Challenges in the intravenous (IV) administration of monoclonal antibodies (mAbs)

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A majority of mAbs have been formulated for intravenous (IV) administration delivery, especially for treatment of cancer where the drug is usually administered in the hospital or an infusion center (Tables1.1 and 4.1). The IV administration is usually given as an infusion rather than a bolus, and thus requires dilution of the mAb formulation, including excipients into appropriate fluids suitable for IV administration. The resulting dilution of the excipients, especially surfactants, which may decrease below the concentration required for prevention of aggregation during agitation, may be an issue and will be discussed later in this chapter. In addition, compounds from the plastic used to manufacture IV bags may impact the stability of the mAb or pose a safety risk.

Extractables and leachables from IV bags and impact on protein/mAb stability

Extractables are compounds released from product contact surfaces after exposure to aggressive solvent conditions that exceed what the drug product normally encounters during normal storage and use, that is, extremes in pH, ionic strength, and temperature. Leachates are a subset of the extractables, which may elute from the product container contact surfaces during normal use and storage conditions (Wakankar et al., 2010). Since there is a potential for exposure of these compounds after dilution of the mAb therapeutic into IV bags, it is important to evaluate the compatibility and safety of the mAb in the IV infusion bags and sets. This can be a daunting process since there is a large selection of IV bag types available, which are made from different plastic materials. Some of the bags may also have stopper components at the filling ports and these may also need to be evaluated. A further complication, especially in Europe, is the recent practice of using a centralized IV additive service where drug is diluted into bags in advance, often requiring freezing and storage prior to shipment to the site for IV administration (Needle, 2008). Thus, assessment of the impact of longer-term storage and freezing–thawing of the drug product in the bags may be required.

The materials and manufacturing processes used by manufacturers are often considered to be proprietary. This makes leachate studies difficult, especially since additives such as plasticizers, polymerization initiators, and stabilizers that are usually used in the manufacture of the IV bags may differ in different plastic materials or even in the same type of plastic materials from each manufacturer (Quackenbos, 1954; Till et al., 1982). The leachates can include organics, metals, and volatile sulfur-containing compounds, which end up as contaminants in the drug product IV solution (Gallelli & Groves, 1993; Jenke, 2002, 2003, 2005; Jenke et al., 2005). The variability of the

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