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March 2012

Over the Counter (OTC) Drugs – Regulatory and Testing Requirements

An Over the Counter (OTC) drug is a category of pharmaceutical products. The FDA defines a pharmaceutical as an article intended for use in the diagnosis, cure, mitigation, treatment or prevention of disease. OTCs are products that have been found to be safe and effective for direct consumer use based on label instructions and warnings and do not require prescriptions. An OTC drug always contains at least one active pharmaceutical ingredient (API), intended to relieve the consumer's symptoms. OTC drugs are subject to slightly more stringent safety and efficacy standards than prescription drugs because consumers must be able to self-diagnose, self-treat and self-manage. They must be safe enough for consumers to use without the supervision of a doctor. OTCs are used to treat a variety of health problems, including headaches, coughs and colds, fever, heartburn, etc. An OTC drug should not be confused with a dietary supplement (vitamins, minerals, etc.), which is regulated differently by the FDA.

OTC drugs are required to receive premarket approval from the FDA or conform to a product monograph for the particular OTC specifying conditions recognizing them as safe, effective and not misbranded. The product monograph is a statement that specifies the kinds and amounts of ingredients a drug or a class of drugs may contain, directions for the drugs use, the conditions in which it may be used and the contraindications to its use. The monograph provides manufacturers with specific guidelines for production, packaging and labeling of OTC products. Monographs for specific categories of OTC drug products can be found in the FDA's Code of Federal Regulations title 21. Drugs that were marketed before May 11, 1972 (the beginning of the OTC Drug Review) may be marketed without specific approval pending publication of a monograph under the ongoing OTC Drug Review. Once a regulation (monograph) concerning a specific class of OTC drugs is final, the drug must either be the subject of an approved New Drug Application (NDA) or comply with the appropriate monograph for the OTC Drug.

An NDA is the way drug sponsors formally propose that the FDA approve a new pharmaceutical to be marketed in the US. It provides enough information for the FDA to determine whether the drug is safe and effective in its proposed uses, if the benefits to the drug outweigh the risks, whether the drug's labeling is appropriate or not, what the labeling should contain and whether the methods used in manufacturing the drug and the controls used to maintain the drug's quality are adequate to preserve the

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drug's identity, strength, quality and purity. The NDA is not necessarily for new drugs, but can be used by a drug that has been marketed for many years to gain FDA compliance as an OTC drug.

If a company wishes to label their product with "meets USP testing requirements", the product must also comply with a testing monograph published by the USP (United States Pharmacopeia). The United States Pharmacopeia is a non–governmental, official public standards–setting authority for prescription and OTC medicines and other healthcare products manufactured or sold in the United States. USP sets standards for the quality, purity, strength and consistency of these products–critical to the public health. USP's standards are recognized and used in more than 130 countries around the globe. These standards have helped to ensure public health throughout the world for close to 200 years.

As with any regulated drug product, there are tests that must be performed on the final OTC product before it can be made available to consumers. Stability studies are performed on all OTC products produced and packaged at P.J. Noyes, unless the product is produced in bulk to be repackaged by the customer or the customer prefers to conduct a study independently (if this is the case, the company is required to provide the results of the stability studies to PJ Noyes). A stability study is the method used to determine the ability of a drug product to remain within the established specifications in its packaging so that it maintains its identity, strength, quality and purity throughout the retest or expiration dating period. Initial stability tests are done to bring a drug to market for the first time, using samples from the first 3 batches that are manufactured. The goal of the stability study is to determine the shelf life (the time period of storage at a specified condition within which the drug product still meets its established specifications) of the product. When a product is sent for stability studies, it undergoes physical attribute, microbial and assay testing at certain intervals over a period of time, which is determined in part by whether the testing is accelerated or ambient.

Accelerated testing is a test for product stability that involves the use of a test environment that is more severe and puts more stress on the product so that expiration dating information can be obtained more quickly to allow the company to bring their product to market sooner than if they had to wait 36 months for the required ambient testing to be completed. Accelerated testing is performed while the

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product is kept at 40ºC ± 2º and 75% ± 5% relative humidity. Testing is typically performed on products at the 0, 1, 2, 3 and 6 month marks. The results of these tests at the given intervals (pass or fail) approximate the expiration dating that can be marked on the product's packaging and allows marketing and sales. For example, when a product that has been undergoing accelerated testing is tested at the 3-month mark and meets all its specifications, the expiration date on the package can be marked as 2 years from the date of manufacture. If the same product is tested again at the 6-month mark and meets all the specifications for the product, the expiration date can be marked as 3 years from the date of manufacture.

Ambient testing is performed while the product is kept at 25ºC ± 2º and 60% ± 5% relative humidity. Testing is performed on all new products or existing products that have changed. Testing intervals are typically 0, 3, 6, 9, 12, 18, 24, 30 (optional) and 36-month marks for a product with a 3-year expiration date. The tests are performed on existing products that have not changed at the 0, 6, 12, 24 and 36-month marks. If an expiration date of more than 3 years is desired, tests may be performed at yearly intervals after the 36-month mark. Even if the product has undergone accelerated testing, ambient testing (with a time frame that extends up to the expiration date) must be completed to determine the expiration date. If the product does not meet the ambient testing specifications to uphold the expiration dating on the product being marketed, the product may have to be recalled. Every year the product is manufactured, samples from one batch must be sent out for ongoing stability testing.

References:

- FDA Code of Federal Regulations Part 21
- USP website: http://www.usp.org/
- Lori Berry, Project Manager
- Consumer Healthcare Products Association (CHPA) Online
- Stability Studies of Drugs & Drug Products: http://stabilitystudy.com/
- Internal SOP QC050

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- RIAC Desk Reference- Ned H. Criscimagna's (Senior Engineer with IIT Research Institute) article, "Accelerated Testing"
- FDA's PowerPoint "Regulation of Nonprescription Drug Products"
- Blue Cross Blue Shield of Tennessee, Inc.

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