The History of Clinical Trials

In honor of International Clinical Trials Day, this interactive timeline depicts the history of clinical trials. Read our summaries of each event and explore the links to the various sources.

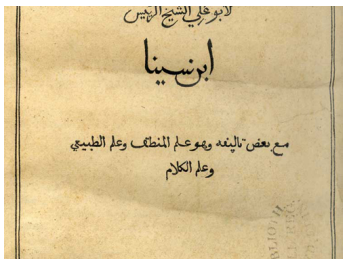
Lilly TRIALS

Options

~500 B.C.E.

Early Documented Experiment

An early documented experiment resembling a clinical trial was recorded in the Book of Daniel of the Bible. Daniel did not want to eat the king's meat or drink his wine. So some youths were fed a diet of meat and wine, while others were fed a diet of peas, beans, and water. At the end of the 10-day experiment, the youths who had been fed peas, beans, and water "appeared fairer and fatter in flesh." Read More >

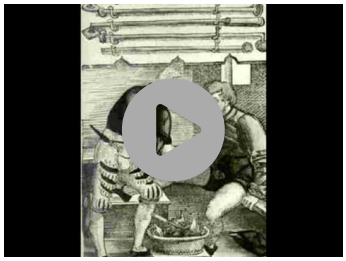


1025

Basis of Modern Clinical Trials Described

In *The Canon of Medicine*, Avicenna described seven practical rules for the experimental use and testing of medicines, forming the basis of modern clinical trials. Read More >

Categories: People



1537

First Clinical Trial of a Novel Therapy

Ambroise Paré, a French military surgeon, accidentally conducted the first clinical trial of a novel therapy because he ran out of the standard therapy on the battlefield and was forced to find an alternative. Paré tested a tincture of egg yolk, turpentine, and oil of roses against the standard therapy of boiling oil for sealing soldier wounds. Read More ›

Categories: People

1667

First Mention of Paid Experimental Subject

The first documented experiment involving a paid subject was noted in a diary entry by Samual Pepys. According to the entry, the local university hired a "poor and debauched man" to have sheep blood "let into his body." Read More ›

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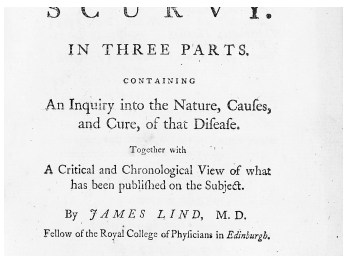

IN THREE PARTS.

CONTAINING

An Inquiry into the Nature, Cauſes, and Cure, of that Diſeaſe.

Together with

A Critical and Chronological View of what has been publiſhed on the Subject.

By JAMES LIND, M. D.

Fellow of the Royal College of Phyſicians in Edinburgh.

1747

First Controlled Trial

Dr. James Lind, a Scottish naval surgeon, conducted the first controlled clinical trial by testing six proposed remedies to treat scurvy in sailors. He found that oranges and lemons were far better than the other five proposed treatments. Read More ›

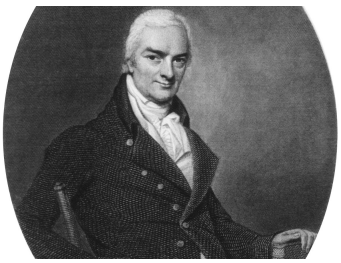
Categories: People

1785

Placebo Enters Medical Usage

The word "placebo" appeared in the George Motherby's *New Medical Dictionary*, which described it as "a commonplace method or medicine." Read More ›

Categories: People



1799

Placebo Effect First Demonstrated

John Haygarth designed a study comparing metal rods ("Perkins tractors"), a common treatment at the time, with wooden rods shaped and painted to look like metallic ones. Haygarth's study was one of the earliest, if not the first, placebo-controlled single-blind studies. Read More ›

Categories: People

1811

Placebo First Defined

The word "placebo" was first defined in *Quincy's Lexicon-Medicum*, a medical dictionary, as "an epithet given to any medicine adapted more to please than benefit the patient." Read More ›

1813

U.S. Vaccine Act

The U.S. Vaccine Act of 1813 was passed, making it the first U.S. federal law addressing consumer protection and therapeutic substances. Read More ›

