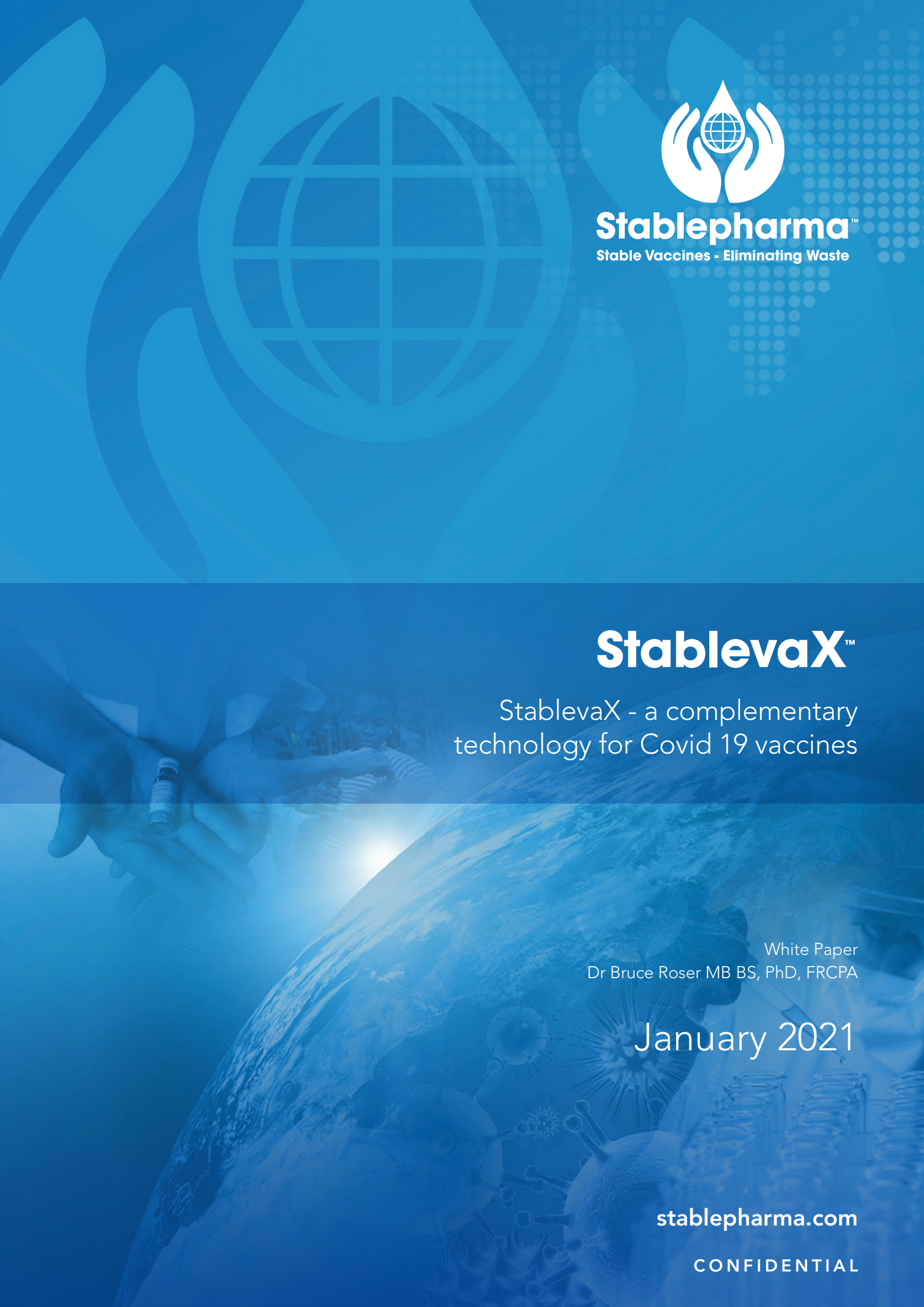
Stablepharma™
Stable Vaccines - Eliminating Waste

StablevaX™

StablevaX - a complementary technology for Covid 19 vaccines



White Paper
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stablepharma.com

Introduction

StablevaX offers a novel approach to vaccine stabilisation that aims to enable otherwise highly thermally-sensitive vaccines to be stored at room temperature.

