Biologics Centennial:
100 Years of Biologics Regulation

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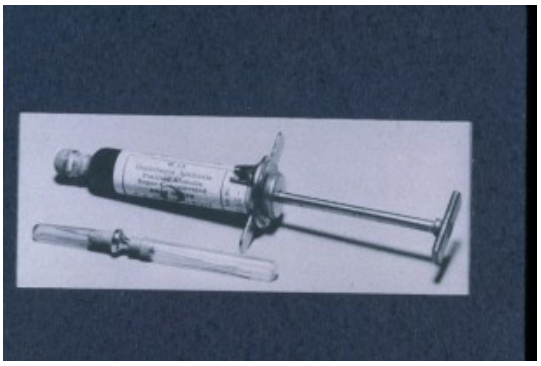
Suzanne White Junod, Ph.D.
FDA Historian

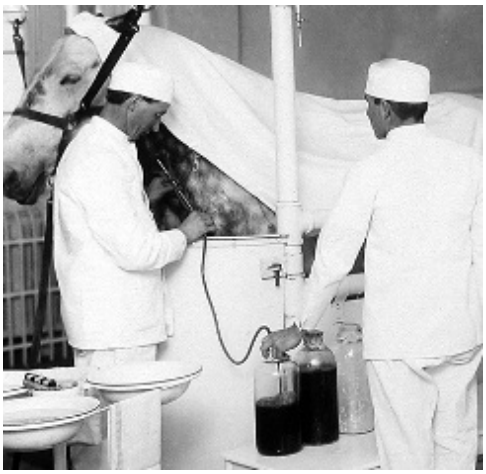
The late 19th century was one of the most exciting times imaginable for physicians and scientists working in biological research arenas around the world. Robert Koch in Germany was investigating and isolating the bacterial organisms responsible for anthrax, rabies, tuberculosis and cholera. In France, Louis Pasteur was studying the microorganisms causing fermentation and spoilage and developed the first laboratory vaccine to protect fowl from chicken cholera. American bacteriologists Theobald Smith and Edmund Salmon introduced the concept of heat killed vaccines and used it first to prepare a vaccine against hog cholera.

This burgeoning science of immunology began rapidly developing new vaccines and anti-toxins that promised to prevent and cure some of the most dangerous and dreaded epidemic diseases afflicting mankind. Researchers Emil von Behring and Shibasaburo Kitasato in Robert Koch's lab, for example, discovered that animals injected with diphtheria and tetanus toxins produced anti-toxins which could be inoculated into other animals to both cure and provide future immunity from these dread diseases. Their serum therapy was tested at Berlin's Charite` hospital at the end of 1891 and the chemical company Hoechst began commercial antitoxin serum production soon after. Mortality rates from diphtheria in Europe dropped dramatically and laboratories in the United States quickly rushed to begin production of these new life-saving biological products.

Municipal, State and National Biologics Regulation

The Hygienic Laboratory in Washington D.C. (the early Public Health Service) began a program to immunize horses to produce serum in large quantities. Likewise, serum production was begun at the Bacteriological Laboratory of the New York City Health Department. What Europe pioneered, the U.S. soon mass produced. Although the first standardized serums were produced in public health departments and state laboratories, commercial manufacturers soon developed expertise in creating the careful temperature controls and sterile conditions required to produce potent sera and vaccines, as well as the injection tools --aseptic syringes-- necessary for injecting these early biological drugs directly into the body, a particularly perilous procedure in the early days of the bacteriological revolution.





Production of diphtheria antitoxin by inoculating horses required great care to maintain purity and avoid contamination. Courtesy of National Archives and Records Administration.

