Commentary: Géraldine Guérin-Peyrou

Solving the viral vector bottleneck during a pandemic

The viral vector bottleneck has been a well-documented challenge for the cell and gene therapy sector in recent years. There is a good reason for this: cell and gene products have become highly successful, with increasing numbers of therapies reaching late-stage clinical trials and approval. Adeno-associated viruses (AAV) are a critical component of research and development of these therapies. However, AAV production has not kept up with demand, and the bottleneck has become progressively more of a challenge. This is especially the case during the COVID-19 pandemic.

Viral manufacturers typically dedicate significant resources to adapting key steps of production for large-scale manufacturing. One solution to this is to develop transfection reagents to achieve transient transfection, a critical step that is indispensible for a reliable AAV manufacturing process. Our company, Polyplus-transfection SA, is currently launching a new transfection reagent for large-scale AAV manufacturing. However, achieving supply of a new product critical to addressing the viral vector bottleneck during the COVID-19 pandemic and global lockdown is a considerable challenge.

The COVID-19 pandemic is an unparalleled situation of international proportions. Many industries have to worry about keeping supply and manufacturing chains going to keep companies in business. The cell and gene therapy sector has the added responsibility of maintaining the development of life-affecting and life-changing therapies. Delays to therapeutic development can affect the lives of patients, many of whom have no alternative treatment options. To maintain the supply of critical transfection reagents, our company has had to take a number of steps.

The origin of COVID-19 in China allowed other governments in the world to see the potential challenges resulting from the outbreak, as well as to take steps to prevent a further spread of the disease. The time gap – between the outbreak in China and the disease's spread to Europe – also enabled companies and supply chains to take steps to mitigate risk prior to the global lockdown. The shortage in reagents to develop COVID-19 tests, vaccines and therapies has been well documented. It is also essential to continue supplying reagents to developers of cell and gene therapies for cancer and other diseases.

For a company such as ours, which supplies reagents to many parts of the cell and gene therapy sector, it is important to plan for the unexpected. There have been a number of times since we were founded in 2001 that the world has experienced challenges to global supply lines, from the shock of the attack on New York City in September 2001 to the eruption a few years later of the Eyjafjallajökul volcano in Iceland. Whilst these events caused short-term disruptions to global supply lines, there have been other purely viral challenges. The SARS pandemic in 2002-04 demonstrated how a coronavirus can spread, and the measures that governments may need to take to quell it.

When the infection started to spread in China, it became critical to move quickly before the SARS-CoV-2 virus reached Europe. The biggest challenge for companies supplying the cell and gene therapy sectors has been to maintain supply chains, both for incoming materials, as well as outgoing products. It was inevitable that obtaining all stock, from raw materials to laboratory equipment, might produce a major obstacle as global supply chains narrowed. As a result, it was essential to considerably increase stock levels before the shutdown actually took effect.

At the other end of production, it was important to move as much finished product as possible to different locations around the world to be ready to supply different customers globally. This especially related to our lead GMP product, a transfection reagent used in the production of viral vectors.

Increasing communication with our partners, including couriers and transporters worldwide, has also proved vital from the outset. As a result, we have been able to maintain global shipments. Appointing, and maintaining relationships with reserve transporters has also proved important. When a transporter in one location is unable to continue operations, another is immediately appointed.

Another aspect of our response has been to tighten safety rules at our laboratories and research and development facilities in France, which has been badly affected by the pandemic.

As with many companies across Europe, we immediately set up home-based offices and working practices for all positions not directly involved with scientific operations in order to protect employees of the operational teams. In addition, a regular turnover of employees was immediately implemented to minimise the number of people on site at the same time. We've also had to divert significant additional resources to different sectors of the company. The supply chain department has been bolstered for managing shipments, with additional resources needed to manage reception and shipments of goods, as well as the significant increases in documentation.

Backup plans and staff are needed should any employees need to self-isolate. Daily management meetings have followed progress and changes in stock and demand. The operations team has received daily reports to inform them about resultant changes and anticipating risks. We have also appointed an international crisis management team that interacts daily to assess immediate issues, threats and plans for any future contingencies.

Indeed, in the middle of the crisis, we were able to launch a new reagent for improving AAV production for large-scale manufacturing. This will provide, in the teeth of a global pandemic, a solution to the viral vector bottleneck.

This article was written by Géraldine Guérin-Peyrou, director of marketing and communication at Polyplus-transfection SA in Illkirch-Graffenstaden, France.