The WHO estimates that up to 50% of all vaccines manufactured currently lose their efficacy before they can be delivered, often as a result of cold-chain failures. Removing the need for a cold chain has the potential to transform vaccine delivery pipelines and dramatically improve vaccine access globally. Here at Stablepharma, our goal is to incorporate this transformative technology into the manufacture process of currently available vaccines to mitigate unnecessary death and disability at the hands of vaccine-preventable diseases.

In light of the ongoing COVID-19 pandemic, the challenge of equitable and efficient vaccine delivery has never appeared starker. Stablepharma believes StablevaX could be a crucial complementary technology to currently available COVID-19 vaccines, especially those using mRNA-based approaches. All of the current vaccines require the cold chain from factory to the patient to maintain potency, with the two mRNA vaccines (Pfizer/BioNTech and Moderna) require -20° to -80° storage. The need for these extreme cold temperatures has severely hindered vaccine roll-out efforts, even in countries with robust healthcare systems, and has already resulted in vaccine doses being wasted. It is vital to ensure comprehensive immunity worldwide to protect nations from subsequent waves of infection, and therefore it is imperative that we have vaccines that can be safely delivered to even the most remote corners of the world.

StablevaX™ technology converts existing vaccines to a thermally stable form so that they can be **easily transported, stored, and stockpiled for long periods at any temperature**, high or freezing, without loss of potency. The aim is to ensure that all vaccines can all be removed from the refrigerated cold chain and stored for months or even years at room temperature.

Our C.S.O and founder Dr Bruce Roser MB BS, PhD, FRCPA identified and patented the process of using the sugar Trehalose to achieve a state of 'suspended animation' in a sugar glass to thermally stabilize many vaccines. Trehalose is a naturally occurring sugar with remarkable chemical stability that can stabilize delicate molecules against very hostile environments. This property is observed naturally in some living organisms, most notably in the case of the "resurrection" plant.

Stablepharma does not make or develop new vaccines - we take existing vaccines and stabilize them in trehalose glass within the pores of a medical grade sponge, using the patented StablevaX™ technology. This sponge is then housed in the barrel of a syringe, which acts both as storage and delivery vessel. By housing the pre-dosed and stable vaccine in an AD syringe, we ensure safe, efficient, and waste-free delivery without the need for a cold chain.

Pre-dosed syringes – just add water

1. Remove sterile wrapping
2. Take up water
3. Blow out air
4. Inject
5. Correct vaccine dose injected

- Just like a normal injection.
- Follows WHO protocol for vaccination.
- Can be used by a paramedic without any extra training.

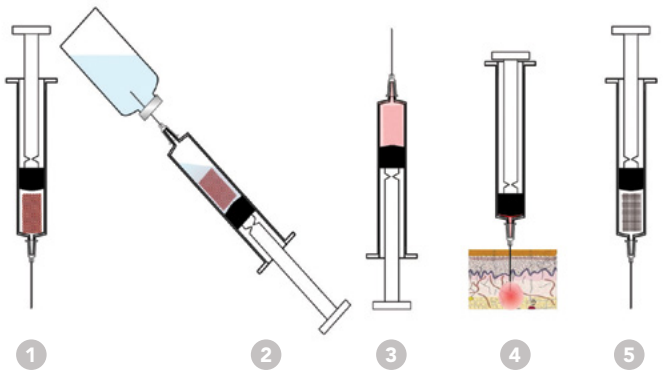

Figure 1 A schematic of the delivery steps for a StablevaX-stabilised vaccine.

Technology & Development Status

StablevaX™ technology, outlined in Figure 1, combines two separate innovations together to deliver a powerful new approach to vaccine storage and administration;

1. Stabilization of the vaccine in a dry trehalose glass, formed within the pores of a medical grade sponge matrix located in the AD injection syringe.

2. Rehydration by aspiration of water, and injection of the full dose by compression of the sponge in a highly efficient procedure at the point of use.

