



Stablepharma™

Stable Vaccines - Eliminating Waste

Illustrative Examples of Extraordinary Stability
of Vaccines When Dried In Trehalose

**A world changing invention
for the stabilisation of vaccines**

June 2020

Updated ref stabilising RNA & Covid 19 vaccines

StablevaX™

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Illustrative Examples of Extraordinary Stability of Vaccines When Dried In Trehalose

Some Illustrative Examples of Extraordinary Stability of Vaccines When Dried In Trehalose

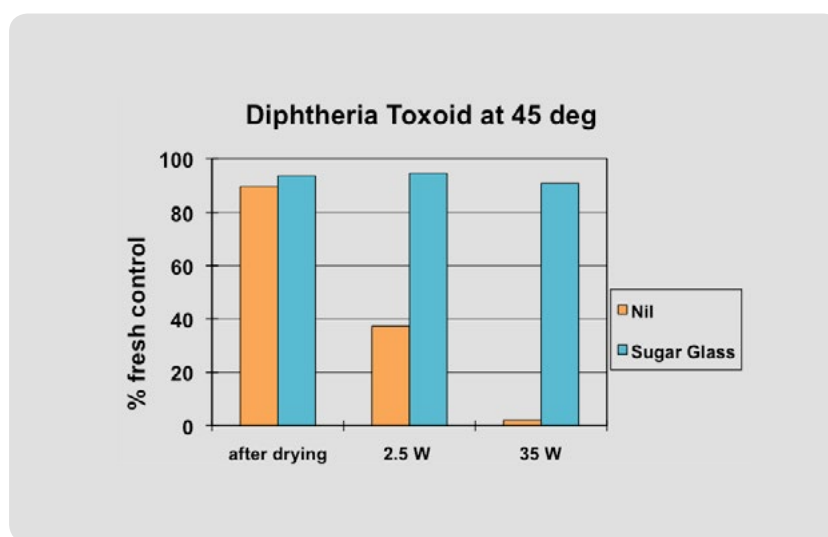
Taken from cumulative past experience in use of trehalose

StableVax technology uses two separate innovations together to develop a powerful new way of storage and delivery of vaccines.

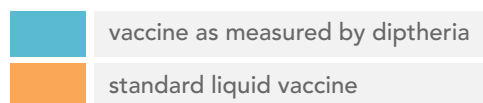
These technologies are

1. stabilisation of the vaccine in a trehalose glass within the pores of a sponge, which is housed and stored in the injection syringe.
2. Rehydration by aspiration of water, and injection of the full dose by compression of the sponge

The following examples illustrate that multiple different vaccines can be effectively stabilised in trehalose. Storage times illustrated are sometimes limited because later data is no longer accessible to Stablepharma

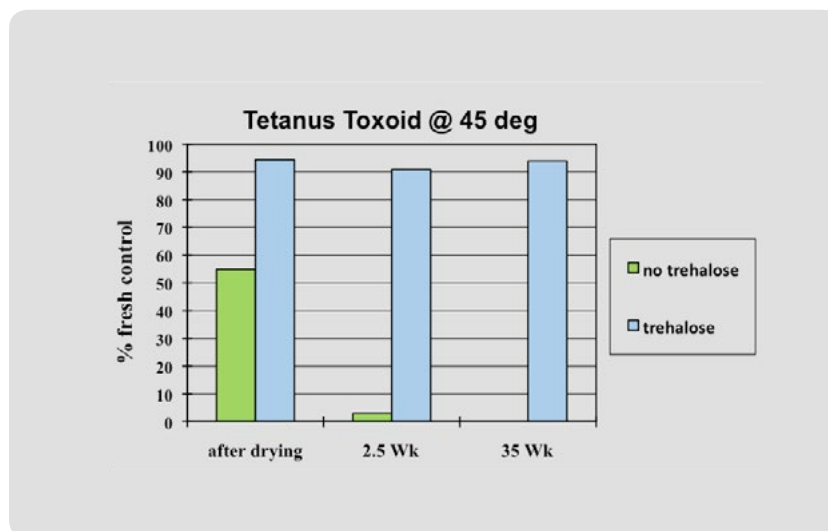


Recovery of stabilised Diphtheria vaccine compared with standard liquid vaccine as measured by diphtheria-specific antibody after storage at 45° for 35 weeks. This result is equivalent to storage at room temperature for over one year.

