

# Preface

For those of us in vaccine analytical and process development, it was apparent that a central resource on analytics would be helpful, especially since many new organizations both in the developed and developing markets are working on new vaccine products. We thus solicited input from a variety of analytical leaders to put together this volume on analytics of vaccines. Historically, vaccines were relatively crude preparations and quality control testing was primarily focused on safety issues such as sterility and absence of adventitious agents as well as a potency testing as a surrogate for clinical performance. With the advent of more modern technology applied to biotech products, testing and release for many modern vaccines are carried out by sophisticated techniques such as Mass Spectrometry, PCR, NMR, HPLC, and Flow cytometry.

Vaccines have had a profound impact on preventing or eliminating many major diseases worldwide. Since vaccines are administered to healthy individuals, it is critical that their safety and efficacy be under strict control by carefully constructing the manufacturing process and the analytical Quality Control packages. Unlike low molecular weight drugs or modern biologics, vaccines have always been considered to be complex products manufactured by complex processes. This has manifested itself in strict control of the manufacturing process often expressed as “the process defines the product.” Corresponding quality control packages are an important part of the release paradigm based on classical safety technology and a potency assay developed at the time of licensure and correlated with clinical efficacy. Although this paradigm still exists today, the application of modern biotechnology analytical methods have opened up vaccine products for further characterization. Nevertheless, the diversity of vaccine products requires the application of a wide array of analytical and QC technologies.

The claim that a vaccine is *Safe* and *Efficacious* can only be asserted through proper control with suitable and capable analytical methods. This necessity was realized over 100 years ago when Milton Joseph Rosenau was the first to test mass produced Small Pox vaccine for potency and purity. (Willrich 2011) During the

twentieth century, as regulation, production fostered a shift from inactivated whole cell vaccines to purified subunit based vaccines because of enhanced safety profiles (Plotkin and Plotkin 2011; Zhao et al. 2013). Combination vaccines that contain multiple antigens required rigorous demonstration of maintenance of the individual components to confer lasting immunity (Galambos and Sewell 1995; Galambos and Sturchio 1996). The testing paradigm has not changed. However, the field is experiencing a shift in needs—rapid response for rapidly emerging Influenza epidemics, flexibility in location of manufacture, horizontal, and philanthropic vaccine production where individual components are furnished by unique entities either academic, government, or industry. Regardless of the evolved development of the field, the need for safety and efficacy remains paramount but their demonstration will require sound analytical control. Sound analytical control fulfills both regulatory oversight, e.g., ICH Q2 guidances and business needs by providing accurate and precise monitoring of critical structural elements from cell bank to drug substance and final drug product dosage form.

This book can serve as a reference for vaccine control for current and future vaccine platforms. The chapters in the book describe release testing and characterization technology applied to commercial vaccines as well as vaccines in late stage clinical development. The editors in conjunction with the contributors structured the book to detail analytical control for all current vaccine modalities. In addition, current topics that are supplemental to the actual implementation of an analytical control and that are confronting vaccine quality control and regulatory organizations are developed; and thus provide a vantage point for those in such endeavors. For these sections, authors offer a trajectory of guidance from experiences as vaccine production; distribution and market expand globally beyond established markets in the United States and Europe in the twenty-first century. Adjuvants, a critical component of most vaccine formulations (and delivery) were not included given their broad scope and mechanisms of immune stimulation and that many other excellent reviews exist at this time. Despite increasing technological improvements the need to have sound analytical control in clinical stages development for the maturation of process and formulation into reliable commercial control to assess safety and efficacy remain. The comprehensive descriptions of each chapter describe how analytical methodologies are employed and structured to support process control, release, and stability. As the intentions of the editors, *Vaccine Analysis*, offers a unique, single point of reference to capture analytical control strategies for all primary vaccine modalities.

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