Extended Abstract

Annals of Clinical Trials and Vaccines Research

Challenges and solutions for maintaining quality and potency of the product in vaccine development

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Immunization is one among the foremost successful and cost-effective health interventions known. Over the past several decades, immunization has achieved eradication of smallpox, lowered the global incidence of polio by 99%, and reduced illness, disability and death from vaccine-preventable diseases. More children are being reached with vaccination. With the addition of preventive campaigns to age groups at risk for meningitis A and yellow fever, access and use of vaccines by age groups other than infants is expanding.

Immunization is a key component behind the efforts taken to meet the Millennium Development Goals, particularly goal 4, which is reducing the child mortality rates. For the first time, the number of children dying each year has fallen below 10 million as a result of the combined impact of improved access to water and sanitation, increased immunization coverage and integrated delivery of essential health interventions. Part of this impact was due to the introduction of several new vaccines to most countries. Vaccines against hepatitis B and Haemophilus influenzae type b have become part of the national immunization program in 179 countries. Additional vaccines against priority diseases, such as pneumonia and diarrhea, have been introduced in many countries of the world and others against chronic diseases such as cervical cancer are following.

Currently, various solutions exist to ensure vaccine quality throughout the cold chain. Although all solutions explained below are available today, in a longer run, we expect more vaccines to become more stable which will have an impact on handing of vaccines through reducing the dependency on the cold chain. Controlled temperature chain approaches can also be considered as long-term solutions since it requires a lengthy process of national regulatory authorities' approval. In shorter term, the biggest challenge for all other available solutions is to incorporate them into immunization programs.

In order to ensure quality and integrity of the vaccine products, their storage and distribution conditions should be monitored continuously. The general practice for temperature monitoring in vaccine refrigerators at the periphery is to use a thermometer. A thermometer, however, only provides a snapshot of the temperature at the point in time when it is checked and cannot be considered as an 'appropriate' monitoring tool. If a temperature value of between +2°C and +8°C is found while checking, health workers may erroneously conclude that the vaccines are safe since this snapshot reading provides a value only when it is checked and does not cover the rest of the daytime/nighttime period. Unless a temperature excursion is seen at the time the temperature is checked with a daily thermometer, most temperature violations go unnoticed

In recent years, quality assurance (QA) and good manufacturing practice (GMP) became increasingly important within the pharmaceutical industry. They are of particular importance within the manufacture of veterinary vaccines since such products have the subsequent specific characteristics: The active ingredients are nearly always produced by the manufacturer. Vaccine production usually requires cultivation steps, including growth of the acceptable organism and therefore the use of drugs of animal origin, which makes it easy to introduce a contaminant and to amplify low levels of contamination. As the end product is not usually subjected to a final sterilization step, prior to final formulation its constituents should be particularly well protected against contamination and crosscontamination.

Manufacture requires the handling of live organisms which are sometimes pathogenic for hurnans and / or animals. The release of these agents, with the possibility of contamination/ cross-contamination, has to be regarded as a serious danger and, depending on the organism involved, the workers and the environment, together with all the materials, should be well protected. Moreover, the extent of risk is further exacerbated by the massive number of animal species and potential pathogenic agents. The variety d manu during of products manufactured is very great but the volume of manufacture is sometimes quite low, so manufacturing operations based on the sharing of equipment and facilities is common. In addition, other activities such as diagnosis and research are frequently linked to manufacture and this may result in opportunities for crosscontamination

Vaccine manufacture may be a complex activity, with risks, which is administered during a complicated environment. Particular aspects of the work are important in relation to potential problems of contamination, for example contamination of the product, cross-contamination, possible amplification of contamination organisms and contamination of workers and the environment. These factors, along side the inherent variability of biological agents and materials and therefore the relative inefficiency of internal control tests in providing adequate reassurance for final products, means the roles of the QA system and GMP are of the utmost crucial in the Vaccine Manufacturing. Not only should the wants of general current GMP for medicinal products be applied but also the precise requirements of particular products. The need to take care of control over all aspects of GMP can't be overemphasized. In this chapter, a summary of QA and GMP, with special attention to a number of the actual requirements of vaccine manufacture, are going to be given. It has to be emphasized that responsible persons in vaccine manufacturing must have an honest knowledge of the wants of QA and GMP, and people liable for research and development have to appreciate the significance of QA.

The quality of vaccines is increasingly guaranteed by the use of robust and reproducible production processes. FDA and other regulatory agencies generated recommendations and guidelines to ensure high-quality levels.

The present talk will be a focus on the discussions of the following areas:

• Why need to assess the quality and the potency of vaccine product from early phase through the late phase vaccine development, even after licensure of the product.

• Strategy thinking and planning in the assessment of the potency and safety of Human Vaccine: in vivo animal assay vs. in vitro assays.

• Cases studies to demonstrate the challenges and solutions to timely evaluate the quality and potency of vaccine products.

• Regulatory considerations of the potency evaluation of vaccine products.