

Safety Data Sheet

1 Identification of the substance/preparation and company

1.1 Product identification

Name: CVD 103-HgR

CVD 103-HgR is a live attenuated bacterial vaccine strain of classical Inaba *Vibrio cholerae* O1. It is the active ingredient in the oral vaccine marketed as Vaxchora™ (Cholera Vaccine, Live, Oral), indicated for active immunization against disease caused by *V. cholerae* serogroup O1.

1.2 Manufacturer identification

Paxvax Berna GmbH
Oberriedstrasse 68
3174 Thörishaus, Switzerland

Phone: +41 31 888 51 63

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2 Hazard identification

Classified Hazards:

Not classified. Exempt from requirements - product regulated as a medicinal product, cosmetic product or medical device.

Label elements:

Exempt from requirements - product regulated as a medicinal product, cosmetic product or medical device.

Hazard(s) not otherwise classified (HNOC):

CVD 103-HgR is the active ingredient in the oral vaccine marketed as Vaxchora™ (Cholera Vaccine, Live, Oral), indicated for active immunization against disease caused by *V. cholerae* serogroup O1. In clinical trials, the most common adverse events (incidence > 3%) following oral administration of the vaccine were tiredness (31%), headache (29%), abdominal pain (19%), nausea/vomiting (18%), lack of appetite (17%) and diarrhea (4%).

An extensive environmental risk assessment of the strain CVD 103-HgR was performed. The study concluded that the strain posed no risk to the environment. The host range of *Vibrio cholerae* is exclusively restricted to human beings.

3 Composition/information on ingredients

The CVD 103-HgR live bacterial vaccine strain consists of a lyophilized powder with non-hazardous excipients.

The concentration of the CVD 103-HgR bulk drug substance is $\geq 1 \times 10^{10}$ CFU/g. The concentration of the Vaxchora vaccine is 4×10^8 to 2×10^9 CFU/dose. Doses up to 1×10^{10} CFU/dose have been safely administered in clinical trials.

4 First aid measures

4.1 First aid instructions

Inhalation: In case of accidental inhalation, remove to fresh air and keep at rest

Skin Contact: In case of accidental skin contact, clean affected areas thoroughly with soap and water.

Eye Contact: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice.

Ingestion: Product is meant to be ingested. If adverse reaction is suspected, do not induce vomiting, seek medical advice immediately and show this container label.

4.2 Description of most important symptoms or effects

Inhalation: None known.

Skin contact: Irritating to skin.

Eye contact: Direct contact with eyes is likely irritating.

Ingestion: The vaccine based on CVD 103-HgR is to be administered orally. In case of accidental ingestion it is known that doses up to 1×10^{10} CFU/dose of strain CVD 103-HgR did not cause adverse reactions in clinical studies.

4.3 General

In case of doubt, seek medical attention.

5 Fire-fighting measures

5.1 Suitable extinguishing media

Not known to be flammable. Water, Foam, CO₂, other chemical extinguishing media may be used.

6 Accidental release measures

6.1 Methods for cleaning up

Clean up all spills immediately, place spilled material in labeled container and inactivate bacteria using 70% isopropanol / water (v/v) solution or 10% bleach solution. After inactivation, the material can be discarded. Dispose of in accordance with applicable local, state, and federal regulations. Spray spill area with 70% isopropanol / water (v/v) solution or 10% bleach solution to inactivate any remaining bacteria. Wash spill area with large quantities of water.

7 Handling and storage

7.1 Handling

General hygiene measures for the handling of this product are applicable.

7.2 Storage

Vaxchora Vaccine

Store at 2°C to 8°C / 36°F to 46°F

Protect against moisture

Protect from light

8 Exposure controls/personal protection

8.1 Exposure Controls

No special measures necessary.

9 Physical and chemical properties

9.1 Appearance

Beige powder

9.2 Odor

Odorless

9.3 Solubility in water

Soluble in water

9.4 pH-value

Neutral

9.5 Additional physical properties

Flammability or explosive limits, vapor pressure, odor threshold, vapor density, relative density, melting/freezing point, initial boiling point and range, flash point, evaporation rate, flammability, partition co-efficient: n-octanol/water, auto-ignition temperature, decomposition temperature, viscosity: Not applicable

10 Stability and reactivity

10.1 Reactivity

Non-reactive.

10.2 Chemical stability

Stable.

10.3 Other

No hazardous reactions known.

11 Toxicological information

11.1 Acute oral toxicity

Strain CVD 103-HgR is non-toxic.

11.2 Inhalation effect

Unknown.

11.3 Irritant effect on skin

Non-irritant.

11.4 Irritant effect on eyes

Non-irritant.

11.5 Sensitization

Non-sensitizing

11.6 Carcinogenicity

Not a potential carcinogen.

12 Ecological information

CVD 103-HgR and the parent strain, *V. cholerae* 569B were compared as for their ability to survive under various conditions reflecting an actual environmental microcosm as well as their ability to enter the viable but non-culturable (VBNC) state (Viret 2004). Data indicate that CVD 103-HgR does not differ significantly from its wild-type parent 569B in terms of survival. CVD 103-HgR survives best in sterilized estuarine water in the

absence of competition with other micro-organisms (10³-fold decrease after 33 days). In non-sterile estuarine water, viability decreased from 10⁵ CFU/ml to non-detectable levels within 14 days, whereas in soil an inoculum of 10⁶ CFU/mL decreased to undetectable levels after 19 days.

Under specific experimental conditions, CVD 103-HgR, just like 569B, is able to enter the VBNC state. Shifting VBNC cells to optimal conditions for growth in artificial seawater allowed for very slow growth at 30°C. However, massive resuscitation did not occur (unpublished results) (Viret 2004).

Overall, these studies show the short-term survival of the vaccine strain in environmental microcosms and emphasise the fact that it presents no selective advantage versus wild type *V. cholerae*. Thus the risk of long-term persistence in the aquatic environment is low.

13 Disposal considerations

13.1 Product

Do not discharge product unmonitored into environment. Dispose of in accordance with applicable local, state, and federal regulations.

14 Transport information

14.1 Road Transport

Non-hazardous goods

Vaxchora Vaccine

Transport at 2°C to 8°C / 36°F to 46°F

Protect against moisture

Protect from light

14.2 Marine Transport

Non-hazardous goods

Vaxchora Vaccine

Transport at 2°C to 8°C / 36°F to 46°F

Protect against moisture

Protect from light

14.3 Air transport

Non-hazardous goods

Vaxchora Vaccine

Transport at 2°C to 8°C / 36°F to 46°F

Protect against moisture

Protect from light

15 Regulatory information

SARA Title III: No chemicals in this material are subject to the reporting requirements of SARA Title III

Massachusetts Right to Know Components: No components are subject

Pennsylvania Right to Know Components: No components are subject

New Jersey Right to Know Components: No components are subject

California Prop 65 Components: This product does not contain any chemicals known to the State of California to cause cancer, birth defects, or any other reproductive harm.

Vaxchora (Cholera Vaccine, Live, Oral) is approved by the US Food and Drug Administration for human use.

16 Other information

This information is based on our present state of knowledge. It should therefore not be construed as guaranteeing specific properties of the products described or their suitability for a particular application.

This safety data sheet is written to provide health, safety and environmental information for people handling this formulated product in the workplace. It is not intended to provide information relevant to medicinal use of the product. In this instance patients should consult prescribing information/package insert/product label or consult their pharmacist or physician. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate safety data sheet for each ingredient.”