Exhibit 307

A History of the FDA and Drug Regulation in the United States

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For a more detailed history, please visit the FDA centennial website at http://www.fda.gov/centennial/history/history.html

1820

Eleven doctors set up the U.S. Pharmacopeia and record the first list of standard drugs.

1848

Drug Importation Act passed by Congress requires U.S. Customs Service inspection to stop entry of tainted, low quality drugs from overseas.

1883

Dr. Harvey W. Wiley becomes the chief chemist at the Bureau of Chemistry's food adulteration studies.

1905

The American Medical Association (AMA) begins a voluntary program of drug approval that would last until 1955. In order to advertise in the AMA and related journals, drug companies must show proof that the drug will treat what they claim.

1906

The original Food and Drug Act is passed by Congress on June 30 and signed by President Theodore Roosevelt. The Act outlaws states from buying and selling food, drinks, and drugs that have been mislabeled and tainted.

1911

In **U.S. v. Johnson**, the Supreme Court rules that the 1906 Food and Drugs Act does not outlaw false medical claims but only false and misleading statements about the ingredients or identity of a drug.

1912

Congress passes the **Sherley Amendment** to overcome the ruling in U.S. v. Johnson. The Act outlaws labeling medicines with fake medical claims that is meant to trick the buyer.

1930

The name of the Food, Drug, and Insecticide Administration is shortened to **Food and Drug Administration (FDA)** under an agricultural appropriations act.

1933

FDA recommends a total rewrite of the out-of-date 1906 Food and Drugs Act.

1937

Elixir Sulfanilamide, contain the poisonous liquid, diethylene glycol, kills 107 persons, many of whom are children, dramatizing the need to establish drug safety before marketing and to pass the pending food and drug law.

1938

Congress passes **The Federal Food, Drug, and Cosmetic (FDC) Act** of 1938, which requires that new drugs show safety before selling. This starts a new system of drug regulation. The Act also requires that safe limits be set for unavoidable poisonous matter and allows for factory inspections.

The Federal Trade Commission is given power to oversee advertising for all FDA-regulated products except prescription drugs.

FDA states that sulfanilamide and other dangerous drugs must be given under the direction of a medical expert. This begins the **requirement for prescription only (non-narcotic) drugs** (see 1951 Durham-Humphrey amendment).

1941

Nearly 300 deaths and injuries result from the use of sulfathiazole tablets, an antibiotic, tainted with the sedative, phenobarbital. In response, FDA drastically changes manufacturing and quality controls. These changes lead to the development of **good manufacturing practices (GMPs).**

1948

The Supreme Court rules in **U.S. v. Sullivan** that FDA jurisdiction extends to retail stores, thereby allowing FDA to stop illegal sales of drugs by pharmacies including barbiturates and amphetamines.

1950

In **Alberty Food Products Co. v. U.S.**, a U.S. Court of Appeals rules that the directions for use on a drug label must include the drug's purpose.

1951

Congress passes the **Durham-Humphrey Amendment**, which defines the kinds of drugs that cannot be used safely without medical supervision. The amendment limits sale of these drugs to prescription only by a medical professional. All other drugs are to be available without a prescription.

1952

A nationwide investigation by FDA reveals that chloramphenicol, an antibiotic, caused nearly 180 cases of often deadly blood diseases. Two years later FDA engages the American Society of Hospital Pharmacists, the American Association of Medical Record Librarians, and later the American Medical Association in a **voluntary program of drug reaction reporting**.

1953

The **Factory Inspection Amendment** clarifies previous law and requires FDA to give manufacturers written reports of conditions seen during inspections and results of factory samples.

1962

Thalidomide, a new sleeping pill, causes severe birth defects of the arms and legs in thousands of babies born in Western Europe. The U.S. media reports on how Dr. Frances Kelsey, a FDA medical officer, helped prevent approval and marketing of Thalidomide in the United States. These reports stirred up public support for stronger drug laws.

Congress passes the **Kefauver-Harris Drug Amendments**. For the first time, these laws require drug makers to prove their drug works before FDA can approve them for sale.

