การพัฒนาสู่ความมั่นคง และความสามารถทางยา ใน ยุคประเทศไทย 4.0

Drugs Security and Capability Development in the Era of Thailand 4.0

การประชุมวิชาการประจำปีสวทช. 31 มีนาคม 2560

ภก.เชิญพร เต็งอำนวย

รองประธานสภาอุตสาหกรรมแห่งประเทศไทย

ประธานคลัสเตอร์ผลิตภัณฑ์สุขภาพและความงามสภาอุตสาหกรรมแห่งประเทศไทย

(/AboutFDA/WhatWeDo/default.htm)

What We Do (/AboutFDA/WhatWeDo/default.htm)

Learn what FDA does and does not regulate, the laws FDA enforces, and more.

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Memoranda of Understanding (MOUs) other ways the FDA collaborates with the public to enhance its public health mission.

Doing Business With FDA (/AboutFDA/business/default.htm)
Ways to reach FDA offices for specific types of questions

Reports, Manuals, & Forms (/AboutFDA/ReportsManualsForms/default.htm)
A collection of various FDA reports, guides, and forms.

About This Website (/AboutFDA/AboutThisWebsite/default.htm)
FDA web policies, accessibility, and support for mobile devices.

Innovation at FDA (/AboutFDA/Innovation/default.htm)
The latest news on FDA efforts to support innovation.

Plain Language (/AboutFDA/PlainLanguage/default.htm)
Discover how FDA is implementing the Plain Writing Act and Plain Language Principles in our communications with you.

Spotlight

- **FDA Leadership Profiles (/AboutFDA/CentersOffices/ucm193757.htm)**
- **FDA Basics (/AboutFDA/Transparency/Basics/ucm2021108.htm)**
- **FDA Strategic Priorities: 2014 - 2018 (/AboutFDA/ReportsManualsForms/Reports/ucm227527.htm)**
- **FDA Organization Charts (/AboutFDA/CentersOffices/OrganizationCharts/default.htm)**
- **Budgets (/AboutFDA/ReportsManualsForms/Reports/BudgetReports/default.htm)**

Building Status

- **Status of White Oak Campus Facilities (/AboutFDA/WorkingatFDA/BuildingsandFacilities/ucm229281.htm)**
- **Status of Headquarters Buildings (excluding White Oak Campus) (/AboutFDA/WorkingatFDA/BuildingsandFacilities/ucm229036.htm)**

