



**FIGURE 19** The impact of various moisture levels on the degradation rate constants of CAVERJECT IMPULSE (as measured by degradation product, PGA<sub>1</sub>, formation at 40°C).

It is also possible for the dried product to absorb atmospheric moisture for container closure systems that leak. Therefore, one must assure that appropriate container closure integrity testing (CCIT) data has been generated for the package system chosen to minimize this risk.

The most important parameter to assess for establishing an appropriate moisture specification is the impact of moisture on product quality. Typically this is evaluated by determining the effect of various moisture levels on product stability. Samples of product in a DCS/DCC package can be prepared at different moisture contents and the resulting stability evaluated. An example of the measured degradation rate constants at 40°C for CAVERJECT IMPULSE determined as a function of moisture content is illustrated in Figure 19. Data such as this can be used to justify an appropriate moisture specification. Note that, as stated earlier, it may be necessary to establish a moisture specification for product at the time of quality control release and a second moisture specification for the product shelf life.

Therefore, the moisture specifications should be established using the following criteria:

1. Evaluate what the process can achieve (at the end of the freeze-dry cycle and through final sealing).
2. Perform moisture absorption isotherms for externally stoppered products to estimate additional moisture uptake.
3. Determine moisture absorption from the package with time and storage condition (i.e., from the closure or diluent chamber).
4. Determine the effect of variable moisture contents on product quality (e.g., stability).