USFDA

FDA is responsible for protecting the public health by assuring the safety, efficacy and security of human and veterinary drugs, biological products, medical devices, nation's food supply, cosmetics, and products that emit radiation.

FDA is also responsible for advancing the public health

by helping to speed innovations that make medicines more effective, safer, and more affordable and

by helping the public get the accurate, science-based information they need to use medicines and foods to maintain and improve their health.

FDA also has responsibility for regulating the manufacturing, marketing and distribution of tobacco products to protect the public health and to reduce tobacco use by minors.

FDA MISSION

- To promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner.
- With respect to such products, protect the public health by ensuring that foods are safe, wholesome, sanitary and properly labelled; human and veterinary drugs are safe and effective; there is reasonable assurance of the safety and effectiveness of devices intended for human use;cosmetics are safe and properly labelled and public health and safety are protected from electronic product radiation.
- Participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements.
- As determined appropriate by secretary, carry out in consultation with experts in science, medicine and public health, and in co-operation with consumers, users, manufacturers, importers, packers, distributors and retailers of regulated products

FDA Regulates

Foods, including:dietary supplements, bottled water, food additives, infant formulas other food products.

Drugs, including: prescription drugs (both brand-name and generic), non-prescription (over-the-counter) drugs

Biologics, including: vaccines, blood and blood products, cellular and gene therapy products, tissue and tissue products, allergenics

Medical Devices, including:simple items like tongue depressors and bedpans, complex technologies such as heart pacemakers, dental devices, surgical implants and prosthetics

FDA Regulation

Electronic Products that give off radiation, including: microwave oven, x-ray equipment, laser products, ultrasonic therapy equipment, mercury vapor lamps, sunlamps

Cosmetics, including: color additives found in makeup and other personal care products, skin moisturizers and cleansers, nail polish and perfume

Veterinary Products, including: livestock feeds, pet foods, veterinary drugs and devices

Tobacco Products, including: cigarettes, cigarette tobacco, roll-your-own tobacco, smokeless tobacco

FDA does not regulates

- Advertising
- Alcohol
- Consumer Products(eg. Paint, child resistant packages and baby toys)
- Drugs of Abuse(with no approved medical use like heroin and marijuana)
- Health Insurance
- Meat and Poultry
- Pesticides
- Water
- Restaurants and Grocery Stores

FDA Regulatory Guidelines

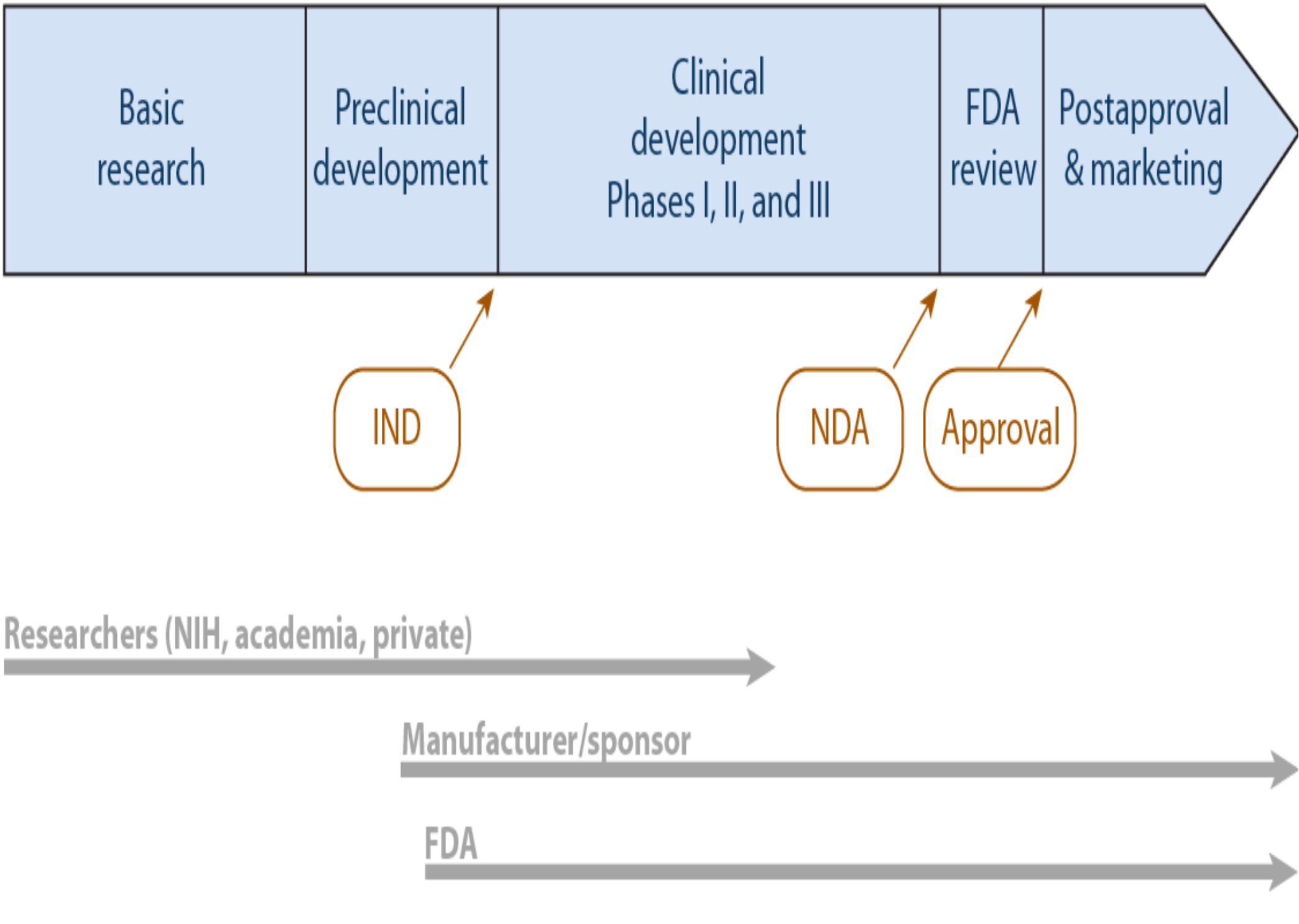
- FDA divides that responsibility into two phases: pre-approval (premarket) and post-approval (post-market)

