Material Safety Data Sheet

BAVARIAN NORDIC

According to Regulation (EC) No. 1907/2006 (REACH), amended by 2015/830/EU

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1. Identification of the substance / preparation and company

1.1 Product identification

Product name:	CVD 103-HgR (Vaxchora)
Product Family:	Vaccine
CAS Number:	N/A
Synonyms:	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 *Vibrio cholerae* serogroup O1.

1.2 Manufacturer identification

Bavarian Nordic Berna GmbH
Oberriedstrasse 68
3174 Thoerishaus,
Switzerland
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2. Hazard identification

Classification	No classifications according to 1272/2008EC
Hazard statements	No hazard statements according to 1272/2008EC
Other Hazards	Risk Group 1 Biological Agent (organism with no or negligible risk)

This information pertains to the occupational use of the product. For patient information, refer to the patient information leaflet as required by legislation on Medicinal Products for Human Use.

3. Composition / information on ingredients

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.

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 ≥1x10^{10} CFU/g. The concentration of the Vaxchora vaccine is 4x10^{8} to 2x10^{9} CFU/dose. Doses up to 1x10^{10} CFU/dose have been safely administered in clinical trials.

4. First aid measures

Inhalation	In case of inhalation, please seek medical advice.
Skin contact	In case of accidental contact with skin, clean affected areas thoroughly with soap and water.
Eye contact	In case of accidental contact rinse eyes immediately with plenty of water and ensure complete irrigation and seek medical advice.
Ingestion	The vaccine based on CVD 103-HgR is to be administered orally. In case of accidental ingestion, it is known that three times the current dose of strain CVD 103-HgR did not cause adverse reactions in adult studies.
General	In case of doubt, seek medical attention

5. Fire-fighting measures

Unusual fire or explosion hazards	Unknown. Not expected
Hazardous combustion products	Unknown. Not expected
Suitable Extinguishing media	Water, foam, CO_2, other chemical extinguishing media
Special firefighting procedures	No special requirements

6. Accidental release measures

Personal precautions	Wear lab coat and gloves
Environmental precautions	For large spills, take precautions to prevent entry into waterways, sewers, or surface drainage systems
Clean up methods	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.
Decontamination procedures:	N/A

7. Handling and storage

Handling Precautions	General hygiene measures for the handling of this product are applicable.
Storage requirements	Bulk CVD 103-HgR Powder: Store at ≤ −20°C Vaxchora Vaccine: Store at 5°C ± 3°C/ 41°F ± 5°F Protect against moisture Protect from light

8. Exposure control / personal protection

Exposure controls	Observe good microbiological practice. Wear laboratory clothing, gloves, and eye protection. Avoid ingestion and accidental exposure in occupational settings.
Environmental exposure	General advice: do not allow uncontrolled discharge of product into the environment.

9. Physical and chemical properties

Appearance	Beige powder
Odor	Odorless
Solubility in water	Soluble in water
pH	Neutral

10. Stability and reactivity

Hazardous reactions	Non-reactive
Chemical stability	Stable
Other	No hazardous reactions known

11. Toxicological information

Acute oral toxicity	Strain CVD 103-HgR is nontoxic
Inhalation effect	Unknown
Irritant effect on skin	Non-irritant
Irritant effect on eyes	Non-irritant
Sensitization	Non-sensitizing
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 indicates 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 10^5 CFU/ml to non-detectable levels within 14 days, whereas in soil an inoculum of 10^6 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 emphasize 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

Product

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

14. Transport Information

Road Transport **Non-hazardous goods**	Bulk CVD 103-HgR Powder Store at ≤−20°C Vaxchora Vaccine Store at 5°C ± 3°C/ 41°F ± 5°F Protect against moisture Protect from light
Marine Transport **Non-hazardous goods**	Bulk CVD 103-HgR Powder Store at ≤−20°C Vaxchora Vaccine Store at 5°C ± 3°C/ 41°F ± 5°F Protect against moisture Protect from light
Air transport **Non-hazardous goods**	Bulk CVD 103-HgR Powder Store at ≤−20°C Vaxchora Vaccine Store at 5°C ± 3°C/ 41°F ± 5°F Protect against moisture Protect from light

15. Regulatory information

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

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.