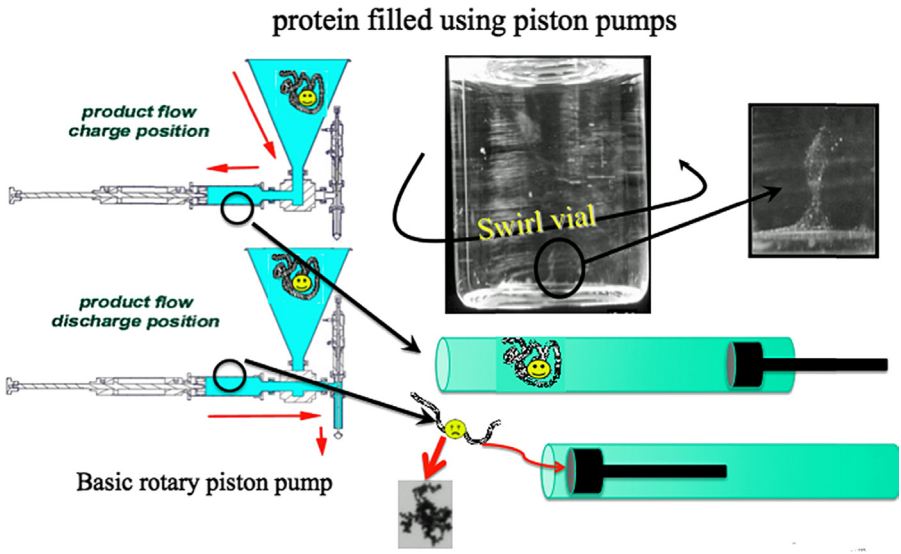

Figure 3.21 Particulate formation in protein solutions filled using rotary piston pumps when filled into vials.

two containers at low and high speeds that represented the typical and fastest filling speeds. After each transfer an aliquot was analyzed by turbidity measurements at 350 nm or by light obscuration using a Hiac particle counter. As the number of transfers increased, the turbidity and number of particles >2 mM increased (see Figure 2 in Cromwell et al., 2006). This was not observed using the rolling diaphragm pump.

Adsorption to surfaces

On adsorption to hydrophobic air–water interfaces solid particles such as stainless steel microparticles will generate aggregates as discussed previously. In addition to this type of adsorption, proteins are also capable of adsorption on solid surfaces that make up typical container closures. Generally the amount of protein that adsorbs to such surfaces is small, on the order of micrograms. Thus, proteins that are delivered at low doses may undergo substantial percentage loss due to surface adsorption. This often can be handled by adding a surface-active excipient such as a surfactant or protein to coat the container closure as is done by the addition of human serum albumin to formulations of erythropoietin (Shimoda & Kawaguchi, 1986). mAbs are high-dose drugs and when formulated at higher concentrations the percentage of mAb lost due to surface adsorption is not significant. One report discusses the loss of a murine mAb during secretion from transgenic plant tissue cultures, which was attributed to adsorption to container surfaces (Doran, 2006). However, these experiments were done in glass shake flasks at low mAb concentrations (2 μg/mL), and thus this result is not surprising.