

[Home](#) [Inspections, Compliance, Enforcement, and Criminal Investigations](#) [Inspections](#) [Inspection Guides](#)

Inspections, Compliance, Enforcement, and Criminal Investigations

Leak Testing Sealed Ampoules of Parenteral Solutions

[\[Previous Chapter¹\]](#) [\[Table of Contents²\]](#) [\[Next Chapter³\]](#)

DEPT. OF HEALTH, EDUCATION, AND
WELFARE PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
ORA/ORO/DEIO/IB

Date: 4/28/72 Number: 6
Related Program Areas:
Drugs, Human and Veterinary; Injectable
Vitamins

ITG SUBJECT: LEAK-TESTING SEALED AMPULS OF PARENTERAL SOLUTIONS

Leak-testing glass ampuls of injectables by means of vacuum- pressure treatment and methylene blue dye solution is recommended by Avis. \1\ Drug manufacturers frequently use this test or some modification of it.

A "leaker" ampul of *[purged]* {{Registered Trademark}} (Meperidine Hydrochloride) colored blue from the dye solution was collected as an exhibit during a recent BUF-DO EI (Albany Resident Post). The blue color of the solution faded within a few hours leaving a clear transparent solution. Storage in the dark overnight, or vigorous shaking of the ampul, allowed the blue color to return to its original intensity.

Additional samples of clear and "blue" ampuls were collected, and experiments were initiated using the ampuls and similar Meperidine HCl solutions made up in the BUF-DO Laboratory. The color loss phenomenon was reproducible using either *[purged]* {{Registered Trademark}} from the ampuls or the "synthetic" solutions. "Blue" solutions at pH 5.6 and 7.6 turned colorless when exposed to incandescent light and/or to daylight in about 45 minutes. Exposure to fluorescent light caused some ampuls to go completely colorless in 2 hours, while others had only a partial loss of color from blue to pale blue in an 8 hour period.

The dye solution consists of deionized water, methylene blue dye at approximately .003% w/v, and trisodium phosphate (the latter used to simplify rinsing the ampuls after the dye test). The same solutions without trisodium phosphate did not exhibit the color change.

The above observations may have extensive implications. For example, leakers having color loss as a result of exposure to light prior to inspection, could escape detection and be marketed. The solution in these defective ampul is adulterated and may be dangerously contaminated.

We emphasize that these observations are limited to one drug. There are many unanswered questions when considering other drugs. Buffalo Laboratory postulates that the trisodium phosphate alters the redox potential of methylene blue, either through a salt effect or by increasing the pH of the ampul contents. Regardless of the mechanism of action, leaker ampuls colored by methylene blue with trisodium phosphate, can become colorless when subjected to light.

We would welcome information from Districts having experience with this problem and/or its solution.

\1\ Avis, Kenneth E.; "Parenteral Preparations", Chapter 36, pp. 498-524 in Remingtons Pharmaceutical Sciences; Edit. Martin, Eric W.; Mack Publishing Co., (1965).

[\[Previous Chapter⁴\]](#) [\[Table of Contents⁵\]](#) [\[Next Chapter⁶\]](#)

Page Last Updated: 04/30/2009

Note: If you need help accessing information in different file formats, see [Instructions for Downloading Viewers and Players](#).

[Accessibility Contact](#) [FDA Careers](#) [FDA Basics](#) [FOIA](#) [No Fear Act](#) [Site Map](#) [Transparency](#) [Website Policies](#)

U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993
Ph. 1-888-INFO-FDA (1-888-463-6332)

[Email FDA](#)



[For Government](#) [For Press](#)

[Combination Products](#) [Advisory Committees](#) [Science & Research](#) [Regulatory Information](#) [Safety](#) [Emergency](#)
[Preparedness](#) [International Programs](#) [News & Events](#) [Training and Continuing Education](#) [Inspections/Compliance](#)
[State & Local Officials](#) [Consumers](#) [Industry](#) [Health Professionals](#) [FDA Archive](#)



U.S. Department of **Health & Human Services**

Links on this page:

1. [ssLINK/UCM070528.htm](#)
2. <http://wcms.fda.gov/FDAgov/ICECI/Inspections/InspectionGuides/InspectionTechnicalGuides/default.htm>
3. [ssLINK/UCM070835.htm](#)
4. [ssLINK/UCM070528.htm](#)
5. <http://wcms.fda.gov/FDAgov/ICECI/Inspections/InspectionGuides/InspectionTechnicalGuides/default.htm>
6. [ssLINK/UCM070835.htm](#)