According to Smithsonian expert, Ray Kondratas, although there had been concern voiced in both the medical and popular literature about the need for regulation, standardization, and quality control of these new biological products, at the turn of the century, nothing lay on the table but talk. (see Ramunas A. Kondratas, "Biologics Control Act of 1902," in J.H. Young, ed., "The Early Years of Federal Food and Drug Control," American Institute for the History of Pharmacy (Madison, WI: 1982)). In 1901, however, that changed quickly after a five year old girl in St. Louis died in the city hospital from tetanus. The admitting physician stated that she had most likely presented at the hospital nine days earlier with spinal meningitis, but was given the diphtheria anti-toxin prophylactically. What struck the municipal health officials investigating the case however, was the fact that when they located the horse from which the anti-toxin had been taken, they learned that the horse named Jim, who had produced over 30 quarts of diphtheria antitoxin in his career, had been destroyed after contracting tetanus. Investigators concluded that instead of destroying all of Jim's contaminated serum, two officials had allowed some of it to be distributed resulting in the deaths of twelve more children throughout St. Louis. Soon thereafter, nine children in New Jersey died from contaminated smallpox vaccine, setting the stage for the adoption of rigorous standards for the emerging biological products industry.

Unlike the fanfare accompanying passage of the Pure Food and Drugs Act of 1906, Theodore Roosevelt's signing of the Biologics Control Act of 1902 on July 1, 1902, was marked by neither comment nor discussion, much less publicity. The medical Society of the District of Columbus had taken the initiative in proposing the legislation, then the commissioners of the District of Columbia shepherded the bill through the District of Columbia Committees of both houses of Congress. Although the Public Health Service had been considering drafting similar legislation, Congress did not consult with the PHS before the legislation was enacted. Instead, it appointed the Surgeon General of the Marine Hospital Service, as well as those of the Army and Navy to a Board whose officials were tasked with promulgating regulations for licensing establishments engaged in the "sale and preparation of viruses, serums, toxins, and anti-toxins and analogous products in international or foreign commerce." Procedures for licensing manufacturing

establishments and expiration dates were included in the Act. Later, under the 1944 PHS Act, biological products, as well as their manufacturing establishments were licensed. In 1948, responsibility for biologics rested with the National Institutes of Health, but in 1972, responsibility for biologics control came to FDA.

Commemorating the Centennial of the 1902 Biologics Control Act

This year, FDA's Center for Biologics Evaluation and Research is honoring the first 100 years of biologics regulation by celebrating the Centennial of the Biologics Control Act. September 23 and 24, 2002 the Center sponsored a science symposium entitled, "Science and the Regulation of Biological Products: From a Rich History to a Challenging Future." The symposium was dedicated to the memory of Harry Meyer, Jr. co-developer of the first licensed rubella virus vaccine, while the Harry Meyer, Jr. lecture was delivered by his friend, colleague, and co-developer, Paul D. Parkman. A Centennial video was shown, and information on the conference as well as the commemorative booklet were presented on a web page.

Meanwhile, at the Smithsonian Institute's National Museum of American History, a case exhibit for the Centennial has been opened to the public. Entitled Safety for Millions: The Biologics Control Act of 1902 Centennial, FDA Historian John Swann and the staff of the museum's Division of Medical Sciences, headed by Ray Kondratas, as well as others at CBER, have worked to assemble an interesting array of artifacts exploring the evolution of biologics research and regulation. From early diphtheria antitoxins and a logbook on their testing from the Hygienic Laboratory in 1895, to diphtheria booklets and early licenses, the artifacts give a glimpse into the earliest U.S. regulation of these biological products. Timely are the exhibit's addition of a smallpox quarantine sign from 1919 and a vial of smallpox vaccine from the 1960s. Unusual polio artifacts including a Polio Pioneer card and pin as well as samples of polio vaccine which highlight the exhibit's portrayal of the 1950s safety debate over the killed (Salk) v. live (Sabin) vaccines against polio, including the Cutter Laboratories vaccine incident that highlighted concerns with regulation and the overall safety of the live polio vaccine. Finally, the exhibit covers the modern day AIDS crisis focusing on the safety of the blood supply and including examples of old blood irradiation devices as well as one of the first AIDS test kits.