Solid Formulation of a Recombinant Anthrax Vaccine

Carrie Schneider, Greg Cantin & Jason Payne - Pfenex Inc.; Jon Telfer & David Smith - Glide Pharma

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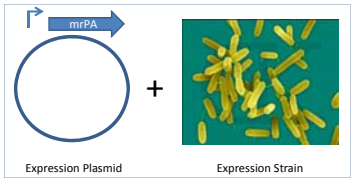
Overview

Pfenex and Glide Pharma have an ongoing collaboration to develop an anthrax vaccine containing the recombinant Protective Antigen (rPA) from *Bacillus anthracis* produced using Pfēnex Expression Technology™, which is suitable for delivery with the Glide SDI® (Solid Dose Injection) technology. This approach will address two important logistical constraints of the currently available vaccine, namely, long term stability during storage at room temperature and ease of administration. Glide's SDI system comprises a re-useable spring powered actuator and a disposable single-use cassette which houses the vaccine formulation. The formulation is a small solid implant packaged in the cassette. In use, the cassette is unpacked and inserted into the actuator. The action of pushing the loaded actuator against the injection site "charges" a spring in the actuator, which at a preset compression value pushes the vaccine rod through the skin and into the subcutaneous tissue. The formulation dissolves and the vaccine is released into the surrounding tissue. In proof of concept studies in humans for Glide's therapeutic development programs, the delivery was found to be preferred to delivery with needle and syringe. Using the company's core technology for recombinant protein expression, Pfenex has manufactured multiple gram quantities of a stable variant of the rPA antigen in a cGMP compliant production process. The mrPA antigen (before formulation into a solid dose) was shown to be highly immunogenic in rabbits in both adjuvanted and non-adjuvanted forms and fully protected the animals from an aerosol spore challenge. Studies to incorporate the antigen into the solid dose formulation have been completed; the physical properties of the implant and protein quality were found to be stable for at least three months after storage at temperatures of up to 40°C.

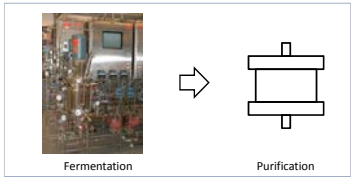
Glide's Solid Dose Injection system

Glide's SDI® (Solid Dose Injection) system comprises a re-useable spring powered actuator and a disposable single-use cassette which houses the vaccine formulated in a small solid implant. Pressing the loaded Glide SDI against the injection site "charges" a spring in the actuator, which at a preset compression value pushes the vaccine through the epidermis and dermis and into the subcutaneous layer. The formulation dissolves, releasing the vaccine into the surrounding tissue

Pfenex's recombinant Protective Antigen



Pfēnex Expression Technology™ combines a selected engineered *Pseudomonas fluorescens* expression strain with a variant of Protective Antigen (mrPA) selected for reduced proteolytic degradation.



High yield fermentation process generates multiple grams per liter of the mrPA antigen

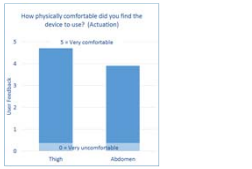
Potent antigen protects 100% of rabbits from a *B. anthracis* aerosol spore challenge in two doses in both adjuvanted and non-adjuvanted liquid forms.

Human Factor Study

The human factor study follows strong progress in Glide's device design optimization program, which is the final development stage prior to manufacturing scale-up.

The study, which enrolled 22 subjects with no prior experience of injection devices, was designed to assess the overall comfort and ease-of-use of the Glide SDI® and to identify any potential improvements in the design's utility.

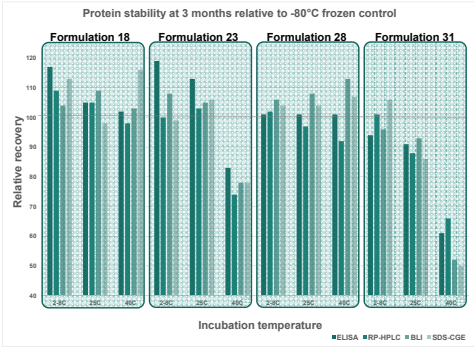
The study assessed the accessibility of potential administration sites with the system. During the trial, the subjects rated their experience, and the results show that users scored the design highly in each of the usability tests undertaken.



Stability

Antigen stability of mrPA in SDI was evaluated by SDS-CGE and RP-HPLC to monitor proteolytic degradation and mrPA content, by ELISA with neutralizing antibodies to evaluate antigenicity and structural stability and BLI to evaluate CMG-2 (ANTXR2) receptor binding.

In selected solid dose formulations, the antigen is stable at up to 40°C for at least 3 months.



Summary

- Glide 's Solid Dose Injector delivery method is preferred to needle and syringe
- Pfenex's process has been developed to manufacture mrPA at high yield, purity.
- The purified mrPA antigen bulk drug substance is stable and potent
- Solid dose formulations with mrPA have been identified that are stable for at least three months at 40°C.

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