Contact FDA

888-INFO-FDA
888-463-6332

Food and Drug Administration
10903 New Hampshire Ave
Silver Spring, MD 20993

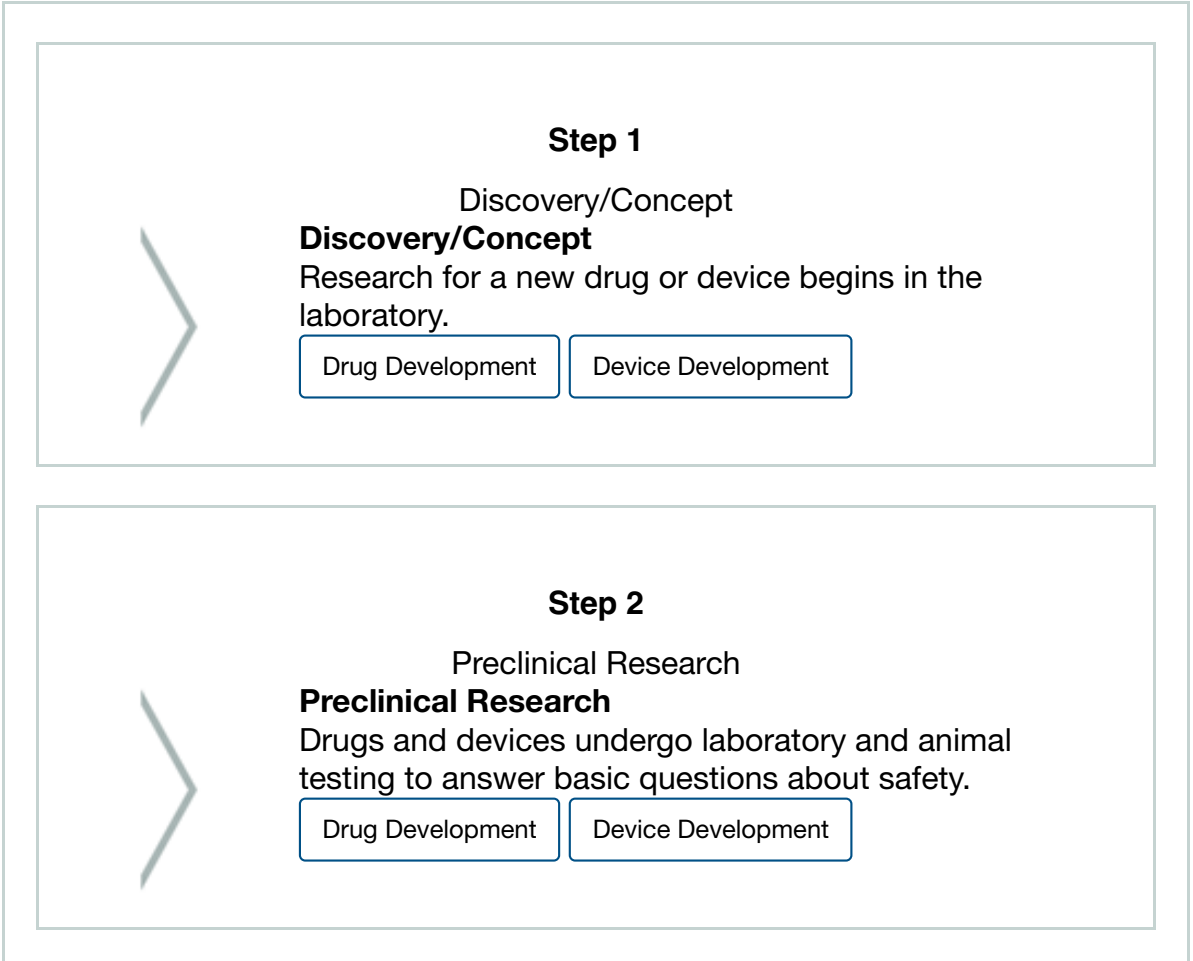
Learn About Drug and Device Approvals

The development of drugs and medical devices follows well-established paths to make sure that they are safe and effective when they reach the public. From concept to approval and beyond, FDA:

- Reviews research data and information about drugs and devices before they become available to the public.
- Watches for drug problems once drugs and devices are available to the public.
- Monitors drug information and advertising.
- Protects drug quality.

Drug and Device Development Processes

The development processes for drugs and devices are similar–each involves five basic steps. However, the processes differ within those steps. Click on either Drug Development or Device Development in the graphic below to learn more.



Step 3

Clinical Research

Clinical Research

Drugs and devices are tested on people to make sure they are safe and effective.

Drug Development | Device Development

Step 4

FDA Review

FDA Review

FDA review teams thoroughly examine all of the submitted data related to the drug or device and make a decision to approve or not to approve it.

Drug Development | Device Development

Step 5

FDA Post-Market Safety Monitoring

FDA Post-Market Safety Monitoring

FDA monitors all drug and device safety once products are available for use by the public.

Drug Development | Device Development

Resources for You

- **Report Side Effects on MedWatch (https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm)**

More in Learn About Drug and Device Approvals (/ForPatients/Approvals/default.htm)

The Drug Development Process (/ForPatients/Approvals/Drugs/default.htm)

The Device Development Process (/ForPatients/Approvals/Devices/default.htm)

Step 1: Discovery and Development

Discovery

Typically, researchers discover new drugs through:

- New insights into a disease process that allow researchers to design a product to stop or reverse the effects of the disease
- Many tests of molecular compounds to find possible beneficial effects against any of a large number of diseases
- Existing treatments that have unanticipated effects
- New technologies, such as those that provide new ways to target medical products to specific sites within the body or to manipulate genetic material

At this stage in the process, thousands of compounds may be potential candidates for development as a medical treatment. After early testing, however, only a small number of compounds look promising and call for further study.

