IMMUNIZATIONS NEWSLETTER

PROVIDING GSA MEMBERS WITH UPDATES ON ADULT IMMUNIZATIONS

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BREAKING NEWS

- August is National Immunization Awareness Month. Check out the CDC website for activities and tools that vaccine advocates can use to educate and motivate others to get immunized.

OF ADJUVANTS AND INNOVATION

When vaccines are developed and discussed, the main focus is on the antigen—the ingredient in the product that provides an immunogenic template for the vaccine recipient to use in developing immunity against a pathogen. Vaccine products contain much more than antigens, though. Diluents, stabilizers, and trace components are present along with special molecules called adjuvants, which provide a needed boost to the antigen's immunogenicity.

At the CDC’s 2016 National Adult and Influenza Immunization Summit (NAIIS) in Atlanta, Georgia, on May 10–12, attendees heard presentations on vaccines in development and learned about research on new adjuvant-containing vaccine products. Adjuvants are pharmacologic or immunologic agents that increase the body’s response to antigens, generally through as yet unexplained mechanisms. For many of the 125 vaccines currently in clinical development, adjuvants could be make-or-break factors just as important as the antigen itself.

SOCIAL RESEARCH/POLICY/PRACTICE

As evidenced recently by the Ebola and Zika virus outbreaks, infectious diseases have the capacity to disrupt the economic, political, and social systems through illness, disability, death, fear, and anxiety. From a pharmacologic standpoint, infectious diseases are generally prevented or treated with one or more of three types of products: small molecules (including most antibiotics), vaccines, and monoclonal antibodies.

As of April of this year, 453 infectious disease products were in one of the three phases of clinical development or under review at the Food and Drug Administration (FDA), Kelly Cappio of the Biotechnology Industry Organization said at NAIIS. Of these, 221 were small molecules, 125 vaccines, and 29 monoclonal antibodies. Among the vaccine
candidates, 19 were pandemic influenza vaccines, 15 staphylococcal vaccines, 14 seasonal influenza vaccines, and 14 respiratory syncytial virus vaccines. For global health and tropical diseases, Cappio said vaccines are especially important interventions in developing countries. Other products target new disease areas and key infections in health care and community settings.

The development process is "long, highly capital intensive, and risky," Cappio concluded. Fewer than 1 in 10 vaccine candidates achieve licensure. Among those currently in development, prospects are brighter for the 11 vaccines that have advanced to phase 3 trials or FDA review and another 48 in phase 2 testing.

Because of the cost and risk involved in vaccine development, marketed products are expensive. This can present policy dilemmas in the health care marketplace.

BIOLOGICAL SCIENCE

Adjuvants are included in vaccine formulations to enhance or shape the immune response, said Leonard Friedland, MD, of GSK Vaccines US, by “acting as substitutes for natural immune defense signals.” The immunogenic components of microbial cells that are used as antigens are not always sufficient to induce an immune response. In nature, certain immune-defense triggers alert the host of the presence of a pathogen. This attracts antigen-presenting cells and T cells and may induce cytokine release or provide costimulation of the T cell, all enhancing the immune response to the antigen itself.

Older patients and others with compromised immune systems may need adjuvanted vaccine to achieve adequate responses. Adjuvants can also alter the need for booster vaccinations; improve responses to poorly immunogenic recombinant antigens; enhance vaccine effectiveness against complex pathogens such as those causing tuberculosis, HIV, or malaria; and provide antigen-sparing effects in situations where vaccine supply is limited, Friedland said.

Licensed and investigational vaccine products include many different types of adjuvants. These include aluminum salts, lipid A analogues, emulsions, double-stranded RNA analogues, the protein flagellin (the structural part of the bacterial flagellum), cationic peptides and liposomes, and phospholipids. During preapproval testing, a vaccine that is adjuvanted faces additional regulatory hurdles. The vaccine developer must demonstrate that the adjuvant is necessary to achieve the desired level of immunity. If more than one adjuvant is included, each must be proven safe independently and then together.

HEALTH SCIENCE

Adjuvanted vaccines against herpes zoster (shingles) and influenza are currently under development, according to GSK and Seqirus representatives who presented at NAIIS.

Clinical results with GSK’s herpes zoster subunit vaccine have been promising, reported Debora Rausch, MD, of the company’s US Vaccines unit. The product uses the glycoprotein E antigen from the viral coat and the three-part AS01 adjuvant system. The liposome-based AS01 system contains a derivative of the lipopolysaccharide component of Salmonella minnesota (MPL) and QS-21, a natural saponin molecule extracted from tree bark. In clinical trials, the zoster formulation has demonstrated a vaccine effectiveness of 97% or more, Rausch said, and good durability, with no apparent waning during the first 4 years after immunization. Adverse events have included local reactions and systemic symptoms such as muscle pain, fatigue, and headache.
The oil-in-water emulsion adjuvant MF59 has increased vaccine effectiveness in tests of a trivalent influenza vaccine, according to James A. Mansi, PhD, of Global Medical Affairs with Seqirus. MF59 was first approved as an adjuvant in 1997, when it was included in the Fluad influenza vaccine formulation, Mansi said. It is composed of squalene stabilized with Tween 80 and Span 85. Squalene is a natural oil produced by the liver in the cholesterol biosynthetic pathway; it is biodegradable and biocompatible, Mansi said. While the liver typically synthesizes squalene in amounts of more than 1 gram per day, the vaccine contains only 10 mg.

In two clinical trials, MF59-adjuvanted influenza vaccine demonstrated consistent effectiveness, Mansi said. The product also produced higher immune responses to the drifted strains that caused so much illness and deaths during the 2014–15 influenza season, Mansi concluded.

The presence of adjuvants in vaccines can produce confusion among consumers and criticism among antivaccine groups, leading patients to question whether they should be immunized. Aluminum and squalene just don’t sound like the kinds of substances people would want to put in their bodies!

To counter such hesitation and misinformation, vaccine advocates can explain that squalene and lipids are natural substances found in the body. Aluminum is the third most common element on earth and is thus ubiquitous in people’s diets. The body is well equipped to bind and excrete the small amount of aluminum in a dose of a vaccine.

In short, the safety of adjuvants is established in preclinical (animal) and clinical (human) testing before FDA licenses vaccines for marketing. While rare adverse effects could emerge when the vaccine is used more widely, these are monitored by the manufacturer and the CDC through its Vaccine Adverse Event Reporting System after marketing. The chances of a person getting the preventable disease, with its morbidity and mortality, are far greater than the risk of adverse events from the adjuvants that help the vaccine work.

SOURCES AND RESOURCES

Cappio K. New vaccines on the horizon: the clinical-stage pipeline. Presented at the National Adult and Influenza Immunization Summit, May 10, 2016, Atlanta, GA.

Friedland L. Adjuvants used in vaccines. Presented at the National Adult and Influenza Immunization Summit, May 10, 2016, Atlanta, GA.

Rausch D. GlaxoSmithKline’s investigational herpes zoster vaccine. Presented at the National Adult and Influenza Immunization Summit, May 10, 2016, Atlanta, GA.

Mansi JA. MF59 adjuvanted influenza vaccine: influenza prevention for vulnerable populations. Presented at the National Adult and Influenza Immunization Summit, May 10, 2016, Atlanta, GA.

Centers for Disease Control and Prevention. Ingredients of vaccines—fact sheet.

Centers for Disease Control and Prevention. Vaccine Adverse Event Reporting System.