The stabilization process used in StablevaX has been found to be effective in preserving 13 different vaccines to date, including common childhood vaccines and live virus vectors. It is also able to preserve recombinant Protective Antigen (rPA) vaccine against Anthrax, which is usually stored at -20 to -80°C, providing a precedent for its use even with highly thermally unstable vaccines (please see 'Examples' deck).usually stored at -20 to -80°C (please see 'Examples' deck)

Animal Trial

Tetanus vaccine stabilized with StablevaX™ has been shown to be effective in a pre-clinical animal trial (please see 'examples deck'). . This study was conducted at the U.K. National Institute of Biological Standards and Control (NIBSC) in September 2016 under the supervision of the MHRA. NIBSC is a World Health Organization (WHO) and UK National Health Service (NHS) affiliated facility.

In this study, groups of 10 Guinea pigs were treated with tetanus vaccine that had been stored one of three ways:

1. At 4°C, as per manufacturer's guidelines
2. At room temperature, after stabilization using StablevaX technology
3. At room temperature, without stabilization

Immunogenicity (anti-tetanus antibody response) and vaccine-derived antigen levels were assayed using an in-house monoclonal antibody capture ELISA assay. The graph shows the Individual antibody levels at 4 and 8 weeks in groups of 10 Guinea Pigs. The data shows that there isn't any significant difference between antibody levels in the group treated with the stabilised vaccine relative to the fresh vaccine.

Medicines & Healthcare products Regulatory Agency

NIBSC

Stablepharma is currently collaborating with the European manufacturer BulBio to progress their adult Tetanus, diphtheria booster (Td) vaccine in the StablevaX™ device through pre-clinical protection trials for potency, followed by First in Human clinical trials in order to obtain regulatory approval to then market the first StablevaX™ vaccine.

A series of animal trials for several other vaccines to assess retention of full protective efficacy are planned for 2021.

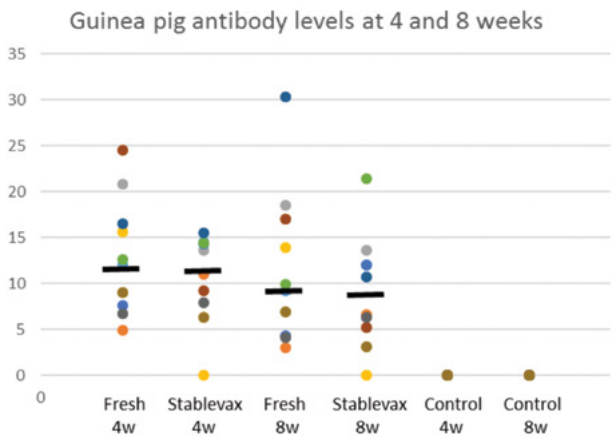

Figure 2 Antibody levels at 4- and 8-weeks post-vaccination with either fresh or stabilised tetanus vaccine, or with a control.

Thermally stabilized vaccine RNA

Background

Several years ago, Dr Bruce Roser's 'not-for-profit' Quadrant Research Foundation in Cambridge was awarded a grant by the WHO to stabilize live oral poliovirus vaccine (OPV). His laboratory collaborated with Dr Phil Minor at NIBSC in London, who contributed expert advice, supplied the OPV, and performed the live virus assays.

The project showed that the virus outer capsid which enclosed the RNA genome prevented the trehalose from entering the virus' core to stabilize the RNA. All attempts to manipulate the capsid to allow entry of trehalose simply destroyed the structure of this notoriously fragile virus. It was originally thought that the capsid was in fact somewhat permeable, but that the RNA in the core could not be stabilized with trehalose. It would not have been a surprising result as RNA is widely known to be notoriously unstable in vitro.

To complete the study for the WHO, the RNA was extracted from the OPV vaccine, purified and dried in our trehalose buffer to establish whether it could be stabilized with trehalose.

