FDA/CDER
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The Unapproved Universe

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All drug products bought from U.S. pharmacies with valid prescriptions have FDA approval, right? *Wrong.*

FDA estimates that there are thousands of illegally marketed unapproved drugs currently on the market. There have been progressive changes to the drug laws since the passage of the 1906 Pure Food and Drug Act. These changes were primarily in response to tragedies that occurred from drugs, resulting in the implementation of stronger drug laws. Yet some drugs are currently marketed as if the laws never changed.

FDA recently instructed companies to stop manufacturing and distributing unapproved single-ingredient, immediate-release oral oxycodone drug products. These products have been sold in the U.S. for years, yet FDA has not evaluated them for safety, effectiveness, manufacturing quality, or proper labeling. Thus, they cannot be legally marketed in the U.S. The onus is on the company to submit applications containing this information to FDA. This is just one example of many where FDA has halted the manufacturing and distribution of drug products because they are unapproved.

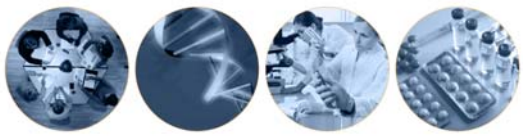
Unapproved Drugs Initiative: This action is part of FDA's Unapproved Drugs Initiative. The goal of this initiative, which began in June 2006, is to remove unapproved new drugs from the market and to encourage manufacturers to seek FDA review and approval for unapproved products. This initiative is the Agency's risk-based enforcement approach to efficiently and rationally bring all unapproved new drugs into the approval process. Unapproved drugs lack evidence demonstrating safety and effectiveness and pose a significant public health concern.

The New Drug Approval (NDA) and Over-the-Counter (OTC) drug monograph processes play an essential role in ensuring that all drugs are both safe and effective for their intended uses. Manufacturers of drugs that lack required approval, including those that are not marketed in accordance with an OTC drug monograph, have not provided FDA with evidence demonstrating that their products are safe and effective. The Agency has serious concerns that drugs marketed without required FDA approval may not meet modern standards for safety, effectiveness, quality, and labeling. One cannot assume that FDA has found all marketed drugs to be safe and effective.

The end result is that all drugs must have FDA approval or comply with an OTC monograph, unless the product is:

–DESI pending or OTC monograph pending: *there are very few DESI pending proceedings that are pending*
–Generally recognized as safe and effective (GRAS/E*):* *it is not likely that any currently marketed prescription drug is GRAS/E*
–Grandfathered: it is not likely that any currently marketed prescription drug product is grandfathered.

The FDA has an interest in taking steps to either encourage the manufacturers of unapproved products to obtain the necessary evidence and comply with the required approval provisions, or remove the products from the market.



CDER Small Business Assistance | Division of Drug Information | Office of Communications
10001 New Hampshire Avenue | Hillandale Bldg, 4th Floor | Silver Spring, MD 20993
(866) 405-5367 or (301) 796-6707
CDERSmallBusiness@fda.hhs.gov
www.fda.gov/smallbusinessdrugs

Compliance Policy Guide: As part of the Unapproved Drugs Initiative, FDA issued a final guidance entitled "Marketed Unapproved Drugs—Compliance Policy Guide (CPG)." This guidance outlines FDA's enforcement policies to bring all unapproved drugs into compliance with the approval process. The FDA uses a risk-based enforcement program in order to concentrate its resources on those products that pose the highest threat to public health and without imposing undue burdens on consumers, or unnecessarily disrupting the market. Unapproved new drugs introduced onto the market after September 19, 2011 are subject to immediate enforcement action at any time, without prior notice and without regard to the enforcement priorities set forth in the CPG. For unapproved new drugs commercially used or sold as of September 19, 2011, the CPG gives highest enforcement priority to the following:

- Drugs with potential safety risks
- Drugs that lack evidence of effectiveness
- Health fraud drugs
- Drugs that present direct challenges to the new drug approval and OTC drug monograph systems
- Unapproved new drugs that also violate the Act in other ways
- Drugs that are reformulated to evade an FDA enforcement action

Sometimes, a company may obtain approval of a new drug application (NDA) for a product that other companies are marketing without approval. We want to encourage this type of voluntary compliance with the new drug requirements. It benefits public health by increasing the assurance that marketed drug products are safe and effective, and reduces the resources that FDA must expend on enforcement. FDA is more likely to take enforcement action against these remaining unapproved drugs in this kind of situation. Once the risk-based assessment has been made, the FDA may take any number of actions, including but not limited to:

- requesting voluntary compliance
- providing notice of action in a Federal register notice
- issuing an untitled letter
- issuing a warning letter, or
- initiating a seizure, injunction, or other proceeding

FDA remains committed to ensuring that all drugs available to the American people have been shown to be safe and effective before entering the market, and meet appropriate standards for manufacturing and labeling. Companies marketing prescription drug products have a corporate responsibility to the American public who expects these products to be safe and effective. The Agency will continue to do *its* part by working with companies and encouraging them to obtain approval, and will take enforcement action when necessary.

The goal remains the same: to reduce consumer exposure to drugs that are not proven safe, effective and of high quality.

Cheers,

Renu Lal, Pharm.D.
CDER Small Business Assistance

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