Categories: Regulatory

1848

U.S. Import Drugs Act

The U.S. Import Drugs Act of 1848 was passed, making it the U.S. federal government's first attempt at drug regulation. Read More ›

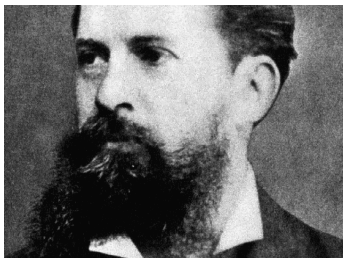
Categories: Regulatory

1862

Origin of U.S. Food and Drug Administration (FDA)

The newly created U.S. Department of Agriculture inherited the responsibility of conducting chemical analyses of agricultural products. Later, this department would come to be known as the Food and Drug Administration (FDA). Read More ›

Categories: Regulatory



1885

Randomization First Used

Charles S. Peirce and Joseph Jastrow first used and described randomization in their article "On Small Differences in Sensation." Read More ›

Categories: People

1902

U.S. Biologics Control Act Passed

The U.S. Biologics Control Act of 1902, also known as the Virus-Toxin Law, first gave the federal government control over the processes used for the production of biological products. It was passed in response to the deaths of 13 children who received a diphtheria antitoxin contaminated with tetanus. Read More ›

Categories: Regulatory

1905

American Medical Association (AMA) Begins Evaluating Drugs

The American Medical Association (AMA) had unsuccessfully pushed for federal evaluation of new medical products. So it formed the Council on Pharmacy and Chemistry to evaluate drugs for quality and safety. Drugs accepted by the Council could carry the AMA's Seal of Acceptance and advertise in the Journal of the American Medical Assocation (JAMA). Read More ›

1906

U.S. Pure Food and Drugs Act Passed

The U.S. Pure Food and Drugs Act of 1906 created regulatory enforcement power for what would later be called the Food and Drug Administration (FDA) and prohibited the interstate transport of misbranded and adultered foods, drinks, and drugs. The Act was signed by President Theodore Roosevelt and became the first comprehensive federal drug law.

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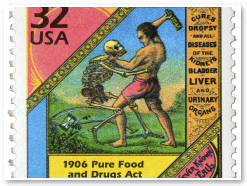

1908

Double-Blinding First Used

W.H.R. Rivers first used and described double-blinding in his study of the influence of alcohol and other drugs on fatigue.

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Categories: People

1911

U.S. v. Johnson Ruling

In the *U.S. v. Johnson*, the Supreme Court ruled that the Pure Food and Drugs Act of 1906 did not prohibit false therapeutic claims. It only prohibited "false and misleading" label claims about the ingredients or identity of the drug. The product involved in the ruling was called Dr. Johnson's Cure for Cancer. Read More ›

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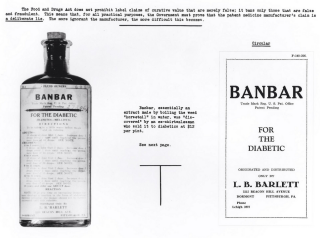

1912

U.S. Sherley Amendment Passed

The Sherley Amendment was passed to remedy the U.S. Pure Food and Drugs Act's failure to address false therapeutic claims. The Amendment prohibited false therapeutic claims "intended to defraud" the consumer. But regulators soon found that proving intent was a difficult task when prosecuting the maker of Banbar, a diabetic "cure." Read More ›

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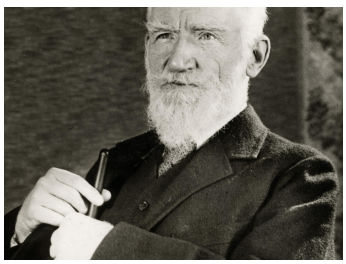

1913

Human Guinea Pig Coined

The playright George Bernard Shaw coined the term "human guinea pig" to negatively equate human and animal research experimentation. Shaw was an antivivisectionist, or someone opposed to experimentation on animals. At that time, Shaw and other vivisectionists were also very critical of human experimentation. Read More ›

Categories: People

1925

Need for Randomization First Described

In his book *Statistical Methods for Research Workers*, R. A. Fisher first stated the requirement of randomization in experimental design. Fisher, a statistician and geneticist, argued that randomization eliminated bias and permitted a valid test of significance. Read More ›

