U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

How Drugs are Developed and Approved

The mission of FDA's Center for Drug Evaluation and Research (CDER) is to ensure that drugs marketed in this country are safe and effective. CDER does not test drugs, although the Center's Office of Testing and Research does conduct limited research in the areas of drug quality, safety, and effectiveness.

CDER is the largest of FDA's five centers. It has responsibility for both prescription and nonprescription or over-the-counter (OTC) drugs. For more information on CDER activities, including performance of drug reviews, post-marketing risk assessment, and other highlights, please see the ***CDER Update: Improving Public Health Through Human Drugs*** **()** The other four FDA centers have responsibility for medical and radiological devices, food, and cosmetics, biologics, and veterinary drugs.

Some companies submit a new drug application (NDA) to introduce a new drug product into the U.S. Market. It is the responsibility of the company seeking to market a drug to test it and submit evidence that it is safe and effective. A team of CDER physicians, statisticians, chemists, pharmacologists, and other scientists reviews the sponsor's NDA containing the data and proposed **labeling (/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm)**.

The section below entitled *From Fish to Pharmacies: The Story of a Drug's Development*, illustrates how a drug sponsor can work with FDA's regulations and guidance information to bring a new drug to market under the NDA process.

From Fish to Pharmacies: A Story of Drug Development

Osteoporosis, a crippling disease marked by a wasting away of bone mass, affects as many as 2 million American, 80 percent of them women, at an expense of $13.8 billion a year, according to the National Osteoporosis Foundation., The disease may be responsible for 5 million fractures of the hip, wrist and spine in people over 50, the foundation says, and may cause 50,000 deaths. Given the pervasiveness of osteoporosis and its cost to society, experts say it is crucial to have therapy alternatives if, for example, a patient can't tolerate estrogen, the first-line treatment.
Enter the salmon, which, like humans, produces a hormone called calcitonin that helps regulate calcium and decreases bone loss. For osteoporosis patients, taking salmon calcitonin, which is 30 times more potent than that secreted by the human thyroid gland, inhibits the activity of specialized bone cells called osteoclasts that absorb bone tissue. This enables bone to retain more bone mass.

Though the calcitonin in drugs is based chemically on salmon calcitonin, it is now made synthetically in the lab in a form that copies the molecular structure of the fish gland extract. Synthetic calcitonin offers a simpler, more economical way to create large quantities of the product.

FDA approved the first drug based on salmon calcitonin in an injectable. Since then, two more drugs, one injectable and one administered through a nasal spray were approved. An oral version of salmon calcitonin is in clinical trials now. Salmon calcitonin is approved only for postmenopausal women who cannot tolerate estrogen, or for whom estrogen is not an option.

How did the developers of injectable salmon calcitonin journey "from fish to pharmacies?"

After obtaining promising data from laboratory studies, the salmon calcitonin drug developers took the next step and submitted an Investigational New Drug (IND) application to CDER. The **IND Web page (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm)** explains the need for this application, the kind of information the application should include, and the Federal regulations to follow.

Once the IND application is in effect, the drug sponsor of salmon calcitonin could begin their clinical trials. After a sponsor submits an IND application, it must wait 30 days before starting a clinical trial to allow FDA time to review the prospective study. If FDA finds a problem, it can order a "clinical hold" to delay an investigation, or interrupt a clinical trial if problems occur during the study.

Clinical trials are experiments that use human subjects to see whether a drug is effective, and what side effects it may cause. The **Running Clinical Trials Webpage (/ScienceResearch/SpecialTopics/RunningClinicalTrials/default.htm)** provides links to the regulations and guidelines that the clinical investigators of salmon calcitonin must have used to conduct a successful study, and to protect their human subjects.

The salmon calcitonin drug sponsor analyzed the clinical trials data and concluded that enough evidence existed on the drug's safety and effectiveness to meet FDA's requirements for marketing approval. The sponsor submitted a New Drug Application (NDA) with full information on manufacturing specifications, stability and bioavailablility data, method of analysis of each of the dosage forms the sponsor intends to market, packaging and labeling for both physician and consumer, and the results of any additional toxicological studies not already submitted in the Investigational New Drug application. The **NDA Web page (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm)** provides resources and guidance on preparing the NDA application, and what to expect during the review process.

New drugs, like other new products, are frequently under patent protection during development. The patent protects the salmon calcitonin sponsor's investment in the drug's development by giving them the sole right to sell the drug while the patent is in effect. When the patents or other periods of exclusivity on brand-name drugs expire, manufacturers can apply to the FDA to sell generic versions. The **Abbreviated New Drug Applications (ANDA) for Generic Drug Products Webpage (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm)** provides links to guidances, laws, regulations, policies and procedures, plus other resources to assist in preparing and submitting applications.

Bringing Nonprescription Drug Products to the Market Under an OTC Monograph

OTC drugs can be brought to the market following the NDA process as described above or under an OTC monograph. Each OTC drug monograph is a kind of "recipe book" covering acceptable ingredients, doses, formulations, labeling, and, in some cases, testing parameters. OTC drug monographs are continually updated to add additional ingredients and labeling as needed. Products conforming to a monograph may be marketed without FDA pre-approval. The NDA and monograph processes can be used to introduce new ingredients into the OTC marketplace. For example, OTC drug products previously available only by prescription are first approved through the NDA process and their "switch" to OTC status is approved via the NDA process. OTC ingredients marketed overseas can be introduced into the U.S. market via a monograph under a Time and Extent Application (TEA) as described in 21 CFR 330.14. For a more thorough discussion of how OTC drug products are regulated visit FDA laws, regulations and guidances that affect small business. Information is also provided on financial assistance and incentives that are available for drug development.

CDER Small Business and Industry Assistance (CDER SBIA)

Drug sponsors which qualify as small businesses can take advantage of special offices and programs designed to help meet their unique needs. The **CDER Small Business and Industry Assistance (CDER SBIA) Webpage (/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/default.htm)** provides links to FDA laws, regulations and guidances that affect small business. Information is also provided on financial assistance and incentives that are available for drug development.

Spotlight

- **The FDA's Drug Review Process: Ensuring Drugs Are Safe and Effective (/Drugs/ResourcesForYou/Consumers/ucm143534.htm)**

Application Types

- **Investigational New Drug (IND) Application (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm)**
- **New Drug Application (NDA) (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/NewDrugApplicationNDA/default.htm)**
- **Abbreviated New Drug Application (ANDA): Generics (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/default.htm)**
- **Therapeutic Biologic Applications (BLA) (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/TherapeuticBiologicApplications/default.htm)**
- **Drug Applications for Over-the-Counter (OTC) Drugs (/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/Over-the-CounterDrugs/default.htm)**