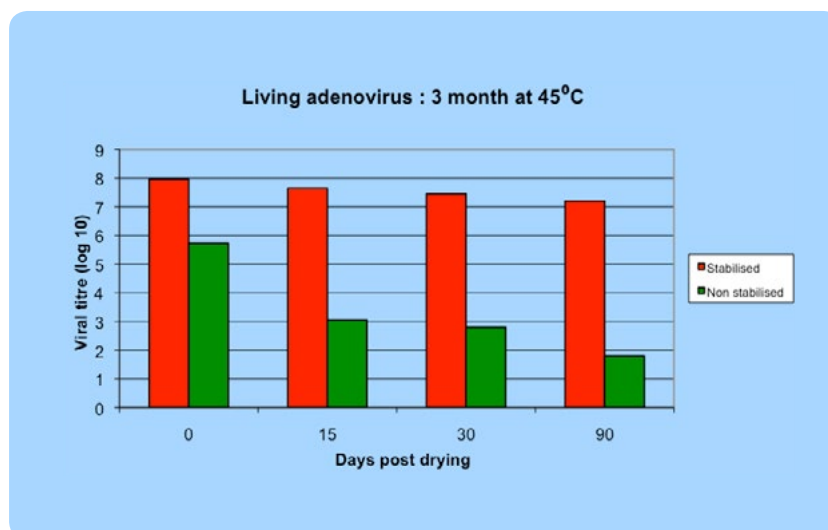




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Recovery of tetanus vaccine compared with standard liquid vaccine. As measured by tetanus-specific antibody. Also equivalent to room temperature storage for over one year.

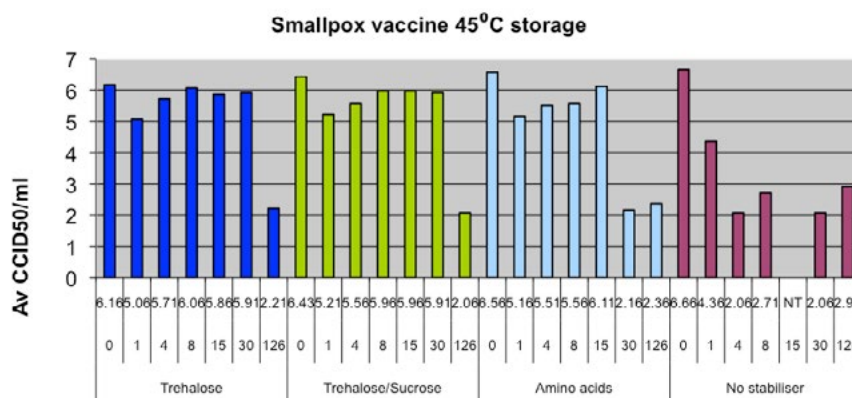


Adenovirus is used as a living vector to deliver DNA-based vaccines. Because of the virus envelope it is not possible to get the trehalose through this surface membrane and inside the virus to preserve the essential molecules. Nevertheless, it shows very useful stability when stored at 45° C for 3 months compared with the non-stabilised virus.



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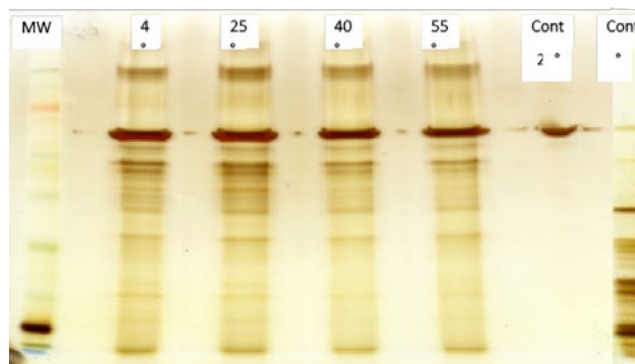
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Modified Vaccine Ankara (MVA) smallpox virus is another vector used to deliver DNA vaccines. In three different stabilisers **TREHALOSE** **TREHALOSE/SUCROSE** and **AMINO ACIDS** compared with virus with **NO STABILISERS**.

