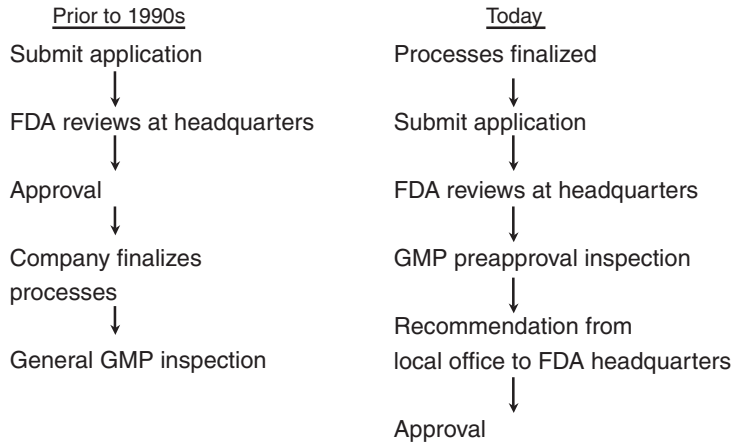

Figure 5-2 Comparison of new drug application/abbreviated new drug application (NDA/ANDA) approval process.

antibiotics, the large majority of parenteral drug products do contain added substances. Nevertheless, it is always the goal of a formulator of a sterile drug product to keep that formulation as simple as possible with a minimum of added substances (excipients).

GENERAL GUIDANCE FOR DEVELOPING FORMULATIONS OF PARENTERAL DRUGS

The final formulation of a parenteral drug product depends on understanding the following factors that dictate the choice of formulation and dosage form.

Route of Administration

Injections may be administered by such routes as intravenous, subcutaneous, intradermal, intramuscular, intra-articular, and intrathecal (chap. 31). The type of dosage form (solution, suspension, etc.) will determine the particular route of administration that may be employed. Conversely, the desired route of administration will place requirements on the formulation. For example, suspensions would not be administered directly into the bloodstream because of the danger of insoluble particles blocking capillaries. Solutions to be administered subcutaneously require strict attention to tonicity adjustment; otherwise irritation of the plentiful supply of nerve endings in this anatomical area would give rise to pronounced pain. Injections intended for intraocular, intraspinal, intracisternal, and intrathecal administration require stricter standards of such properties as formulation tonicity, component purity, and limit of endotoxins because of the sensitivity of tissues encountered to irritant and toxic substances.

If the route of administration must be intravenous, then only solutions or microemulsions can be the dosage form. If the route of administration is to be subcutaneous or intramuscular, then the likely type of dosage form is a suspension or other microparticulate delivery system.

Pharmacokinetics of the Drug

Rates of absorption (for routes of administration other than intravenous or intra-arterial), distribution, metabolism, and excretion for a drug will have some effect on the selected route of administration and, accordingly, the type of formulation. For example, if the pharmacokinetic profile of a drug is very rapid, modified release dosage formulations may need to be developed. The dose of drug and the dosage regimen are affected by pharmacokinetics, so the size (i.e., concentration) of the dose will also influence the type of formulation and amounts of other ingredients in the formulation. If the dosage regimen requires frequent injections, then a multiple dose formulation must be developed, if feasible. If the drug is distributed quickly from the injection site, complexing agents or viscosity-inducing agents may be added to the formulation to retard drug dissolution and transport.