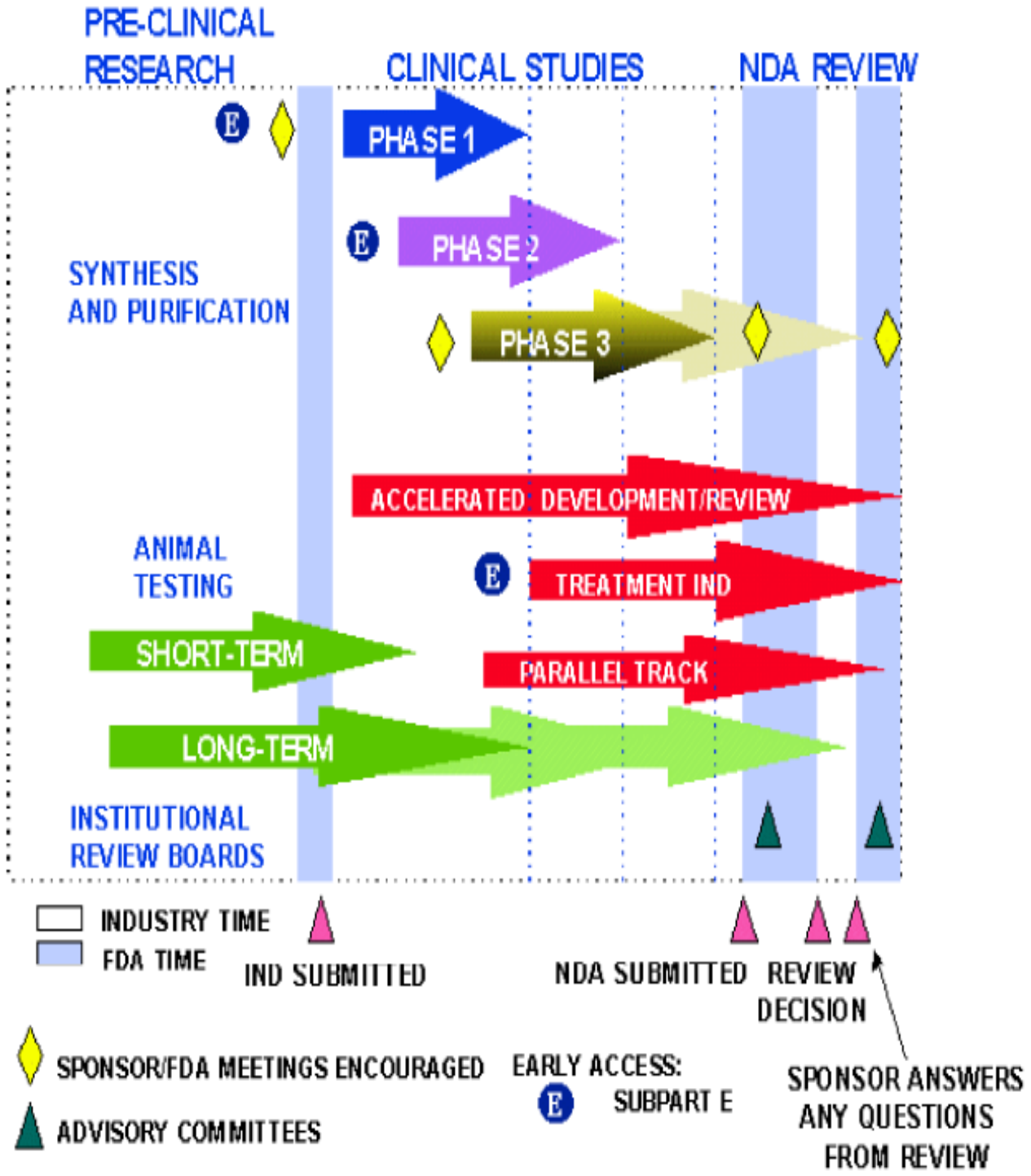
- First, FDA reviews the safety and effectiveness of new drugs that manufacturers wish to market in the United States; this process is called premarket approval or pre-approval review.
- Second, once a drug has passed that threshold and is FDA-approved, FDA acts through its post-market or post-approval regulatory procedures.

- A drug may not be sold unless it has FDA approval.
- The agency continues its oversight of drug safety and effectiveness as long as the drug is on the market.

USFDA Approval for New Drugs

- To get an approval,
- the manufacturer must demonstrate the drug's safety and effectiveness according to criteria specified in law and agency regulations,
- ensure that its manufacturing plant passes FDA inspection, and
- obtain FDA approval for the drug's labeling—a term that includes all written material about the drug, including, for example, packaging, prescribing information for physicians, and patient brochures.


Basic research
Preclinical development
Clinical development Phases I, II, and III
FDA review
Postapproval & marketing
IND
NDA
Approval
Researchers (NIH, academia, private)
Manufacturer/sponsor
FDA


PRE-CLINICAL RESEARCH
CLINICAL STUDIES
NDA REVIEW
E
PHASE 1
E
PHASE 2
SYNTHESIS AND PURIFICATION
PHASE 3
ACCELERATED DEVELOPMENT/REVIEW
ANIMAL TESTING
E
TREATMENT IND
SHORT-TERM
PARALLEL TRACK
LONG-TERM
INSTITUTIONAL REVIEW BOARDS
INDUSTRY TIME
FDA TIME
IND SUBMITTED
NDA SUBMITTED
REVIEW DECISION
SPONSOR/FDA MEETINGS ENCOURAGED
ADVISORY COMMITTEES
EARLY ACCESS:
E
SUBPART E
SPONSOR ANSWERS ANY QUESTIONS FROM REVIEW

Investigational New Drug (IND) Application

- FDA requires data from clinical trials—formally designed, conducted, and analysed studies of human subjects—to provide evidence of a drug's safety and effectiveness.

- Before testing in humans—called clinical testing—the drug's sponsor (usually its manufacturer) must file an investigational new drug (IND) application with FDA.

- The IND includes information about the proposed clinical study design, completed animal test data, and the lead investigator's qualifications.

Investigational New Drug (IND) Application

- It must also include the written approval of an Institutional Review Board, which has determined that the study participants will be made aware of the drug's investigative status and that any risk of harm will be necessary, explained, and minimized.
- The application must include an "Indication for Use" section that describes what the drug does and the clinical condition and population for which the manufacturer intends its use.

