

to a level of e.g. 1–5. A flavor profile may hence be established, and this can then be reestablished at several time points in the room-temperature storage. It is not recommended to evaluate results from higher temperatures (although they may be carried out).

1.2 Subjective Appearance Testing

Solutions, particularly parenteral solutions, may have a tendency to discolor slightly. Often it is not possible, within analytical sensitivity, to establish either the source of the color or the level of the substance causing it. In this case it is a good practice to use a color standard to describe the “intensity” of the discoloration. Roche, for instance, uses the so-called Roche Color Standard (RCS), which uses a compound (the identity of which is a secret) that can be reliably reproduced and has exceptional color stability. Making up serial dilutions of this compound then gives solutions of different “slight” discolorations; they are denoted RSC#1, #2, etc., so that a solution can always be compared in this fashion. It is a bit like the old-fashioned Dubosque colorimeter (which can be used with advantage in this type of situation). The principle of the Dubosque colorimeter is to have a view of two test tubes from the top. One is the control, and the other is the solution being matched. It is possible to adjust the length of the light path in the second tube, and this is done until the intensity matches that of the standard. The length of the path is then an indication of the “concentration.”

The RCS (and similar types of numbers) are difficult to analyze, but a Dubosque colorimeter gives numbers that follow Beer’s law and are logarithmically proportional to concentration (although the proportionality factor cannot be known). In this fashion the “decomposition” could be represented simply as a first-order reaction, where the concentration, X , of the decomposition product would be given by

$$X = X_{\infty}[1 - \exp(-qt)] \quad (10.1)$$

or

$$\ln \left[1 - \frac{X}{X_{\infty}} \right] = -qt \quad (10.2)$$

where q is a constant, t is time, and X_{∞} is found by iteration. This allows (from accelerated studies) a visual estimate of the worst appearance that a product could take on. The appearance of tablets can be treated differently and will be discussed later.

2. PARENTERAL SOLUTIONS

In parenteral solutions, physical stability includes interaction with a container and changes in chemical composition that give rise to physical changes. The latter will be discussed first.

One manifestation is slight discoloration. Thiamine hydrochloride solutions, for instance, may discolor slightly without showing detectable changes in content of parent compound. Such discolorations can be followed as described immediately