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Regulatory strategies and considerations in monoclonal antibody R&D including biosimilars/biobetters

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Monoclonal antibodies (mAb or moAb) are antibodies that are made by identical immune cells that are all clones of a unique parent cell. Monoclonal antibodies can have monovalent affinity, in that they bind to the same epitope (the part of an antigen that is recognized by the antibody). Given almost any substance, it is possible to produce monoclonal antibodies that specifically bind to that substance; they can then serve to detect or purify that substance. This has become an important tool in biochemistry, molecular biology, and medicine. In particular, mAbs have been used in various diagnostic tests, anti-cancer and anti-viral-therapies, and autoimmune therapies, such as rheumatoid arthritis, Crohn's Disease, Ulcerative Colitis, and to help prevent acute rejection of transplanted organs, such as kidneys transplants, as well as treatments for moderate-to-severe allergic asthma. Biosimilar antibodies are highly similar versions of "innovator" (or "originator") antibodies with the same amino acid sequence but produced from different clones and manufacturing processes. As a consequence, biosimilar mAbs may include possible differences in glycosylation and other microvariations such as charge variants that may affect quality, safety and potency. Biosimilars may also be follow-on biologics and can also refer to second- and third- generation antibodies, which may have enhanced properties, such as greater affinity or longer action, often referred to as "biobetters". In contrast to the low-cost generic versions of small molecules that are off patent, it is currently not possible to produce exact copies of large proteins and glycoproteins, such as antibodies, owing to their structural complexity. Nevertheless, tremendous progress has been made in bioproduction and analytical sciences, and it is now possible to produce proteins and glycoproteins that are highly similar to reference products with little or no clinically-meaningful differences. The European Medicines Agency pioneered the regulatory framework for approval of these products, and now the US and most regulatory authorities have regulatory processes for the approval of biosimilar mAbs. The US Food and Drug Administration is one of the few regulatory authorities that has a regulatory pathway for biosimilars that are interchangeable, meaning that additional studies have been conducted supporting that they may be substituted for the reference product by a pharmacist without the intervention of the health care provider who prescribed the reference product. FDA recently published guidance explaining the additional studies that would need to be conducted to support approval of an interchangeable biosimilar. This presentation will look at principally the EMA and US approaches to regulating biosimilar mAbs including interchangeable biosimilar mAbs and biobetter mAbs. The development of legal and regulatory pathways for biosimilars mAbs will continue to raise much debate among lawmakers, regulators, originator and generic industry, patent attorneys, academia and health care professionals.

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