FDA/CDER SBIA CHRONICLES

SEPTEMBER 11TH, 2014

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COMING SOON:

CDER DIRECT, AN ON-LINE APPLICATION FOR COMPANIES TO CREATE AND SUBMIT SPL FILES FOR REGISTRATION AND LISTING.

TUNE INTO OUR Webinar ON SEPT. 16TH

Additional Resources:

- Overview of the Drug Registration and Listing Webinar

- SPL Standard Training

- For technical questions on electronic submissions, e-mail: SPL@fda.hhs.gov

- For regulatory questions about registration or drug listing, email: eDRLS@fda.hhs.gov.

Registration and Drug Listing

If your firm, domestic or foreign, manufactures or commercially distributes (among other activities) a human drug product within the U.S., you are subject to drug firm registration and drug listing requirements. Registration and drug listing allows FDA to develop and maintain a catalog of all drug products marketed in the U.S. Registration information provides the locations and contact information for drug establishments and determines sites for inspection. Drug product listing information provides an inventory of all drug products in circulation as well as manufacturing information, including inactive ingredients incorporated into marketed drug products. The FDA relies on registration and listing information for administering many key programs, including post-marketing surveillance; user fee assessments; counterterrorism; monitoring of drug shortages and availability; and determining products that are being marketed without an approved application. The electronic drug establishment registration and drug listing system (eDRLS) also populates electronic listing databases such as DailyMed and the National Drug Code (NDC) Directory, ultimately improving the accuracy and inclusiveness of these databases. Do not confuse registration with Generic Drug User Fee Act (GDUFA) self-identification or drug approval. In fact, registration of a drug establishment, or assignment of an NDC, does not in any way denote approval of a firm's product.

Who should register? Section 510 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) requires firms that participate in the manufacture or processing of human drugs to register with the FDA. The term "manufacture" is defined broadly and includes the manufacture, preparation, propagation, compounding, or processing of a drug. These activities include any form of manipulation, sampling, testing or control procedures that are applied to the final product or to any part of the process. Activities that may fall within the scope of drug manufacturing include analysis; active pharmaceutical ingredient (API) or final dosage form (FDF) analytical testing; API or final dosage form manufacture; importation; labeling; packaging; particle size reduction; positron emission tomography drug production; drug recovery/salvaging activities; drug sterilization; and, repackaging or relabeling of any drug package.

In addition, firms that commercially distribute human drugs within the U.S., or that offer human drugs for import into the U.S., must register. Commercial distribution is defined as any distribution of a human drug except for investigational use, excepting internal or interplant transfer of a bulk drug substance between registered establishments within an affiliated company.

Who should list? At the time of registration, certain domestic or foreign firms must **list** all drugs manufactured, prepared, propagated, compounded, or processed for commercial distribution in the US. Human drugs requiring listing include APIs or other unfinished drugs requiring further processing, labeling, or packaging; prescription drugs and over-the-counter drugs (whether or not the subject of an approved application); and homeopathic drugs.

Substances that are ***not*** subject to the listing requirements (because they are not drugs) include foods and dietary supplements; drug intermediates (substances used in the chemical synthesis of active ingredients); and inactive ingredients (such as excipients, colorings, flavorings, emulsifiers, lubricants, preservatives, or solvents). These are things that may become components of drugs in the future but have not yet been combined with an active ingredient.

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Foreign establishments whose product will be imported into the U.S. must be electronically registered with the FDA before the import process begins. Compliance officers at the U.S. border verify that a foreign firm is registered and its products that enter the U.S. have been listed. Each foreign establishment must also identify one U.S. agent as part of its registration information. The U.S. agent must physically reside or maintain a place of business in the U.S. The U.S. agent provides critical services that include assisting FDA in communications with the foreign drug establishment, responding to questions concerning the establishment's products, and assisting FDA in scheduling inspections of the establishment. A U.S. agent can represent multiple establishments from multiple companies. An establishment can only assign one U.S. agent at a time, but can change the agent at any time.

Private labeler distributors (PLDs) are firms that do not participate in the manufacture or processing of a drug, but instead market and distribute under their own trade name and label a drug product made by someone else. PLDs are not obligated to register or list, as they distribute drugs that they do not manufacture or process. However, they are permitted to submit listing information. If a PLD does not elect to submit drug listing information directly to the FDA, the registered establishment producing the drug(s) is responsible for listing the drug on behalf of the PLD, and must obtain a Labeler Code that uniquely identifies the PLD for which it manufactures or processes the drug.

Exemptions to the registration and listing requirements (per 21 CFR 207.10) include:
- Pharmacies, hospitals, clinics, & public health agencies that regularly dispense medication upon prescription from a practitioner, but do not manufacture or process drugs for sale other than in the regular course of professional practice;
- Practitioners licensed to prescribe or administer drugs and who manufacture or process drugs solely for use in their professional practice;
- Persons who perform non-release testing in research, teaching, or chemical analysis. However, establishments that perform any form of analysis or stability tests on drugs intended for U.S. commercial distribution must register;
- Foreign drug establishments whose drugs do not enter the U.S. market and are imported to the U.S. only for purposes of processing and re-exportation;
- Manufacturers of harmless inactive ingredients that are excipients, colorings, flavorings, emulsifiers, lubricants, preservatives, or solvents that become components of drugs.

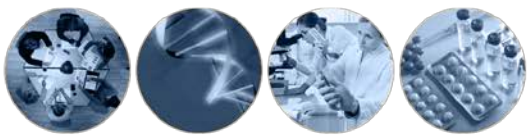
When to register and list? An owner or operator of an establishment must register within five days after beginning the manufacture or processing of a drug or drugs for commercial distribution. Firms should renew registration information annually between October 1st to December 31st of each calendar year. Additionally, at the time of registration, firms should also submit a list of every drug in commercial distribution. Updates to listing information must be submitted every June and December of each calendar year. However, FDA encourages firms to submit updates more frequently as changes occur, including labeling updates. A drug listing update should include information for drugs that have been introduced into commercial distribution and have not been previously listed, as well as any changes to information for previously listed drugs. Because the drug listing system is a key repository for labeling, it is important to keep this information up to date.

How to register and list? Firms must submit drug establishment registration and drug listing electronically, unless FDA grants a waiver to submit in paper format. To submit electronically, firms must create an electronic submissions gateway (ESG) account, obtain a DUNS number, and submit Structured Product Labeling (SPL). For details, please view our new **Human Drug Establishment Registration and Drug Listing Compliance** web-based learning course.

Note that FDA does not charge any fee to register or list. Failure to register and provide listing information in accordance with section 510 of the Food, Drug, and Cosmetic Act are prohibited acts and may cause the drug to be misbranded. In addition, per 21 CFR 207.39, any representation that creates an impression that an NDC or registration number denotes FDA approval is misleading and constitutes misbranding.

Cheers,
Renu Lal, Pharm.D.
CDER Small Business and Industry Assistance

Issues of this newsletter are archived at http://www.fda.gov/cdersmallbusinesschronicles



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