# Q&A: Monoclonal Antibodies

1. **What are monoclonal antibodies?**
   - **Antibodies** are proteins generated by the immune system to defend ourselves from diseases. **Monoclonal antibodies (mAbs)** are engineered antibodies that mimic human antibodies. They are expressed from a single type of immune cell to create identical copies, hence the name *monoclonal.*

2. **Are mAbs biologics?**
   - Yes – biologics (also known as biopharmaceuticals or biological medical products) are derived from natural sources rather than being chemically synthesized, and include vaccines, hormones, gene therapies, insulin, plasma-derived medicines, and antibodies.

3. **How are mAbs made?**
   - mAbs are produced in a lab, with support from molecular biology and protein and genetic engineering. There are multiple different methods.
   - In general, the process involves isolating the cells that make antibodies – often from people who have recovered from an infection – and cloning them to ultimately manufacture them at scale in large bioreactors.

**Figure 1: Manufacturing monoclonal antibodies**


Source: *Understanding the Complexities of Monoclonal Antibody Development and Manufacturing*, AstraZeneca, 2022.

4. **What is the difference between mAbs and vaccines?**
   - Vaccines work by inducing the production of antibodies in our bodies. A vaccine is administered to healthy individuals to enable an immune response (including the generation of antibodies). This takes a few weeks, after which we are primed to fight infection if exposed to a given pathogen.

- Administering mAbs directly provides our body with the most powerful antibodies to protect ourselves from or treat an infection, therefore working almost immediately.
- Another way of rapidly providing such a line of defence is by transfusing blood plasma (rich in antibodies) obtained from convalescent individuals. However, this method cannot be brought to an industrial scale and is not considered feasible in most low- and middle-income countries (LMICs).

**5. Are mAbs new?**

- No – mAbs have been used for over 30 years, but mostly for non-communicable diseases such as cancer and autoimmune diseases, and primarily in high-income countries.
- But the use of mAbs for infectious diseases is a more recent development. Of the first 100 antibody-based drugs approved in the US, only seven were for an infectious disease. Recently, there have been breakthroughs with approvals of mAbs for Ebola, optimized mAbs for respiratory syncytial virus (RSV), and several mAbs that were used during COVID-19 pandemic. On the near horizon, there are also mAbs in the pipeline for malaria, HIV, and other pandemic pathogens.

**6. How expensive are mAbs?**

- Monoclonal antibodies are among the world's most expensive treatments.
- The current mAbs market is based on high prices and low volumes. In the US, mAb treatments for cancer can exceed USD $10,000 per month. The recently approved optimized RSV mAb to protect newborns from deadly respiratory infections is about USD $400-500 per shot.
- Despite the high prices, in 2019, seven of the 10 best-selling novel drugs were mAbs.

**7. Why are mAbs so expensive and can prices go down?**

- Compared to small molecules, mAbs are expensive to make due to complex biomanufacturing processes and resource-intensive regulatory requirements. In addition, the lack of an established market and limited visibility on demand can keep prices high.
- There are opportunities to decrease development and manufacturing costs through novel, higher-yield technologies and more disruptive innovations that are in the pipeline to further simplify antibody-based therapies and their manufacturing.
- Product optimization could also decrease costs, for example by increasing potencies and therefore reducing dose requirements.
- Due to weight-based dosing, mAbs for infants and small children can also be produced at lower cost.

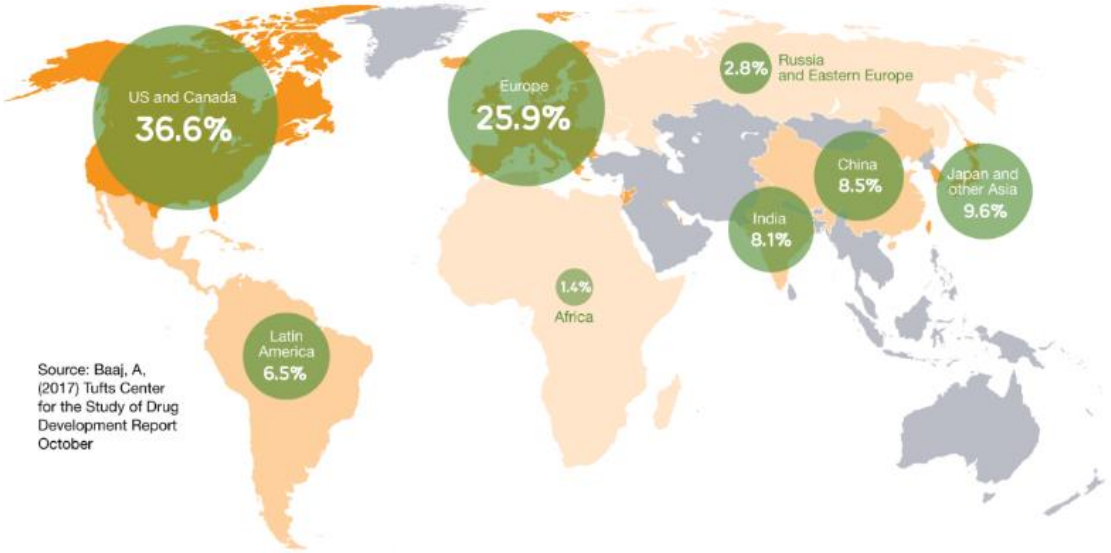
**8. Are there generic versions of mAbs?**

- Yes. Generic versions of mAbs are called *biosimilars*. However, given that biosimilars are more complicated to develop than small molecule generics and there is a less established market, there is less biosimilar manufacturing capacity globally. In addition, regulatory equivalence is harder to establish for copies of antibodies or other biologic products than for small molecules medicines. It is estimated to be 50-100 times more expensive to develop and manufacture biosimilars than small molecule generics, largely due to the length of the process and the regulatory requirements. In fact, even where biosimilars exist, for example for cancer, prices can still be out of reach at around USD $500 per month.