Development

Once researchers identify a promising compound for development, they conduct experiments to gather information on:

- How it is absorbed, distributed, metabolized, and excreted
- Its potential benefits and mechanisms of action
- The best dosage
- The best way to give the drug (such as by mouth or injection)
- Side effects (often referred to as toxicity)
- How it affects different groups of people (such as by gender, race, or ethnicity) differently
- How it interacts with other drugs and treatments
- Its effectiveness as compared with similar drugs

Step 2: Preclinical Research

Before testing a drug in people, researchers must find out whether it has the potential to cause serious harm, also called toxicity. The two types of preclinical research are:

- In Vitro
- In Vivo

FDA requires researchers to use good laboratory practices (GLP), defined in medical product development regulations, for preclinical laboratory studies. The GLP regulations are found in **21 CFR Part 58.1: Good Laboratory Practice for Nonclinical Laboratory Studies**

(http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=58). These regulations set the minimum basic requirements for:

- study conduct
- personnel
- facilities
- equipment
- written protocols
- operating procedures
- study reports
- and a system of quality assurance oversight for each study to help assure the safety of FDA-regulated product

Usually, preclinical studies are not very large. However, these studies must provide detailed information on dosing and toxicity levels. After preclinical testing, researchers review their findings and decide whether the drug should be tested in people.

CFR - Code of Federal Regulations Title 21

The information on this page is current as of April 1 2016.

For the most up-to-date version of CFR Title 21, go to the Electronic Code of Federal Regulations (eCFR).[6]

TITLE 21--FOOD AND DRUGS
CHAPTER I--FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES
SUBCHAPTER A--GENERAL
PART 58GOOD LABORATORY PRACTICE FOR NONCLINICAL LABORATORY STUDIES[9]

Authority: 21 U.S.C. 342, 346, 346a, 348, 351, 352, 353, 355, 360, 360b-360f, 360h-360j, 371, 379e, 381; 42 U.S.C. 216, 262, 263b-263n.
Source: 43 FR 60013, Dec. 22, 1978, unless otherwise noted.

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7. /scripts/cdrh/cfdocs/search/default.cfm?FAQ=true
8. http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Databases/ucm135680.htm
9. ./CFRSearch.cfm?CFRPart=58&showFR=1

FDA

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Contact FDA

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Step 3: Clinical Research

What are the Clinical Trial Phases?

Embedded Video

Watch this video to learn about the three phases of clinical trials.

While preclinical research answers basic questions about a drug's safety, it is not a substitute for studies of ways the drug will interact with the human body. "Clinical research" refers to studies, or trials, that are done in people. As the developers design the clinical study, they will consider what they want to accomplish for each of the different Clinical Research Phases and begin the Investigational New Drug Process (IND), a process they must go through before clinical research begins.

On this page you will find information on:

- Designing Clinical Trials
- **Clinical Research Phase Studies**
- **The Investigational New Drug Process**
- **Asking for FDA Assistance**
- **FDA IND Review Team**
- **Approval**

Designing Clinical Trials

Researchers design clinical trials to answer specific research questions related to a medical product. These trials follow a specific study plan, called a protocol, that is developed by the researcher or manufacturer. Before a clinical trial begins, researchers review prior information about the drug to develop research questions and objectives. Then, they decide:

- Who qualifies to participate (selection criteria)
- How many people will be part of the study
- How long the study will last
- Whether there will be a control group and other ways to limit research bias
- How the drug will be given to patients and at what dosage
- What assessments will be conducted, when, and what data will be collected
- How the data will be reviewed and analyzed

Clinical trials follow a typical series from early, small-scale, Phase 1 studies to late-stage, large scale, Phase 3 studies.

Clinical Research Phase Studies

Phase 1

Patients: 20 to 100 healthy volunteers or people with the disease/condition.

Length of Study: Several months

Purpose: Safety and dosage

Approximately 70% of drugs move to the next phase

Phase 2

Patients: Up to several hundred people with the disease/condition.

Length of Study: Several months to 2 years

Purpose: Efficacy and side effects

Approximately 33% of drugs move to the next phase

Phase 3

Patients: 300 to 3,000 volunteers who have the disease or condition

Length of Study: 1 to 4 years

Purpose: Efficacy and monitoring of adverse reactions

Approximately 25-30% of drugs move to the next phase

Phase 4

Patients: Several thousand volunteers who have the disease/condition

Purpose: Safety and efficacy

Learn more about **Clinical Trials (/ForPatients/ClinicalTrials/ucm20041753.htm)**.

The Investigational New Drug Process

Drug developers, or sponsors, must submit an Investigational New Drug (IND) application to FDA before beginning clinical research.

