



Vaccine safety

A specialised group within EFPIA

THE ROLE OF THE VACCINE INDUSTRY

One of the highest priorities for vaccine manufacturers, as well as for government agencies that regulate the industry, is the safety of vaccines. Since vaccines are administered to prevent disease among people potentially at risk of infection, manufacturers must be held accountable to the highest standards of safety and quality. Unlike medicines that are used to cure illness or to alleviate symptoms, vaccines are given to large and diverse groups of people worldwide, with no perceived or immediately obvious health benefit to the person who is vaccinated.

REINFORCING VACCINE SAFETY MEASURES

The vaccine industry continues to work with regulatory authorities, the scientific community and academic institutions to address vaccine safety issues. In addition to ongoing surveillance studies, there are other safety measures currently under consideration, such as:

- vaccine traceability (i.e., using detachable / peel-off stickers on vials or syringes to provide information in readable form or through bar coding);
- vaccine registers to record patient vaccination data, and
- the enhancement of established programs such as adverse event monitoring and alerting systems at European level.

A TIGHTLY REGULATED ENVIRONMENT VACCINE LICENSING IN EUROPE

Since 1995, biotechnological vaccines or innovative vaccines may be licensed through the centralised procedure established by the European Agency for Evaluation of Medicinal Products (EMA). Consequently, community-marketing authorisations are granted for the EU-member countries. Vaccines that are not eligible for the centralised procedure by EMA, may be licensed by national regulatory authorities, according to the mutual recognition procedure (MRP). Whatever the registration procedure used, EMA also provides advice on measures necessary to ensure the safe and effective use of these products, for instance by evaluating information from a database on Adverse Drug Reaction (ADR) reports.

These biological products cannot be commercialised until they have been

tested by an official medicines control laboratory (OMCL) according to specific guidelines on batch release established by the European Directorate for the Quality of Medicines (EDQM).

Since December 2001, EMA has put into operation an electronic system, called EudraVigilance. EudraVigilance is a data-processing network and database management system for the exchange and evaluation of Individual Case Safety Reports (ICSR). The system allows rapid exchange of information on adverse reactions and medicines' safety among all stakeholders (i.e., the competent authorities of the Member States, as well as Iceland, Liechtenstein and Norway, and the vaccine manufacturer).

PRE-LICENSING – THREE PHASES OF CLINICAL TRIALS

Before a vaccine is licensed, it is thoroughly tested to establish its quality, safety and efficacy. This period of vaccine development may take at least ten years. Even before becoming a candidate vaccine for investigation among human volunteers, the vaccine and its clinical development program are first reviewed by regulatory authorities and Ethics Review Committees. Throughout the succeeding period of clinical research, each vaccine batch passes rigorous quality control tests, complying with Good Manufacturing Practices that demonstrate absolute consistency in terms of safety, potency and purity.

Pre-licensing clinical trials are first carried out among a small number of healthy volunteers to test the safety

of various vaccine doses and to document any short-term side effects. The second phase of clinical trials may include as many as several hundred volunteers, and is designed to generate more information regarding the vaccine's safety and its potential to induce a protective immune response, which is referred to as the vaccine's "immunogenicity."

The third phase may involve thousands to tens of thousands of volunteers, and is carried out to confirm that the vaccine prevents the disease (i.e., vaccine efficacy) with minimal side effects (safety and tolerance). Once the vaccine has passed the requirements for quality, safety and efficacy, it can then be submitted to the authorities for licensing.

VACCINE EVALUATION NEVER STOPS

Vaccine pharmacovigilance or “vaccinovigilance,” is the continual evaluation and monitoring of a vaccine’s safety after it has received marketing authorisation.

After a vaccine is licensed for use, ongoing large-scale post-marketing surveillance studies assess the vaccine’s impact on the disease in the community. During these large-scale vaccine effectiveness studies, vaccine safety monitoring continues, which may include reports of rare events or of events not noted during the clinical development programme.

Such studies may also reveal positive outcomes, such as the post-marketing surveillance studies that were carried out among children in Europe where mass vaccination against invasive Hib (*Haemophilus influenzae* type b) disease or invasive meningococcal C disease showed levels of vaccine protection that were superior to those than had been anticipated from the clinical trial results.

Vaccine manufacturers are mandated to prepare detailed reports and analysis of all “serious adverse events” that occur after a vaccination session (whether or not the event can be attributed to the vaccine), which are then sent to the competent regulatory authorities.

VACCINE MISCONCEPTIONS – THEN...



Courtesy of the National Library of Medicine

... AND NOW

Today, as diseases begin to disappear from communities, a sense of false security fosters the misconception that vaccination is no longer necessary. However, when vaccination is stopped, the disease may return. In Ireland and the United Kingdom, for example, recent outbreaks of childhood measles have occurred due to inadequate coverage of MMR (Measles-Mumps-Rubella) vaccine caused by unsubstantiated allegations linking the vaccine to autism or inflammatory bowel disease.

Many childhood illnesses that occur frequently during the first year of life are accompanied by fever or malaise. Children in their first year are also susceptible to diseases such as Sudden Infant Death Syndrome (SIDS) and developmental disorders, and later to diabetes. With so many millions of vaccines given worldwide every year during this time of a child’s life, the laws of probability reveal that a serious adverse event may occur during any period following vaccination.

CHALLENGES IN A CHANGING GLOBAL ENVIRONMENT

With increasingly tighter government regulations and a public expectation for effective vaccines at zero risk, communication campaigns that promote the benefits of immunisation may consequently be carried out in an environment that no longer sees the disease but only focuses on reports of adverse events. While no medical intervention is 100% risk-free, the risk of a serious illness or complication from a vaccine-preventable disease is much greater than the chance of any complication from the vaccine. The polio immunisation campaigns that were carried out during the 1950s and 1960s were hugely successful and

Public concerns about vaccine safety date back to 1798 when Edward Jenner tested cowpox as a means to vaccinate against smallpox. Early anti-vaccination groups called the procedure “unnatural” with the potential to produce animal disease as well as bovine characteristics in humans. Fear of smallpox disease, however, was greater than any concerns over the vaccine – on 8 May 1980, after years of the global immunisation campaign, the Thirty-third World Health Assembly officially confirmed the eradication of smallpox.

Consequently, adverse events that occur close to the time of vaccination may not be due to the vaccine itself – but occur as a coincidence. Reports of adverse events following vaccination may be misinterpreted or misunderstood by assuming that the vaccine necessarily caused the event. While there is a temporal association between the event and the vaccination, this association is not considered sufficient to establish causality.

Individual case reports of adverse events may be based on anecdotal case reports or on data that do not adequately support a causal association. Such reports may reflect incomplete reporting, unverified diagnoses, and lack of background information to determine how many other persons who did not receive the vaccine experienced the same disorder. For this reason, individual case reports alone are often not considered sufficient evidence to establish a causal association and may require further investigation.

driven by direct evidence of the crippling disease.

During the subsequent course of successful vaccination campaigns, there may come a point in time when adverse events such as redness at the injection site or brief fever become more frequent than the actual number of cases of disease. Today, public confidence in vaccines must be reinforced to maintain the highest possible acceptance of vaccination. Communicating the benefits of vaccination to those who are focused on risk requires consistent messages that are based on solid scientific data.

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