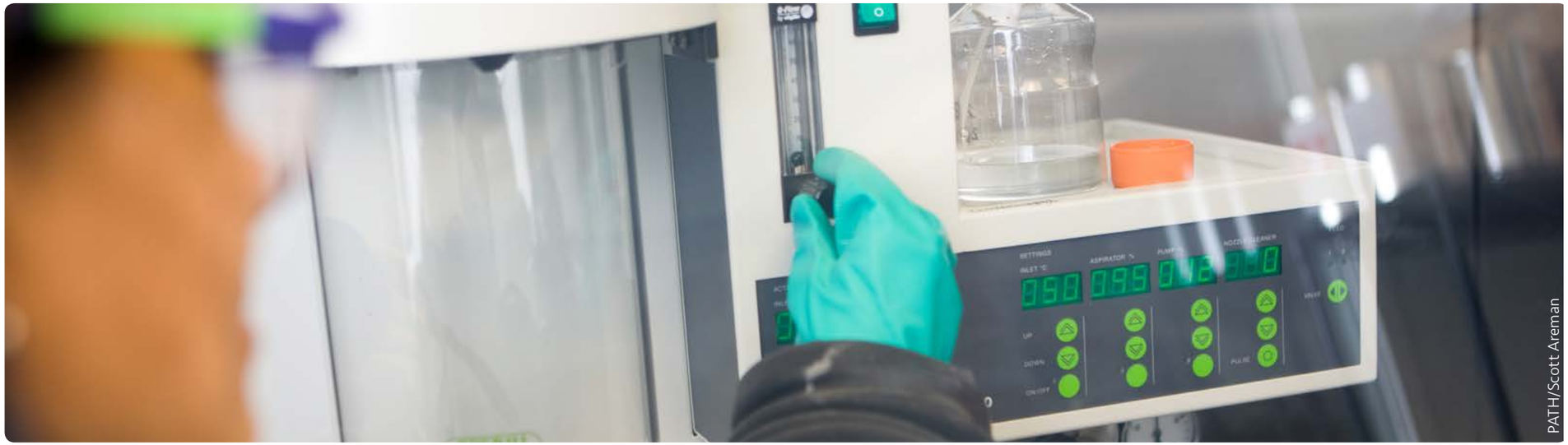
PATH/Scott Areman

Summary of stability data for investigational formulations of vaccines

Produced by Working in Tandem, Ltd., for the PATH Vaccine and Pharmaceutical Technologies Group.

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As of May 9, 2012

Background

This set of tables is an update of the orginal "Stability data for commonly used vaccines and novel formulations," produced by Working in Tandem, Ltd., and PATH in 2008.

This set of tables summarizes stability data for research or novel vaccine formulations. An accompanying set of tables summarizes stability data for commonly used, licensed vaccines.

These tables are not intended to be an exhaustive list of all vaccine formulations in research and development. The vaccines and formulations included in the tables have been selected using publicly available information to provide examples of stability data for the vaccines listed.

Approach

Information on the type, presentation, formulation, and stability of vaccines was compiled from information available in the public domain.

Vaccines were categorized according to whether they are:

a) Vaccines against a single pathogen.
b) Combination vaccines, i.e., against several pathogens, but formulated to be delivered in a single injection (e.g., diphtheria, pertussis, tetanus [DTP] and measles, mumps, rubella [MMR]).
c) Platform technologies (e.g., vectors) that can or are being developed as vaccines against a number of pathogens.

Notes to tables summarizing stability of investigational formulations of vaccines

Vaccines	These tables are not intended to be exhaustive and do not include all vaccines for each target. The vaccines listed have been selected to provide representative information for each target.
Formulation	The investigational "stabilized" formulation of the vaccine is shown.
Main stabilizing excipients	The primary stabilizing excipients in the formulation according to publicly available information are shown (if known).
Adjuvant	The type of adjuvant (if present in the formulation) is indicated.
Damaged by freezing	Yes/No is based on published information on whether the vaccine is damaged by freezing. Vaccines with aluminum salt adjuvants are assumed to be damaged by freezing (freeze sensitive) unless there is available information stating this is not the case. Lyophilized vaccines are assumed not to be damaged by freezing, unless othewise stated.