In the IND application, developers must include:

- Animal study data and toxicity (side effects that cause great harm) data
- Manufacturing information
- Clinical protocols (study plans) for studies to be conducted

- Data from any prior human research
- Information about the investigator

Asking for FDA Assistance

Drug developers are free to ask for help from FDA at any point in the drug development process, including:

- Pre-IND application, to review FDA guidance documents and get answers to questions that may help enhance their research
- After Phase 2, to obtain guidance on the design of large Phase 3 studies
- Any time during the process, to obtain an assessment of the IND application

Even though FDA offers extensive technical assistance, drug developers are not required to take FDA's suggestions. As long as clinical trials are thoughtfully designed, reflect what developers know about a product, safeguard participants, and otherwise meet Federal standards, FDA allows wide latitude in clinical trial design.

FDA IND Review Team

The review team consists of a group of specialists in different scientific fields. Each member has different responsibilities.

- ***Project Manager:*** Coordinates the team's activities throughout the review process, and is the primary contact for the sponsor.
- ***Medical Officer:*** Reviews all clinical study information and data before, during, and after the trial is complete.
- ***Statistician:*** Interprets clinical trial designs and data, and works closely with the medical officer to evaluate protocols and safety and efficacy data.
- ***Pharmacologist:*** Reviews preclinical studies.
- ***Pharmakineticist:*** Focuses on the drug's absorption, distribution, metabolism, and excretion processes.Interprets blood-level data at different time intervals from clinical trials, as a way to assess drug dosages and administration schedules.
- ***Chemist:*** Evaluates a drug's chemical compounds. Analyzes how a drug was made and its stability, quality control, continuity, the presence of impurities, etc.
- ***Microbiologist:*** Reviews the data submitted, if the product is an antimicrobial product, to assess response across different classes of microbes.

Approval

The FDA review team has 30 days to review the original IND submission. The process protects volunteers who participate in clinical trials from unreasonable and significant risk in clinical trials. FDA responds to IND applications in one of two ways:

- Approval to begin clinical trials.

- Clinical hold to delay or stop the investigation. FDA can place a clinical hold for specific reasons, including:
  - Participants are exposed to unreasonable or significant risk.
  - Investigators are not qualified.
  - Materials for the volunteer participants are misleading.
  - The IND application does not include enough information about the trial's risks.

A clinical hold is rare; instead, FDA often provides comments intended to improve the quality of a clinical trial. In most cases, if FDA is satisfied that the trial meets Federal standards, the applicant is allowed to proceed with the proposed study.

The developer is responsible for informing the review team about new protocols, as well as serious side effects seen during the trial. This information ensures that the team can monitor the trials carefully for signs of any problems. After the trial ends, researchers must submit study reports.

This process continues until the developer decides to end clinical trials or files a marketing application. Before filing a marketing application, a developer must have adequate data from two large, controlled clinical trials.

More in The Drug Development Process (/ForPatients/Approvals/Drugs/default.htm)

Step 1: Discovery and Development (/ForPatients/Approvals/Drugs/ucm405382.htm)

Step 2: Preclinical Research (/ForPatients/Approvals/Drugs/ucm405658.htm)

Step 3: Clinical Research (/ForPatients/Approvals/Drugs/ucm405622.htm)

Step 4: FDA Review (/ForPatients/Approvals/Drugs/ucm405570.htm)

Step 5: FDA Post-Market Safety Monitoring (/ForPatients/Approvals/Drugs/ucm405579.htm)

Step 4: FDA Review

If a drug developer has evidence from its early tests and preclinical and clinical research that a drug is safe and effective for its intended use, the company can file an application to market the drug. The FDA review team thoroughly examines all submitted data on the drug and makes a decision to approve or not to approve it.

Find out how the **FDA is Speeding Up the Approval Process (/ForPatients/Approvals/Fast/ucm20041766.htm)**.

New Drug Application

A New Drug Application (NDA) tells the full story of a drug. Its purpose is to demonstrate that a drug is safe and effective for its intended use in the population studied.

A drug developer must include everything about a drug—from preclinical data to Phase 3 trial data—in an NDA. Developers must include reports on all studies, data, and analyses. Along with clinical results, developers must include:

- Proposed labeling
- Safety updates
- Drug abuse information
- Patent information
- Any data from studies that may have been conducted outside the United States
- Institutional review board compliance information
- Directions for use

FDA Review

Once FDA receives an NDA, the review team decides if it is complete. If it is not complete, the review team can refuse to file the NDA. If it is complete, the review team has 6 to 10 months to make a decision on whether to approve the drug. The process includes the following:

- Each member of the review team conducts a full review of his or her section of the application. For example, the medical officer and the statistician review clinical data, while a pharmacologist reviews the data from animal studies. Within each technical discipline represented on the team, there is also a supervisory review.
- FDA inspectors travel to clinical study sites to conduct a routine inspection. The Agency looks for evidence of fabrication, manipulation, or withholding of data.
- The project manager assembles all individual reviews and other documents, such as the inspection report, into an “action package.” This document becomes the record for FDA review. The review team issues a recommendation,

and a senior FDA official makes a decision.

