

authorities that resuspension can be readily achieved by a patient, medical practitioner or nurse, by simple shaking prior to administration.

Aqueous injections that are designed for multiple dosing must contain an antimicrobial preservative, unless it can be shown that the preparation itself has sufficient antimicrobial properties to be self-preserving. Preservatives must not be used when the volume to be routinely administered in a single dose exceeds 15 mL. Preservatives must not be used if the product is intended to be injected intracister-nally, epidurally or intrathecally (or any other route giving access to the cerebrospinal fluid), or if it is injected into the eye. Unpreserved injections should be presented in single-dose containers (ampoules or pre-filled syringes) rather than vials. This is because vials allow more than one dose to be withdrawn and therefore may become contaminated with micro-organisms if used for multiple doses.

### Infusions

Infusions are sterile aqueous solutions or emulsions with water as the continuous phase. They are usually made isotonic with respect to blood. They are large volume parenterals, typically ranging in volume from 100 mL to 1000 mL, but they may be larger. Infusions do not contain antimicrobial preservatives. Solutions for infusion are clear and free from visible particles. Emulsions do not show any sign of phase separation.

### Concentrates for injection or infusions

Concentrates for injection or infusion are sterile solutions intended for injection or infusion only after dilution. They are diluted to a prescribed volume usually with an aqueous liquid such as saline (0.9% w/v sodium chloride) or water before administration. After dilution, they comply with the requirements for injections or infusions given above.

### Powders for injection or infusion

Powders for injection or infusion are dry solid, sterile substances sealed in their final container. When dispensed, a volume of the prescribed sterile diluent (usually an aqueous liquid) is added and shaken with the powder. This should rapidly form either a clear, particle-free solution or a uniform suspension. After dissolution or suspension they comply with the requirements for injections or infusions.

Freeze-dried (lyophilized) products for parenteral use are considered to be powders for injection or infusion. Freeze-drying is often used for drug substances that are not stable in solution (e.g. degrade by hydrolysis). In this process, a solution of the drug is prepared, sterilized by filtration and filled into the final container (usually a vial). The solution is then freeze-dried by reducing the temperature and applying a vacuum, so that the water in the drug solution is removed by sublimation, leaving a sterile plug of the drug substance in the vial which is then closed and sealed. For further details of this process see Chapters 17 and 29.

## Absorption from injection sites

### Factors affecting absorption from the injection site

For a drug to exert its pharmacological effect (i.e. provide a clinical action) it must be able to reach its appropriate site of action. The movement of a drug from the site of administration (injection site) into the bloodstream is the process of drug absorption. From this it can be seen that there is no absorption process if the drug is injected intravenously into the bloodstream or into a similar fluid of distribution such as the cerebrospinal fluid (intrathecal and intracisternal injections), or directly into the site of action e.g. intra-articular or intraocular injections. In contrast, drugs that are injected intradermally, subcutaneously or intramuscularly must undergo absorption to reach the systemic circulation. This occurs by diffusion of the drug through the tissues surrounding the injection site followed by penetration through the walls of blood capillaries or the lymphatic system. Both the subcutaneous area and muscle tissue are richly supplied with blood capillaries. Lymph vessels are found extensively in subcutaneous tissue and in connective tissue sheaths around muscles, but are found only in small numbers within muscle tissue itself.

Subcutaneous and intramuscular injections may be either solutions or suspensions. Intradermal injections are usually solutions, but generally are only used for diagnostic purposes (e.g. allergy testing) and act locally at the site of administration. When aqueous solutions of drugs are administered by subcutaneous or intramuscular injection drug absorption is usually comparable to that seen with