1. Identification

1.1. Product identifier

Product Identity	AFSTYLA® – Antihemophilic Factor (Recombinant) Single Chain
Alternate Names	

1.2. Relevant identified uses of the substance or mixture and uses advised against

Intended use	See Technical Data Sheet.
Application Method	See Technical Data Sheet.

1.3. Details of the supplier of the safety data sheet

Company Name	CSL Behring GmbH Emil-von-Behring Straße 76 35041 Marburg Germany
Emergency	
U.S. 24 hour Emergency Telephone No.	Emergency Response: (800) 424-9300 Emergency Product Information: (800) 504-5434
Customer Service EU: CSL Behring GmbH	+49 (64 21) 39-0
Customer Service U.S.: CSL Behring LLC	(610) 878-4000

2. Hazard(s) identification

2.1. Classification of the substance or mixture

No applicable GHS categories.

2.2. Label elements

Using the Toxicity Data listed in section 11 and 12 the product is labeled as follows.

No applicable GHS categories.

[Prevention]:
No GHS prevention statements
[Response]:
No GHS response statements
[Storage]:
No GHS storage statements
[Disposal]:
No GHS disposal statements

3. Composition/information on ingredients

This product contains the following substances that present a hazard within the meaning of the relevant State and Federal Hazardous Substances regulations.

Ingredient/Chemical Designations	Weight %	GHS Classification	Notes
Sucrose CAS# 0000057-50-1	**~ 0.6%**	**Not Classified**	**[1] [2]**

[1] Substance classified with a health or environmental hazard.
[2] Substance with a workplace exposure limit.
[3] PBT-substance or vPvB-substance.
*The full texts of the phrases are shown in Section 16.

Non Hazardous Ingredients:
Single-chain recombinant Factor VIII, Active ingredient
L.Histidine, Polysorbate 80, Calcium chloride di-hydrate, Sodium chloride
Water For Injection, USP, (7732-18-5), Volume adjustment

4. First aid measures

4.1. Description of first aid measures

General In all cases of doubt, or when symptoms persist, seek medical attention. Never give anything by mouth to an unconscious person.

Inhalation Remove to fresh air, keep patient warm and at rest. If breathing is irregular or stopped, give artificial respiration. If unconscious place in the recovery position and obtain immediate medical attention. Give nothing by mouth.

Eyes Irrigate copiously with clean water for at least 15 minutes, holding the eyelids apart and seek medical attention.

Skin Remove contaminated clothing. Wash skin thoroughly with soap and water or use a recognized skin cleanser.

Ingestion Rinse from mouth and seek medical guidance. Induce vomiting only as directed by medical personnel. Never give anything by mouth to an unconscious person.

4.2. Most important symptoms and effects, both acute and delayed

Overview

Potential Health Effects:
No adverse health effects anticipated with normal handling and use in appropriate medical setting. Medical implications of therapeutic use are described in product package insert.

Emergency Overview: This product is a sterile prescription pharmaceutical. It is to be administered only at the order of a licensed physician. This product is safe when used for its intended purpose and administered as directed by a physician. In addition, no adverse health effects are anticipated as a result of incidental contact or exposure to this product by those handling it or administering it in a therapeutic setting. More detailed information is available in the product package insert. Please report adverse events in patients using this product to the manufacturer at the telephone number listed above.

Eye/skin contact: No data. No adverse health effects reported nor anticipated.
Skin Absorption: This product is not absorbed through the skin.
Ingestion: Not intended for oral use. Relatively non-toxic if ingested.
Chronic Effects/Carcinogenicity: None known or anticipated under normal handling and exposure conditions.
See section 2 for further details.

5. Fire-fighting measures

5.1. Extinguishing media

Packaging material fires may be extinguished with water, carbon dioxide, or dry chemical

5.2. Special hazards arising from the substance or mixture

Hazardous decomposition: None known.

5.3. Advice for fire-fighters

Product is not flammable. The only potential fire hazard would involve packaging material.
Packaging material fire may produce carbon monoxide and other gaseous asphyxiates plus airborne particulate matter.

Firefighting personnel should respond with appropriate protective clothing, firefighting gear, and breathing equipment as trained. All other personnel should exit the area and proceed to a gathering point in an area unaffected by the fire and smoke.

ERG Guide No. N/A ----

6. Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Put on appropriate personal protective equipment (see section 8).

6.2. Environmental precautions

Use good personal hygiene practices. Wash hands before eating, drinking, smoking or using toilet. Promptly remove soiled clothing and wash thoroughly before reuse.

6.3. Methods and material for containment and cleaning up

Large Spill: Absorb spills with material suitable for aqueous solutions and dispose in solid waste container, or mop spilled material with detergent/water or bleach/water solution and dispose in sanitary sewer. Ventilate area, if desired.
Small Spill: Clean area of spill with wetted toweling and dispose in solid waste container, or follow procedure for large spills.

7. Handling and storage

7.1. Precautions for safe handling

Handle containers carefully to prevent damage and spillage.

