When products are prepared aseptically in unlicensed units there is usually no possibility of quality control of the product before release and use. Consequently quality assurance of the aseptic process is of paramount importance to ensure the quality of the product.

This quality assurance includes:

- validation of the equipment, processes, techniques and staff involved in the preparation
- control of the process by use of Standard Operating Procedures, monitoring, training, competency assessment, supervision, self-inspection and change control.

### 10.1 Validation

Validation is performed when an aseptic unit is commissioned when any new equipment, process, technique or member of staff is introduced into the process and at defined intervals. The purpose is to show that under simulated conditions aseptic products can be consistently prepared to the required quality using the defined process. Any subsequent changes should be assessed in the same manner to ensure that they do not compromise that quality.

Validation methods are described in the appendices but it must be remembered that they only represent the capabilities of the aseptic processing system as tested. To ensure the reproducibility of quality of the product strict adherence to the validated Standard Operating Procedures is essential.

### 10.2 Control of the aseptic process

10.2.1 All key elements and manipulative steps in the aseptic process, from the starting material to the finished product, should be controlled by
comprehensive Standard Operating Procedures to ensure that the process consistently produces a product of the requisite quality.

10.2.2 Key elements of the aseptic process include:

- entry of personnel and materials into the processing area
- completing all required documentation for each product including worksheets, labels, etc.
- maintaining the integrity of the aseptic processing area, and monitoring the workstation and its environment
- handling and preparation of starting materials, especially disinfection before transfer into the critical zone
- correct loading and positioning of materials within the critical zone of the controlled workspace
- good aseptic processing techniques during manipulation of the product, including ‘no-touch’ of critical surfaces
- segregation and flow of materials to ensure no inadvertent cross-contamination or substitution of products
- performance and recording of in-process checks where appropriate
- removal of product and waste materials from the processing area followed by effective cleaning.

10.2.3 All aseptic processing must be carried out and supervised by competent staff.

10.2.4 Staff should be fully conversant with all the relevant Standard Operating Procedures before being deemed competent to work in the aseptic preparation unit.

10.2.5 Regular updating of staff on the procedures should be undertaken, documented and the extent of knowledge assessed.

10.2.6 No deviation should be allowed from the Standard Operating Procedures. Should exceptional circumstances necessitate consideration of deviation, this should only be sanctioned by an appropriately experienced and authorised senior member of staff and fully documented. If the changed procedure then becomes normal practice the procedures should be rewritten and revalidated in the usual way to take account of the changed circumstances.

10.2.7 There should be a formal written procedure for the assessment of any proposed change which may affect product quality and if the change is
implemented it must be widely communicated to and acknowledged by all members of the aseptic team.

10.2.8 Standard Operating Procedures should be written and implemented for all equipment used for aseptic processing. Where appropriate, equipment should be regularly calibrated and the accuracy of volume measuring devices validated.

10.2.9 All staff working in aseptic processing should be made fully aware of the potential consequences of any deviation from the validated procedure, both to the integrity of the product and to the intended recipient. Regular reminders of the critical nature of the process should be provided.

10.2.10 Staff involved in aseptic processing should be taught to recognise upper limb disorders or repetitive strain injuries and to use techniques to minimise these conditions wherever possible.61

10.3 Some principles and examples of good aseptic technique

10.3.1 Before starting a session of work put on a fresh pair of sterile gloves. If the gloves have been used to prepare a previous product during that session of work, check them for damage and if none is found disinfect them using sterile 70% alcohol before commencing preparation of the next product.

10.3.2 Wherever possible use double-wrapped, sterilised disposable equipment to avoid the need for disinfection of the outer surface before transfer into the critical zone.

10.3.3 Syringes or needles packed in strips should be separated before transfer into the critical zone to reduce the potential for particle dispersion.

10.3.4 Where the outer surface of materials has to be disinfected before transfer into the critical zone use the spray and wipe technique with sterile 70% alcohol and a sterile wipe (see 12.3).

10.3.5 When transferred into the critical zone allow all materials to dry before proceeding with the preparation.

10.3.6 Position the product in the critical zone so that there is unobstructed airflow over and around it.
10.3.7 Keep the critical zone uncluttered and free from previous waste.

10.3.8 Avoid reaching over the product to access equipment or dispose of waste.

10.3.9 Swab the surfaces of bungs that will be penetrated and the necks of ampoules with a fresh sterile 70% alcohol impregnated wipe and allow to dry before proceeding.

10.3.10 Use a strict ‘no-touch’ technique to avoid any contact with any surface which will be in contact with the sterile fluid path.\textsuperscript{63} Note: Additional procedures to protect the operator may be determined by the hazardous nature of the product, e.g. radiation protection considerations for radio-pharmaceuticals.

10.3.11 Peel open over-wrapped items pointing towards the air stream from the HEPA filter. Do not tear paper wrappers.

10.3.12 Use closed systems wherever possible.

10.3.13 Where ampoules have to be used make only one withdrawal immediately after opening and discard any remainder (see Chapter 2, definition 9).

10.3.14 When opening glass ampoules cover the neck with a freshly opened sterile 70% alcohol swab before snapping open.

10.3.15 When withdrawing from glass ampoules use a sterile filter straw or filter needle to remove glass particles. Replace the filter straw or needle with a fresh sterile needle before adding the solution to another container.

10.3.16 When using vials avoid aerosols by using pressure equalisation within the syringe or venting devices.

10.3.17 When making additions to infusion bags wherever possible suspend them so that the additive port is in the HEPA-filtered air stream rather than on the work surface.
10.3.18 Take care to insert needle through the centre of the additive port, keeping the needle straight to avoid puncturing the bag. Consider the effect of multiple insertions through the additive port and take steps to minimise if necessary.

10.3.19 Use an appropriate gauge of needle that will minimise damage to rubber bungs whilst still maintaining an acceptable flow rate.

10.3.20 Ensure that all tubing is clear of fluid and securely clamped before removal from the critical zone.

10.3.21 Clean up all drips or spillage of product immediately and disinfect the work surface and gloves between products.