VACCINE MANUFACTURING – EXTENSIVE EXPERTISE AND STRONG TRACK RECORD

Wacker Biotech has an outstanding track record and more than 20 years of experience as a contract development and manufacturing organization (CDMO) producing biologics, live microbial products and vaccines using microbial hosts. Our experience, capabilities and capacities allow us to provide full service from process transfer and/or development to (pre)clinical and commercial manufacturing. Wacker Biotech has profound expertise in the process development and manufacturing of a variety of vaccine products, including live attenuated, inactivated, (conjugated) polysaccharide and protein-based vaccines.

Past, Present and Future Vaccines

Vaccination draws on a long history of development and has evolved into a cost-effective and efficacious approach for the prevention of infectious diseases. The first successful immunization trials against human smallpox were conducted in the late 18th century using the lymph of cowpox-infected subjects.[1, 2, 3] In searching for the causes of disastrous diseases in the two centuries that followed, this breakthrough laid the groundwork for the discovery of numerous pathogens, progressively leading to whole pathogen (live attenuated, inactivated) and subunit (polysaccharide, toxoid) vaccines.[4]

During the 1990s, the use of protein-based and conjugate vaccines started to rise, with the aim of reducing adverse reactions to whole pathogen antigens and to induce stronger and longer-lasting immunity than could be achieved through unconjugated polysaccharides.[5]

Today, most approved bacterial vaccine products are conjugated (polysaccharides) and protein/toxoid antigens, which have gradually replaced traditional whole pathogen and polysaccharide products. This reflects a paradigm shift in vaccine production towards well-defined antigens, which in fact make up a large portion of the vaccine candidates currently evaluated in clinical trials.[5]

More Than 20 Years of Vaccine Manufacturing Experience

Wacker Biotech has an outstanding CDMO track record and uses a variety of microbial hosts to produce all types of established and future vaccine products. Our work rests on a foundation of more than 20 years of experience as a CDMO for vaccines, with deep expertise in manufacturing live attenuated, inactivated, (conjugated) polysaccharide and protein-based vaccine products.

Our production sites are home to state-of-the-art biosafety level 1 (Halle, Jena) and 2 (Amsterdam) facilities, as well as an explosion-proof room (Amsterdam) for manufacturing vaccine products under ICH and GMP quality guidelines. Our stainless steel fermenters range in capacity from 270 L to 1,500 L, and our single-use reactors can accommodate volumes