- **The FDA has 30 days to review an IND application**.
- Unless FDA objects, a manufacturer may then begin clinical testing.

Clinical Trials

- With IND status, researchers test in a small number of human volunteers the safety they had demonstrated in animals.
- These trials, called Phase I clinical trials, attempt, in FDA's words, "to determine dosing, document how a drug is metabolized and excreted, and identify acute side effects."
- If the sponsor considers the product still worthy of investment, it continues with Phase II and Phase III clinical trials.

New Drug Application (NDA)

- Once a manufacturer completes the clinical trials, it submits a new drug application (NDA) to FDA's Center for Drug Evaluation and Research (CDER).
- The NDA contains not only the clinical trial results, but also information about the manufacturing process and facilities, including quality control and assurance procedures.
- The application includes a product description (chemical formula, specifications, pharmacodynamics, and pharmacokinetics); the indication (specifying one or more diseases or conditions for which the drug would be used and the population who would use it); labeling; manufacturing description; and a proposed Risk Evaluation and Mitigation Strategy (REMS), if appropriate.
- During the NDA review, CDER officials evaluate the drug's safety and effectiveness data, analyze samples, inspect the facilities where the finished product will be made, and check the proposed labeling for accuracy.

FDA Review

- FDA considers three overall questions in its review of an NDA:

- Whether the drug is safe and effective in its proposed use, and whether the

  benefits of the drug outweigh the risks.
- Whether the drug's proposed labeling (package insert) is appropriate, and what it should contain.
- Whether the methods used to manufacture the drug and the controls used to maintain the drug's quality are adequate to preserve the drug's identity, strength, quality, and purity.

- FDA approves an application based on its review of the clinical and non-clinical research evidence of safety and effectiveness, manufacturing controls and facility inspection, and labeling.

- An approval may include specific conditions, such as required post-approval studies (or post- approval clinical trials, sometimes referred to as Phase IV clinical trials) that the sponsor must conduct after marketing begins.

- FDA has 180 days to review an NDA.
- If it finds deficiencies, such as missing information, the clock stops until the manufacturer submits the additional information.
- If the manufacturer cannot respond to FDA's request (e.g., if a required study has not been done, making it impossible to evaluate safety or effectiveness of the drug), the manufacturer may voluntarily withdraw the application.

- If and when the manufacturer is able to provide the information, the clock resumes and FDA continues the review.

- When FDA makes a final determination, it sends the applicant a “complete response letter.”

- If FDA decides to not approve an application, regulations state that the letter must describe the specific deficiencies the agency identified and recommend ways for the applicant to make the application viable.

- An unsuccessful applicant may request a hearing.

- Regulators identify the reasons for which FDA can reject an NDA, which include problems with clinical evidence of safety and effectiveness for its proposed use, manufacturing facilities and controls, labeling, access to facilities or testing samples, human subject protections, and patent information.

How FDA Regulates Approved Drugs

- FDA's role in ensuring a drug's safety and effectiveness continues after the drug is approved and it appears on the market.
- FDA acts through its post-market regulatory procedures after a manufacturer has sufficiently demonstrated a drug's safety and effectiveness for a defined population and specified conditions and the drug is FDA-approved.
- Manufacturers must report all serious and unexpected adverse reactions to FDA, and clinicians and patients may do so.
- FDA oversees surveillance, studies, labeling changes, and information dissemination, among other tasks.

Drug Developed

Drug sponsor develops a new drug compound and seeks to have it approved by FDA for sale in the United States.

Animals Tested

Sponsor must test new drug on animals for toxicity. Multiple species are used to gather basic information on the safety and efficacy of the compound being investigated/researched.

IND Application

The sponsor submits an Investigational New Drug (IND) application to FDA based on the results from intial testing that include, the drug's composition and manufacturing, and develops a plan for testing the drug on humans.

FDA's Center for Drug Evaluation and Research (CDER) evaluates new drugs before they can be sold.

The center's evaluation not only prevents quackery, but also provides doctors and patients the information they need to use medicines wisely. CDER ensures that drugs, both brand-name and generic, are effective and their health benefits outweigh their known risks.

IND REVIEW

FDA reviews the IND to assure that the proposed studies, generally referred to as clinical trials, do not place human subjects at unreasonable risk of harm. FDA also verifies that there are adequate informed consent and human subject protection.

3

PHASE 1

20-80

The typical number of healthy volunteers used in Phase 1; this phase emphasizes safety. The goal here in this phase is to determine what the drug's most frequent side effects are and, often, how the drug is metabolized and excreted.

4

PHASE 2

100's

The typical number of patients used in Phase 2; this phase emphasizes effectiveness. This goal is to obtain preliminary data on whether the drug works in people who have a certain disease or condition. For controlled trials, patients receiving the drug are compared with similar patients receiving a different treatment--usually a placebo, or a different drug. Safety continues to be evaluated, and short-term side effects are studied.

At the end of Phase 2, FDA and sponsors discuss how large-scale studies in Phase 3 will be done.

5

PHASE 3

1000's

The typical number of patients used in Phase 3. These studies gather more information about safety and effectiveness, study different populations and different dosages, and uses the drug in combination with other drugs.

FDA's New Drug Application (NDA)Review

10 Drug Labeling

FDA reviews the drug's professional labeling and assures appropriate information is communicated to health care professionals and consumers.

8-9 Application Reviewed

After an NDA is received, FDA has 60 days to decide whether to file it so it can be reviewed. If FDA files the NDA, the FDA Review team is assigned to evaluate the sponsor's research on the drug's safety and effectiveness.

7 NDA Application

The drug sponsor formally asks FDA to approve a drug for marketing in the United States by submitting an NDA. An NDA includes all animal and human data and analyses of the data, as well as information about how the drug behaves in the body and how it is manufactured.

6 Review Meeting

FDA meets with a drug sponsor prior to submission of a New Drug Application.