**9. Where are mAbs produced now?**

- Manufacturing of mAbs currently occurs mostly in North America, Europe and some Asian markets. However, there are some LMICs with mAbs manufacturing capacity, including India and Brazil.

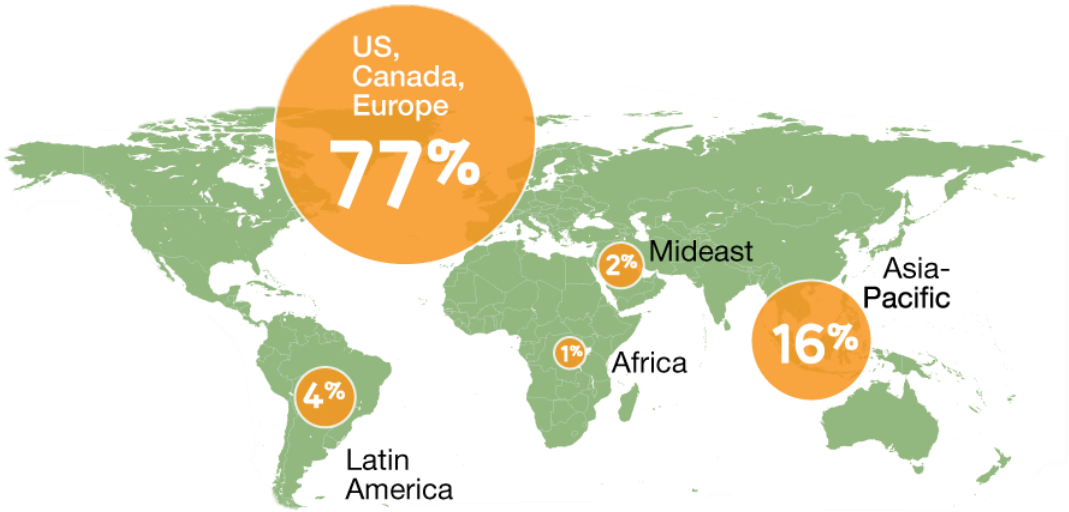
**Figure 2: Concentration of global biopharmaceutical manufacturing**




**10. Are mAbs being used in LMICs?**

- Current use of mAbs in LMICs is negligible. The entire African region makes up only 1% of the global mAbs market. This is not representative of the burden of disease. For example, 99% of deaths from RSV occur among children in LMICs, yet 99% of sales of the mAb *pavilizumab* to prevent such infection occur in the US and Europe. The more recent optimized RSV mAb (*nirsevimab*) is not even available yet in LMICs, despite representing a clear advantage in these countries by requiring only a single shot for the season.

**Figure 3: Estimated global market for monoclonal antibodies**




Source of maps: *Expanding access to monoclonal antibody-based products: A global call to action,* Wellcome, IAVI, 2020.

**11. Are mAbs suitable for LMICs?**

- In most cases, mAbs are given as intravenous (IV) solution (infusions) and require cold chain and frequent doses to complete the treatment or prevention cycle. However, there have been promising recent developments, such as oncology mAbs that have been approved with subcutaneous formulations and mAbs that are engineered to last longer (long-acting formulations). In addition, some use cases for mAbs would target patients already in a hospital or clinical setting, making administration requirements for injectable formulations less of a barrier.

**12. Why do we need mAbs if we have other, simpler tools?**

- Some challenges persist in managing infectious diseases that mAbs may be able to address. For example, mAbs could be used by vulnerable populations who currently have limited options including the very young, elderly, and immunocompromised.
- It is important to clarify that mAbs are not substitutes for vaccines in preventing diseases, as vaccine-induced protection tends to last for years or life (depending on the disease). However, they can be complementary in certain cases.
- mAbs can also fill gaps where vaccines do not exist yet or can take time to be developed, such as for new pandemic pathogens.
- mAbs that provide longer periods of protection could also simplify existing programs such as mass drug administration campaigns or replace and/or complement other existing options with complex dosing schedules.
- Finally, mAbs are very specific against the pathogen they target, implying high efficacy and fewer side effects than with other treatments.

**13. Are there mAbs in the WHO Model List for Essential Medicines (EML)?**

- A limited number of mAbs have been recently added to the WHO EML, mainly for cancer (two mAbs for melanoma were added in 2019). However, several others, such as for lung cancer, have been rejected. The WHO Expert Committee noted the benefits for patient survival but rejected the lung cancer mAbs due to their prohibitively high prices that would redirect substantial resources from other priorities in limited health budgets, especially given the high burden of disease. The Committee explicitly encouraged work to address the high price of mAbs to facilitate increased access.