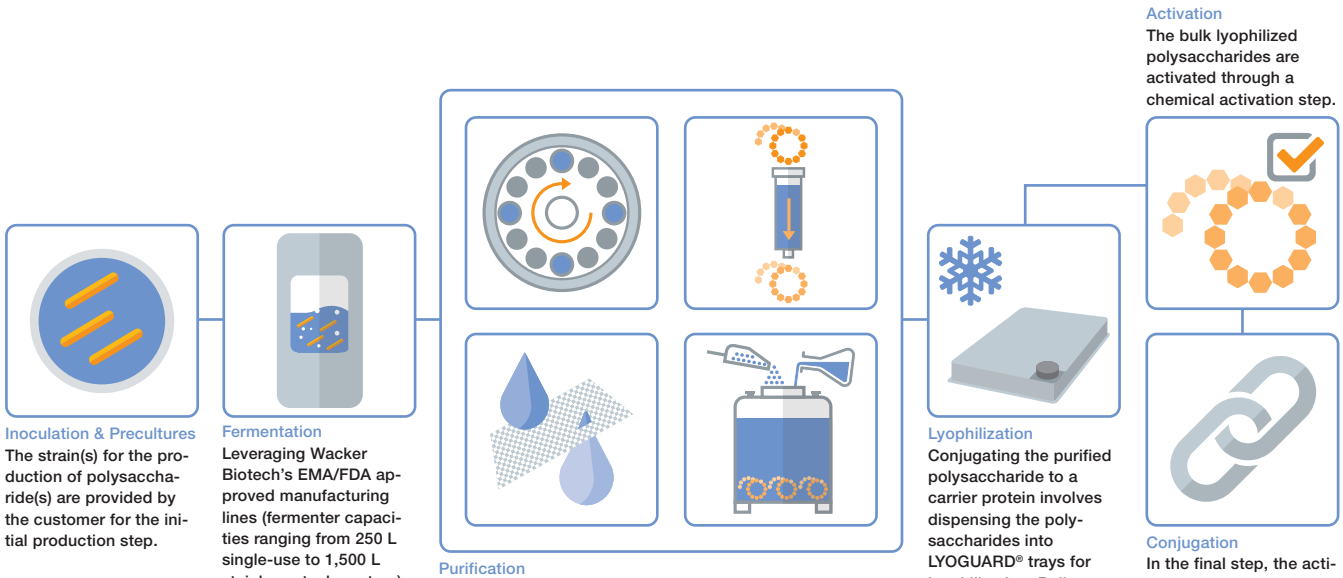
Vaccine Capabilities and Capacities

- >20 years of vaccine manufacturing experience
- From bench to commercialization (preclinical, phase I to III, commercial product)
- Process and analytical transfer, development and validation
- >650 GMP batches manufactured and released
- Inactivated, live attenuated, (conjugated) polysaccharide and protein-based vaccines
- Cutting-edge capacities
  - 270 L, 350 L, 2 x 1,500 L stainless steel bioreactors
  - Single-use bioreactors for volumes of up to 250 L
  - Biosafety level 1 (Halle, Jena, Amsterdam) and level 2 (Amsterdam) facilities
  - Explosion-proof room (Amsterdam)
  - Bulk lyophilization of up to 65 L
  - Fill-and-finish facility (DIN 2R to 20R vials) for up to 20,000 vials per batch

Selection of Vaccine Strain Experience

- *Escherichia coli*
- *Corynebacterium diphtheriae*
- *Haemophilus influenza B*
- *Klebsiella oxytoca*
- *Neisseria meningitidis A, C*
- *Pseudomonas aeruginosa*
- *Salmonella typhi*
- *Saccharomyces cerevisiae*
- *Vibrio cholerae*

Conjugated Polysaccharide Vaccine Production Overview



Inoculation & Precultures
The strain(s) for the production of polysaccharide(s) are provided by the customer for the initial production step.

Fermentation
Leveraging Wacker Biotech's EMA/FDA approved manufacturing lines (fermenter capacities ranging from 250 L single-use to 1,500 L stainless steel reactors) allows customers to adjust the scale of GMP processes to meet the needs of each project and development phase.

Purification
Purification of the polysaccharide from the fermentation broth usually includes several steps, such as:
- Centrifugation of the pathogen after chemical/thermal inactivation
- Concentration of intermediate product by ultrafiltration and/or depth filtration
- Precipitation of the polysaccharide using inorganic salts and/or organic solvents (explosion-proof rooms and equipment required)
- Chromatography steps

Lyophilization
Conjugating the purified polysaccharide to a carrier protein involves dispensing the polysaccharides into LYOGUARD® trays for lyophilization. Bulk lyophilization runs of up to 65 L are supported.

Activation
The bulk lyophilized polysaccharides are activated through a chemical activation step.

Conjugation
In the final step, the activated polysaccharides are chemically conjugated to the carrier protein(s).

of up to 250 L. Furthermore, at our site in Amsterdam, we operate a modern GMP fill-and-finish facility for aseptic filling operations of DIN 2R to 20R up to 20,000 vials per batch as well as bulk lyophilization up to 65 L. Wacker Biotech has produced and released more than 650 GMP vaccine batches for clinical (phase I to III) and commercial applications. We can provide quick, flexible and efficient solutions for customer-specific process development and process transfer, complemented by tailored analytics for quality control. Our expertise and capabilities make us a highly reliable partner for manufacturing classic vaccines as well as frontline and emerging future vaccine products. In addition to manufacturing a variety of live attenuated, inactivated and protein-based vaccines, Wacker Biotech also has a great deal of experience in manufacturing (conjugated) polysaccharide vaccines for clinical and commercial applications. A schematic overview of how such conjugated polysaccharides are typically produced at Wacker Biotech is provided in the figure above.

References

[1] Gross et al. 1998. Int. J. Infect. Dis. 3(1).
[2] Pead 2017. Pediatrics. 139(4).
[3] Riedel et al. 2005. Proc. Byl. Univ. Med Cent. 18(1).
[4] Plotkin 2014. Proc. Natl. Acad. Sci. USA. 111(34).
[5] Micoli et al. 2019. Expert Rev. Vaccines. 18(9).

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