toxoids), which could be confused. Keep them separate. Look-alike packaging as well as sound-alike names can easily confuse any conscientious practitioner.

An online publication describing storage and handling requirements for currently recommended vaccines is available from the Centers for Disease Control and Prevention (CDC). Included in the publication are shipping and storage recommendations for specific vaccines, how to reconstitute them, information about vaccines' shelf life before and after reconstitution, and special handling instructions (3).

Biologics for Active Immunity

Bacterial Vaccines

A vaccine is a suspension of attenuated (live) or inactivated (killed) microorganisms or fractions thereof that are administered to induce immunity and prevent disease. Originally, the organism is grown in a suitable broth medium in a controlled environment of temperature, pH, and oxygen tension. To reduce the potential for hypersensitivity reactions to the finished product, the medium, whenever possible, should consist of chemically defined ingredients.

Following a suitable amount of time for bacterial growth, the culture is processed in two steps. If the vaccine is to be inactivated microorganisms, the organisms are treated with phenol or formaldehyde. Heat and phenol or heat and acetone are employed for the typhoid fever vaccine. Next, the organisms are separated from the medium through centrifugation and suspended in sterile water or 0.9% sodium chloride for injection. If necessary, the preparation may be further purified by several methods, including dialysis and/or additional centrifugation.

A live attenuated vaccine can also be produced by genetic alteration of the pathogenic organisms. This allows the organism to survive and multiply but not produce the disease. Usually, several base pairs of DNA in a key region of the gene structure are eliminated or altered. Thus, the organism is incapable of reverting to its more pathogenic form.

Another way to create a vaccine is to employ purified antigen subunits produced with use of recombinant DNA. With subunit vaccines, the genes that code for the desired antigen are introduced into the nonpathogenic organisms. There is no potential to harm the patient because there is no possibility that a pathogenic organism can be created from only a limited number of components of the original organism. Also, the subunit vaccine can be expected to have a lower incidence of side effects. As an example, the hepatitis B vaccine is produced through recombinant DNA technology by common baker's yeast, into which the gene for the hepatitis B surface antigen (HBsAg) has been inserted.

To date, subunit vaccines have had limited clinical utility because of inability to produce a sufficient, specific immune response. However, alternative biotechnologic strategies have been employed to produce subunit vaccine immunogens and adjuvant-active compounds that can be added to enhance the immune response.

The final vaccine may contain one single immunogen (monovalent), or it may contain multiple immunogens (polyvalent, trivalent) to promote immunity against the same disease state. The final product may also be a mixed vaccine. For example, MMR vaccine is a single product with three immunogens for three viral diseases. A mixed biologic may contain a vaccine and a toxoid in the same product, as with diphtheria, tetanus, and pertussis (DTP). Another example of a mixed biologic is the combination vaccine Pediarix (diphtheria and tetanus toxoids and acellular pertussis adsorbed, hepatitis B [recombinant], and inactivated poliovirus vaccine [IPV]) introduced in late 2002.

The strength of a vaccine may be expressed as total number of organisms, total protective units per milliliter or dose, or micrograms of immunogen in each milliliter or in each dose of vaccine.

A current list of vaccines licensed in the United States is posted at www.fda.gov/cber/.

Viral Vaccines

Viruses cannot be grown on inanimate media employed to grow bacteria and so