Data for accuracy and assessment of error or uncertainty for residual moisture methods are presented in detail (56).

Vapor Pressure Moisture Methodology

Vapor pressure moisture methodology has added a new piece of information to the evaluation of residual moisture in the freeze-dried final container. Rey (personal communication) used water vapor pressure methodology to determine the moisture content of the headspace in several freeze-dried biological products using and electro-optical dew point measurement instrument (Fig. 19). This information has agreed with results from gravimetric, Karl Fischer, TG, and TG/MS testing for both high and low residual moisture levels in vials. Verifying high residual moisture levels in freeze-dried biologicals is important since excessive residual moisture levels have led to decreases in product potency and therefore decreases in product stability.

Figure 20 shows the condensation temperatures for three lots of α-interferon with residual moisture values near 1.0% (Table 2), which are within the moisture limit for the product (3.0%). The condensation temperatures are very low (between −11.8°C and −24.3°C) and are relatively close to one another. The corresponding water vapor pressure moisture values are low, between 2.05 and 6.67 μg of water per vial, indicative of only small amounts of moisture in the vial headspace. Antihemophilic factor (Table 2) similarly has a low residual moisture (1.05%), a condensation temperature of −42°C, and a very low vapor pressure moisture within the vial headspace (0.2 μg water/vial). In contrast, the condensation temperature graphs for the sequence of U.S. pertussis vaccines, lots 8,

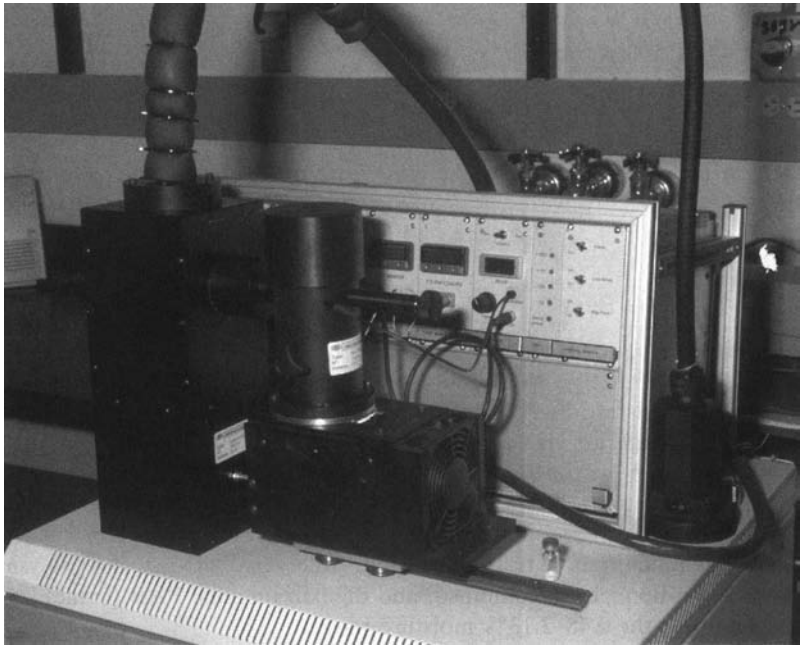

FIGURE 19 Instrument for the measurement of vapor pressure moisture within sealed vials (JMD Electronique, Montelier, France).