The stabilisers are fully protective at 45° C for 30 days but not by 126 days.

Anthrax (rPA) 18 month Stability



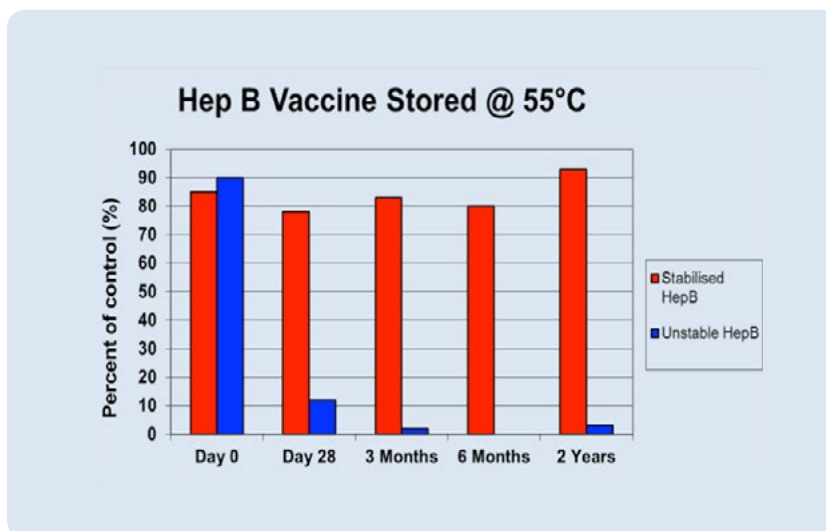
Recombinant Anthrax Protective Antigen stabilised and stored at various temperatures for 18 months.

SDS Agarose- molecular-sizing gel electrophoresis is used to measure the size of proteins and their fragments. They are loaded at the top. Aggregates of damaged molecules have difficulty penetrating the gel and remain at the top. The intact molecule is seen as the darkest band about a third of the way down. Damaged protein which is fragmented forms a series of bands of different sizes running further into the gel.

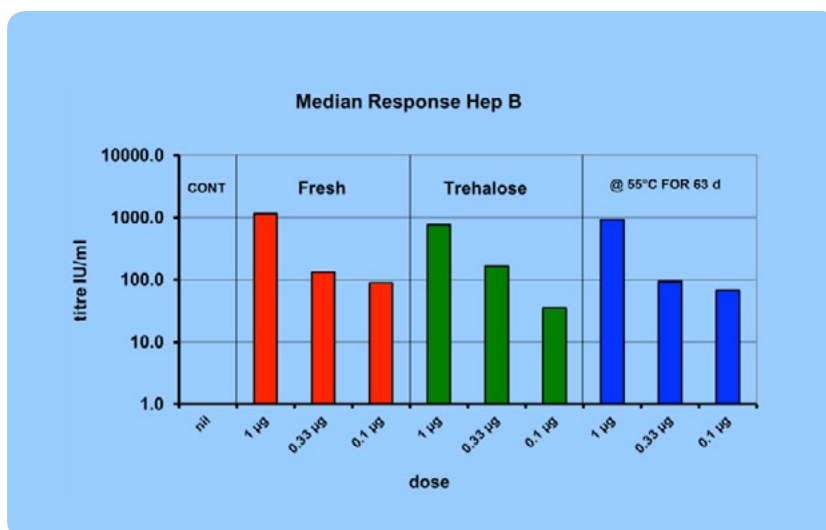
Track 1 (labelled MW) is a series of different proteins used to give an idea of the size of the Anthrax molecules. The samples in tracks 2-5 (4 to 55 degrees) are heavily overloaded to emphasize the fragment bands. There is no difference in the molecules dried and stored in trehalose buffer in any track showing good preservation at all temperatures. The start material which is frozen (labelled Cont -20°) shows the original single dark band of intact protein. It is loaded with less material and the faint bands of degraded protein are not seen. Protein without trehalose stored at 4 degrees is fully degraded (labelled Cont 4°).



Illustrative Examples of Extraordinary Stability of Vaccines When Dried In Trehalose



Commercial Hepatitis B vaccine is listed as stable for 1 Month at 37°C. Hep B vaccine when dried in **trehalose** is stable for up to 2 years at 55°C. At this temperature non-stabilised **Hep B** is rapidly degraded.



