DEVELOPMENT OF A SOLID DOSE INJECTION (SDI®) RECOMBINANT ANTHRAX VACCINE

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Glide TECHNOLOGIES

Developing patient centric devices & diagnostics

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ABSTRACT

Glide Technologies is a UK development company focused on solid dose formulations of therapeutics and vaccines, and non-invasive diagnostics. 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 formulation. Pressing the loaded Glide SDI® against the injection site "charges" a spring in the actuator, which at a preset compression force pushes the vaccine into the subcutaneous layer. The formulation dissolves, releasing the API or vaccine antigens into the surrounding tissue.

Recent studies have confirmed the ability of the Glide SDI® to consistently deliver a solid dose formulation to the subcutaneous layer in a well-established model of human skin (porcine neck). Several studies have been conducted to confirm the utility and ease-of-use of the system's design and operation in naïve human volunteers. In proof of concept studies conducted in humans with Glide's other pipeline products, the delivery was found to be preferred to injection with a needle and syringe.

Previous work at Glide has shown that experimental solid dose vaccines against seasonal influenza, diphtheria, and *H. influenzae* could be successfully prepared and were capable of generating protective immune responses in animal models.

Glide Technologies and Pfenex have collaborated to develop an anthrax vaccine containing the recombinant Protective Antigen (rPA) from *Bacillus anthracis* produced using Pfenex Expression Technology™ and formulated and delivered using the Glide SDI®. 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.

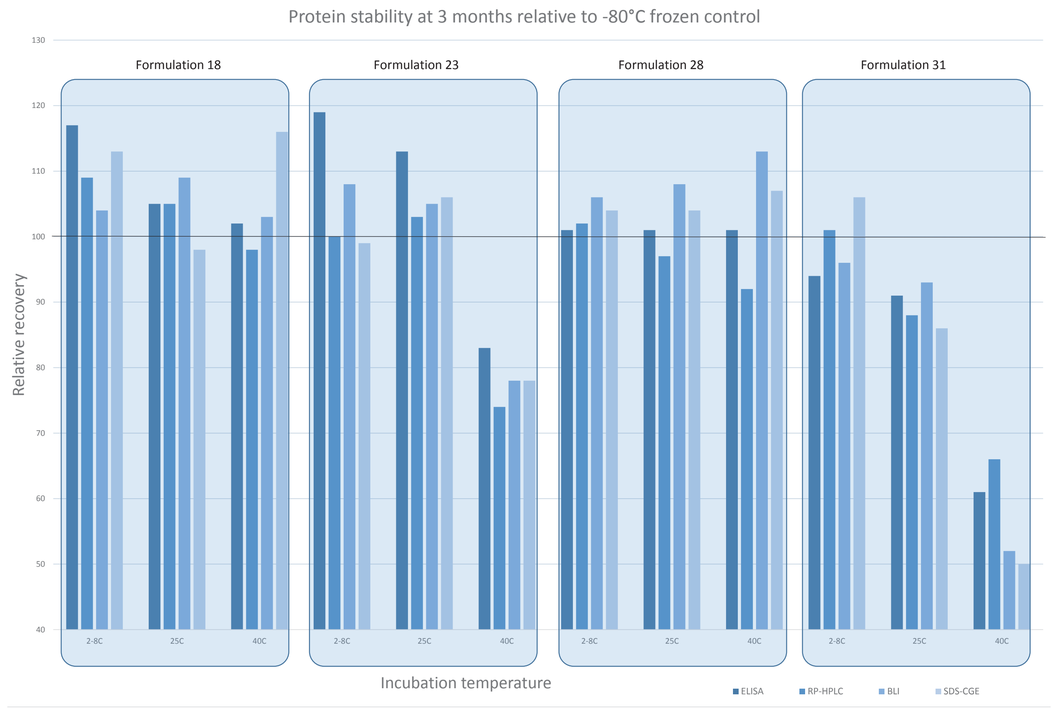
The Pfenex mrPA antigen (before formulation into a solid dose) was shown to be highly immunogenic in rabbits in both adjuvanted and non-adjuvanted forms and fully protected the animals from an aerosol spore challenge. Studies to incorporate the antigen into a solid dose formulation have been completed; the physical properties of the formulation and protein quality were found to be stable for at least three months after storage at temperatures of up to 40°C, making this a promising candidate for the next generation anthrax vaccine.

ANTHRAX VACCINE DEVELOPMENT

The Vaccine Technologies to Advance Next Generation Anthrax Vaccine program aims to develop a new anthrax vaccine with the target product profile of a temperature stable solid dose injection (SDI®) formulation, which will not require cold chain storage and distribution, and, which induces rapid onset of an immune response.
Glide Technologies formulated the anthrax antigen (mutant recombinant protective antigen - mrPA) provided by Pfenex in its proprietary SDI® drug delivery systems.
Samples were analysed using four protein analysis methods to assess protein content and quality at the three month timepoint (T-3):

- SDS-CGE/PAGE to monitor content and proteolytic degradation
- Reverse phase HPLC (RP-HPLC) to monitor degradation
- Bio-layer interferometry (BLI) to monitor the ability of mrPA to bind to the capillary morphogenic gene-2 (CMG-2) receptor
- ELISA to evaluate the relative antigenicity using structurally-sensitive monoclonal antibodies that bind to different structural domains of mutant mrPA

The value at T-3 for the samples was expressed as a percentage of the T-3 -80°C sample.



HUMAN FACTOR STUDY

The human factor study follows strong progress in the company's device design optimisation programme, 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 when self-administered. Additionally, 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. It is anticipated that the device will be further optimised for administration by a nurse/physician.

CONCLUSIONS

- The formulations stabilise mrPA for 3 months at 40°C
- Glide SDI® device use is simple, intuitive and comfortable

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