Stoppered vials are removed and oversealed with either a screw cap or an aluminum foil tear-off cover. This prevents ingress resulting if any stoppers were dislodged or "popped up" during storage.

Leak Testing of Containers

Prior to the introduction of DIN ampoules, bespoke "test-tube" type ampoules were used with a diameter of 10 mm. The large diameter caused some problems in sealing and therefore each batch of ampoules was tested for leaks by immersion in a dye. With the introduction of industry standard DIN ampoules, this practice continued until a review of one year's production showed no leaks, and the practice was no longer necessary. Now noninvasive sensing methodologies are available that can assure the quality of the internal atmosphere (see sect. "Oxygen Headspace Measurement").

Since 2005 the capillary leak adaptor (8) has been replaced by specially sourced ampoules with a parallel-sided neck for the last centimeter. These are stoppered with standard 13-mm diameter igloo closures and the seal is sufficiently good for the headspace gas to remain unchanged with respect to its oxygen content for at least 24 hours if undisturbed. On sealing, the closure is slightly lifted a matter of seconds before the ampoules are flame sealed. This process has been shown routinely to deliver final oxygen headspace well below 1% residual oxygen.

Labeling

Generally ampoules/vials are labeled to indicate the unique batch identifier, product name, manufacturer, and storage conditions. An example of a typical label is shown in Figure 9A.

On establishment by WHO, the ampoules/vials are overlabeled to indicate their new international status, the new label has opaque backing to occlude the previous label, as in the example below (Fig. 9B). Overlabeling is preferred to removal of the previous label for quality assurance reasons.

Test and Inspection

Visual inspection and monitoring of product quality is carried out by the processing team at all stages of the process; this is to detect any potential problems, for example, splashing during dispensing, broken or damaged ampoules, poor freeze-drying (collapse), and poor sealing or capping. All comments are noted in the Product Record.

In addition, the following are recorded/tested:

Fill weight and CV
Dry weight and CV
Residual moisture and CV
Residual oxygen content

All of the above are recorded in the Product Record, which is reviewed by a team consisting of production, processing, and development personnel, prior to release of the batch. In addition, reconstitution time, biological activity/potency, and stability are determined subsequently by the relevant scientist.