Chapter 12

Biotechnology Regulations

12.1 The Regulatory Framework

- NIH was the first federal agency to assume regulatory responsibility over biotechnology
  - In 1974, NIH published research guidelines for recombinant DNA techniques
  - Continued monitoring until 1984
- Government published the “Coordinated Framework for Regulation of Biotechnology”
  - Joint responsibility of the NIH, the USDA, and the EPA
  - Established as formal policy in 1986

12.1 The Regulatory Framework

- "Coordinated Framework for Regulation of Biotechnology"
  - Biotechnology products would not pose regulatory and scientific issues that are substantially different from those posed by traditional products

12.1 The Regulatory Framework

Table 12.1 PRIMARY FEDERAL REGULATORY AGENCIES IN THE UNITED STATES

Regulatory Oversight of Biotechnology Products

Agency	Product Regulated
U.S. Department of Agriculture	Plants, plant pests (including microorganisms), animal vaccines
Environmental Protection Agency	Microbial/plant pesticides, other toxic substances, microorganisms, animals producing toxic substances
Food and Drug Administration	Food, animal feeds, food additives, human and animal drugs, human vaccines, medical devices, transgenic animals, cosmetics

Major Laws that Empower Federal Agencies to Regulate Biotechnology

Law	Agency
The Plant Protection Act	USDA
The Meat Inspection Act	USDA
The Poultry Products Inspection Act	USDA
The Eggs Products Inspection Act	USDA
The Virus Serum Toxin Act	USDA
The Federal Insecticide, Fungicide, and Rodenticide Act	EPA
The Toxic Substances Control Act	EPA
The Food, Drug, and Cosmetics Act	FDA, EPA
The Public Health Service Act	FDA
The Dietary Supplement Health and Education Act	FDA
The National Environmental Protection Act	USDA, EPA, FDA

Source: www.fda.gov.

12.2 U.S. Department of Agriculture

- Created in 1862
- Advancement and Regulations of Agriculture
  - Regulating plant pests, plants, and veterinary biologics
    - **Biologics** – any medical preparation made from living organisms or their products

12.2 U.S. Department of Agriculture

- Animal and Plant Health Inspection Service (APHIS)
  - Branch of USDA responsible for protecting agriculture from pests and diseases
  - Genetically engineered plants and insects are potentially invasive so are treated as plant pests

12.2 U.S. Department of Agriculture

- Permitting Process
  - Requires several years of field trials to investigate everything about the plant
    - Disease resistance, drought tolerance, reproductive rates
  - Precautions must be taken to prevent accidental cross-pollination

12.2 U.S. Department of Agriculture

- Ultimate objective for grower is to harvest a marketable product
  - Petition APHIS for deregulated status
  - Three broad areas to evaluate the petition
    - Plant pest consequences
    - Risks to other organisms
    - Weed consequences

12.2 U.S. Department of Agriculture

- Alternative system to fast-track some new agricultural products called **notification**
  - Six criteria must be met
    - The new agricultural product must be one of only a limited number of eligible plant species
    - The new genetic material must be confined to the nucleus of the new plant
    - The function of the genes being introduced must be known
    - If to be used for food, the new genes cannot cause the production of a toxin, an infectious disease, or any substance used medically
    - If the gene is derived from a plant virus, it cannot have the potential to create a new virus
    - The new genetic material must not be derived from animal or human viruses

12.2 U.S. Department of Agriculture

- If to be used for food, the new genes cannot cause the production of a toxin, an infectious disease, or any substance used medically
- If the gene is derived from a plant virus, it cannot have the potential to create a new virus
- The new genetic material must not be derived from animal or human viruses

12.3 The Environmental Protection Agency

- Established in 1970 with responsibilities including
  - Protecting endangered species
  - Establishing emission standards for cars
  - Regulating pesticides and herbicides
    - Regulates any plant that is genetically engineered to express proteins that provide pest control
  - Supervising the use of herbicide-tolerant plants

12.3 The Environmental Protection Agency

- Experimental Use Permits
  - Plan to create a plant that expresses pesticidal proteins
    - If field test will involve 10 acres or more of land or 1 acre or more of water, then need an **experimental use permit (EUP)**
  - First EUP issued in July 1985 to Advanced Genetic Sciences for use of two genetically altered strains of naturally occurring bacteria that could potentially protect crops from frost damage

12.3 The Environmental Protection Agency

- Deregulation and Commercialization
  - Product approved for market
  - EPA spends about one year reviewing the data collected, concentrating on four areas of concern:
    - Source of gene, how it is expressed, and the nature of the pesticide-protein produced
    - Health effects of the bioengineered plant
    - The environmental fate of the pesticide protein
    - The effects on nontarget species