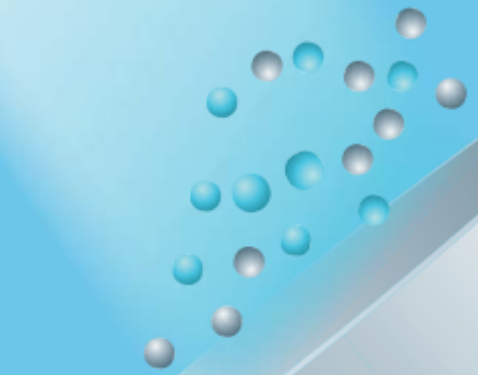
11 Facility Inspection

FDA inspects the facilities where the drug will be manufactured.

FASTER APPROVALS

The **Accelerated Approval** program allows earlier approval of drugs that treat serious diseases and that fill an unmet medical need. The approval is faster because FDA can base the drug's effectiveness on a "surrogate endpoint," such as a blood test or X-ray result, rather than waiting for results from a clinical trial.

The **Fast Track** program helps reduce the time for FDA's review of products that treat serious or life-threatening diseases and those that have the potential to address an unmet medical need. Drug sponsors can submit portions of an application as the information becomes available ("rolling submission") instead of having to wait until all information is available.



12 FDA Drug Approval

FDA reviewers will approve the application or issue a response letter.

FDA's Post-Approval Risk Assessment Systems

PHASE 4

Because it's not possible to predict all of a drug's effects during clinical trials, monitoring safety issues after drugs get on the market is critical. The role of FDA's post-marketing safety system is to detect serious unexpected adverse events and take definitive action when needed.

Once FDA approves a drug, the post-marketing monitoring stage begins. The sponsor (typically the manufacturer) is required to submit periodic safety updates to FDA.

www.fda.gov/medwatch
(800) FDA-1088 (322-1088) phone
(800) FDA-0178 (322-0178) fax

MEDWATCH

FDA's MedWatch voluntary system makes it easier for physicians and consumers to report adverse events. Usually, when important new risks are uncovered, the risks are added to the drug's labeling and the public is informed of the new information through letters, public health advisories, and other education. In some cases, the use of the drug must be substantially limited. And in rare cases, the drug needs to be withdrawn from the market.

Generic Drug Review Process ANDA

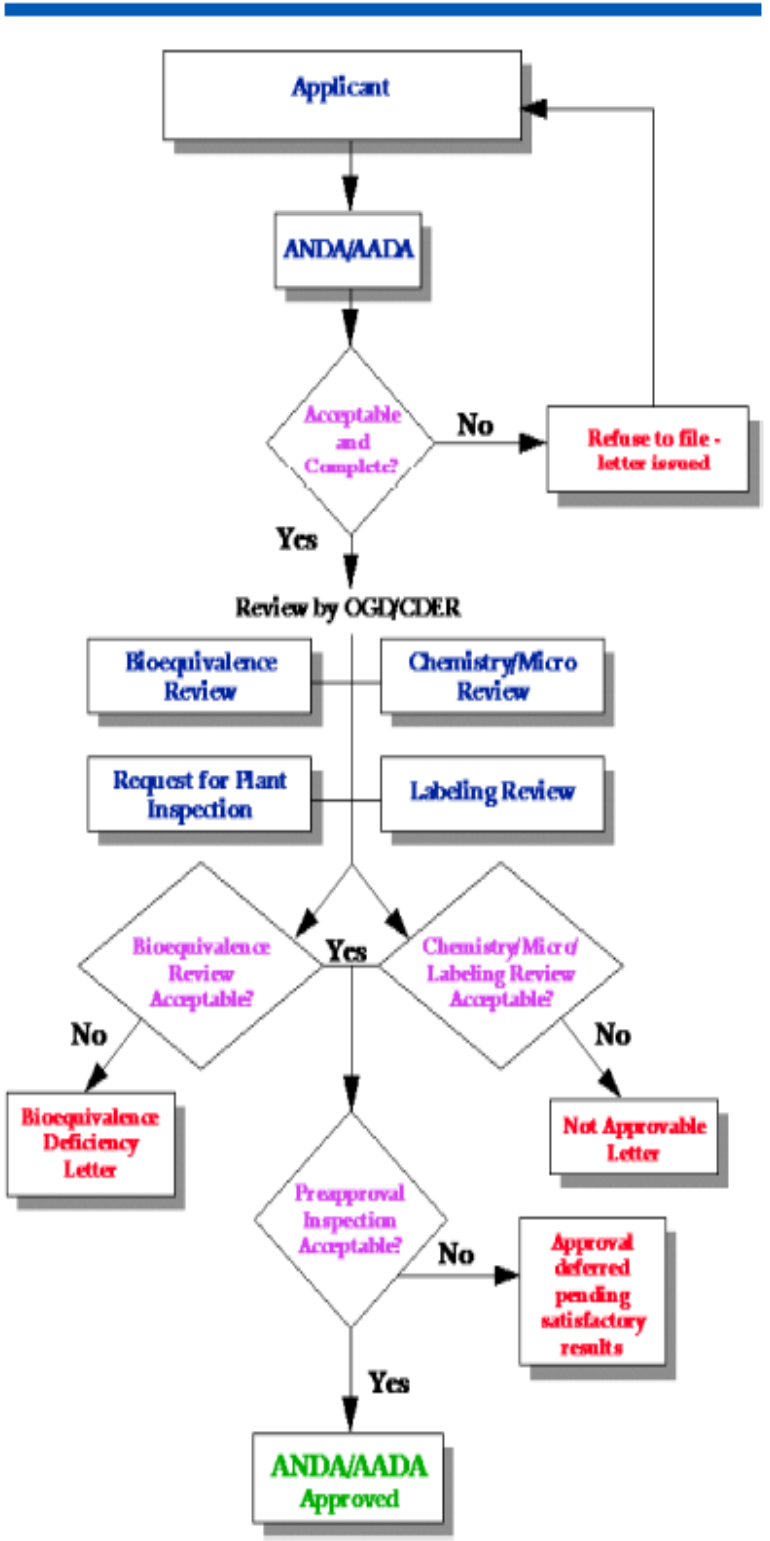
- An important part of CDER's mission is to assure that safe and effective generic drugs are available to the American people.
- This work is accomplished in CDER's Office of Generic Drugs (OGD).
- The information below provides an understanding of how CDER works to assure the safety and effectiveness of generic drug products.

