

## Appendix 2.1

### HISTORICAL REVIEW AND TREND ANALYSIS OF VACCINE ESTABLISHMENT AND PRODUCT LICENSURE IN THE UNITED STATES (1902-67)<sup>1</sup>

#### The First Golden Era of Vaccines (1903-26)

From 1903 to 1916, the number of manufacturing establishments licensed to produce vaccines in the United States rose from 0 to 38, and the number of vaccine products licensed in this country rose from 0 to 367.

A sharp drop in both the number of licensed establishments and the number of licensed products occurred between 1916 and 1918. During World War I, many German and other European manufacturers ceased their American activity, so their licenses were revoked.

For the 9 years after World War I, vaccine licensure in this country significantly increased. By 1926, 40 manufacturing establishments held licenses for 422 products. Two factors probably contributed to the rapid escalation of vaccine activity immediately after the war. First, the medical profession at the time had little to offer patients in terms of effective treatment of infectious diseases, so prevention of such diseases may have been accorded a higher priority than treatment. Second, medical schools were developing research capabilities on which to base their educational programs, so medical science was growing. Thus, the combination of emphasis on prevention of infectious diseases and scientifically based medical research may have led to an increase in new vaccine products.

#### Decline During the Depression Years (1927-31)

From 1927 to around 1931, very few licenses were issued and several were revoked. The number of licensed vaccine manufacturing establishments during this period dropped from 40 to 33, and the cumulative number of licensed products dropped from 431 to 421. Quite possibly, some vaccine manufacturers were forced out of the vaccine business by the country's economic depression.

#### Second Golden Era of Vaccines (1932-40)

From 1932 to 1940, the vaccine business underwent tremendous growth. The number of manufacturers rose from 33 to 52, and the cumulative number of products rose from 448 to an all time high of 607. This growth may have reflected the accumulation of benefits derived from new scientific breakthroughs. Biologists and microbiologists were better able than ever before to isolate and grow organisms; vaccine technologies were improving; immunochemistry techniques were being refined; and the use of clinical trials helped scientists assess vaccine safety and efficacy in humans. With the inevitability of World War II looming, the American Government also may have encouraged the development and production of vaccines to supply U.S. armed forces.

#### Increasing Reliance on Antibiotics (1941-54)

A few years prior to the peak of vaccine activity in 1938, the first clinically successful sulfa drug, sulfapyridine, was introduced into medical practice. Within a few years, the emphasis on disease prevention through vaccination shifted to disease treatment with antibiotics. Antibiotics were often less expensive and less troublesome to administer than were vaccines, and the introduction of antibiotics eroded a growing effort to conduct epidemiologic studies of, and to prevent, pneumococcal diseases. (See appendix 1.1.)

From 1950 on, vaccine product and establishment licensure activity in this country generally declined. Several factors may have contributed to the overall—and continuing—decline. First, American pharmaceutical companies increased their emphasis on the discovery and development of antibiotics rather than immunizing agents. Antibiotics were popular, apparently effective, and profitable. In 1951, Congress passed the Humphrey-Durham Act which gave several drugs, including antibiotics, prescription status; this may have increased the promotion and use of antibiotics. Further, the pharmaceutical industry expanded its scope of research and production into several areas of therapeutics that were more profitable than were vaccines. The discovery of chloramphenicol, the tetracycline, and synthetic penicillin furthered the emphasis 'on treatment—rather than prevention—of infectious diseases.

<sup>1</sup>The number of licensed manufacturing establishments and licensed vaccine products in the United States for each year from 1903 through 1979 are represented in graphic form in figures 3 and 4 in ch. 2 of this report.