Categories: People

1937

Sulfanilamide Disaster

A new liquid preparation of sulfanilamide, a drug used to treat strep throat, killed over 100 people. The solvent used to suspend the active ingredient was a poison and the drug had not been tested in animals or humans prior to marketing. The disaster prompted a public outcry and passage of the U.S. Food, Drug, and Cosmetic Act. Read More ›

Categories: Regulatory

1938

U.S. Food, Drug, and Cosmetic Act Passed

The U.S. Food, Drug, and Cosmetic Act of 1938, which was signed by President Franklin Roosevelt, was passed to overhaul the 1906 law. It granted the U.S. Food and Drug Administration (FDA) new authority, including enforcement of the requirement that drugs must be proven safe before marketing. Read More ›

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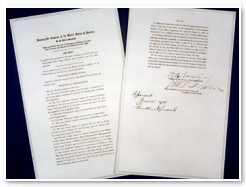

1947

Nuremberg Code Published

The Nuremberg Code, a landmark document on medical ethics, was formulated in response to the atrocities of World War II. The Code was based on a memorandum by Dr. Andrew Ivy and described ten research ethics principles for human experimentation. The first of these principles stated that the "voluntary consent of the human subject is absolutely essential." Read More ›

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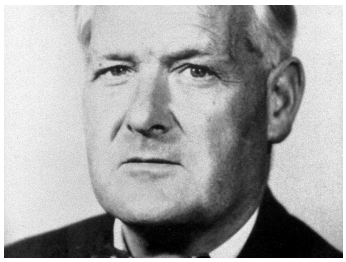

1948

Randomization Popularized

A. Bradford Hill published a study using randomization, which led to widespread use of randomization in clinical trial design. Hill was testing a promising antibiotic called streptomycin for the treatment of tuberculosis, but he was short on drug supply. This shortage is what prompted Hill to randomly assign patients to treatment and control groups. Read More ›

Categories: People

1949

International Code of Medical Ethics Adopted

The International Code of Medical Ethics described the duties of physicians in general, of physicians to the sick, and of physicians of doctors to each other. It was adopted by the World Medical Assocation (WMA) at the World Medical Assembly in London. Read More ›

Categories: Regulatory

1953

Origin of Institutional Review Boards (IRBs) in U.S.

The U.S. National Institutes of Health (NIH) began requiring that all clinical research in its Bethesda center obtain review from a human subjects protection review panel. The rules governing institutional review boards were later expanded and revised in 1966, 1971, and 1974. Read More ›

Categories: Regulatory

1958

U.S. Kefauver Hearings

U.S. Senator Estes Kefauver held hearings on the drug industry beginning in 1958. The hearings brought attention to the poor state of clinical trials under the 1938 drug law. However, amendments to that law were not passed until 1962, when the thalidomide tragedy served as a catalyst.

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1961

U.S. Food and Drug Administration (FDA) Began Regulating Clinical Trials

The U.S. Food and Drug Administration (FDA) began using its authority to regulate clinical trials in 1961, though this authority had been granted with the passage of the 1938 Food, Drug, and Cosmetic Act. Read More ›

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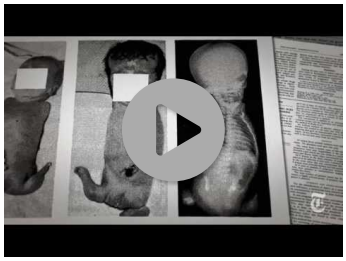

1961

Thalidomide Tragedy

Thalidomide was found to have caused severe birth defects in thousands of children. The drug had been used as a sedative and for the treatment of morning sickness in Europe. This tragedy made clear the need for rigorous testing of drugs prior to their introduction on the market. Read More ›

Categories: Regulatory

1962

U.S. Passage of Kefauver-Harris Amendments

Amendments to the U.S. Food, Drug, and Cosmetic Act created a framework requiring drug manufacturers to prove a drug was both safe and effective. The amendments were sponsored by Sen. Estes Kefauver and Rep. Oren Harris and signed into law by President Kennedy. Read More ›