FDA Approval

In cases where FDA determines that a drug has been shown to be safe and effective for its intended use, it is then necessary to work with the applicant to develop and refine prescribing information. This is referred to as “labeling.” Labeling accurately and objectively describes the basis for approval and how best to use the drug.

Often, though, remaining issues need to be resolved before the drug can be approved for marketing. Sometimes FDA requires the developer to address questions based on existing data. In other cases, FDA requires additional studies. At this point, the developer can decide whether or not to continue further development. If a developer disagrees with an FDA decision, there are mechanisms for formal appeal.

FDA Advisory Committees

Often, the NDA contains sufficient data for FDA to determine the safety and effectiveness of a drug. Sometimes, though, questions arise that require additional consideration. In these cases, FDA may organize a meeting of one of its Advisory Committees to get independent, expert advice and to permit the public to make comments. These Advisory Committees include a Patient Representative that provides input from the patient perspective. Learn more about FDA Advisory Committees.

More in The Drug Development Process (/ForPatients/Approvals/Drugs/default.htm)

- Step 1: Discovery and Development (/ForPatients/Approvals/Drugs/ucm405382.htm)
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- Step 3: Clinical Research (/ForPatients/Approvals/Drugs/ucm405622.htm)
- Step 4: FDA Review (/ForPatients/Approvals/Drugs/ucm405570.htm)
- Step 5: FDA Post-Market Safety Monitoring (/ForPatients/Approvals/Drugs/ucm405579.htm)

Step 5: FDA Post-Market Safety Monitoring

Even though clinical trials provide important information on a drug's efficacy and safety, it is impossible to have complete information about the safety of a drug at the time of approval. Despite the rigorous steps in the process of drug development, limitations exist. Therefore, the true picture of a product's safety actually evolves over the months and even years that make up a product's lifetime in the marketplace. FDA reviews reports of problems with prescription and over-the-counter drugs, and can decide to add cautions to the dosage or usage information, as well as other measures for more serious issues.

Supplemental Applications

Developers must file a supplemental application if they wish to make any significant changes from the original NDA. Generally, any changes in formulation, labeling, or dosage strength must be approved by FDA before they can be made.

INDs for Marketed Drugs

If sponsors want to further develop an approved drug for a new use, dosage strength, new form, or different form (such as an injectable or oral liquid, as opposed to tablet form), or if they want to conduct other clinical research or a post-market safety study, they would do so under an IND.

Manufacturer Inspections

FDA officials conduct routine inspections of drug manufacturing facilities across the United States, and abroad if approved products are manufactured overseas. Manufacturers may be informed of inspections in advance, or the inspections may be unannounced. Inspections may be routine or caused by a particular problem or concern. The purpose of these inspections is to make sure that developers are following good manufacturer practice. FDA can shut down a facility if minimum standards are not met.

Drug Advertising

FDA regulates prescription drug advertisements and promotional labeling. By law, a developer is prohibited from advertising unapproved uses of their product.

All advertisements, such as product claims or reminder ads, cannot be false or misleading. They must contain truthful information about a drug's effectiveness, side effects, and prescribing information. These advertisements can be found in medical journals, newspapers, and magazines, and on the Internet, television, or radio.

Promotional labeling differs from drug advertisements in the way it is distributed. Pharmaceutical companies give out brochures or other promotional materials to physicians or consumers. The drug's prescribing information must accompany promotional labeling. Learn more at **Prescription Drug Advertising (http://www.fda.gov/Drugs/ResourcesForYou/Consumers/PrescriptionDrugAdvertising/default.htm)**.

Generic Drugs

New drugs are patent protected when they are approved for marketing. This means that only the sponsor has the right to market the drug exclusively. Once the patent expires, other drug manufacturers can develop the drug, which will be known as a generic version of the drug. Generic drugs are comparable to brand name drugs and must have the same:

- Dosage form
- Strength
- Safety
- Quality
- Performance characteristics
- Intended use

Because generic drugs are comparable to drugs already on the market, generic drug manufacturers do not have to conduct clinical trials to demonstrate that their product is safe and effective. Instead, they conduct bio-equivalence studies and file an Abbreviated New Drug Application. Learn more at **Generic Drugs: Questions and Answers. (/Drugs/ResourcesForYou/Consumers/QuestionsAnswers/ucm100100.htm)**

Reporting Problems

FDA has several programs that allow manufacturers, health professionals, and consumers to report problems associated with approved drugs.