A generic drug product is one that is comparable to an innovator drug product (also known as the reference listed drug (RLD) product as identified in the FDA's list of Approved Drug Products with Therapeutic Equivalence Evaluations) in dosage form, strength, route of administration, quality, performance characteristics and intended use.

Abbreviated new drug applications (ANDA's) are submitted to FDA's Center for Drug Evaluation and Research, Office of Generic Drugs for review and approval.

Once approved an applicant may manufacture and market the generic drug product provided all patent protection and exclusivity associated with the RLD have expired.

Generic drug applications are termed "abbreviated" in that they are not required to provide clinical data to establish safety and efficacy, since these parameters have already been established by the approval of the innovator drug product (first approved version of the drug product marketed under a brand name).


Applicant
ANDA/AADA
Acceptable and Complete?
No
Refuse to file - letter issued
Yes
Review by OGD/CDER
Bioequivalence Review
Chemistry/Micro Review
Request for Plant Inspection
Labeling Review
Bioequivalence Review Acceptable?
Yes
Chemistry/Micro/ Labeling Review Acceptable?
No
No
Bioequivalence Deficiency Letter
Not Approvable Letter
Preapproval Inspection Acceptable?
No
Approval deferred pending satisfactory results
Yes
ANDA/AADA Approved

Therapeutic Goods Administration

Regulation of Medicines in Australia

- The Australian community expects that the medicines and medical devices in marketplace are safe and of high quality, to a standard at least equal to that of comparable countries.
- The objective of TGA which came into effect in 1991, is to provide a national framework for the regulation of therapeutic goods in Australia and ensure their quality, safety and efficacy.
- The regulatory frame work is based on risk management approach designed to ensure public health and safety, while at the same time freeing industry form any unnecessary regulatory burden.

Introduction

- The Therapeutic Goods Administration is the main government agency responsible for enforcing the regulations of medicines in Australia.
- There are also a number of committees which play an equally important role as a government agency in the regulation of medicines.
- They are involved in the pre-market assessment of medicines, post-market vigilance, and regulation of advertisements of medicines, etc.
- These committees include members who are non-government officials such as healthcare practitioners, professionals, industr representatives and consumers.
- Any product for which therapeutic claims are made must be entered in **Australian Register of Therapeutic Goods** (ARTG – computer based database) before product can be supplied in Australia

- In Australia, medicines can be classified as **registered medicines or listed medicines**, depending on their ingredients and claims made.
- **Registered medicines** can be further classified as **non-prescription (low risk) registered medicines and as prescription (high risk) registered medicines**.
- All medicines which are **for export only** are considered as **listed medicines.**
- Registered medicines are of higher risk than listed medicines, therefore, the degree of control imposed on registered medicines is higher than that of listed medicines;
- Registered medicines are evaluated for safety, quality and efficacy while listed medicines are evaluated for safety and quality only.

- Rigid control has been placed on the supply of medicines in Australia.
- First, all medicines, registered or listed, must be submitted to a pre-market assessment before they can be supplied in Australia.
- The degree of control imposed over a medicine is directly related to the risk level of that medicine.
- Secondly, all Australian manufacturers of medicines are required under the Therapeutic Goods Act to hold a licence which certifies compliance with the Code of Good Manufacturing Practice.
- Overseas manufacturers are also required to provide evidence to prove that they have met similar standards of Good Manufacturing Practice as the Australian manufacturers.
- Thirdly, there are also post-market vigilance activities such as investigating problems, conducting inspections of manufacturing sites and testing samples of medicines, etc., carried out by the Therapeutic Goods Administration and relevant committees to ensure that medicines are of an acceptable standard.

Therapeutic Good

- A therapeutic good is broadly defined in the Therapeutic Goods Act 1989 as a good which can be represented in any form and which is for therapeutic use.

- It can be a medicine or a medical device.
- In general, a therapeutic good is used in or in connection with :
- 1. preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury; or
- 2. influencing, inhibiting or modifying a physiological process;or
- 3. testing the susceptibility of persons to a disease or ailment;or
- 4. influencing, controlling or preventing conception; or
- 5. testing for pregnancy; or
- 6. the replacement or modification of parts of the anatomy.

Classification of Therapeutic Goods

Therapeutic Goods Administration

- The Therapeutic Goods Administration's overall control of the supply of medicines in Australia is exercised through five main processes:
- 1. pre-market evaluation and approval of medicines intended for supply in Australia;
- 2. licensing of manufacturers in accordance with international standards under Good Manufacturing Practice;
- 3. post-market monitoring, through sampling, adverse event reporting, surveillance activities, and response to public inquiries;
- 4. development, maintenance and monitoring of the systems for registering and listing of medicines
- 5. the assessment of medicines for export.

REGULATION OF Therapeutic Goods

- Pre-Market Assessment
- Licensing of Manufacturers
- Post market vigilance

Pre-Market Assessment

- All medicines must be either listed or registered in the Australian Register of Therapeutic Goods before they can be supplied in Australia.
- They are also required to undergo an assessment before they can be listed or registered.

- However, there are a few procedures which are common to both listed and registered medicines.
-
- 1. A sponsor submits an application to the Therapeutic Goods Administration for listing or registering a medicine in the Australian Register of Therapeutic Goods.
- He may refer to Schedules 4 and 5 of the Therapeutic Goods Regulations 1990 to determine whether the medicine is list able or registrable.
- A fee is required when the application is accepted for evaluation.
- 2. The Therapeutic Goods Administration evaluates the application or it refers the application to an external committee for evaluation.
- 3. If the application is accepted, an AUST L or AUST R number will be issued for the medicine and the medicine can be listed or registered in the Australian Register of Therapeutic Goods.
- 4. If the application is rejected, the sponsor may appeal.

Licensing of Manufacturers

- Australian manufacturers of medicines must be licensed under the Therapeutic Goods Act 1989.
- Their manufacturing processes must comply with principles of Good Manufacturing Practice.
- The aim of licensing is to protect public health by ensuring that medicines meet definable standards of quality assurance and are manufactured in conditions which are clean and free of contaminants.

- Applications for a manufacturing licence are assessed through an inspection of the manufacturing premises, i.e. an audit.

- Auditors from the Therapeutic Goods Administration conduct audits of the manufacturing premises and a licence is issued only after all the requirements have been met.

