FIGURE 1 Lyophilized biological reference materials produced at NIBSC, showing 5-mL and 3-mL ampoules, crimp topped, and screw-capped vials.

material irrespective of the volume of material originally dispensed into that particular container. The between-container variation in fill weight must be insignificant compared to the uncertainty of the assay in which it will be used.

Within the Quality Management System, the target for variability of fill weight for a 1-mL fill of aqueous (or similar viscosity) material in ampoules is a CV of 0.25% or less, for a 1-mL fill of more viscous materials it is 1% or less. In addition, material filled into vials has a target CV of 1%, due to the lesser precision of the peristaltic pump on the vial-filling machine compared with the piston dispenser used for ampoules.

During any filling run at least 1% to 2% of the containers filled are selected at intervals for "check-weighing," as a measure of the variability of the material dispensed over the period of the fill (see sect. "Monitoring of the Dispensing Process").

Some reference materials, for instance those that are qualitative or "positive/negative" controls, may not require such tight limits and for other materials (e.g., cellular suspensions or adjuvanted vaccine materials) the nature of the material, in particular its viscosity, may make such a tight CV of fill difficult to achieve.

WHO criteria: "standards must be stable, it is WHO policy not to set expiry dates for International Biological Standards and Reference Reagents." Stability is determined by various factors including the intrinsic properties of the material, the moisture content of the freeze-dried material, and the oxygen and moisture content of the headspace gas within the container.

Since, in general, WHO standards are produced without a defined shelf life they are processed using heat-sealed glass ampoules (in preference to