12.4 Food and Drug Administration

- Charged with making sure that the foods we eat and the medicines we use are safe and effective
- Food and Food Additives
  - FDA serves as a consultant
  - Studies focus on
    - Unexpected or undesirable effects
    - Evaluation of the protein to see if it is substantially the same as naturally occurring proteins in food
  - If food additive poses no foreseeable threat, FDA can grant generally-recognized-as-safe (GRAS) status

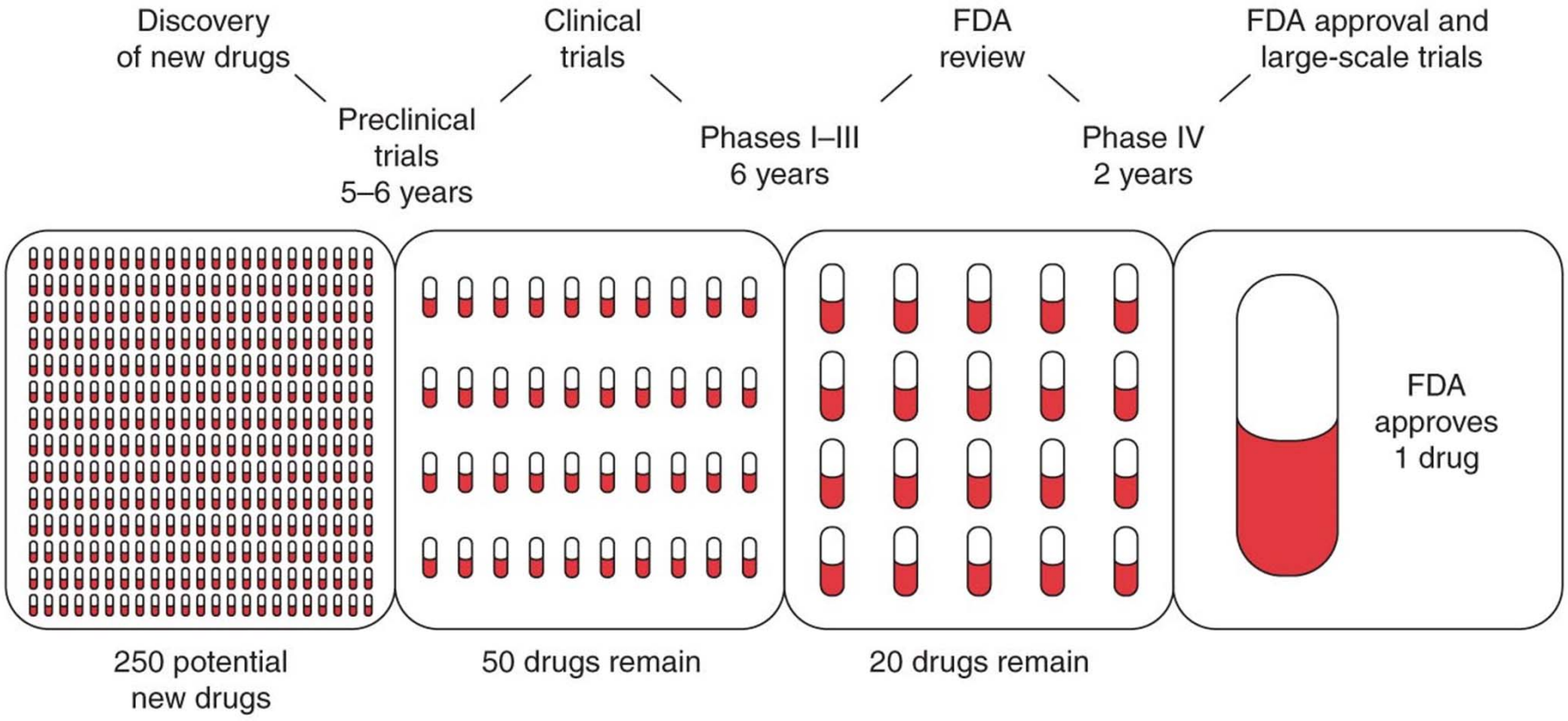
12.4 Food and Drug Administration

- The Drug Approval Process
  - **Investigational new drug (IND) application**
    - FDA considers results of previous experiments, the nature of the substance itself, and the plans for additional testing
- Good Laboratory Practice (**GLP**) and Good Manufacturing Practice (**GMP**)
  - Regulations instituted by FDA to govern animal studies of pharmaceutical products
    - Follow written protocols, have adequate facilities, provide proper animal care, record data properly, and conduct valid toxicity tests

12.4 Food and Drug Administration

- Phase Testing of Drugs
  - **Phase I (safety)** – between 20 and 80 healthy volunteers take the medicine
  - **Phase II (efficacy)** – test new treatment on 100-300 patients who actually have the illness
  - **Phase III (comparative benefit to other current drugs)** – testing on 1,000-3,000 patients in double-blinded tests
- FDA approval as an **NDA** (new drug authorization)

