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In general, what is a viral vaccine and what are their strengths and weaknesses?

Viral vaccines contain either inactivated or attenuated viruses with the aim of inducing a protective immune response in the recipients against the respective infectious disease. The induction of this immune memory is made up of two parts; antibodies which bind to an invading virus and prevent proliferation and also the cellular immune memory which has multiple pathways to prevent and eliminate viral infection. Such vaccines are available against a variety of viral diseases, including mumps, measles, rubella, and influenza. The Oxford/AstraZeneca vaccine against COVID-19 is of a slightly different type of viral vaccine, containing a weakened and modified adenovirus originally isolated from chimpanzees, this virus has been genetically modified to express the spike gene from the SARS-CoV-2 virus. The corona vaccines developed by Moderna and BioNTech/Pfizer, on the other hand, contain no virus particles at all but instead the mRNA coding selected structures of the coronavirus. They rely on the ability of the vaccinated person's body cells to synthesize and present the antigens against which the body's immune system subsequently reacts.

Vaccines are key to combating viral diseases because viruses do not possess a metabolism of their own and thus offer fewer and more challenging targets for therapeutics than, for example, bacteria that can be targeted with antibiotics. All viruses mutate and change their surface structures over time. If this affects the structures targeted by the vaccine, this can reduce the effectivity of the vaccine to an extent that a new vaccine is needed. This is the case for influenza vaccine of which some components change each year.

What are some issues and obstacles faced by the pharmaceutical industry in bringing vaccines to market? How are companies working to overcome these obstacles?

A frequent issue is a lack of clinical data, information on the protective correlates of immunity. Such information is important to design a vaccine and to determine reliable parameters for the evaluation of a vaccine's efficacy. Gathering a larger number of samples from patients who have recovered from a natural infection and with different medical conditions is helpful, but this is often difficult for a variety of reasons. A further issue is the limitations of animal models. The antigens that mice, rabbits, and even primates recognize, as well as the mechanisms of protective immunity, are often not the same as in humans. Further advances in bioinformatics, systems biology and high-throughput screening could lead to progress here. Developing experimental human challenge infections has also been proposed, but this raises ethical questions. Then there are financial issues. While the costs of developing vaccines can go into the billions, some countries that are most affected by disease are unable to afford to immunize their population. Philanthropists have sometimes stepped into the breach to cover the shortfall. But governments in all countries must be made aware that stemming an outbreak at an early stage elsewhere can stop it from reaching their own populations.

Patient safety is always of paramount importance when developing any new pharmaceutical. Can you describe how current GMP guidelines are ensuring vaccine safety for patients?

Current GMP guidelines cover three areas: ensuring the quality of the starting material, controlling the manufacturing process, and testing the vaccine product.

Traditional viral vaccines start with a cell line and viral seed. Both of these components require comprehensive safety testing to ensure there has been no contamination. Contamination can come from two sources; either there is the contamination in the starting materials or there is a breakdown in the GMP manufacture and contamination enters at this point. There are well prescribed regulations on the portfolio of the testing that is required to be performed on the starting materials. Suppliers must certify to have performed the appropriate tests and the laboratories carrying out these tests must have completed the required regulatory audits.

It is important to establish and validate the manufacturing process to ensure that the conditions are reproducible between production batches. If recombinant DNA technology is involved, the molecular integrity of the gene being expressed and the phenotypic and genotypic characteristics of the host cell after long-term cultivation (i.e., end of production testing) should be established.

A considerable number of QC tests must be performed to analyze the final product. Most vaccines are administered as injectables, so sterility testing and endotoxin testing are important for patient safety.

In light of the current COVID 19 pandemic can you detail the products and services Merck offers to the industry and how these assets can be leveraged to bring safe vaccines to market quickly and efficiently?

As a global life science supplier, we expedite companies and institutions involved in COVID-19 response, vaccine research, and the development of therapeutics. Our relevant offerings, from raw materials to products and services for research and manufacturing, are accessible from a single web page.

Events around the spread of COVID-19 and its impact on public health continue to evolve. During this extraordinary time, we are committed to providing researchers, developers, and manufacturers with the products and services they need to aid the COVID-19 response. Our top priorities are staff safety, meeting the needs of our customers, providing accurate and timely information, and ensuring sourcing and business continuity.

We have mobilized a global task force to actively evaluate the supply chains of not only our own products but also the key raw materials we procure from suppliers in order to mitigate any potential disruption. Our business continuity plans embody our commitment to supplying our customers in all markets and providing timely support to the scientific efforts under way around the world, with products and services to support the detection of the coronavirus and the development of vaccines and therapies.

Inevitably, there will be future viruses that need vaccines developed quickly. How will Merck continue to offer its current and future clients the tools and technologies to effectively bring new treatments to patients?

In times when vaccines are urgently needed, QC testing must be particularly swift and straightforward without compromising the dependability of results. Speeding up product release has its benefits in the best of times, but during a pandemic every day matters to save lives. Easy to learn procedures that won't go wrong are immensely crucial when production is being ramped up, as tasks may need to be performed by staff with less experience. At the time the pandemic struck, we at Merck were in the fortunate position that our QC portfolio already comprised well-established rapid and automated technologies that deliver earlier results and help to streamline workflows, including user-friendly rapid sterility and bioburden testing systems. Without us, most of the corona vaccine projects around the globe wouldn't have been possible. BioNTech recently thanked us for our partnership, but we are at least as grateful to them for the chance of being an essential part of their incredible project. In close collaboration with BioNTech, we recently agreed to significantly accelerate our supply of the urgently needed lipids for producing the Pfizer-BioNTech Covid-19 vaccine. We are also further strengthening our own capabilities and capacities for the development and production of mRNA.

Check for our consolidated COVID-19 related offerings: sigmaaldrich.com/covid-19.html