their function is to bind to the pathogen as needed. Immunoglobulin is metabolized by the body if not needed for immunologic purposes.

PRODUCTION OF BIOLOGICS

Biologics are produced by manufacturers licensed to do so in accordance with the terms of the federal Public Health Service Act (58 Stat. 682) approved on July 1, 1944, and each product must meet specified standards as administered by the Center for Biologics Evaluation and Research of the FDA (1). Each lot of a licensed biologic is approved for distribution when it has been determined that the lot meets the specific control requirements for that product. Licensing includes approval of a specific series of production steps and in-process control tests as well as end product specifications that must be met lot by lot.

Generally, each lot of a biologic product must pass rigid control requirements before it may be distributed for general use. Provisions generally applicable to biologic products include tests for potency, general safety, sterility, purity, water (residual moisture), pyrogens, identity, and constituent materials. Constituent materials include preservatives, diluents, and adjuvants, which generally should meet compendial standards; extraneous protein in cell-cultured vaccines (which, if other than serum originating, is excluded); and antibiotics other than penicillin added to the production substrate of viral vaccines, for which compendial monographs on antibiotics and antibiotic substances are available. Additional safety tests on live vaccines and certain other items are also required.

Biologics to be administered by injection are packaged and labeled in the same manner as other injections. In addition, the label of a biologic product must include the title or proper name (the name under which the product is licensed under the Public Health Service Act); the name, address, and license number of the manufacturer; the lot number; the expiration date; and the recommended individual dose for multiple-dose containers. The package label also includes the preservative and its amount; the number of containers if more than one; the amount of product in the container; the recommended storage temperature; a statement, if necessary, that freezing is to be avoided; and such other information as FDA regulations may require to ensure safe and effective use of the product.

With few exceptions, most biologics are stored in a refrigerator (2°C to 8°C, or 35°F to 46°F), and freezing is avoided. Besides the biologic substance that is harmed by freezing, the container may be broken due to the expansion of an aqueous vehicle resulting in loss of product. Diluents packaged with biologics should not be frozen. Some products are to be held at specified temperatures during shipment.

The expiration date for biologic products varies with the product and the storage temperatures. Most biologic products have an expiration date of a year or longer after the date of manufacture or issue. The stated date on each lot determines the dating period, which begins on the date of manufacture and beyond which the product cannot be expected to retain the required safety, purity, and potency. The dating period may be comprised of an in-house storage period during which the lot is held under prescribed conditions followed by a period after issue. The individual monographs for biologics usually indicate both, the after-issue time frame for use and (in parentheses) the permissible in-house storage period.

STORAGE, HANDLING, AND SHIPPING OF BIOLOGICS

Biologics are sensitive to extreme temperatures, and exposure to heat or freezing can decrease their potency and dramatically reduce their effectiveness. Poor storage, handling, and shipping conditions for these products not only waste the intrinsic value of the products but waste money as well. Biologics are expensive and can add significantly to one's inventory costs. An inventory of vaccines and other immunologic products can amount to tens of thousands of dollars or more.