

Vaccines available against JE

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Evaluating JE Vaccines

- Due to the rarity of JE disease, efficacy studies are impractical and vaccines are licensed based on an accepted correlate of protection
 - It is generally accepted that individuals with a serum neutralizing antibody titre of at least 1:10 are protected from JEV disease
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- Seroprotection: PRNT₅₀ titer ≥ 10
 - Seroconversion: PRNT₅₀ titer of ≤ 10 at baseline and ≥ 10 at time of serum sampling, or a 4-fold rise from a baseline titer of ≥ 10
 - Most PRNT₅₀ titers based on using vaccine virus and not wild-type strains.
 - Different virus strains are used as vaccines and no reference reagents for standardizing PRNT titers between vaccines.

All JE vaccines are based on genotype III viruses

- Beijing-1
- Nakayama
- P3
- 821564 XZ
- SA14-14-2
 - Live SA14-14-2/PHK (CD.JEVAX)
 - JE-ChimeriVax (IMOJEV)
 - Inactivated SA14-14-2/Vero, IC51 (IXIARO, JESPECT, JEEV)



Major classes of licensed JE vaccines

Inactivated mouse brain-based JE vaccines

- First licensed in Japan in 1954

Live attenuated JE vaccines

- First licensed in China in 1988

Inactivated Vero cell-based JE vaccines

- First licensed in China in 1998, Japan/US/Europe in 2009

Live attenuated chimeric JE vaccines

- First licensed in Australia in 2010

Licensed JE Vaccines

Class	Company	Strain (all G3)
Inactivated mouse brain-based	Green Cross , AdImmune Corp, VaBiotech JE VAX (Biken) – used as reference for non-inferiority for new generation vaccines	Nakayama
	GPO	Beijing-1
Inactivated Vero cell-based	Biken, Kaketsuken	Beijing-1
	Liaoning Chengda, Beijing Tiantan	Beijing P-3
	Valneva/Novartis/CSL , Biological E*	SA 14-14-2
	Bharat Biotech	Kolar strain (JEV 821564XY)
Live attenuated	Chengdu Institute of Biological Products (CDIBP)* , Wuhan Institute of Biological Products, Lanzhou Institute of Biological Products	SA 14-14-2
Chimeric live attenuated	Sanofi Pasteur*	SA 14-14-2

Bold = internationally distributed, *WHO prequalified

Inactivated mouse brain-derived JE vaccines

- Manufactured by inoculating 2-week old mice intracerebrally
- Brains harvested and purified, formalin inactivated
 - Possibility for variation in purification procedures and vaccine quality across manufacturers
- Excipients include gelatin and sodium glutamate
- Typically given as 2-3 dose primary series + booster(s)
- Many manufacturers no longer producing
- No mouse brain-derived vaccines are WHO prequalified



Inactivated Vero cell JE vaccines

- Vero cell derived
- Formalin-inactivated
- Two dose regimen plus boosters that vary by product (e.g., IXIARO and JESPECT are 0 and 28 days)
- Pediatric (0.25mL) and adult (0.5mL) doses
- Inactivated Vero cell products licensed in the US, Europe, Japan, China, India
- Aluminium hydroxide adjuvanted (0.1%, 250µg) (no gelatin) (Exceptions: Biken and Kaketsuken products)
- Typically licensed from 6 months – 1 year of age in endemic countries, 2 months of age in non-endemic countries
- JEEV is WHO prequalified
 - 2 doses @ 12-35 months and 18-49 years of age



Live attenuated JE vaccines

- Based on Genotype 3 SA 14-14-2 strain
- Grown on primary hamster kidney cells
- Internationally distributed product “CD.JEVAX”, manufactured by Chengdu Institute of Biological Products
- Includes gelatin, saccharose, human serum albumin, and sodium glutamate
- Often given, and prequalified, as single dose
 - In some countries a second dose is recommended at 2 years of age.
- Vaccine is licensed in China, India, South Korea, Thailand, Nepal, Sri Lanka, DPRK, Laos, Cambodia, Myanmar, Malaysia and Vietnam.
- CD.JEVAX is WHO prequalified (following construction of GMP-compliant facility)
 - One dose at ≥ 8 months of age



Chimeric Vaccine

- Single product “IMOJEV”- live vaccine made using recombinant DNA technology
 - Replaced prM and E coding sequences of the yellow fever live attenuated 17D vaccine virus with the SA 14-14-2 live attenuated JE vaccine virus
- Contains mannitol, lactose, glutamic acid, potassium hydroxide, histidine, human serum albumin, and sodium chloride
- Licensed in Australia, Malaysia, Brunei, Philippines, Thailand, Myanmar
- Manufacturer recommendation to give as single dose with pediatric booster
- IMOJEV is WHO prequalified
 - Single dose at ≥ 9 months of age + paediatric booster



ChimeriVax™ technology – YF 17D live vector

Tom Monath & Farshad Guiralhoo, Acambis / Sanoofi Pasteur

ChimeriVax™ technology – YF 17D live vector

Yellow fever 17D genome cloned as cDNA



Exchange coat protein genes of JE SA14-14-2/PHK



Chimeric cDNA → transcribe to RNA

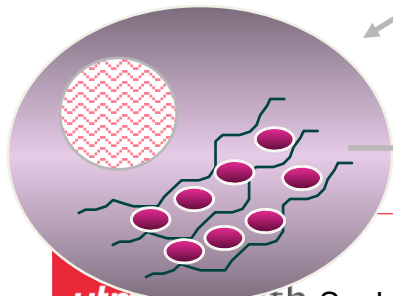


Transfect mRNA

Envelope is heterologous virus containing SA14-14-2 antigens

Grow virus in cell culture

RNA replicative 'engine' is YF 17D



Example Characteristics

Company	Name	Technology	Admin/ Doses per manufacturer recommendations	Age	Presentation	Shelf-Life
Green Cross	JenceVac	Inactivated mouse brain	SC 3 doses + boosters	12-23 months for primary series	Liquid 1 dose vial	18 months
Valneva/ Novartis/ CSL	IXIARO/ JESPECT ¹	Inactivated Vero cell	IM 2 doses + adult booster	≥2 months in non-endemic areas	Liquid 1 dose pre-filled syringe	24 months
CDIBP	CD.JEVAX ²	Live attenuated PHK cell	SC 1 dose	≥8 months	Lyophilized 1 and 5 dose vials	18 months
Sanofi Pasteur/ GPO	Imojev ²	Chimeric live attenuated Vero cell	SC 1 dose + paediatric booster	≥9 months	Lyophilized 1 and 4 dose vials	36 months

¹ “Sister” product JEEV (BioE) is WHO prequalified (12-35 months and 18-49 years)

² WHO prequalified

All products stored at 2-8° C