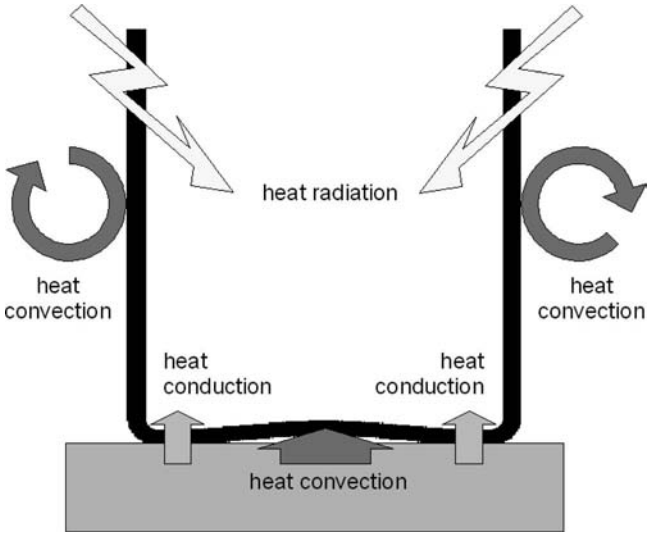

FIGURE 1 Heat transition paths for a glass vial during lyophilization processes.

2. Primary drying: During the primary drying step, frozen water is removed from the suspension by sublimation. To accelerate sublimation, application of a vacuum and gentle heating from the bottom of the vial are common techniques. Heating of the vial from the bottom side can cause glass breakage due to local temperature gradients because of an insufficient heat transition.
3. Secondary drying: In the secondary drying step, remaining nonfrozen water, not sublimated during the primary drying step, is removed. Secondary drying is accomplished at higher temperatures. During the drying processes three mechanisms of heat transition can arise: heat radiation, heat conduction through the bottom of the vial, and heat convection (14) (Fig. 1). The major heat fraction is introduced into the vial by convection, whereas heat radiation and heat conduction are of minor importance.
4. Sterilization and filling of the glass vials can cause damages on the surfaces (glass-to-glass or glass-to-metal contacts, chatter marks, etc.), whereas shipping to and storing at a different site can cause further mechanical loads. Improper handling (e.g., dropping of the vial) can also lead to failure if the impact point is at the site of a defect or residual stress is not removed during the annealing process.

In the pharmaceutical industry, specifications for mechanical stability of a container are very strict because failure of a glass container is unacceptable for safety and economic reasons. Even small flaws on the container can lead to nonsterile conditions inside the product, which can, in the worst case, endanger human health or life. They can also start propagating via subcritical crack growth and finally lead to a time-delayed failure. Therefore, the highest priority for both packaging supplier and pharmaceutical company is to achieve a "zero container-breakage" during production, processing, and usage in combination with low cost and low-cycle times.