Summary of stability data for investigational formulations of vaccines

Abbreviations

Ad	adenovirus
$AlOH_3$	aluminum hydroxide
$AlPO_4$	aluminum phosphate
aP	acellular pertussis
BCG	Bacille Calmette Guerin
CAN-BD	carbon dioxide-assisted nebulization with a bubble dryer
CDC	Centers for Disease Control and Prevention (USA)
CRM_{197}	nontoxic form of diphtheria toxin (cross-reacting material)
DC-chol	3 -[N-(N ,N -dimethylaminoethane)-carbamoyl] cholesterol hydrochloride
ds	double stranded
DT	diphtheria tetanus (toxoids)
ETEC	enterotoxigenic *Escherichia coli*
F/T	freeze-thaw
GSK	GlaxoSmithKline
HA	haemagglutinnin
HAV	hepatitis A virus
HepB	hepatitis B virus
Hib	*Haemophilus influenzae* type B
HIV	human immunodeficiency virus
HPV	human papillomavirus
HydRIS	hypodermic rehydration injection system
ID	intradermal
IM	intramuscular
IN	intranasal
IPV	inactivated poliovirus vaccine
IVI	International Vaccine Institute
JHBSPH	Johns Hopkins Bloomberg School of Public Health
LPV	lipid particle vaccine
LT	(heat) labile toxin (of *E.coli*)
$MgCl_2$	magnesium chloride
MVA	modified vaccinia Ankara
NE	nano-emulsion
NIH	National Institute of Health
OPV	oral poliovirus vaccine
PATH	Program for Appropriate Technology in Health
PCPP	poly[di(carboxylatophenoxy)phosphazene]
PS-PCV	polysaccharide-protein conjugate vaccine
rBCG	recombinant Bacille Calmette Guerin
SC	subcutaneous
SIIL	Serum Institute of India Ltd
TC-chol	cholesteryl N-(trimethylammonioethyl) carbamate chloride
TTSA	type III secretion apparatus (*Shigella*)
VLP	virus-like particle
wP	whole-cell pertussis

Summary of stability data for investigational formulations of vaccines

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Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Freeze-thaw	Available stability data				Notes
										2°–8°C	25°C	37°C	>37°C	
Vaccines against single pathogens														
Cholera														
V. cholerae C7258 (El Tor Biotype, Ogawa Serotype)	Finlay Instutue, Nanobiocel Group	Cuba, Spain	Inactivated bacteria	Oral	Spray dried	Methacrylic copolymers (Eudragit L30D-55, FS30D)	No	No	No data					Used enteric polymers Eudragit® L30D-55 and FS30D
Cholera vaccine strain 638 (El Tor Biotype, Ogawa Serotype)	Finlay Institute	Cuba	Live attenuated bacteria	Oral	Lyophilized	Not known	No	No		≥ 12 months (2)				
Dengue														
ChimeriVax Tetravalent Dengue	Sanofi Pasteur	France	Live attenuated recombinant	Injected	Lyophilized	Not known	No	No			1 month (3)	7 days (3)		
DenVax	CDC, Inviragen	Not known	Live attenuated virus	SC or ID	Liquid	Trehalose, recombinant HSA, F127 (polyoxyethylene-polyoxypropylene block copolymer)	No	No	F/T resistant (4)	11 weeks (4)	7 days (4)	8 hours (4)		
					Lyophilized		No	No		> 6 months (4)		14 days (4)		
Enterotoxigenic *E.coli* (ETEC)														
ACE 527	JHBSPH, PATH, Pierrel Research USA TD Vaccines A/S	USA	Live attenuated bacterium	Oral	Lyophilized (fast-dissolving tablet)	Sucrose, trehalose	None	No		≥ 12 months (5)	≤ 1 week (5)	< 1 week (5)		
Travelers diarrhea vaccine	Intercell	Austria	Recombinant protein	Skin patch	LT dried onto patch	Not known	No	Not known		≥ 22 months (6)	6 months (6)		40°C: 1 month (6)	
***Haemophilus influenzae* type b (Hib)**														
No novel formulations were identified for which stability data are available.														
Hepatitis A (HAV)														
No novel formulations were identified for which stability data are available.														
Hepatitis B (HepB)														
Shanvac-B	Shantha Biotechnics, PATH	India	Recombinant protein	IM	Spray dried	Trehalose, mannitol	$AlOH_3$	Not known		≥ 2 years (7)		≥ 2 years (7)		
Shanvac-B	Shantha Biotechnics, PATH, Arecor	India	Recombinant protein	IM	Liquid	Phosphate, histidine	$AlOH_3$	Yes				≥ 6 months (8)	45°C: ≥ 6 months (8) 55°C: ≥ 9 weeks (8)	
Shanvac-B	Shantha Biotechnics, PATH, Arecor	India	Recombinant protein	IM	Liquid	Phosphate, histidine, propylene glycol	$AlOH_3$	No	F/T resistant (9)			≥ 12 months (9)		
HBsAg-NE	Univesity of Michigan, NanoBio	Not known	Recombinant protein	Mucosal (probably IN)	Liquid	$W_{80}5EC$	Nano-emulsion	Not known		≥ 12 months (10)	6 months (10)		40°C: ≥ 6 weeks (10)	

Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Available stability data: Freeze-thaw	2°–8°C	25°C	37°C	>37°C	Notes
Human immunodeficiency virus (HIV)														
No novel formulations were identified for which stability data are available. Some of the vectors listed in the platform technologies table below are being evaluated as HIV vaccines.														
Human papillomavirus (HPV)														
No novel formulations were identified for which stability data are available.														
Influenza - seasonal														
Nanopatch (microneedles coated with Fluvax)	University of Queensland	Australia	Inactivated virus (split)	ID	Coated microneedles	Trehalose	No	Not known			23°C: ≥ 6 months (11)			
pfMBP-HA fusion protein	Nature Technology Corporation	USA	Recombinant protein	Injected	Not known	Compatible with standard formulations	Recombinant flagellin	Not known					75°C: 40 minutes (12)	
Microneedles coated with influenza virus	Georgia Institute of Technology	USA	Inactivated virus	ID	Coated microneedles	Trehalose	No	Not known				≥ 1 day (13)		
Inactivated influenza nano emulsion	NanoBio	USA	Inactivated virus	IN	Liquid (oil-in-water nanoemulsion)	$W_{80}5EC$	Nano-emulsion	Not known		1 month (14)	1 month (14)			
Influenza virosomes	University of Groningen	The Netherlands	Virosomes	Injected	Lyophilized (inulin stabilizer)	Inulin	Virosomes	No			20°C: ≥ 12 weeks (15)		42°C: ≤ 3 weeks (15)	
Influenza virosomes	Pevion	Switzerland	Virosomes	Not known	Lyophilized	Sucrose, DC-chol, TC-chol	Virosomes	No	≥ 12 months (16)	≥ 12 months (16)	≥ 12 months (16)			
Dry powder influenza vaccine	University of N Carolina at Chapel Hill	USA	Inactivated virus (whole)	IN	Spray-freeze-dried	Trehalose	No	Not known		≥12 weeks (17)	≥ 12 weeks (17)	2 weeks (17)		
Dry powder influenza vaccine	University of Groningen	The Netherlands	Subunit	Pulmonary, injected	Lyophilized	Trehalose, inulin	No	Not known			Inulin 20°C: ≥ 6 months (18)		Trehalose: 45°C: ≥ 6 months (18)	
Dry powder influenza vaccine	University of Groningen	The Netherlands	Subunit	Pulmonary	Spray dried	Inulin	No	Not known			20°C: ≥ 3 years (19)			
Dry powder influenza vaccine	PowderJect	USA		Epidermal (ID)	Spray-freeze-dried	Trehalose, mannitol, dextran	No	Not known					40°C: 3 months (20)	No longer in development
Inactivated influenza vaccine	Stabilitech	UK	Inactivated virus	SC	Lyophilized	Not known	No	No					45°C: ≥ 6 months (56)	
Thermostable IM flu	Variation Biotechnologies Inc	USA	LPV	Injected	Preclinical	Not known	Lyophilized	No					40°C: > 6 months (21)	Oral pill formulation also being developed
Influenza - pandemic														
Whole inactivated H5N1	University of Groningen	The Netherlands	Inactivated virus (whole)	Injected	Freeze dried	Inulin	No	No			1 year (22)		40°C: 3 months (22)	
H5N1	Apogee Technology	USA	Not known	Injected	Not known	PCPP	PCPP	Not known					40°C: > 30 hours (23)	Quoted stability at 40°C is half-life of H5N1
ND1.1 (Ad-HA-dsRNA) (H5)	Vaxart	USA	Live virus vector (adenovirus 4 and/or 7)	Oral	Dried capsules	Not known	dsRNA (TLR3 agonist)	Not known			Room temp: 1 month (24)			
Recombinant MVA	Erasmus University	The Netherlands	Live virus vector	Injected	Not known	Not known	No	Not known				37°C: > 4 weeks (25)		

Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Available stability data					
									Freeze-thaw	2°–8°C	25°C	37°C	>37°C	Notes
Japanese encephalitis														
Vero-cell derived JE vaccine	Kitasato Institute	Japan	Inactivated virus (whole)	Injected	Liquid	Glycine, sorbitol	No	Not known		≥ 12 months (26)	28°C: ≥ 12 months (26)			
Malaria														
No novel formulations were identified for which stability data are available. Some of the vectors listed in the platform technologies table below are being evaluated as malaria vaccines.														
Measles														
Measles vaccine dry powder (MVDP)	University of Colorado, SIIL	USA, India	Live attenuated virus	Pulmonary	Dry powder (CAN-BD)	Myo-inositol, +/- sorbitol or mannitol	No	Not known			6 months (27)	1 week (28)		
Measles vaccine	Aridis Pharmaceuticals, SIIL	USA, India	Live attenuated virus	Pulmonary, injected	Spray dried	Trehalose, sucrose, divalent cations, L-arginine	No	Not known				8 weeks (29)		
Measles vaccine	Transform Pharmaceuticals	USA, India	Live attenuated virus	SC	Liquid	Trehalose, sucrose, gelatin	No	Not known					40°C: 8 hours (30)	High throughput sceening to identify formulations with improved stability following reconstitution
Measles vaccine	Stabilitech	UK	Live attenuated virus	SC	Lyophilized	Not known	No	No	Resistant to ≥ 5 F/T cycles (-20°C/37°C) (52)			6 days (52)		
Meningococcus: single serogroup and combination vaccines														
MenAfrivac (meningitis group A)	SIIL, PATH	India	PS-PCV	IM	Spray-dried	Trehalose	$AlPO_4$	Not known					40°C: ≥ 20 weeks (7) 60°C: ≥ 2 weeks (7)	
Mumps														
No novel formulations were identified for which stability data are available.														
Pertussis: acellular (aP) and whole-cell (wP)														
No novel formulations were identified for which stability data are available.														
Pneumococcus														
Trivalent pneumococcal vaccine	Sanofi Pasteur	France	Recombinant /purified proteins	Injected (assumed)	Liquid	Aluminum-salt adjuvants	$AlPO_4$, $AlOH_3$ or phosphate-treated $AlOH_3$	Yes				1 week (31)		
Polio: oral polio vaccine (OPV)														
Trivalent OPV	Sapporo Medical University	Japan	Live attenuated virus	Oral	Lyophilized	Sorbitol	No	No				≥ 7 days (32)		
Trivalent OPV	Institut Pasteur	France	Live attenuated virus	Oral	Liquid	$MgCl_2 + D_2O$	No	No				3-7 days (33)	45°C: ≤ 3 days (33)	
Polio: inactivated polio vaccine (IPV)														
No novel formulations were identified for which stability data are available.														

Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Available stability data					
									Freeze-thaw	2°–8°C	25°C	37°C	>37°C	Notes
Rabies														
No novel formulations were identified for which stability data are available.														
Rotavirus														
Bacillus subtilis spores expressing VP6 (34)	Tufts University	Not known	Recombinant bacteria	IN or Oral	Lyophilized	None	Cholera toxin	Not known						Spores claimed to be heat stable; no data available
Rotavirus vaccine (35)	Aridis Pharmaceuticals, Johns Hopkins	USA	Live attenuated virus	Oral	Thin film	Not known	No	Not known						Developed to be room temperature stable; no data available
Rubella														
No novel formulations were identified for which stability data are available.														
Shigella														
IpaD (*Shigella* type III secretion system, TTSA)	University of Kansas	USA	Recombinant /purified proteins	Injected	Liquid	Sucrose, dextrose	$AlOH_3$	Yes		≥ 3 months (36)				Formulation composed of IpaD (*Shigella*) plus four other TTSA proteins from other gram-negative pathogens
PrgI (*Salmonella* type III secretion system, TTSA)	University of Kansas	USA	Recombinant /purified proteins	Injected	Liquid			Yes						Formulation composed of PrgI (*Salmonella*) plus two other TTSA proteins from other gram-negative pathogens
Tetanus toxoid														
Tetanus toxoid fragment C expressed on B subtilis spores	Tufts University	USA	Recombinant bacteria	IN, sublingual	Lyophilized	None	No	No					45°C: ≥ 12 months (41)	
Tetanus toxoid bioneedeles	Netherlands Vaccine Institute	The Netherlands	Recombinant /purified proteins	IM	Lyophilized	Trehalose	$AlPO_4$	No				≥ 3 weeks (42)	60°C: ≥ 1 week (42)	
Tuberculosis														
Some of the vectors listed in the platform technologies table below are being evaluated as tuberculosis vaccines.														
AERAS-422 rBCG	Aeras	USA	Live recombinant bacterium (BCG)	ID	Lyophilized	Mannitol, trehalose, sucrose, sodium glutamate	No	No				4 weeks (37)		
AERAS-402/Crucell Ad35	Crucell, Aeras, CDC	The Netherlands, USA	Live virus vector (adenovirus)	Pulmonary	Spray dried	Mannitol, cyclodextrin, trehalose,	No	Not known		≥ 12 months (38)	≥ 12 months (38)	≥ 5 weeks (38)		
BCG microspheres	Pharmaceutical Research Center, Tehran	Iran	Live attenuated bacterium (BCG)	Oral	Liquid (microspheres)	Alginate	No	Not known		5 weeks (39)				
BCG microspheres	Harvard University	USA	Live attenuated bacterium (BCG)	Pulmonary	Spray dried	L-leucine	No	Not known		4 months (40)	30 days (40)			

Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Available stability data: Freeze-thaw	2°–8°C	25°C	37°C	>37°C	Notes
Typhoid														
Vi-CRM197	Novartis Vaccines Inst for Global Health	Italy	PS-PCV	Injected	Liquid	None	No	Not known		> 3 months (43)			40°C: > 8 weeks (43)	
Vi-Diphtheria toxoid conjugate vaccine	IVI, NIH, Shantha	USA	PS-PCV	Injected	Liquid	None	No	No	Resistant to 20 F/T cycles (44)		NOT stable at 5 weeks (44)	NOT stable at 5 weeks (44)		
PrgI (*Salmonella* type III secretion system, TTSA)	University of Kansas	USA	Recombinant /purified proteins	Injected	Liquid	Sucrose, dextrose	$AlOH_3$	Yes					40°C: < 6 months (57)	Formulation composed of PrgI (*Salmonella*) plus two other TTSA proteins from other gram-negative pathogens
Vivotif (Ty21a)	University of Kansas, Aridis	USA	Live attenuated bacterium	Oral	Foam dried	Trehalose or sucrose	No	Not known				≤ 4 weeks (45)		
Vivotif (Ty21a)	Aridis Pharmaceuticals	USA	Live attenuated bacterium	Oral	Foam dried	Trehalose, methionine, gelatin	No	Not known			12 weeks (46)	≤ 4 weeks (46)		Stabiliers to increase "transition temperature" of Ty21a by 10°C identified, but no stability studies conducted
Yellow fever														
XRX-001 (Inactivated YF vaccine)	Xcellerex	USA	Inactivated virus	Injected	Liquid	Proprietary stabilizers	$AlOH_3$	Yes		≥ 6 months (47)	≥ 8 weeks (47)			
YF vaccine (cell-culture)	Biomanguinhos	Brazil	Live attenuated virus	Injected	Lyophilized	Hydrolysed gelatin, sugar, amino acids	No	No				≥ 2 weeks (48)		
Combination vaccines														
Combination vaccines containing diphteria and/or tetanus and/or pertussis, with/without other antigens														
Diphtheria tetanus	Xstal Bio, School of Pharmacy, London	UK	Recombinant /purified proteins	IM	Protein-coated microcrystals	L-glutamine	$AlOH_3$ or $AlPO_4$	Not known				≥ 2 weeks (49)	45°C: ≥ 2 days (49)	Stablity at 37°C was the same as control, non-stabilized DT
Infanrix (DTaP), Daptacel (DTaP)	GSK, Sanofi, PATH	Belgium France	Recombinant /purified proteins	IM	Liquid	Propylene glycol, PEG 300, glycerol	$AlOH_3$ $AlPO_4$	No	Resistant to F/T (49)					
Combination vaccines containing measles and/or mumps and/or rubella														
No novel combination formulations identified which have stability data														