7.2. Conditions for safe storage, including any incompatibilities

Incompatible materials: None known.

Store and transport in accordance with the conditions specified in the product package insert.
Store locked up or accessible for authorized persons or their representatives only.

7.3. Specific end use(s)

No data available.

8. Exposure controls and personal protection

8.1. Control parameters

Exposure

CAS No.	Ingredient	Source	Value
0000057-50-1	Sucrose	OSHA	TWA: 15mg/m3 (total) 5 mg/m3 (resp)
		ACGIH	TWA: 10 mg/m3
		NIOSH	TWA: 10 mg/m3 (total) 5 mg/m3 (resp)
		Supplier	No Established Limit

Carcinogen Data

CAS No.	Ingredient	Source	Value
0000057-50-1	Sucrose	OSHA	Select Carcinogen: No
		NTP	Known: No; Suspected: No
		IARC	Group 1: No; Group 2a: No; Group 2b: No; Group 3: No; Group 4: No;

8.2. Exposure controls

Respiratory None required.

Eyes None required to provide protection against this product. Eye protection may be required by procedure of administration.

Skin None required for protection against the product. Medical-grade examination or surgical gloves may be required by procedure of administration.

Engineering Controls Not Applicable

Other Work Practices Use good personal hygiene practices. Wash hands before eating, drinking, smoking or using toilet. Promptly remove soiled clothing and wash thoroughly before reuse.

9. Physical and chemical properties

Appearance	White to off-white powder (lyophilized)
Physical Form of Pure Concentrate	Readily soluble, with almost colorless to slightly opalescent solution
Odor	Unspecified
Odor threshold	Not Measured
pH	6.9 +/- 0.5
Melting point / freezing point	Not applicable (Decomposition)
Initial boiling point and boiling range	Unspecified
Flash Point	NA
Evaporation rate (Ether = 1)	Unspecified
Flammability (solid, gas)	Not Applicable
Upper/lower flammability or explosive limits	**Lower Explosive Limit:** NA **Upper Explosive Limit:** NA
Vapor pressure (Pa)	Unspecified
Vapor Density	Unspecified
Specific Gravity	Unspecified
Molecular weight	~170 kDa

Solubility in Water	Complete
Partition coefficient n-octanol/water (Log Kow)	Not Measured
Auto-ignition temperature	NA
Decomposition temperature	Unspecified
Viscosity (cSt)	Not Measured

9.2. Other information

No other relevant information.

10. Stability and reactivity

10.1. Reactivity

Hazardous Polymerization will not occur.

10.2. Chemical stability

Stable for period indicated on the label when stored at conditions specified in product package insert.

10.3. Possibility of hazardous reactions

No data available.

10.4. Conditions to avoid

Keep away from light.

10.5. Incompatible materials

None known.

10.6. Hazardous decomposition products

None known.

11. Toxicological information

Acute toxicity

Single intravenous injection at doses up to 1500 IU/kg was well tolerated in cynomolgus monkeys and rats. The NOAEL was considered to be 1500 IU/kg for both species.

Repeat-Dose Toxicity Study:

Repeat-dose toxicity in rats and cynomolgus monkeys after intravenous injection at doses up to 1250 IU/kg (rats) and 500 IU/kg (monkeys) for up to 28 days was well tolerated with no adverse changes. Under the conditions of these studies, the NOAEL was designated to the highest dose tested, ie 1250 IU/kg for rats and 500 IU/kg for monkeys.

Local Tolerance:

Intravenous, intra-arterial and perivenous injection was well tolerated in the rabbit with no local or systemic signs of reaction to treatment.

Safety Pharmacology:

In accordance with the ICH guideline S6, the safety pharmacology investigations were included in the 28 day repeated dose toxicity studies in rats (neurobehavioral tests) and monkeys (cardiovascular variables). Under the conditions of these studies, the NOAEL was designated to the highest dose tested, ie 1250 IU/kg for rats and 500 IU/kg for monkeys. A further in-depth investigation of potential effects of rVIII-SingleChain on hemodynamic and electrophysiological parameters or respiratory variables was conducted in dogs and monkeys after IV administration of rVIII-SingleChain at (cumulative) doses up to 1550 IU/kg under anesthetized or telemetered conditions. No adverse cardiovascular effects, clinical signs or behavioral effects were observed. Therewith, the NOAEL for cardiovascular

and respiratory parameters was considered to be at least 1550 IU/kg, and that for neurobehavioral parameters at least 1250 IU/kg.

Thrombogenicity:
The thrombogenic potential was evaluated in the Wessler stasis model in rabbits. rVIII-SingleChain showed only a minimal prothrombotic potential at the highest administered dose of 1000 IU/kg with no statistically significant effects at the lower doses of 150, 300 or 500 IU/kg, leading to the designation of a NOAEL of 500 IU/kg.

Genotoxicity:
The active components of rVIII-SingleChain are recombinant counterparts of naturally occurring human plasma proteins. Mutagenic effects of FVIII are not expected since there is no direct interaction with DNA to anticipate damage of DNA or interaction with DNA binding proteins. Therefore, no studies with regard to the mutagenic potential of AFSTYLA® were performed.

