Monoclonal Antibodies
Functional Improvements at SPC Shelf-Life Limits

Richard V Parry*, Terry Chapman ‡, Monika Ali Khan*, Maria Connolly* and Andrew G Watts‡

* Bath ASU, A15 Fiveways Light Industrial Estate, Westwells Road, Corsham, SN13 9RG

‡Department of Pharmacy and Pharmacology, University of Bath, Claverton Down, Bath, BA2 7AY

Introduction

Monoclonal antibody (mAb) therapeutics are one of the fastest growing sectors in the pharmaceutical industry and have already established themselves as frontline therapies in oncology.

These drugs are often assigned short shelf lives once prepared for administration, typically 24 to 48 hours.

However, SPC's for some of these drugs recommend they be used **immediately** following preparation.

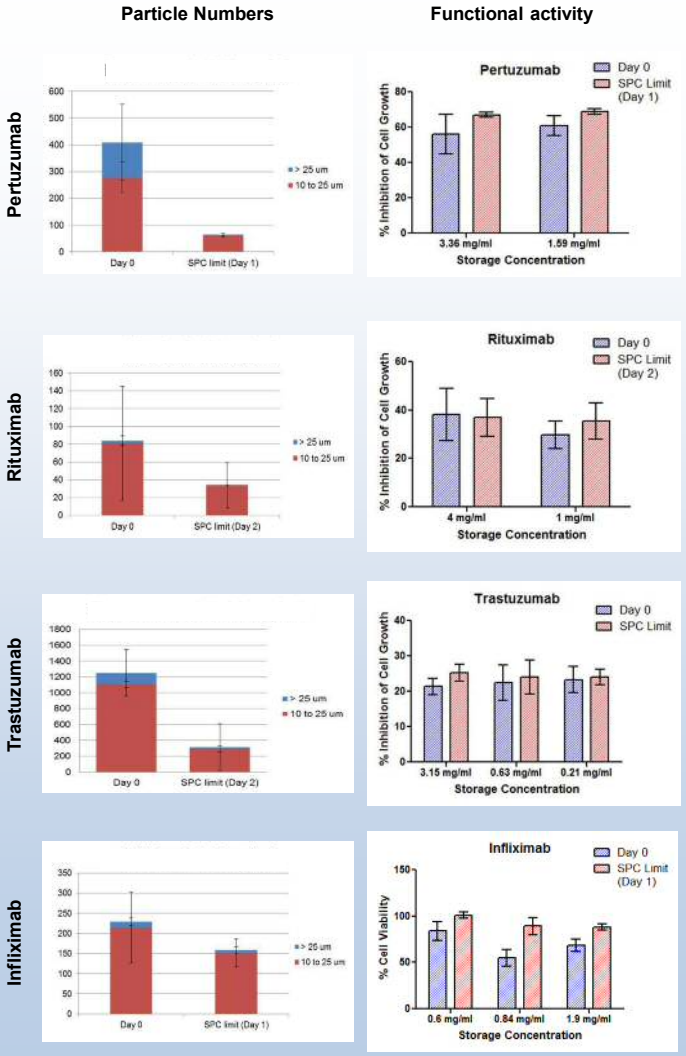
Aim

To evaluate the **physical**, **chemical** and **functional** stability of several mAb therapeutics and compare the (quality) characteristics of these drugs immediately after preparation with those at the limit of their SPC assigned shelf-life. The monoclonal antibodies analysed included Pertuzumab, Rituximab, Trastuzumab and Infliximab.

Methods

All tests were performed using the commercially available monoclonal antibodies. Infusion bags were aseptically prepared by Bath ASU in a grade A cleanroom environment (Class II Biological safety cabinets) using a suitably validated process and operator. A total of 4 infusion devices at each test concentration were prepared with 0.9% NaCl solution as diluent. All products were stored in light protective bags at +4°C. Approximately 0.5ml was withdrawn into 3ml polypropylene syringes under aseptic conditions at each time point tested (immediately following preparation and at the SPC assigned shelf limit) and assayed immediately. Physical/Chemical analysis of each antibody was performed using SE-HPLC, circular dichroism (VT-CD), SDS-page, pH, visual inspection, dynamic light scattering (DLS), FlowCAM® imaging (Fluid Imaging Technologies) and LC-mass spectroscopy (LCMS). Functional activity was measured using cell based assays that were specific for each antibody.

Results



Discussion

Analysis of the stability data generated from SE-HPLC, VT-CD, pH, visual inspection, SDS-page, LC-MS and DLS techniques, revealed that no significant differences could be detected between freshly prepared samples and those tested at the limit of their assigned SPC shelf-life. However, FlowCAM ® imaging of samples did demonstrate significant differences in the number of sub-visible particles (>10um) present. Surprisingly, samples tested at the limit of their shelf-life consistently contained fewer protein aggregates than freshly prepared samples. In addition, results from cell based functional activity tests demonstrated, consistently, that samples tested at the limit of their shelf-life had equivalent, or greater, functional activity than freshly prepared samples.

Conclusion

Differences have been observed between the characteristics of several mAb therapeutics tested immediately after preparation and at the limit of their shelf-life. Surprising, we found the mAb's at the limit of their shelf-life to be of equivalent, or better, functional activity with fewer aggregates.