- Audits are conducted before a licence is issued, and at regular intervals after the licence has been granted -- generally every 15 to 24 months, depending on the complexity of the manufacturing process and whether previously identified deficiencies have been corrected.

Post-Market Vigilance

- In Australia, post-market vigilance activities include the following:
- 1. investigating problems which have been reported through the Adverse Drug Event Reporting System;
- 2. conducting inspections of the manufacturing premises to ensure their compliance with the relevant Code of Good Manufacturing Practice;
- 3. conducting laboratory testing of products on the market and if necessary, conducting recalls of deficient medicines; and
- 4. conducting surveillance activities.

The Medicines and Healthcare products Regulatory Agency (MHRA)

- UK regulatory body
- MHRA is a government body which was set up in 2003 to bring together the functions of the Medicines Control Agency (MCA) and the Medical Devices Agency (MDA).

How does licensing and authorisation work?

- Licences for medicines are granted only when a product meets high standards of safety and quality and works for the purpose intended.
- The regulatory system also imposes rigorous standards on medicines manufacturers and wholesale dealers who trade in them.
- A licence, also referred to as a **marketing authorisation,** from the MHRA is required before any medicine can be used to treat people in the UK.

- To begin the process,companies and/or researchers must apply to the MHRA for permission to test drugs through clinical trials, if these trials are to be conducted in the UK.

- In order to receive permission to run a trial, they must first satisfy the MHRA that they have met strict safety criteria.

- All the test results from these trials on how well the medicine works and its side effects, plus details of what the medicine contains, how it works in the body, and who it is meant to treat, are then sent to the MHRA for detailed assessment.

- The assessment team is made up of experts from different relevant specialities, each of whom has undergone additional training in medicines Assessment.
- In the past, all this information used to be supplied in paper format; now it is supplied electronically, to minimise procedural delays.
- The MHRA also has to comply with strict time frames and performance targets for the licensing of Medicines.
- Once the MHRA is satisfied that the medicine works as it should, and that it is acceptably safe, it is given a marketing authorisation or product licence.

MHRA monitors safety and quality standards

- Regular inspections of good and safe practice
- Annual routine sampling of around 3,000 marketed medicines at manufacturers' premises, wholesalers, and pharmacies, proactive medical device programme.
- Publishing standards on ingredients and expected quality for medicines (British Pharmacopoeia)
- Ongoing reports from healthcare professionals, patients, and manufacturers,
- Assessment of misleading or incorrect information, including:
- • Adverts
- • Product labelling
- • Product information leaflets.
- Gathering intelligence about illegally manufactured imported and counterfeit medicines and medical devices.
- Managing the General Practice Research Database (GPRD), information from which is used to detect healthcare trends and monitor the safety and risk benefit of market licensed medicines

General Practice Research Database

- The government entrusts the MHRA to manage the General Practice Research Database (GPRD)
- The GPRD is an internationally recognised database which is used to research safety and effectiveness issues of licensed medicines as well as improve the understanding of disease.
- The database contains the anonymised records of patients registered at more than 480 family doctor (GP) practices across the UK.
- It is the largest/most validated population based database of its kind in the world, detailing illness, investigations, and treatment.

European Medicines Agency (EMA)

- The European Medicines Agency (EMA) is a decentralised body of the EU.
- The mission of the Agency is to foster scientific excellence in the evaluation and supervision of medicines, for the benefit of public and animal health serving over 500 million users of medicinal products.
- Responsible for centralised procedure and co-ordination of EU network + plays a role in stimulating innovation and research in the pharmaceutical sector.

- One of the 15 independent European Community agencies
- Composed of a secretariat (EMEA staff), management board, scientific committees, working parties and expert groups (members nominated by EU/EEA Member States)
- Mobilises existing scientific and inspection resources of the EU/EEA for
- – evaluation of centralised medicinal products
- – preparing of guidelines on safety/quality/efficacy
- – coordination of verification of compliance with principles of GMP, GCP, GLP

- Responsible for issuing and supervising national marketing authorisations (pharmacovigilance, inspections, sampling and testing)
- Authorisation of clinical trials on their territor y
- Authorisation and supervision of manufacture and importation on their territory
- Supervision of GLP Test facilities
- Nominating members to EMEA Scientific Committees, working parties and other groups

EMA is not responsible

- Evaluation of all medicines in the EU
- Controlling, advertising of medicines
- Research/development of medicines
- Price and reimbursement
- Clinical trial approval
- Medical devices
- EU healthcare policie

