Crystallization may be performed from the solvent or aqueous phase. Na, K, and penicillin concentrations, pH, and temperature need to be adjusted for crystallization. Excess amounts of Na or K are added to the penicillin-rich solvent before crystallization in an agitated vessel. The crystals are separated by a rotary vacuum filter. The crystals may be washed and predried with anhydrous butyl alcohol to remove some impurities. Large horizontal belt filters are used for collection and drying of the crystals. Usually warm air or radiant heat is used for drying.

Crystalline penicillins G or V are sold as an intermediate or converted to 6-APA (6-aminopenicillanic acid), which is used for production of semisynthetic penicillins. The enzyme penicillin acylase is used for cleavage of penicillin G or V to produce 6-APA. Some bacteria, *E. coli, B. megaterum,* and *P. melanogenum,* as well as some molds produce the enzyme.

Production costs for penicillin production utilizing glucose as a substrate were calculated in 1982 as $19/kg. Prices of penicillin have decreased in recent years, from $31.73/kg in 1996 to $15/kg in 2000. This has put pressure on penicillin manufacturers to reduce production costs. The most important costs in penicillin production are raw materials (35%) and utilities (14%). By using cheaper raw materials, as molasses or starch, and genetically improved strains producing higher penicillin yields, the production costs may be reduced significantly.

Worldwide, approximately 26,000 tons of penicillin G and 10,000 of penicillin V are produced annually. Penicillins for medical applications and feed have an annual demand of $4,400 million. More than 80% of the penicillin produced is utilized for the synthesis of 6-APA and other intermediates.

A.2.4. Production of High-Fructose Corn Syrup (HFCS)

High-fructose corn syrup (HFCS) is a low-calorie sweetener commonly used in beverages, desserts, and other sweet foods. Until 1935, the only syrup available was 42 DE (dextrose equivalent) acid-converted corn syrup. In 1940, enzymes were commercially available and corn starch was hydrolyzed enzymatically to produce corn syrups. In the early 1960s the first crystalline dextrose derived from corn was marketed. The commercial production of the enzyme glucose isomerase, which converts glucose to its sweeter (approx. 1.7 times) isomer fructose, was a major milestone. The first HFCS was produced in 1967 and contained 15% fructose. Further process improvements yielded 42% and 55% fructose-containing HFCS. The original conversion process was batch; however, immobilized enzyme technology was later used for the production of HFCS by continuous operation. United States sales of HFCS exceeded 9.58 million tons in 1999.

Three major HFCS products differ by their fructose content, 42%, 55%, and 90%. HFCS containing 42% fructose is mainly used in most of the food products utilizing liquid sweeteners. HFCS with higher levels of fructose (55%) are mainly used in soft drinks as a replacement for sucrose and in jams and jellies (90%) as a low-calorie sweetener.

Production of HFCS from corn starch is an enzymatic process. The process scheme may be divided into 18 steps and five major operations (Fig. A.5). Those operations are dextrose production by enzymatic hydrolysis of corn starch, primary physical and chemical treatment of dextrose syrup, isomerization of dextrose to 42% fructose, secondary