The **result was surprising** and showed that the trehalose drying technology not only prevented RNA disintegration, but the molecule was intact even at 45°C as shown by gel electrophoresis (Figure 3)

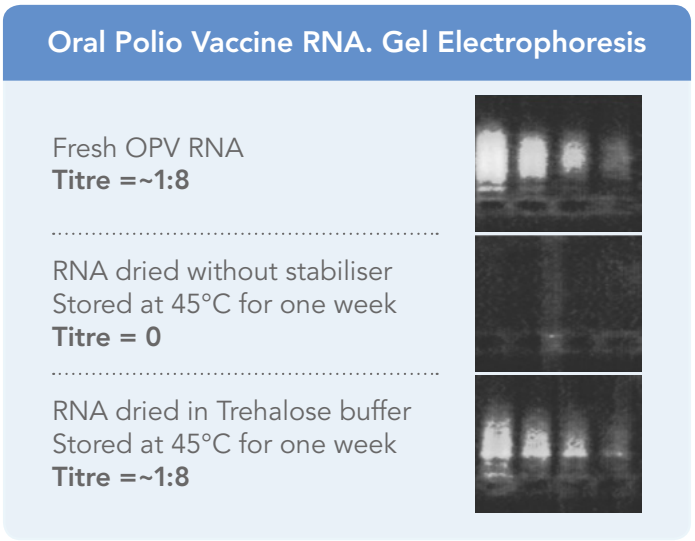

Figure 3 A 2-fold serial dilution comparison of OPV-derived RNA levels, measured using gel electrophoresis, following different storage approaches.

The result indicated that the stabilizing ability of an inert trehalose glass was more powerful than we had believed at the time and might enable development of a new class of thermally stable nucleic-acid-based vaccines.

mRNA COVID-19 vaccines stabilized with StablevaX™?

Our technology may have considerable promise in rendering mRNA Covid 19 vaccines stable at even high ambient temperatures, enabling their safe distribution worldwide.

While the Stablepharma technology preserves the molecular structure of oral polio vaccine RNA as judged by gel electrophoresis, it is important to point out that this RNA has not yet been tested for its functionality.

Current mRNA Program:

Stablepharma has recently initiated a SARS-Cov2 RNA program to test whether the StablevaX technology can stabilize the lipid nanoparticle/mRNA vaccine at higher temperatures. Stablepharma is establishing a strategic partnership with two major academic institutions in the UK in order to work jointly on this vaccine stabilization program.

We are using a 3-step approach to stabilize SARS-CoV-2 mRNA vaccine of which the first step is to establish that naked CoV-2 mRNA can be stabilized in trehalose in the same way as naked poliovirus RNA.

Co-Development Proposal

Based on the previous work and our ongoing mRNA program, we believe that the opportunity to thermally stabilize an mRNA vaccine at elevated temperatures is well worth pursuing. This will be crucial in delivering RNA vaccines to remote potential reservoirs of Covid infection.

With the right partnering approach such as a commercial co-development agreement, this work could be fast tracked at a reasonable cost and if successful the contribution to world health could be a landmark event, especially since mRNA vaccines have great potential to immunize against other diseases.

What we specifically need from a partnering process or a co-development agreement is:

1. **Investment** to create a dedicated science team, with the necessary specialized equipment.
    - Stablepharma has the laboratory space and standard laboratory equipment available along with a competent and experienced management team to oversee the project.
    - The company is currently in discussion with two UK University's with the aim for them to contribute their expertise in the science of Lipid nanoparticle encapsulation of antigens, including RNA.
2. **Access** to the samples of the commercial, thermally unstable, COVID-19 vaccine and data on analytical techniques.

Summary

Whilst Stablepharma is not directly involved in the efforts to develop new treatments or prophylaxis against the COVID-19 pandemic to date, we potentially offer an important contribution to the logistical problems of storage, stockpiling, distribution, and safe delivery of these products worldwide.

This applies to all the different types of vaccine that require storage in a cold chain but is of particular urgency and relevance with mRNA-based vaccines.

Stablepharma stands ready to make its technologies widely available in the global fight against the COVID-19 pandemic and would be willing and able, with additional resources, to conduct Research and Development to co-develop the stabilized version of these vaccines in partnership with vaccine manufacturers and developers.

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