilators, are often used in the course of a single anesthetic, at times simultaneously. It has been recognized for some time that perioperative medication errors are a significant potential source of morbidity and, rarely, mortality.[1-4] Interest in medication errors has extended to regulatory agencies, the Federal Government, and the general public.

The recognition and identification of an object depends on shape, color, brightness, and contrast. As these elements become increasingly distinctive, identification of the object becomes faster and more accurate.[5-7] Therefore, although multiple factors contribute to medication errors, consistency and clarity of pharmaceutical and syringe labeling, in accordance with human factors, are important elements in their prevention.

Statement:
The primary consideration in the design of labels for pharmaceutical containers should be patient safety and the reduction of medication errors. This is particularly true for the potent medications used in the practice of anesthesiology. Therefore, ASA supports the manufacture and use of pharmaceuticals with labels meeting the following standards, which are consistent with those established by American Society for Testing and Materials International (ASTM International):

1. **Label Content:** The drug's generic name, concentration, and volume or total contents of the vial or ampoule should be the most prominent items displayed on the label of each vial or ampoule containing pharmaceuticals for use in the practice of anesthesiology. In addition, the drug's proprietary name, manufacturer, lot number, date of manufacture, and expiration date should also be included on the label.

2. **Font:** The text on the label should be designed to enhance the recognition of the drug name and concentration as recommended in ASTM International standards D4267, *Standard Specification for Labels for Small- Volume Parenteral Drug Containers* and D6398, *Standard Practice to Enhance Identification of Drug Names on Labels* (Section 7). These standards include recommendations for the font size, extra space for separation around the drug name, and the use of additional emphasis for the initial syllable, or a distinctive syllable, of similar drug names.

3. **Contrasting Background:** Maximum contrast between the text and background should be provided by high-contrast color combinations as specified in Section 6.3.1 of ASTM International Standard D6398, which also minimize the impact of color blindness:

Text	Background
Black	White
Blue	Yellow
White	Blue
Blue	White

4. **Color:** Nine classes of drugs commonly used in the practice of anesthesiology have a standard background color established for user-applied syringe labels by ASTM International standard D4774, *Standard Specifications for User Applied Drug Labels in Anesthesiology*. For these drugs, the color of the container's top, label border, and any other colored area on the label, excluding the background as required for maximum contrast, should be the color corresponding to the drug's classification. The color would be that established in Standard D4774 and therefore identical to the color of the corresponding syringe label.

Drug Class	Pantone Color
Induction Agents	Yellow
Tranquilizers	Orange 151
Muscle Relaxants	Florescent Red 805
Relaxant Antagonists	Florescent Red 805/White Diagonal Stripes
Narcotics	Blue 297
Narcotic Antagonists	Blue 297/White Diagonal Stripes
Major Tranquilizers	Salmon 156
Narcotic/Tranquilizer Combinations	Blue 297/Salmon 156
Vasopressors	Violet 256
Hypotensive Agents	Violet 256/White Diagonal Stripes
Local Anesthetics	Grey 401
Anticholinergic Agents	Green 367

5. **Bar coding:** Essential information including the drug's generic name, concentration, and volume of the vial or ampoule should be bar coded at a location on the vial or ampoule which will not interfere with the label's legibility, as specified in ASTM International Standard D6398 Section 8.

References:

1. Curie M, Mackay P, Morgan C, Runciman WB, Russell WJ, Sellen A, Webb RK, Williamson JA. The "wrong drug" problem in anaesthesia: an analysis of 2000 incident reports. *Anaesthesia and Intensive Care* 1993; 21:596-601
2. Fasting 5, Gisvold SE. Adverse drug errors in anesthesia, and the impact of coloured syringe labels. *Can J Anesth* 2000; 47:1060-1067.
3. Merry AF, Webster CS. Labeling and drug administration error. *Anaesthesia* 1996; 51:987-988.
4. Foster P. Drug syringe labeling. *Anaesthesia.* 2003; 58:99-100.
5. Treisman A. Feature and objects in visual processing. *Scientific American* November 1986 pp 114-125.
6. Triesman A. Features and Objects. *Quarterly J of Exp Psychology* 1988; 40A (vol 2) 201-237.
7. Kosslyn SM. Aspects of a cognitive neuroscience of mental imagery. *Science* 1988; 240:1621-1626.

Note: For referenced ASTM International standards, visit the ASTM Web site *www.astm.org or contact ASTM customer service at service@astm.org*