



Figure 3.19 Generation of aggregates during bioprocessing.

processes used during preparation of DP. During production of the bulk DS exposure to shear and stress during agitation as well as different solution conditions that include pH, ionic strength, and temperature can lead to aggregate formation. Preparation of DP from bulk DS involves several unit operations such as tangential flow filtration for concentration and buffer exchange, freeze-thawing in cryogenic vessels for bulk storage, filtration and filling into final DP containers, and solid dosage form processes such as freeze-drying and spray drying. Aggregates can form during these unit operations. The resulting DP may also aggregate as a result of long-term storage conditions such as pH, ionic strength, and temperature (Schreiber, 2002). In addition, agitation and exposure to temperature excursions during shipping can lead to protein aggregation. Once shipped, aggregates can also be generated during handling of the final DP for administration to the patient, and this aspect will be discussed further in a later chapter.

Specific examples of mAb aggregation

Aggregation of a mAb during long-term storage

As discussed previously, altered conformation of proteins can lead to aggregation. An interesting example of this is for an IgG₂ mAb where it was shown that disulfide isoforms, which contribute to conformational changes, can govern the aggregation behavior of this antibody (Perico, Purtell, Dillon, & Ricci, 2009). Three disulfide