lesser slope and with a minimum at pH 7. Cyclodextrins have also been used in stabilization of monoclonal antibodies (Ressing et al., 1992).

Cyclodextrins (CDs) are powerful complexing agents, and much work has centered about their use in drug solubilization and stabilization. They are the subject of a fair amount of pharmaceutical research. For instance, Scalia et al. (1998) have described the complexation of butyl-methoxydibenzoilmethane with hydroxypropyl-β-cyclodextrin. Veiga and Ahsan have described the interaction between tolbutamide and β-cyclodextrins. The tolbutamide phase solubility diagram, in this case, shows a maximum in solubility at a concentration of β-CD of 0.008 M. Such maxima are usually ascribed to the limit of solubility of the complex. Ventura et al. (1998) have described the interaction between papaverine and modified and natural β-cyclodextrins. The phase-solubility diagram is such that the papaverin solubility increases monotonically (in a straight line or curved) with β-CD concentration. Ventura et al. (1997) have shown the increase in aqueous solubility of ursodesoxycholic and chenodesoxycholic acids by complexation with β-CDs.

Miyake et al. (1999) have demonstrated the inclusion compounds of itraconazolone with 2-hydroxypropyl-β-cyclodextrin in propylene glycol solution. Antoniadou-Vyza et al. (1997) have reported that the hydrolysis rate constant of methocarbamol is reduced almost 50% when complexed with hydroxypropyl-β-cyclodextrin. Vianna (1998) et al. showed that complexes of dexamethasone acetate with cyclodextrin showed marked improvement in aqueous solution stability and gave rise to first-order decomposition. Másson et al. (1998) have shown that chlorambucil and indomethacin have greatly improved (first-order) aqueous stability when complexed with a variety of cyclodextrins. Diazepam behaved in different manners depending on the particular cyclodextrin used.

Less common ligands such as dextran stabilize porcine pancreatic elastase (Chang et al., 1993).

3. PHOTOLYSIS

Attention is given to light stability in the 1993 ICH guidelines, although at the time of this writing, testing methods are not finalized. This is exemplified in lines 471–473:

> Light testing should be an integral part of stress testing. [The standard conditions for light testing are still under discussion and will be considered in a further ICH document.] (471–473).

In photolysis, light ($h\nu$) is absorbed by the solution and activates a species in it. ($h\nu$) here represents a quantum of light, where h is Planck's constant ($h = 6.626 \times 10^{-27}$ erg s) and ν (in units of s^{-1}) is the frequency of the light. The activated species (denoted by [*]) then returns to ground state, it either

1. Emits light (of a different frequency ν'); this is referred to as fluorescence or phosphorescence
2. Causes the activated species to decompose, in which case one deals with photolysis. The simplest sequences in photolysis would, therefore, be

$$A + (h\nu) \rightarrow [A^*] \tag{5.14}$$

$$[A^*] \rightarrow \text{products} \tag{5.15}$$