THERMOSTABILIZATION OF ADENOVIRUS-VECTORED VACCINES, REMOVING THE NEED FOR CONTINUAL COLD-CHAIN STORAGE

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Challenges around affordable and reliable supply of vaccines that need to be transported and maintained in the cold-chain to remain effective are a hindrance to realizing their full potential. We will describe preparation for GMP manufacture and Phase I clinical trial of a new technology for vaccine thermostabilisation. We will also describe application of the same technology to a novel veterinary vaccine which is entering advanced development.

The sugar-matrix thermostabilisation (SMT) technology involves application of vaccine in a simple disaccharide-based buffer to a non-woven matrix, similar to a pad of filter paper. This is followed by drying at ambient temperature and pressure (i.e. without a freezing step, enhancing suitability for freeze-sensitive products). The materials and process are simple and cheap.

We have previously shown that SMT allows for the storage of viral vectored vaccines such as modified vaccinia virus Ankara (MVA) and adenovirus vectors at up to 45^{o}C for several months with minimal losses[1,2]. More recently we have shown the technique can improve stability of various other vaccine types, ranging from virus-like particles through to enveloped RNA viruses. In many cases, the level of thermostability achieved would allow for “last mile” vaccine distribution via the ‘extended controlled temperature chain’ (ECTC), or even allow prolonged storage at uncontrolled ambient temperature. This would decrease distribution-associated costs/ losses and increase vaccination feasibility in hard-to-reach areas.

We have now received funding for GMP manufacture and Phase I clinical trial of an SMT-formulated adenovirus-vectored rabies vaccine, ChAdOx2 RabG. We will describe the production of custom wet-laid non-woven matrices with optimized SMT performance, using processes and materials suitable for use as an input to a GMP process. We will further describe the development of simple apparatus suitable for executing the process for pilot GMP batches, the optimization of the drying process and excipient composition, and the application of frequency modulation spectroscopy for non-destructive analysis of residual moisture content. Finally, we will describe the application of the technology to a formulation of ChAdOx1 RVF, an adenovirus-vectored vaccine against Rift Valley Fever Virus which is being developed for both human and veterinary use. In this case, SMT is applied to an ultra-low-cost drug substance designed for veterinary use (cell lysate which has been clarified and ultrafiltered but not chromatographically purified), emphasizing the suitability of the approach for low-cost and One Health applications.

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2. Dulal, P., et al., Potency of a thermostabilised chimpanzee adenovirus Rift Valley Fever vaccine in cattle. Vaccine, 2016. 34(20): p. 2296-8.