Ingredient	Oral LD50, mg/kg	Skin LD50, mg/kg	Inhalation Vapor LD50, mg/L/4hr	Inhalation Dust/Mist LD50, mg/L/4hr	Inhalation Gas LD50, ppm
Sucrose CAS Number: 0000057-50-1	No data available	No data available	No data available	No data available	No data available

Note: When no route specific LD50 data is available for an acute toxin, the converted acute toxicity point estimate was used in the calculation of the product's ATE (Acute Toxicity Estimate).

Classification	Category	Hazard Description
Acute toxicity (oral)	---	Not Applicable
Acute toxicity (dermal)	---	Not Applicable
Acute toxicity (inhalation)	---	Not Applicable
Skin corrosion/irritation	---	Not Applicable
Serious eye damage/irritation	---	Not Applicable
Respiratory sensitization	---	Not Applicable
Skin sensitization	---	Not Applicable
Germ cell mutagenicity	---	Not Applicable
Carcinogenicity	---	Not Applicable
Reproductive toxicity	---	Not Applicable
STOT-single exposure	---	Not Applicable
STOT-repeated exposure	---	Not Applicable
Aspiration hazard	---	Not Applicable

12. Ecological information

12.1. Toxicity

No ecological damage or persistence in the environment expected under normal conditions of use or with proper disposal. Environmental fate and transport of this product have not been studied.

Aquatic Ecotoxicity

Ingredient	96 hr LC50 fish, mg/l	48 hr EC50 crustacea, mg/l	ErC50 algae, mg/l
Sucrose CAS Number: 0000057-50-1	Not Available	Not Available	Not Available

12.2. Persistence and degradability

There is no data available on the preparation itself.

12.3. Bioaccumulative potential

Not Measured

12.4. Mobility in soil

No data available.

12.5. Results of PBT and vPvB assessment

This product contains no PBT/vPvB chemicals.

12.6. Other adverse effects

No data available.

13. Disposal considerations

13.1. Waste treatment methods

This material should be disposed of in accordance with local, state and / federal regulations. Not classified as Hazardous waste.
EWC-Code: 180109 (070599)

Observe all federal, state and local regulations when disposing of this substance.
Waste must be disposed in accordance with federal, state and local environmental regulations. Uncontaminated product may be disposed by flushing down the sanitary sewer, or by mixing with a liquid sorbent and then placing mixture in the solid waste container for disposal. Incineration is the preferred method of disposal for any contaminated product.

14. Transport information

	DOT (Domestic Surface Transportation)	IMO / IMDG (Ocean Transportation)	ICAO/IATA
14.1. UN number	Not Applicable	Not Regulated	Not Regulated
14.2. UN proper shipping name	Not Regulated	Not Regulated	Not Regulated
14.3. Transport hazard class(es)	**DOT Hazard Class:** Not Applicable **DOT Label:** ---	**IMDG:** Not Applicable **Sub Class:** Not Applicable	**Air Class:** Not Applicable
14.4. Packing group	Not Applicable	Not Applicable	Not Applicable

14.5. Environmental hazards

IMDG Marine Pollutant: No

14.6. Special precautions for user

No further information

15. Regulatory information

Regulatory Overview	The regulatory data in Section 15 is not intended to be all-inclusive, only selected regulations are represented.
Toxic Substance Control Act (TSCA)	All components of this material are either listed or exempt from listing on the TSCA Inventory.
WHMIS Classification	Not Regulated

US EPA Tier II Hazards

Fire: No
Sudden Release of Pressure: No
Reactive: No
Immediate (Acute): No
Delayed (Chronic): No

EPCRA 311/312 Chemicals and RQs:
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

EPCRA 302 Extremely Hazardous:
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

EPCRA 313 Toxic Chemicals:
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

Proposition 65 - Carcinogens (>0.0%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

Proposition 65 - Developmental Toxins (>0.0%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

Proposition 65 - Female Repro Toxins (>0.0%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

Proposition 65 - Male Repro Toxins (>0.0%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

N.J. RTK Substances (>1%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

Penn RTK Substances (>1%):
To the best of our knowledge, there are no chemicals at levels which require reporting under this statute.

16. Other information

The information and recommendations contained herein are based upon data believed to be correct. However, no guarantee or warranty of any kind, expressed or implied, is made with respect to the information contained herein. We accept no responsibility and disclaim all liability for any harmful effects which may be caused by exposure to our products. Customers/users of this product must comply with all applicable health and safety laws, regulations, and orders.

The full text of the phrases appearing in section 3 is: Not Applicable

This is the first version in the GHS SDS format. Listings of changes from previous versions in other formats are not applicable.

The information contained herein is based upon data considered true and accurate. CSL Behring makes no warranties, express or implied, as to the adequacy of the information contained herein. This information is offered solely for the user's consideration, investigation, and verification. Report to the manufacturer any allegations of health effects resulting from handling or accidental contact with this material.

End of Document