

What Is The Latest FDA Thinking About Expiration Dates On Medical Gases?

Many medical gas manufactures (including majors) have applied expiration date stickers to their cylinders for years. A typical expiration date interval was "Five Years". Prior to 2003, this was consistent with the FDA's enforcement of the Good Manufacturing Practices. The actual regulation is from 21 CFR § 211.137:

***Expiration dating.** (a) To assure that a drug product meets applicable standards of identity, strength, quality, and purity at the time of use, it shall bear an expiration date determined by appropriate stability testing described in Sec. 211.166....*

In March 2003, the FDA issued Draft Guidance for Medical Gases. In the Draft Guidance, the FDA explains what they consider to be "Current Good Manufacturing Practice (CGMP)". For example:

Medical gases are subject to the requirements in § 211.137 - Expiration dating.

To ensure that a medical gas meets applicable standards of identity, strength, quality, and purity at the time of use, each container must bear an expiration date determined by appropriate stability testing described in § 211.166 (§ 211.137(a)).

Expiration dates must be related to any storage conditions stated on the label, as determined by stability studies described in § 211.166 (§ 211.137(b)).

Expiration dates must appear on the labeling in accordance with the requirements of § 201.17 (§ 211.137(d))....

To summarize, as of March 2003.... We were required to use expiration dates ... *AND* ... we were required to conduct a stability study to justify the expiration date. Also in the draft guidance, the FDA said the following about stability studies:

The Agency recommends that the testing program take into account the compatibility of the valve assembly, the acceptability of the valve packing and the valve seal used, the type of cylinder, and any other factor that can have an effect on the stability of the medical gas. Each medical gas would be tested for stability in the exact container closure system that it is marketed in, such as steel high-pressure cylinders, aluminum high-pressure cylinders, and cryogenic containers.

The FDA's concern is the stability of the cylinder and valve. They know that most medical gases are stable elements.

Enforcement Discretion

When the regulations simply are not practical, the FDA uses "enforcement discretion" to explain why they do not enforce certain requirements. Usually, this enforcement discretion is reasonable and in the best interest of industry. We learn by experience (sometimes painful) what the FDA enforces.

Here is an excerpt from an FDA Warning Letter issued to our industry:

The drug product does not bear an expiration date determined by appropriate stability testing [21 CFR 211.137(a)]. For example, the expiration date placed by your firm on the labels for Oxygen USP is not based on results from a written program to test the stability

of the product in its container- closure system as required by 211.166(a)(4). The expiration date used is copied from the labeling applied to the "H" cylinders used as the source gas for transfilling.

Latest Agency Thinking

The Draft Guidance may not be the latest agency thinking about expiration dating. In a recent message from the FDA to a firm in the medical gas equipment business, the FDA stated, "The agency is currently developing guidance pertaining to stability testing and expiration dating of medical gases. Pending publication of FDA guidance on this subject, our policy has been to use enforcement discretion with respect to the requirement in 21 CFR 211.137 that medical gases, as drug products, bear an expiration date. Please be aware, however, that if a manufacturer chooses to apply an expiration date to a medical gas, it must be supported by a stability study as required by 21 CFR 211.166. If the choice is made to label the product with an expiration date, it could be on a separate sticker in a manner similar to the lot number."

Recommended Practice

AsteRisk recommends that you consider not using an expiration date until the FDA and CGA agree upon a stability study/expiration date practices. When the stability study is completed, we recommend that you adopt the industry accepted expiration date.

If you have questions about this, or other FDA issues, please contact Tom Badstubner: tom@asteriskllc.com or 508-883-0927.