Advance Understanding of Buffer Behavior during Lyophilization

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Introduction

Therapeutic proteins are becoming an ever increasing important class of drugs in the pharmaceutical industry. Since the turn of the century, there has been a significant increase in the number of biologics ranked in the top ten blockbuster drugs. In 2012, seven out of the ten blockbusters were categorized as biologics with Humira®, a tumor necrosis factor (TNF) inhibitor leading sales at US $ 9.3 billion [24]. Due to the challenges of maintaining long-term stability in aqueous solution, many proteins are formulated as lyophilized or freeze-dried powder. In fact, roughly half of all commercial biologics are lyophilized products with Remicade, a TNF-α monoclonal antibody, leading sales at US $ 8.2 billion in 2012 [24].

The diverse modalities of biologics (e.g., monoclonal antibody, antibody drug conjugates, fusion proteins, enzymes) and the different routes of administration (e.g., intravenous, subcutaneous, intramuscular) require critical consideration of the type of buffer, stabilizers, and bulking agents used in the formulation. For example, solutions administered by the parenteral route typically formulated at a pH of 4–8 to minimize pain upon injection, which then dictate to some extent the range and type of buffers used. The types of buffers used in some of the best-selling lyophilized biologics are listed in Table 1.

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