Categories: Regulatory, People

1963

U.S. Food and Drug Administration (FDA) Required Informed Consent

The U.S. Food and Drug Administration (FDA) established 21 CFR 130.3, which was later incorporated in 45 CFR 46, requiring clinical investigators to certify informed consent as required by the Kefauver-Harris amendments. Read More ›

Categories: Regulatory

1964

Declaration of Helsinki Adopted

The Declaration of Helsinki established the first set of formal international principles to guide the protection of human participants in medical research. It was adopted by the World Medical Association (WMA) at the World Medical Assembly in Helsinki. The Declaration has been revised over time, but it remains a standard in medical research ethics and has been codified into laws in countries around the world. Read More ›

Categories: Regulatory

1966

United Nations Prohibited Medical Experimentation Without Consent

Article 7 of the International Covenant on Civil and Political Rights (ICCPR), which was adopted by United Nations General Assembly, prohibited medical experimentation without consent. Read More ›

Categories: Regulatory

1966

Independent Review Required in U.S.

The U.S. Surgeon General issued a policy statement requiring that human subject research have independent prior review, thus creating the need for institutional review boards. Read More ›

Categories: Regulatory

1966

Dr. Henry Beecher's Article Published

Dr. Henry Beecher published his influential essay "Ethics and Clinical Research," spurring a reconsideration of research practices and serving as the foundation for today's ethical codes and committees. Beecher described ethical lapses in research conducted by renowned physicians, scientists, and universities and published in the world's leading journals. His exposure of these lapses prompted a public realization that poor treatment of human subjects was not limited to Nazi doctors. Read More ›

Categories: People, Regulatory

1972

Discovery of Tuskegee Study

The Associated Press published a story about the Tuskegee syphilis experiment, creating a public outcry. The study, which was called "Tuskegee Study of Untreated Syphilis in the Negro Male," was conducted by the Public Health Service and the Tuskegee Institute beginning in 1932. The researchers had not informed the men of the study or its real purpose, nor had they offered the men penicillin after it became the standard treatment in 1947. Read More ›

Categories: Regulatory

1974

U.S. National Research Act Passed

In response to the Tuskegee study, the U.S. National Research Act of 1974 was passed, creating the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission was tasked with identifying research ethics principles, as well as mechanisms to ensure those principles were followed. Read More ›

Categories: Regulatory

1974-1978

First National Bioethics Commission in U.S.

As mandated by the National Research Act, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research met to deliberate research ethics principles. The Commission first convened during an intensive four-day period at the Smithsonian Institution's Belmont Conference Center and then during monthly deliberations over the course of four years.

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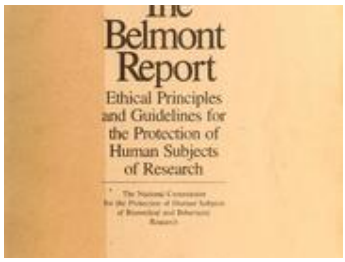
1978

Society for Clinical Trials Organized

The Society for Clinical Trials, an international professional organization, was created to develop and discuss the design and analysis of clinical trials. Read More ›



1979

Belmont Report Released in U.S.

The Belmont Report summarized the ethical recommendations identified during deliberations of the National Commmission for the Protection of Human Subjects of Biomedical and Behavioral Research. It described basic ethical principles to guide research on human subjects and served as a basis for subsequent federal regulation. Read More ›

Categories: Regulatory

1981

Human Subjects Research Regulations Revised in U.S.

The U.S. Department of Health and Human Services (HHS) and the Food and Drug Administration (FDA) revised the regulations governing human subjects research. These revisions were intended to make the regulations more consistent with the recommendations in the Belmont Report. Read More ›

Categories: Regulatory

1982

International Guidelines for Biomedical Research Involving Human Subjects Released

The World Health Organization (WHO) and the Council for International Organizations of Medical Sciences (CIOMS) released the "International Guidelines for Biomedical Research Involving Human Subjects." The document was intended to help countries apply the principles of the Declaration of Helenski and the Nuremberg Code and to provide universal guidelines that could be used globally. Read More ›

Categories: Regulatory

1991

The Common Rule Published in U.S.