- **MedWatch (http://www.fda.gov/Safety/MedWatch/default.htm)** is a gateway for reporting problems with medical products (drugs and devices) and learning about new safety information. You can subscribe to regular **MedWatch safety alerts (/Safety/MedWatch/ucm228488.htm)**.
- **Medical Product Safety Network (MedSun) (http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/Medsun/searchReportText.cfm)** monitors the safety and effectiveness of medical devices. FDA recruits 350 healthcare providers throughout the United States to report any medical device problems that result in serious injury or death. Each month, FDA publishes the MedSun newsletter. The newsletter gives consumers important information about medical device safety.

Active Surveillance

Under the Sentinel Initiative, FDA is developing a new national system to more quickly spot possible safety issues. The system will use very large existing electronic health databases—like electronic health records systems, administrative

and insurance claims databases, and registries—to keep an eye on the safety of approved medical products in real time. This tool will add to, but not replace, FDA's existing postmarket safety assessment tools. Learn more about the **Sentinel Initiative (/Safety/FDAsSentinelInitiative/ucm2007250.htm)** and its major activities.

More in The Drug Development Process (/ForPatients/Approvals/Drugs/default.htm)

- **Step 1: Discovery and Development (/ForPatients/Approvals/Drugs/ucm405382.htm)**
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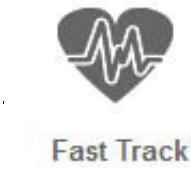
Fast Track, Breakthrough Therapy, Accelerated Approval, Priority Review

Speeding the availability of drugs that treat serious diseases are in everyone's interest, especially when the drugs are the first available treatment or if the drug has advantages over existing treatments. The Food and Drug Administration has developed four distinct and successful approaches to making such drugs available as rapidly as possible:

- Priority Review
- Breakthrough Therapy
- Accelerated Approval
- Fast Track

Because each of these approaches implies speed, there can be confusion about the specific meaning of each and the distinctions among them.



(/ForPatients/Approvals/Fast/ucm405399.htm)

Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need.
Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)

(/ForPatients/Approvals/Fast/ucm405397.htm)

A process designed to expedite the development and review of drugs which may demonstrate substantial improvement over available therapy.
Breakthrough Therapy (/ForPatients/Approvals/Fast/ucm405397.htm)

Accelerated Approval

(/ForPatients/Approvals/Fast/ucm405447.htm)

These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint.
Accelerated Approval (/ForPatients/Approvals/Fast/ucm405447.htm)

Priority Review

(/ForPatients/Approvals/Fast/ucm405405.htm)

A Priority Review designation means FDA's goal is to take action on an application within 6 months.
Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)

Resources for You

- **MedWatch (https://www.accessdata.fda.gov/scripts/medwatch/)**

More in Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review (/ForPatients/Approvals/Fast/default.htm)

Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)

Fast Track

Fast track is a process designed to facilitate the development, and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier. Fast Track addresses a broad range of serious conditions.

Determining whether a condition is serious is a matter of judgment, but generally is based on whether the drug will have an impact on such factors as survival, day-to-day functioning, or the likelihood that the condition, if left untreated, will progress from a less severe condition to a more serious one. AIDS, Alzheimer's, heart failure and cancer are obvious examples of serious conditions. However, diseases such as epilepsy, depression and diabetes are also considered to be serious conditions.

Filling an unmet medical need is defined as providing a therapy where none exists or providing a therapy which may be potentially better than available therapy.

Any drug being developed to treat or prevent a condition with no current therapy obviously is directed at an unmet need. If there are available therapies, a fast track drug must show some advantage over available therapy, such as:

- Showing superior effectiveness, effect on serious outcomes or improved effect on serious outcomes
- Avoiding serious side effects of an available therapy
- Improving the diagnosis of a serious condition where early diagnosis results in an improved outcome
- Decreasing a clinical significant toxicity of an available therapy that is common and causes discontinuation of treatment
- Ability to address emerging or anticipated public health need

A drug that receives *Fast Track* designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval
- More frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers
- Eligibility for *Accelerated Approval and Priority Review, if relevant criteria are met*
- *Rolling Review*, which means that a drug company can submit completed sections of its Biologic License Application (BLA) or New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. BLA or NDA review usually does not begin until the drug company has submitted the entire application to the FDA

Fast Track designation must be requested by the drug company. The request can be initiated at any time during the drug development process. FDA will review the request and make a decision within sixty days based on whether the drug fills an unmet medical need in a serious condition.

