same in all cases. One would assume that it would be the absolute (total) amount of decomposition product that would be of importance, so that expressing the toxicity limitation as a percentage is not appropriate.

In cases where the Leeson–Mattocks model holds (but not in other cases of zero-order reactions), the above dilemma may be prevented by making the smaller dosage forms proportionally smaller, since the term V in Eq. (7.13) then becomes smaller as well.

Regulations are never immutable, and it may well be that at some future date such regulations will be modified to meet the stated need.

9. NONSTOICHIOMETRIC INTERACTIONS WITH WATER

It is sometimes a pharmaceutical practice to "coat" labile pharmaceuticals. One such example is vitamin A beadlets, which are an emulsion of vitamin A ester in a gelatin solution, which has then been converted into drops and dried. The beadlets are therefore a matrix of gelatin with droplets of oil in the interior. The protection offered is one against oxidation.

10. PARENTERAL SOLID PRODUCTS

When an injectable product is insufficiently stable in solution to allow marketing of a ready-made solution, there are still ways to develop a marketed product.

In the far past, there were so-called powder-filled products. Here a solid drug substance was made under exceedingly "clean" conditions so that it emerged from its synthesis as "completely" free of foreign material. In such a case it could be filled into a vial, sterilized by suitable means (heat, ethylene oxide (not used of injectables anymore), or γ-ray sterilization). Excipients used (sodium chloride, for instance) would have to be equally clean, and the practice is not, to the author's knowledge, used much any more.

Aside from the sepsis issue, there was also the problem with rate of dissolution, and from both these aspects, lyophilization offers a better (but probably more expensive) alternative.

10.1. Lyophilized Products

The process is one where a solution of the drug (+ excipients) is made and aseptically filtered. The solution is then aseptically filled into vials, which are loaded into a sterile lyophilization oven. This has cooling coils in its shelves and can be evaluated to very high vacuum.

The vials containing the solution are transferred to the oven, and coolant at very low temperature ($< 30°C$) is flowed through the tray coils. The solution freezes, and then a vacuum is applied of such magnitude (P_v torr) that it is lower than the vapor pressure of ice at the given temperature (P_i torr). This causes the ice to sublime, and then there remains a cake that either is crystalline and has an exceedingly high surface or is amorphous and also possesses a high surface area.

When this, at time of use, is reconstituted with water or diluent, the dissolution is, in both cases, rapid and the "original" solution is regained.