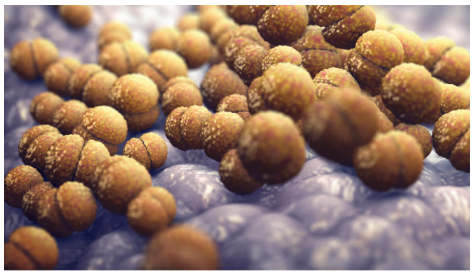
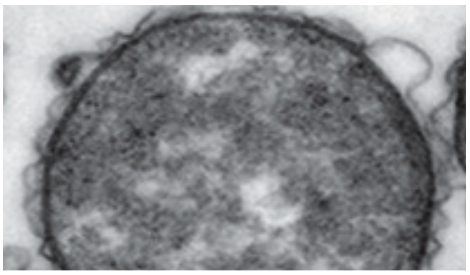
Vaccsheet

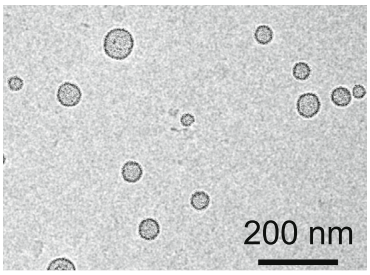
Avacc® 13: Nonamen® – An outer membrane vesicle vaccine protecting against *Neisseria meningitidis* serogroup B



Neisseria meningitidis



High blebbing mutant



Outer membrane vesicles

Introduction

Intravacc developed Nonamen, an outer membrane vesicle (OMV) vaccine based on 9 serotypes of the major protective antigen PorA to achieve broad protection. The detergent-free production process results in highly stable OMVs with low reactogenicity.

Competitive advantages

The vaccine contains 9 different serotypes of the variable antigen PorA which protect against a wide range of *Neisseria meningitidis* strains. The manufacturing process is scalable and gives a high yield, ensuring a low cost of goods. The vaccine complies with all requirements laid down in the European Pharmacopoeia and GMP.

Vaccine strains

Three vaccine strains have been genetically engineered, each harboring 3 PorA genes at carefully selected loci representing different *Neisseria* serotypes. Further genetic modifications result in enhancement of vesicle formation and reduction of the LPS related toxicity while maintaining the intrinsic adjuvant properties. Together the 3 vaccine strains comprise antigens of 9 different Neisseria serotypes strains. The vaccine strains have been adapted to a specifically developed animal-component-free production medium. GMP master and working seedlots have been prepared and tested.

Process

The Upstream Process (USP) is a highly robust process based on growth of bacteria in a bioreactor. The USP was developed to enable extraction of OMVs applying a detergent-free process.

Purification and formulation are according to standard protocols. This production process yields approximately 50.000 doses from a 40L harvest, (van de Waterbeemd et al. 2013).

The patented detergent-free production process, ensures that immunogenic outer membrane lipoproteins are retained within the vaccine.

Stability

Genetic stability testing has shown that the strains are stable for many generations. The nonavalent OMV vaccine is stable for at least 24 months.

Protection

Nonamen is protective in rabbits and mice based on the induction of serum bactericidal antibody responses, which is the accepted correlate of protection. Specifically, the vaccine induces bactericidal antibodies against all 9 PorA's.

Safety

A repeated dose toxicology study was performed under GLP regime. Rabbits were vaccinated intramuscularly 5 times with OMVs containing either 7.5 or 15 µg PorA. Only a minimal rise in body temperature (< 1°C) was observed 4 hours after immunization. No major local or systemic pathological abnormalities were observed (Kaaijk et al. 2013).

GMP

Equipment and documentation are in place to manufacture and test the vaccine under GMP.

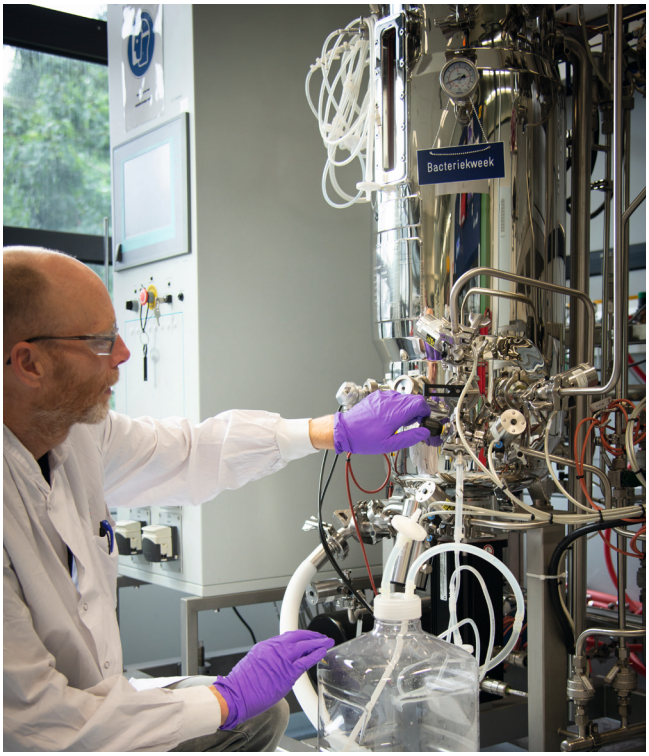
Key assets Intravacc vaccine:

- Chemically defined media, free of animal components
- Dedicated genetic engineering to minimize LPS toxicity and optimize antigen composition
- Robust production process
- Patented technology (OMV extraction WO/2013/006055)
- GMP procedures for preparation and testing are in place, as are GMP seedlots and Bill of Testing.
- Broad protection by nine PorA's and high retention of additional protective antigens by a mild extraction process
- Low reactogenicity in animals.

Partnering opportunity

Intravacc offers:

- A license on:
  - The 3 vaccine strains each comprising 3 porA genes
  - Patented DSP technology allowed in the US, pending in multiple countries ncluding the EU, US and Asia
  - The trademark Nonamen registered in the EU
- Co-development of the Nonamen vaccine until market introduction
- Expert knowhow, infrastructure and equipment to enable a short time to market.



Refereces

- Van de Waterbeemd B, Zomer G, Kaaijk P, Ruiterkamp N, Wijffels RH, van den Dobbelsteen GP, van der Pol LA. PLoS One. 2013 May 31;8(5):e65157
- Kaaijk P, van Straaten I, van de Waterbeemd B, Boot EP, Levels LM, van Dijken HH, van den Dobbelsteen GP. Vaccine. 2013 Feb 4;31(7):1065-71

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