

Table 7-1 Examples of Rubber Closure Components

Component type	General purpose
Elastomer	Base material—natural, butyl or halobutyl, silicone
Curing (vulcanizing) agent	Forms cross-links to shape the rubber. Common agents are sulfur, zinc oxide, and peroxide
Accelerator	Increases curing rate. One example used to be 2-mercaptobenzothiozole
Activator	Increases efficiency of accelerator. Common agents are zinc oxide and stearic acid
Antioxidant	Resists aging (e.g., phenol)
Plasticizer	Aids in the shaping process
Filler	Modifies hardness (e.g., carbon black)
Pigments	Provides color

elastomer material was the natural latex rubber liquid obtained from the *Hevea brasiliensis* tree. An increase in demand for rubber during World War II as well as the threat of strategic blockade of rubber shipments led to developments in the production of synthetic rubbers. Synthetic rubbers include styrene-butadiene rubber (SBR), neoprene [poly-(2-chloro-1,3-butadiene)], nitrile rubber, and butyl rubber. Butyl rubber is the most commonly used elastomer for pharmaceutical applications today because of its superior oxygen/moisture barrier (36). Neoprene is a halogenated synthetic rubber, which is available for more oil-based products.

Chemistry

Rubber stoppers are composed of the elastomer, a curing agent, an activator, a filler, as well as additional compounds to control cure rate, color, and resistance properties (Table 7-1). The curing agent, or vulcanizing agent, forms the cross-links in the rubber that provides the shape, the elasticity, and the resiliency to the rubber. Sulfur is the most common curing agent for elastomers with chemically unsaturated backbones (37). An activator, typically a metal oxide with a fatty acid, is used to accelerate the rate at which the sulfur reacts with the unsaturated polymer. The most common activator is zinc oxide combined with stearic acid (38). An accelerator, typically a sulfenimide, and a retarder, often benzoic acid, salicylic acid, and phthalic anhydride, can be added to further control the rate of vulcanization. Fillers are added to reduce tack, adjust color, and often to increase hardness and durability. Common fillers include carbon black, clay, calcium carbonate, and precipitated silica. Additional additives can include antioxidants and antiozonates as well as colorants.

Manufacturing

The basic steps in the manufacture of rubber closures involve the following (3):

1. Raw materials are tested usually at a minimum for identity and purity.
2. Batch ingredients are weighed usually within $\pm 1\%$ tolerances.
3. Batch ingredients are mixed.
4. The mix is tested to insure cure characteristics.
5. The mix is placed on an extruder to create pellets, strips, or sheets.
6. The rubber is molded by injection, compression, or transfer.
7. The molded sheets are trimmed.
8. The stoppers are washed to remove trim and mold lubricants.
9. During post extraction, the stoppers are baked and autoclaved, if applicable.
10. The stoppers are tested for conformance by chemical and physical testing.
11. The stoppers are packed and shipped.

The two major steps in the production of rubber products are the compounding of the components followed by curing. In the compounding process, the rubber is masticated, or broken down by heat and shearing with a mixer. Mastication, breaks down the polymer, increasing its viscoelasticity, and enables the incorporation of additives such as fillers. Following mastication, the remaining additives, with the exception of the curing agents are added and mixed