The EU regulatory system for medicines

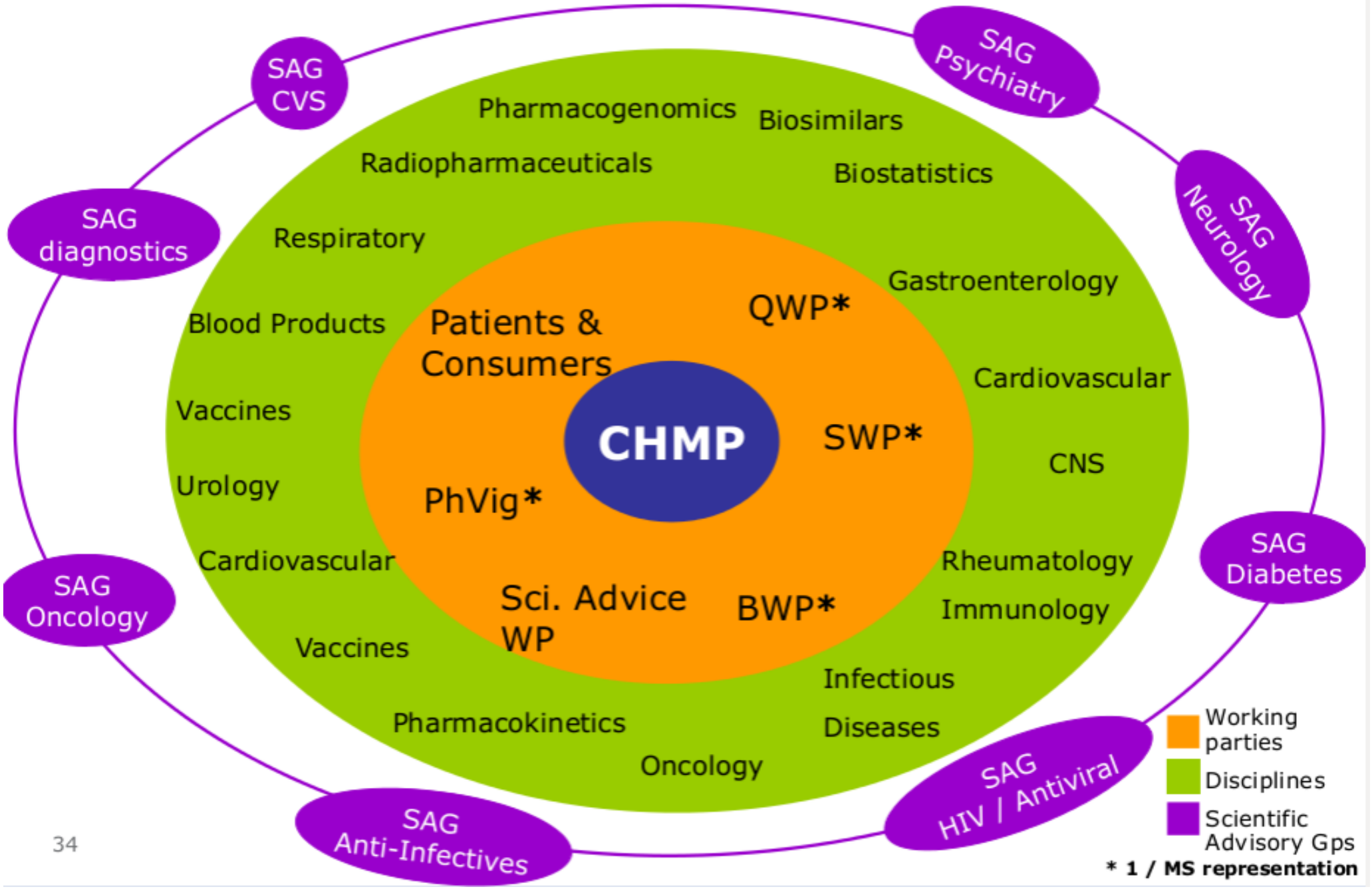
- The European medicines regulatory system is based on a network of medicines regulatory authorities from the 31 EEA Member States, the European Commission and the European Medicines Agency (EMA)
- The network is supported by a pool of many thousands of experts drawn from right across Europe, allowing it to source the best possible scientific expertise for the regulation of medicines in the EU and to provide scientific advice of the highest quality.
- The diversity of the experts involved in the regulation of medicines in the EU encourages the exchange of knowledge, ideas and best practices between scientists striving for the highest standards for medicines' regulation.

EU Member States: 28

The European Economic Area (EEA) is formed of the 28 EU Member States plus:

The EMA’s scientific committees

- The EMA has seven scientific committees that carry out its scientific assessments:
- • Committee for Medicinal Products for Human Use
- • Pharmacovigilance Risk Assessment Committee
- • Committee for Medicinal Products for Veterinary Use
- • Committee for Orphan Medicinal Products
- • Committee on Herbal Medicinal Products
- • Committee for Advanced Therapies
- • Paediatric Committee

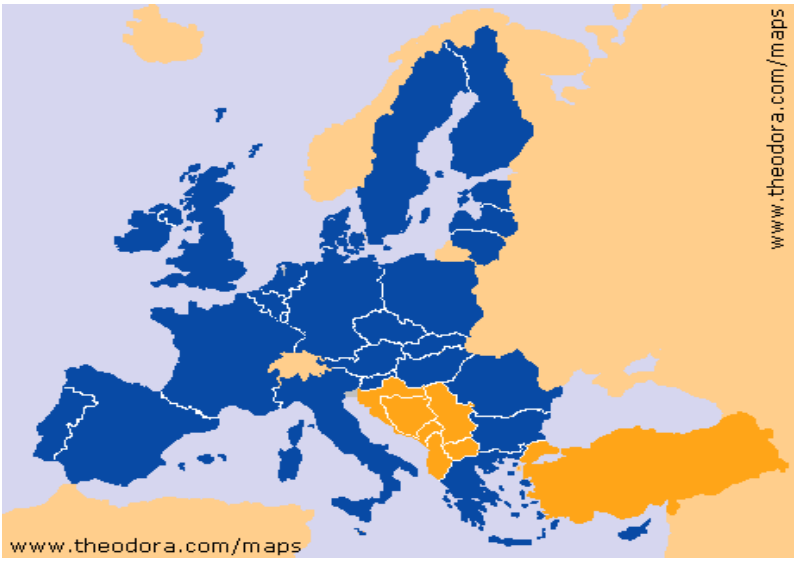

SAG CVS
SAG Psychiatry
SAG diagnostics
SAG Neurology
SAG Oncology
SAG Diabetes
SAG Anti-Infectives
SAG HIV / Antiviral
Pharmacogenomics
Biosimilars
Radiopharmaceuticals
Biostatistics
Respiratory
Gastroenterology
Blood Products
Patients & Consumers
QWP*
Cardiovascular
Vaccines
CHMP
SWP*
CNS
Urology
PhVig*
Cardiovascular
Rheumatology
Sci. Advice WP
BWP*
Immunology
Vaccines
Infectious Diseases
Pharmacokinetics
Oncology
Working parties
Disciplines
Scientific Advisory Gps
* 1 / MS representation

The EU procedures of marketing authorisations

Centralised Procedure (via EMA)

Mutual Recognition procedure

Decentralised Procedure



Better Resource Utilisation
Harmonised Scientific Opinions
Harmonised Information to Doctors / Patients

Centralised Procedure

- Under the centralised procedure, pharmaceutical companies submit a single marketing-authorisation application to the EMA.
- The EMA's Committee for Medicinal Products for Human Use (CHMP) or Committee for Medicinal Products for Veterinary Use (CVMP) carries out a scientific assessment of the application and gives a recommendation on whether or not to grant a marketing authorisation.
- Once granted by the European Commission, the centralised marketing authorisation is valid in all EU Member States.
- This allows the marketing-authorisation holder to market the medicine and make it available to patients and healthcare professionals throughout the EU on the basis of a single marketing authorisation.
- The use of the centralised procedure is compulsory for certain medicines and most innovative medicines go through this procedure.