Summary of stability data for investigational formulations of vaccines

As of May 9, 2012

Vaccine	Manufacturer/ developer	Country	Vaccine type	Delivery route	Formulation	Main stabilizing excipients	Adjuvant	Damaged by freezing	Available stability data: Freeze-thaw	2°–8°C	25°C	37°C	>37°C	Notes
Platform technologies and live vectors														
Adenovirus vectors														
AERAS-402/Crucell Ad35	Crucell, Aeras, CDC	The Netherlands, USA	Live virus vector	Pulmonary	Spray dried	Mannitol, cyclodextrin, trehalose, dextran	No	Not known		≥12 months (38)	≥12 months (38)	≥ 5 weeks (38)		
Adenovirus type 5 (Ad5)	NovaLabs, Oxford University	UK	Live virus vector	Injected	HydRIS (Air/filter-dried)	Trehalose, sucrose	No	Not known				≥ 15 months (51)	45°C: ≤ 6 months (51)	
Adenovirus (subtype not known)	Stabilitech	UK	Live virus vector	Injected	Liquid and lyophilized	Not known	No	Not known		Liquid: ≥ 6 months (52)		Lyophilized: ≥ 3 months (52)		
Adenovirus type 5 (Ad5)	University of Michigan	USA	Live virus vector	Injected	Lyophilized	Sucrose, trehalose, sorbitol, gelatin	No	No	Resistant to F/T damage (58)	≥ 150 days (58)				
Adenovirus type 5 (Ad5)	University of Texas	USA	Live virus vector	IN	Liquid	Mannitol, sucrose, pluronic F68	No	No	Resistant to F/T damage (53)		9 days (53)			
Ad5 (MRKAd5gag HIV)	Merck	USA	Live virus vector	Injected	Liquid	Sucrose, ethanol, histidine, EDTA	No	Not known	Resistant to F/T damage (54)	≥ 24 months (data) (54) 7 years (est.) (54)	13 days (54)			
Vaccinia and other pox virus vectors														
Recombinant MVA (modified vaccinia Ankara)	Erasmus University	The Netherlands	Live virus vector	IM	Lyophilized	Not known	No	No				≥ 4 weeks (25)		
Recombinant MVA (modified vaccinia Ankara)	NovaLabs, Oxford University	UK	Live virus vector	Injected	HydRIS (Air/filter-dried)	Trehalose, sucrose	No	No				≥ 12 months (51)	45°C: ≤ 4 months (51)	
Bacterial vectors														
Salmonella typhi (Ty21a)	University of Kansas, Aridis	USA	Live attenuated bacterium	Oral	Foam dried	Trehalose or sucrose	No	Not known				≤ 4 weeks (45)		
Salmonella typhi (Ty21a)	Aridis Pharmaceuticasls	USA	Live attenuated bacterium	Oral	Foam dried	Trehalose, methionine, gelatin	No	Not known			12 weeks (46)	≤ 4 weeks (46)		Stabiliers to increase 'transition temperature' of Ty21a by 10°C identified, but no stability studies conducted
DNA vaccines														
DermaVir	Genetic Immunity	USA	Plasmid DNA	Trans-cutaneous	Nanoparticles	Mannitol	No	Not known		> 8 weeks (55)		≤ 3 weeks (55)		
Plasmid DNA	Vical Inc	USA	Plasmid DNA	IM	Lyophilized	Trehalose, PVP	No	No						No long term stability data presented, only ability of excipients to protect DNA during lyophilization process (50)

Summary of stability data for investigational formulations of vaccines

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