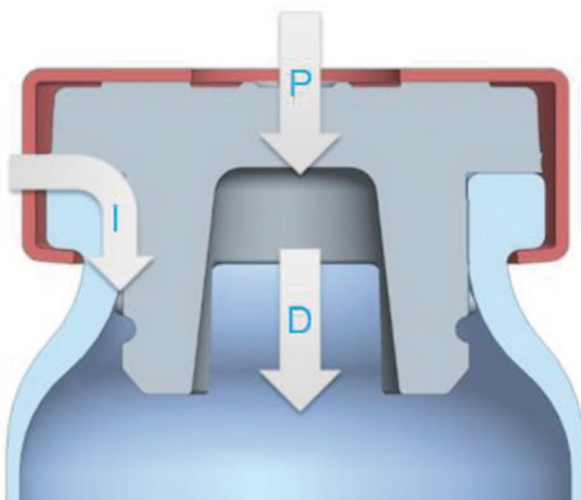


Fig. 5 Moisture making its way into freeze-dried vials



Moisture Absorption/Desorption and Permeability Behavior

Lyophilization is a process that is applied if the drug product on the longer run is not stable in an aqueous medium, and where identity, strength, quality, and purity can only be guaranteed if the product is brought in the form of a lyophilized cake. Upon storage, it is therefore also of importance to keep moisture away from the freeze-dried product. In general, the lower the active dose is, the more important it is to shield the product from moisture. This shielding can be done via appropriate choices of packaging components and crimping conditions.

For a lyophilized drug product there are three principal routes by which, after packing, it can be “contaminated” with water: ingress of water via the closure/vial interface ((I) in the Fig. 5), desorption of water from the elastomeric closure (D), and permeation of water through the closure (P) (Fig. 5).

The ingress route will be given attention under the section CCI of this chapter. The desorption and permeation routes will be discussed here.

Elastomeric closures for parenteral use, at the end of their manufacturing process, are always subjected to a washing and drying process³. The purpose of this process is to bring the closures in a controlled state of microbiological and particulate cleanliness, and to satisfy regulatory requirements that are imposed by various regulations [5–6]. During the washing and rinsing phases of this process, the closures are for a certain period exposed to water, while also in the step before washing the closures for a certain time remain in wet condition. This means that right before and during the washing and rinsing there is time for the closures to absorb water. The absorption of the water takes place at the surface of the stopper and will not reach into the bulk of it. Most of the water will be dried off during the drying

³ Most of the time this washing and drying process is combined with a siliconization process of the closures.