The centralised procedure

Regulatory review Process

- **1 Marketing Authorisation** valid EU
- **1 Invented name** (Tradename)
- **1 Common Labelling** (22 languages identical)
  - Summary of Product Characteristics (SPC)
  - User Package Leaflet & Package Labelling
- **Maximum time limit**
  - **210 days** Evaluation → Opinion

Centralised Procedure (CP) - Mandatory Scope (1)

- Medicinal products developed by means of one of the following biotechnological processes:
- Recombinant DNA technology
- Controlled expression of gene coding for biologically active proteins
- Hybridoma and monoclonal antibody methods

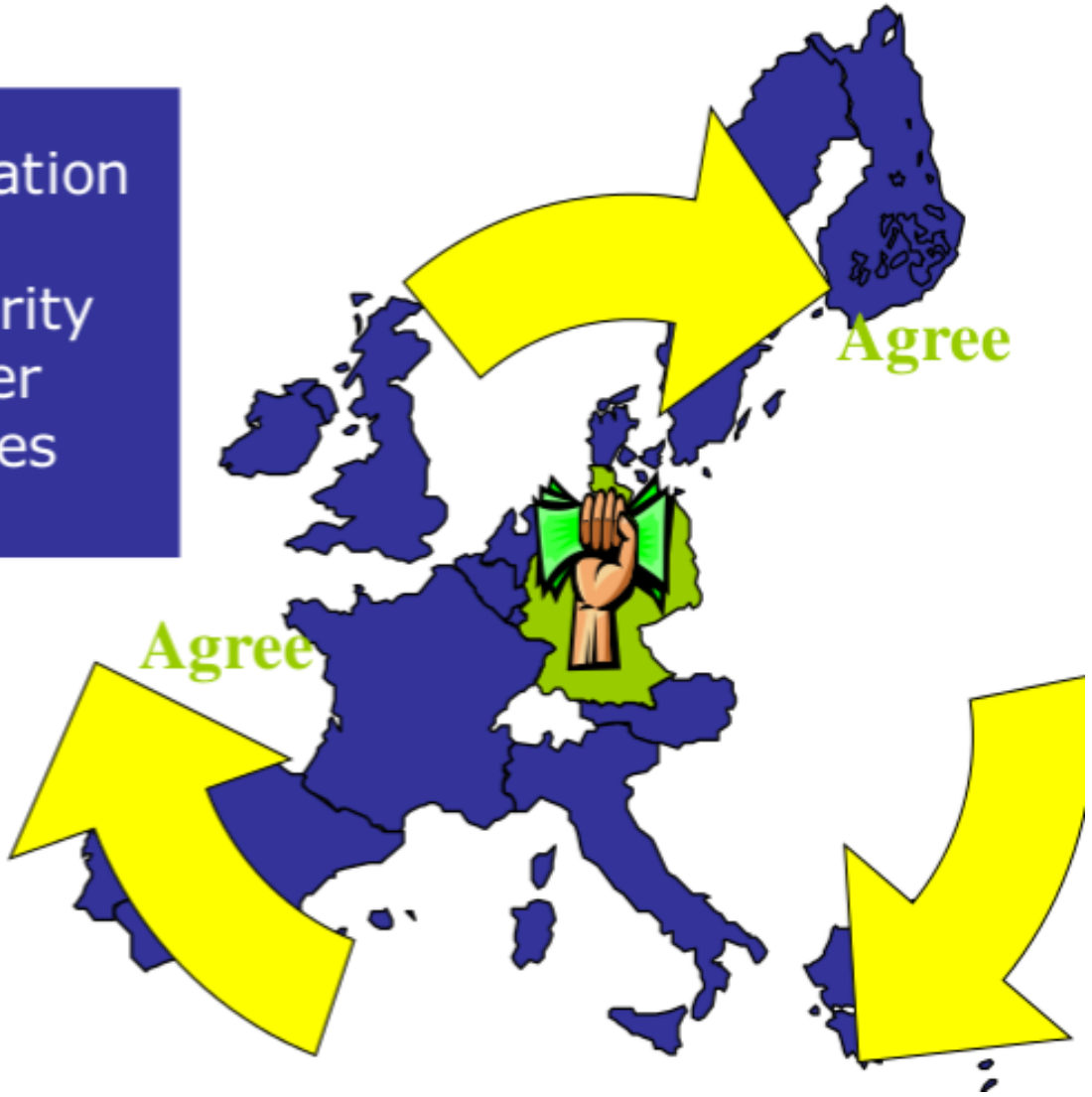
Mutual Recognition

Procedure where companies that have a medicine authorised in one EU Member State can apply for this authorisation to be recognised in other EU countries.

This process allows Member States to rely on each other’s scientific assessments.

The mutual recognition procedure

One initial National Authorisation issued by:
-1 National Regulatory Authority
- recognised by up to 29 other National Regulatory Authorities



Decentralised Procedure

where companies can apply for the simultaneous authorisation of a medicine in more than one EU Member State if it has not yet been authorised in any EU country and it does not fall within the mandatory scope of the centralised procedure;

Structure of EU Marketing Authorization Applications (MAAs)

The Common Technical Document (CTD)

MODULE 1
Administrative and regional information, "Risk Management", "Risk Reduction" and Pharmacovigilance Plans
MODULE 2
Overviews and summaries of Modules 3 to 5
MODULE 3
Quality (manufacturing process, control methods, analytical tests)
MODULE 4
Pre- clinical investigations (animal models)
MODULE 5
Clinical investigation (Phases I to III)

Ministry of Health, Labour and Welfare

- The mission of the Ministry of Health, Labour and Welfare is to enable people to live fulfilling lives with a greater sense of security.
- The Ministry is therefore responsible for systems that are closely related to the individual lives of the people and which concern medical care, long-term care, pensions, labour, childcare, and public assistance

- PMDA
- – Pharmaceutical and Medical Devices Agency
- – Japanese counterpart to the FDA operational aspects of drug development
- MHLW
- – Ministry of Health, Labour and Welfare
- – Japanese counterpart to the Dept of HHS
- - Higher degree of involvement in drug development
- – Ensures that public’s interest is taken into account
- –Ultimately responsible for drug approval

- PMDA
- To identify possible regulatory issues and provide possible solutions
- Very high concern for safety
- Safety confirmation studies and post-
- marketing data are increasing in oncology