ABSTRACT

Monoclonal antibodies (mAbs) were initially used as laboratory reagents, later they were adopted as clinical diagnostic reagents, and eventually as therapeutic agents. The development of therapeutic mAbs commenced in the early 1980s and by 1986 the first mAb for human use "Orthoclone OKT3®" was approved by the US Food and Drug Administration (FDA). The next wave of antibody products were mostly anticancer agents which were approved in the US and Europe in the 1990s. The technological evolution from murine-based therapeutic mAbs to chimeric (part murine part human protein), humanized, and fully human antibodies has led to a reduction in immune-mediated clearance and hypersensitivity, improved the safety and feasibility of repeated administration making them therapeutically viable. Since the commercialization of the first therapeutic mAb, these products have become a dominant component of the biopharmaceutical market generating revenues of several billion dollars. The area of biosimilar antibody development is positioned for substantial growth with regulatory agencies like the European Medicines Agency (EMA) coming up with new guidelines on similar biological medicinal products followed by Health Canada, the US FDA and others, addressing biosimilar product development. With few of the blockbuster mAbs going off-patent in the next decade, companies with expertise in manufacturing biosimilar mAbs with the right kind of business and regulatory strategy are likely to have good value proposition.

KEYWORDS: Antibodies; biosimilars; European Medicines Agency; guidelines; monoclonal antibodies; regulations.

Introduction

Antibodies (Abs) are a key component of the adaptive immune response, playing a central role both in the recognition of foreign antigens and the stimulation of an immune response to them. Over a century ago Paul Ehrlich postulated that, if a compound could be made that selectively targeted against a disease-causing organism, then a toxin for that organism could be delivered along with the agent of selectivity (Ehrlich, 1900). The mouse hybridoma technology in 1975 as described by Köhler and Milstein was the triggering event that led to the development of antibody technology and emergence of therapeutic mAbs (Köhler and Milstein, 1975). This technology turned the magic bullet concept into a realistic option. Abs are grouped into five classes based on the sequence of their heavy chain constant regions: IgM, IgD, IgG, IgE and IgA (Louis et al., 2010). The mAbs are monospecific Abs that are the same because they are made by identical immune cells that are all clones of a unique parent cell. The Abs have monovalent affinity, in that they bind to the same epitope. They are structurally complex, and may have several functional domains within a single molecule, depending on the isotype (antigen-binding region, complement-binding region, constant part interacting...