



Subpart I – Laboratory Controls: Meeting GMP Requirements

By John Stomp

This article provides a comprehensive review of all of the requirements listed below for maintaining compliance with GMP regulation Subpart I: Laboratory Controls. Auditing applications for each requirement is also provided.

- [21 CFR 211.160 General Requirements](#)
- [21 CFR 211.165 Testing and Release for Distribution](#)
- [21 CFR 211.166 Stability Testing](#)
- [21 CFR 211.167 Special Testing Requirements](#)
- [21 CFR 211.170 Reserve Samples](#)
- [21 CFR 211.173 Laboratory Animals](#)
- [21 CFR 211.176 Penicillin Contamination](#)

ARTICLE EXCERPT

211.165 – Testing and Release for Distribution

Introduction

This particular regulation is concerned solely with GMP requirements for release of a drug product into the marketplace. The requirements include: written procedures, records, sampling plans, testing of each individual batch of product, accept/reject criteria, valid test methods and final product specifications. The purpose of this regulation is to ensure that only pure, high quality and effective drug products are distributed to the consumer.

Each Batch of Product

GMP regulation 211.65 requires each individual batch of drug product be tested by the Quality Laboratory for compliance with final specifications of identity and strength of the active ingredient. For example, this could include weight, size and hardness for compressed tablets, as each of these attributes is related to the amount of active ingredient that will be released into the individual's system (bioavailability). There are also provisions in this regulation that allow for release of the product, pending some test results. This provision applies to sterility and pyrogen testing of sterile products, and short-lived radiopharmaceuticals. Testing must be conducted as soon as possible, and there is a risk of recall if test results fail



acceptance criteria. This risk is minimized when there is sufficient history that these products always pass the particular tests that are awaiting results.

Microbiological Testing

Sterile product aside, there is a requirement for products susceptible to microbiological contamination be tested. Solid oral dosage forms usually do not require this type of testing, because they do not provide an environment to foster the growth of microorganisms (too dry). Liquid dosage forms can provide a growth environment if they do not contain alcohol or sufficient preservatives that inhibit growth of microorganisms. Liquid antacids are a good example of products that are susceptible to microorganism contamination. These products contain ingredients that will foster growth. Such products need to be tested for microbiological contamination.

Sampling and Testing

GMP requires that sampling plans and test methods for each type of drug product be in the form of written procedures. Procedures must also include the number of samples that will be tested per batch. It is important to understand that the number of samples tested must be adequate. Many USP/NF tests specify the number of samples to be used. For example, 10 tablets may be required for weight, content and uniformity. The key fact here is that the size of the sample is based on a recognized reference (USP/NF), and it is wise to follow it.

Acceptance Criteria

GMP regulation 211.165 requires that acceptance criteria for sampling and testing by the Quality Unit be adequate to assure batches of drug product meet specifications. Criteria for acceptance must include accept/reject limits. Compliance with the regulation will be acceptable, as long as sampling is statistically sound. The best approach for assuring a statistically valid plan is to use ASQ sampling plans and USP/NF test methods whenever possible. Use of in-house sampling plans and test methods will have to be justified whenever they are used to accept or reject a batch of drug product.

END ARTICLE EXCERPT



FDA Compliance Digest

Published by enKap

enKap

ENGAGED KNOWLEDGE APPLICATION

This article excerpt is compliments of the FDA Compliance Learning Community of enKap (<http://www.enkap.com>). This article was published in its entirety in the July 2010 Issue of the *FDA Compliance Digest* .

For more information on the FDA Compliance Digest please go to:
<http://www.enkap.com/page/fda-compliance-digest>