Once a drug receives *Fast Track* designation, early and frequent communication between the FDA and a drug company is encouraged throughout the entire drug development and review process. The frequency of communication assures that questions and issues are resolved quickly, often leading to earlier drug approval and access by patients.

More in Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review (/ForPatients/Approvals/Fast/default.htm)

- **Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)**
- **Breakthrough Therapy (/ForPatients/Approvals/Fast/ucm405397.htm)**
- **Accelerated Approval (/ForPatients/Approvals/Fast/ucm405447.htm)**
- **Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)**

Breakthrough Therapy

Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that are intended to treat a serious condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over available therapy on a clinically significant endpoint(s).

To determine whether the improvement over available therapy is substantial is a matter of judgment and depends on both the magnitude of the treatment effect, which could include duration of the effect, and the importance of the observed clinical outcome. In general, the preliminary clinical evidence should show a clear advantage over available therapy.

For purposes of Breakthrough Therapy designation, clinically significant endpoint generally refers to an endpoint that measures an effect on irreversible morbidity or mortality (IMM) or on symptoms that represent serious consequences of the disease. A clinically significant endpoint can also refer to findings that suggest an effect on IMM or serious symptoms, including:

- An effect on an established surrogate endpoint
- An effect on a surrogate endpoint or intermediate clinical endpoint considered reasonably likely to predict a clinical benefit (i.e., the accelerated approval standard)
- An effect on a pharmacodynamic biomarker(s) that does not meet criteria for an acceptable surrogate endpoint, but strongly suggests the potential for a clinically meaningful effect on the underlying disease
- A significantly improved safety profile compared to available therapy (e.g., less dose-limiting toxicity for an oncology agent), with evidence of similar efficacy

A drug that receives Breakthrough Therapy designation is eligible for the following:

- All Fast Track designation features
- Intensive guidance on an efficient drug development program, beginning as early as Phase 1
- Organizational commitment involving senior managers

Breakthrough Therapy designation is requested by the drug company. If a sponsor has not requested breakthrough therapy designation, FDA may suggest that the sponsor consider submitting a request if: (1) after reviewing submitted data and information (including preliminary clinical evidence), the Agency thinks the drug development program may meet the criteria for Breakthrough Therapy designation and (2) the remaining drug development program can benefit from the designation.

Ideally, a Breakthrough Therapy designation request should be received by FDA no later than the end-of-phase-2 meetings if any of the features of the designation are to be obtained. Because the primary intent of Breakthrough Therapy designation is

to develop evidence needed to support approval as efficiently as possible, FDA does not anticipate that Breakthrough Therapy designation requests will be made after the submission of an original BLA or NDA or a supplement. FDA will respond to Breakthrough Therapy designation requests within sixty days of receipt of the request.

More in Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review (/ForPatients/Approvals/Fast/default.htm)

- Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)
- Breakthrough Therapy (/ForPatients/Approvals/Fast/ucm405397.htm)
- Accelerated Approval (/ForPatients/Approvals/Fast/ucm405447.htm)
- Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)

Accelerated Approval

When studying a new drug, it can sometimes take many years to learn whether a drug actually provides a real effect on how a patient survives, feels, or functions. A positive therapeutic effect that is clinically meaningful in the context of a given disease is known as “clinical benefit”. Mindful of the fact that it may take an extended period of time to measure a drug’s intended clinical benefit, in 1992 FDA instituted the *Accelerated Approval* regulations. These regulations allowed drugs for serious conditions that filled an unmet medical need to be approved based on a surrogate endpoint. Using a surrogate endpoint enabled the FDA to approve these drugs faster.

In 2012, Congress passed the Food and Drug Administration Safety Innovations Act (FDASIA). Section 901 of FDASIA amends the Federal Food, Drug, and Cosmetic Act (FD&C Act) to allow the FDA to base accelerated approval for drugs for serious conditions that fill an unmet medical need on whether the drug has an effect on a surrogate or an intermediate clinical endpoint.