The Advisory Committee on Investigational Drugs meets for the first time. This was the **first meeting of a committee to advise FDA** on product approval and policy on an ongoing basis.

1966

FDA contracts with the National Academy of Sciences/National Research Council to measure the **effectiveness of 4,000 marketed drugs** approved on the basis of safety alone between 1938 and 1962.

The **Fair Packaging and Labeling Act** requires all consumer products, in interstate commerce, to be honestly and informatively labeled.

1968

FDA forms the **Drug Efficacy Study Implementation (DESI)** to carry out recommendations of the National Academy of Sciences Investigation of the effectiveness of drugs first sold between 1938 and 1962.

1970

FDA requires the first **patient package insert**, medicines must come with information for the patient about risks and benefits.

1972

Over-the-Counter Drug Review begins to enhance the safety, effectiveness and appropriate labeling of drugs sold without prescription.

1973

The U.S. Supreme Court upholds the 1962 drug effectiveness law and approves FDA's action to control entire classes of products.

1982

FDA issues Tamper-resistant Packaging Regulations to prevent poisonings such as deaths from cyanide placed in Tylenol capsules. Congress passes the Federal Anti-Tampering Act in 1983, making it a crime to tamper with packaged consumer products.

1984

Drug Price Competition and Patent Term Restoration Act (Hatch-Waxman Act) increases the availability of less costly generic drugs by allowing FDA to approve applications for generic versions of brand-name drugs without repeating the research that proved the safety and effectiveness of the brand-name drugs. The Act also allowed brand-name companies to apply for up to five years additional patent protection for the new medicines they developed to make up for time lost while their products were going through FDA's approval process.

1989

The FDA issued guidelines asking drug makers to decide if a drug is likely to have **usefulness in elderly people** and to include elderly people in studies when applicable.

1991

In 1981, the FDA and the Department of Health and Human Services published a ~~policy~~ on protecting people in research. In 1991, this policy is adopted by more than a dozen federal agencies involved in human subject research and becomes known as the **Common Rule**.

1993

FDA launches **MedWatch**, a system designed to collect reports from health professionals on problems with drugs and other medical products.

FDA issues guidelines for measuring **gender differences in responses to medication**. Drug companies are encouraged to include patients of both sexes in their research of drugs and to study any gender-specific effects.

1995

FDA declares **cigarettes** to be "drug delivery devices." Limits are issued on marketing and sales to reduce smoking by young people.

1998

FDA introduces the **Adverse Event Reporting System (AERS),** a computerized database designed to store and study safety reports on already marketed drugs.

The **Demographic Rule** requires that a marketing application review data on safety and effectiveness by age, gender, and race.

The **Pediatric Rule** requires drug makers of selected new and existing drugs to conduct studies on drug safety and effectiveness in children.

1999

Creation of the **Drug Facts Label** for OTC drug products. The law requires all over-the-counter drug labels to have information in a standard format. These ***drug facts*** labels are designed to give the user easy-to-find information.

2000

The U. S. Supreme Court, upholds an earlier decision from Food and Drug Administration v. Brown & Williamson Tobacco Corp. et al. and rules 5-4 that **FDA does not have authority to regulate tobacco as a drug**.

2002

The Best Pharmaceuticals for Children Act, in exchange for studying the drug in children, the drug maker gets six months of selling their product without competition.

2003

The Pediatric Research Equity Act gives FDA the right to ask drug companies to study the effectiveness of new drugs in children.

2004

FDA advises medical professionals to limit the use of a pain reliever called Cox-2, a nonsteroidal anti-inflammatory drug (NSAIDs). Studies had shown that long-term use raised chances of heart attacks and strokes. The warning is also added to the over-the-counter NSAIDs' *Drug Facts* label.

Medicines used in hospitals must have a bar code to prevent patients from receiving the wrong medicine.

2005

The **Drug Safety Board** is formed, consisting of FDA staff and representatives from the National Institutes of Health and the Veterans Administration. The Board advises the Director, Center for Drug Evaluation and Research, FDA, on drug safety issues and works with the agency in sharing safety information to health professionals and patients.

The Future