Trehalose-stabilised vaccine is fully potent when used to vaccinate animals.

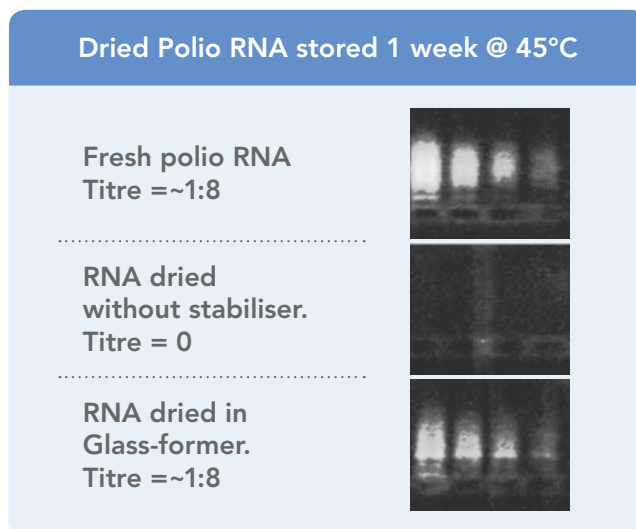
Antibody responses found in groups of ten mice to 3 different doses of Hepatitis B vaccine stored at **55°C for 2 months** compared with the responses to **fresh vaccine** or fresh vaccine dried in trehalose but **not stored**.

Covid 19 - Stablepharma technology will stabilise virus vaccine RNA at high temperatures

We have identified that a large proportion of the current front runner Covid 19 vaccines solutions include RNA, a notoriously thermally unstable molecule.

Live poliovirus vaccines cannot be stabilised due to the impermeability of the capsid.

However, when the RNA is extracted from the virus, it can be stabilised for storage at 45°C using the StablevaX glass forming trehalose technology. The titre, analysed by Agarose gel electrophoresis, is the same as fresh RNA.

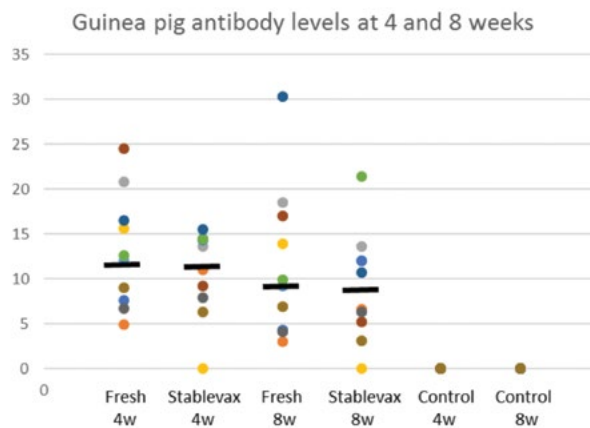


Naked RNA vaccines could therefore probably be rendered thermally stable using the StablevaX technology.

By stabilising a Covid 19 vaccine using Stablepharma 's complimentary technology distribution and stockpiling without the need for the Cold Chain could be possible.

Formal Confirmation - Successful Animal Trials at NIBSC

6 years of R&D work concluded with an independent study conducted by UK's National Institute for Biological Standards and Control (NIBSC) that confirmed a StablevaX version of the tetanus vaccine delivered the same level of antibody response as the existing fresh vaccine produced by leading pharmaceutical companies.



- NIBSC conducted the StablevaX study under the supervision of the UK Medicines & Healthcare products Regulatory Agency.
- National Institute for Biological Standards and Control is a World Health Organisation (WHO) and UK National Health Service affiliated facility.
- The graph shows the level of antibodies detected in animals at 4 and 8 weeks are essentially identical in the two groups.
- Having achieved this milestone of successful testing in Animals we are now able to move forward to the next milestone of Clinical Trials in Humans.

