identify the material throughout its existence. All information, including the original request, agreed criteria, documentation, anomalies in processing, and any tests undertaken, is included in a batch record referred to as the product record. Product records are stored for at least the lifetime of the material.

Additional measurements/criteria carried out at NIBSC: Processing is carried in a controlled environment with respect to temperature and environmental cleanliness. Although there is no formal specification for a maximum permissible microbial content or for sterility per se (materials distributed by NIBSC are not for administration to humans), a high microbial content could interfere with the final assay procedure in which the material is to be used or cause increased degradation of the active material.

The microbial content of the bulk material is determined on arrival for processing, on samples removed during processing, and on the final product.

The dry weight of the freeze-dried material is measured and is compared with the expected dry weight of the material in the formulation.

The final freeze-dried material must completely reconstitute within a reasonable period (typically less than 2 minutes) with occasional gentle agitation.

Process Description

*Equipment Used**

The Institute has three pharmaceutical grade filling machines for different uses, a Bausch and Strobel AVF5090 ampoule dispensing/sealing machine, a Bausch and Strobel FVF5060 vial-filling machine, and a Schubert Paxal ARN584 vial-dispensing/capping machine. There is also other small-scale filing equipment used for pilot studies and laboratory work.

Currently, we use three production freeze dryers, manufactured by Serail (Argenteuil, France), a CS100 (usable capacity 20,000 5-mL ampoules, shelf area 6 m^2), a CS15 (capacity 3500 5-mL ampoules or shelf area 1 m^2), and a CS150 (capacity 24,000 5-mL vials, shelf area 12 m^2). This latter dryer is set up with a negative pressure isolator and dedicated filling machine to allow its use for the freeze-drying of infectious materials (see sect. "Recent Developments").

For development work we have two laboratory-scale Virtis Genesis machines, which are fully PC controlled and so can reliably model the production units, when devising and assessing potential drying cycles.

We have various measuring and monitoring equipment, including balances, temperature and vacuum measuring devices, which are used during processing to monitor the various stages of the process. All equipment has a defined maintenance and where necessary calibration program (traceable to national standards) within the Division's formal Quality Management System. In addition, all critical equipment has alarms to indicate malfunction and where possible automatic reversion to conditions "safe" for the product.

*Note: Details of any named equipment used should not be taken as a recommendation or endorsement for use but is purely for information.