A surrogate endpoint used for accelerated approval is a marker - a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit, but is not itself a measure of clinical benefit. Likewise, an intermediate clinical endpoint is a measure of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on irreversible morbidity and mortality (IMM).

The FDA bases its decision on whether to accept the proposed surrogate or intermediate clinical endpoint on the scientific support for that endpoint. Studies that demonstrate a drug’s effect on a surrogate or intermediate clinical endpoint must be “adequate and well controlled” as required by the FD&C Act.

Using surrogate or intermediate clinical endpoints can save valuable time in the drug approval process. For example, instead of having to wait to learn if a drug actually extends survival for cancer patients, the FDA may approve a drug based on evidence that the drug shrinks tumors, because tumor shrinkage is considered *reasonably likely to predict* a real clinical benefit. In this example, an approval based upon tumor shrinkage can occur far sooner than waiting to learn whether patients actually lived longer. The drug company will still need to conduct studies to confirm that tumor shrinkage actually predicts that patients will live longer. These studies are known as phase 4 confirmatory trials.

Where confirmatory trials verify clinical benefit, FDA will generally terminate the requirement. Approval of a drug may be withdrawn or the labeled indication of the drug changedif trials fail to verify clinical benefit or do not demonstrate sufficient clinical benefit to justify the risks associated with the drug (e.g., show a significantly smaller magnitude or duration of benefit than was anticipated based on the observed effect on the surrogate).

Priority Review

Prior to approval, each drug marketed in the United States must go through a detailed FDA review process. In 1992, under the Prescription Drug User Act (PDUFA), FDA agreed to specific goals for improving the drug review time and created a two-tiered system of review times – *Standard Review* and *Priority Review*. A Priority Review designation means FDA's goal is to take action on an application within 6 months (compared to 10 months under standard review).

A *Priority Review* designation will direct overall attention and resources to the evaluation of applications for drugs that, if approved, would be significant improvements in the safety or effectiveness of the treatment, diagnosis, or prevention of serious conditions when compared to standard applications.

Significant improvement may be demonstrated by the following examples:

- evidence of increased effectiveness in treatment, prevention, or diagnosis of condition;
- elimination or substantial reduction of a treatment-limiting drug reaction;
- documented enhancement of patient compliance that is expected to lead to an improvement in serious outcomes; or
- evidence of safety and effectiveness in a new subpopulation.

FDA decides on the review designation for every application. However, an applicant may expressly request priority review as described in the Guidance for Industry Expedited Programs for Serious Conditions – Drugs and Biologics. It does not affect the length of the clinical trial period. FDA informs the applicant of a Priority Review designation within 60 days of the receipt of the original BLA, NDA, or efficacy supplement. Designation of a drug as "Priority" does not alter the scientific/medical standard for approval or the quality of evidence necessary.

More in Fast Track, Breakthrough Therapy, Accelerated Approval, and Priority Review (/ForPatients/Approvals/Fast/default.htm)

Fast Track (/ForPatients/Approvals/Fast/ucm405399.htm)

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Accelerated Approval (/ForPatients/Approvals/Fast/ucm405447.htm)

Priority Review (/ForPatients/Approvals/Fast/ucm405405.htm)

Parallel Track

Another mechanism to permit wider availability of experimental agents is the "parallel track" policy (Federal Register of May 21, 1990) developed by the U.S. Public Health Service in response to AIDS. Under this policy, patients with AIDS whose condition prevents them from participating in controlled clinical trials can receive investigational drugs shown in preliminary studies to be promising.

บทสรุป

แนวทางขับเคลื่อนในการสร้างความมั่นคง

และความสามารถทางยาของประเทศไทยในยุค 4.0 คือการกำหนดเป้าหมายและแนวทางการพัฒนาผลิตภัณฑ์กลุ่มสุขภาพและผู้สูงอายุให้สอดคล้องกับความสามารถของประเทศในเชิงเศรษฐศาสตร์และสร้างความร่วมมือของภาคการวิจัยและภาคอุตสาหกรรมตั้งแต่ต้นทางโดยการสนับสนุนของภาครัฐทุกภาคส่วนเพื่อขับเคลื่อนร่วมกันสู่ผลลัพธ์เชิงพาณิชย์ในเวลาที่เหมาะสมและทันต่อความต้องการในการพัฒนาขีดความสามารถในการแข่งขันของประเทศ

Fast Track

Breakthrough Therapy
Accelerated Approval
Priority Review

Parallel Track

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ขอบคุณครับ

Thank you

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