Currently available vaccines suitable for StablevaX

■	Cholera
■	Dengue
■	Diphtheria
■	Hepatitis A
■	Hepatitis B
■	Hepatitis E
■	Haemophilus influenzae type b (Hib)
■	Human papillomavirus (HPV)
■	Influenza
■	Japanese encephalitis
■	Malaria
■	Measles
■	Meningococcal meningitis
■	Mumps
■	Pertussis
■	Pneumococcal disease
■	Poliomyelitis
■	Rabies
■	Rotavirus
■	Rubella
■	Tetanus
■	Tetanus Diphtheria
■	Tick-borne encephalitis
■	Tuberculosis
■	Typhoid
■	Varicella
■	Yellow Fever

Pipeline vaccines suitable for StablevaX

■	Campylobacter jejuni
■	Chagas Disease
■	Chikungunya
■	Dengue
■	Enterotoxigenic Escherichia coli
■	Enterovirus 71 (EV71)
■	Group B Streptococcus (GBS)
■	Herpes Simplex Virus
■	HIV-1
■	Human Hookworm Disease
■	Leishmaniasis Disease
■	Malaria
■	Nipah Virus
■	Nontyphoidal Salmonella Disease
■	Norovirus
■	Paratyphoid fever
■	Respiratory Syncytial Virus (RSV)
■	Schistosomiasis Disease
■	Shigella
■	Staphylococcus aureus
■	Streptococcus pneumoniae
■	Streptococcus pyrogenes
■	Tuberculosis
■	Universal Influenza Vaccine
■	Covid 19 (most of the currently under development vaccines)

EMA and FDA approvals for trehalose-stabilised pharmaceuticals 2018

	Trade Name	Generic Name	Indication	Nature
1	Adcetris	brentuximab/vedotin	Hodgkins disease	Mab/conjugate
2	Advate	recombinant Hu Factor VIII	Haemophilia A	recombinant protein
3	Avastin	bevacizumab	anti cancer	monoclonal antibody
4	Blincyto	blinatumomab	Acute Lymphoblastic Leukaemia ALL	monoclonal antibody
5	Cosentyx	secukinumab	Psoriasis	monoclonal antibody
6	Gazyvaro	obinutuzumab	Chronic lymphocytic leukaemia CLL	monoclonal antibody
7	Herceptin	trastuzumab	anti cancer	monoclonal antibody
8	Ixinity	trenonacog alfa recombinant factor IX	haemophilia B	peptide
9	Lucentis	ranibizumab	Macular degeneration	monoclonal antibody
10	Lymphoseek	tilmanocept	imaging	^{99m} Tc
11	MabThera	rituximab	non-hodgkin lymphoma	monoclonal antibody
12	Orbactiv	Oritavancin	infection	antibiotic
13	Raplixa	Fibrocaps fibrin sealant	bleeding	thrombin fibrinogen
14	Tanzeum	albiglutide	Type 2 diabetes	conjugated peptides
15	Cryotop®	Vitrification Kit	freezing embryos	Buffer
16	Cryotop®	Thawing Kit	thawing embryos	Buffer
17	Gems	Vitrification Kit	freezing embryos	Buffer
18	Gems	Thawing Kit	thawing embryos	Buffer
19	Vonvendi	Von Willebrands factor recombinant	Bleeding	Recombinant Protein
20	imfinzi	durvalumab	apoptosis blocking	monoclonal antibody
21	Fasenra	benralizumab	severe asthma	monoclonal antibody
22	Ocrevus	Ocrelizumab	Multiple Sclerosis	monoclonal antibody
23	Cyltezo	adalimumab	Rheumatoid arthritis	monoclonal antibody
24	Gazyva	obinutuzumab	leukaemia	monoclonal antibody
25	Rituxan Hycela™	rituximab and hyaluronidase human	lymphoma	monoclonal antibody

Vaccines stabilised using Stablevax technology in the Laboratory

1	tetanus toxoid
2	diphtheria toxoid
3	pertussis
4	meningitis A conjugate
5	recombinant Hepatitis B
6	Hemophilus influenzae b
7	Escherichia coli
8	Salmonella typhi
9	MVA
10	Botulism
11	Anthrax
12	Adenovirus
Plus, the following adjuvants	
a.	aluminium hydroxide
b.	aluminium phosphate
c.	calcium phosphate

Stablepharma Ltd, 4 Queen Street, Bath BA1 1HE
Telephone 01225 581 220 | email nchild@stablepharma.com