12.4 Food and Drug Administration



12.4 Food and Drug Administration

- Biotech company will file for a **Biological License Agreement (BLA)**
  - If seeking approval of a biologically derived product such as a viral therapy, blood compound, vaccine, or protein derived from animals
- FDA reviews information that goes on label and inspects the facilities where drug will be manufactured as part of approval process

12.4 Food and Drug Administration

- Exceptions to Phase Testing Procedure
  - FDA allows approval of drugs and vaccines intended to counter biological, chemical, and nuclear terrorism without first proving their safety and worth in Phase II and Phase III trials
  - Also true for orphan drugs – drugs with a small number of beneficiaries but with great benefit

12.5 Legislation and Regulation: The Ongoing Role of Government

- Regulation of biotechnology, like other industries, is a matter of politics as well as science
  - Stem cells
  - Labeling of foods that contain GMOs

12.5 Legislation and Regulation: The Ongoing Role of Government

Table 12.2 EXAMPLES OF SHARED RESPONSIBILITIES BY FEDERAL REGULATORY AGENCIES

New Trait/ Organism	Regulatory Review Conducted by	Reviewed for
Viral resistance in food crop	USDA	Safe to grow
	EPA	Safe for the environment
	FDA	Safe to eat
Herbicide tolerance in food crop	USDA	Safe to grow
	EPA	New use of companion herbicide
	FDA	Safe to eat
Herbicide tolerance in ornamental crop	USDA	Safe to grow
	EPA	New use of companion herbicide
Modified oil content in food crop	USDA	Safe to grow
	FDA	Safe to eat
Modified flower color in ornamental crop	USDA	Safe to grow
Modified soil bacteria degrades pollutants	EPA	Safe for the environment

Source: www.fda.gov.

12.6 Introduction to Patents

- A **patent** gives an inventor or researcher exclusive rights to a product and prohibits others from making, using, or selling the product for a certain number of years
- Regulated by the U.S. Patent and Trademark Office (USPTO)
  - 1980 first patent for a bacterium with a unique gene sequence
  - 2,000 patents granted since for plant, animal, and human genes

12.6 Introduction to Patents

- Strong patents = strong business for biotech companies
  - But these patents have stirred considerable controversy
- To win a patent, discovery
  - Must be novel
  - Must be nonobvious
  - Must have some utility

12.6 Introduction to Patents

Table 12.3 PATENTS, TRADEMARKS, AND TRADE SECRETS

Patents provide rights for up to 20 years for inventions in these broad categories:

Utility patents protect useful processes, machines, articles of manufacture, and compositions of matter. Some examples are fiber optics, computer hardware, and medications.

Design patents guard the unauthorized use of new, original, and ornamental designs for articles of manufacture. The look of an athletic shoe, a bicycle helmet, and the *Star Wars* characters are all protected by design patents.

Plant patents are the way we protect invented or discovered, asexually reproduced plant varieties. Hybrid tea roses, Silver Queen corn, and Better Boy tomatoes are all types of plant patents.

Trademarks protect words, names, symbols, sounds, or colors that distinguish goods and services. Trademarks, unlike patents, can be renewed forever as long as they are being used in business. The roar of the MGM lion, the pink of the Owens-Corning Pink Panther, and the shape of a Coca-Cola bottle are familiar trademarks.

Copyrights protect works of authorship, such as writings, music, and works of art that have been tangibly expressed. The Library of Congress registers copyrights that last the life of the author plus 50 years. *Gone With The Wind* (the book and the film), Beatles recordings, and video games are all copyrighted.

Trade Secrets are information that companies keep secret to give them an advantage over their competitors. The formula for Coca-Cola is the most famous trade secret.

Source: www.uspto.gov/web/offices/ac/ahrpa/opa/museum/1intell.htm

12.6 Introduction to Patents

- Patents are enforced for up to 20 years from earliest date of filing
- Must file an application that
  - Adequately describes the product
  - Discloses the best use of the product

12.6 Introduction to Patents

- Patenting DNA Sequences
  - Applicants must assert a utility for the claimed invention that is specific, substantial, and credible
    - Specific utility – must know exactly what the DNA sequence does
    - Substantial utility – defines a real-world use
    - Credible utility – must convince the patent office that the application is backed by sound science

12.7 Biotechnology Products in the Global Marketplace

- Biotechnology Is a Global Enterprise
  - World community is still in preliminary negotiations about the regulation of biotechnology products
- As a model, the European Union (EU) has created the European Agency for the Evaluation of Medicinal Products (EMEA)
  - Once a product is approved, can be marketed in all 15 countries in the EU