development process for ADCs are not currently in the scope of this book. As a brief summary, the mAb that will be conjugated with drug is no longer the final drug product, but rather an intermediate. The drug conjugates are linked to the mAb usually through a cysteine or lysine residue. There are several different linker chemistries that have been used or proposed (Casi & Neri, 2012), and an important consideration is that the linker needs to be stable during systemic circulation to ensure low levels of free drug, whereas it needs to be cleavable after insertion of the ADC into cells so that sufficiently high doses of free drug can be released into the targeted cell. Thus, stability assessments of the linker as well as of the conjugated mAb are critical for successful pharmaceutical development. The final drug product is the conjugated mAb and since many of the drugs are hydrophobic the physicochemical stability of the conjugated mAb will be dependent on the drug–antibody ratio (DAR) as well as the process used to conjugate the mAb (Wakankar et al., 2010). The process of linking the drug results in a heterogeneous population of mAbs with different DAR. Thus, an important part of the development process requires full characterization as a function of DAR and a consistent manufacturing whereby produced lots have similar distribution of species and essentially the same average value for the DAR.

Other developments for the next wave of mAb therapeutics are development of bispecifics that have two different Fabs that bind to different cellular targets (Rouet & Christ, 2014; Thakur & Lum, 2010). Single-chain mAbs have also been developed (Sheets et al., 1998) that may require different strategies than that used for full-length mAbs and mAb fragments. Again these new mAb agents have not been covered in this book, and undoubtedly as they become an important source of new therapies, will need to be discussed in more detail.

The development of mAbs as therapeutic agents has come a long way from the early failures, and it is clear from the huge number of mAb therapies in development and clinical trials that this class of protein biotherapeutics will continue to be a prominent weapon for many diseases, especially in the treatment of cancers.

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