The U.S. Department of Health and Human Services (HHS) published the Federal Policy for the Protection of Human Subjects as part 46 of Title 45 of the Code of Federal Regulations. Fifteen agencies and department subsequently codified this policy, earning it the name "The Common Rule." Other federal statutes and regulations have requirements related to human subjects research, but the Common Rule is the primary set of requirements. Read More ›

Categories: Regulatory

1996

International Good Clinical Practice Guidelines Issued

The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) issued guidelines for Good Clinical Practice (GCP). ICH-GCP is a harmonized standard that "protects the rights, safety and welfare of human subjects, minimises human exposure to investigational products, improves quality of data, speeds up marketing of new drugs and decreases the cost to sponsors and to the public." Read More ›

Categories: Regulatory

2000

World Health Organization (WHO) Issued Institutional Review Board (IRB) Guidelines

The World Health Organizations issued operational guidelines for ethics committees "to facilitate, support, and ensure quality of the ethical review of biomedical research in all countries around the world." Read More ›

Categories: Regulatory

2000

ClinicalTrials.gov Released

The U.S. National Library of Medicine (NLM), in collaboration with the Food and Drug Administration (FDA) and others, released the first version of ClinicalTrials.gov, which primarily listed clinical trials funded by the National Institutes of Health (NIH). Read More ›

2007

International Clinical Trials Registry Platform (ICTRP) Released

The World Health Organization (WHO) released the first version of the International Clinical Trials Registry Platform (ICTRP). It included a search portal to access studies registered in various international registries. WHO had previously stated in 2006 that all clinical trials should be registered. Read More ›

2007

ClinicalTrials.gov Expanded

With the Food and Drug Administration Admendments Act of 2007 (FDAAA), U.S. Congress expanded the requirements for submission to ClinicalTrials.gov. These requirements included registration of more types of trials, adding new registration information, submission of summary results, and inclusion of adverse events for certain trials. Read More ›

Categories: Regulatory

2008

ClinicalTrials.gov Results Provided

ClinicalTrials.gov began allowing sponsors and investigators to submit the results of clinical studies. Read More ›

2008

Declaration of Helskinki Amended

The World Medical Association (WMA) General Assembly amended the Declaration of Helsinki to promote trial registration and results dissemination. Two added principles stated that registration and results dissemination were ethical obligations. Read More >

Categories: Regulatory

2013

European Medicine Agency (EMA) Expands Trial Database

The European Medicines Agency (EMA) released a new version of the European Clinical Trials Database (EudraCT) to include summary results. Read More >

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1537 First Clinical Trial of a Novel Therapy

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Painting of Samuel Pepys by John Hayls (1600–1679)

1747 First Controlled Trial
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1785 Placebo Enters Medical Usage

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Portrait of John Haygarth by J.H. Bell

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Title page of *Quincy's Lexicon-Medicum* by National Library of Medicine (NLM)

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1848 U.S. Import Drugs Act

1862 Origin of U.S. Food and Drug Administration (FDA)
U.S. Food and Drug Administration logo by Food and Drug Administration (FDA)

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Portrait of Charles Peirce by National Oceanic and Atmospheric Administration/Department of Commerce

1902 U.S. Biologics Control Act Passed

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1906 U.S. Pure Food and Drugs Act Passed

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U.S. Postal Service stamp commemorating the 1906 Pure Food and Drugs Act by Smithsonian National Postal Museum

1908 Double-Blinding First Used
Portrait of W.H.R. Rivers by Henry Maull

1911 *U.S. v. Johnson* Ruling

1912 U.S. Sherley Amendment Passed
Banbar label and circular by Food and Drug Adminisatration (FDA)

1913 Human Guinea Pig Coined
Photo of George Bernard Shaw by Unknown

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Elixir Sulfanilamide bottles by Food and Drug Administration (FDA)

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1958 U.S. Kefauver Hearings
U.S. Senator C. Estes Kefauver (D-TN) by Biographical Directory of the United States Congress

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1961 Thalidomide Tragedy

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1962 U.S. Passage of Kefauver-Harris Amendments

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After signing the Kefauver-Harris Amendments, U.S. President Kennedy presented a pen to Dr. Frances O. Kelsey by Food and Drug Administration (FDA)

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1972 Discovery of Tuskegee Study

YouTube Video

Group of men who were test subjects in the Tuskegee Study by National Archives and Records Administration

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