

1. Identification of the Substance/Preparation and Company

Commercial product name: Dermogesic® non-flammable cold spray
 Active ingredient(s): 1,1,1,3,3-Pentafluoropropane (HFC-245fa)
 1,1,1,2-Tetrafluoroethane (HFC-134a)
 Synonyms: HFC-245fa: Pentafluoropropane, R-245fa
 HFC-134a: Tetrafluoroethane, Fluorocarbon 134a, HFA-134a, Norflurane
 Presentation: Aerosol can containing 100ml of the active ingredients in the ratio 95%
 HFC-245fa / 5% HFC 134a
 Intended use: Vapo-coolant for clinical use as a topical cryo-analgesic and cold spray

Manufacturer: Acorus Therapeutics Ltd
 Address: Office Village
 Chester Business Park
 Chester UK
 CH4 9QZ
 Telephone: +44 (0) 1244 625152
 Fax: +44 (0) 1244 625151

2. Composition/Information on Ingredients

Hazardous Components:

| CAS No. | EINECS Name | Chemical formula(e) | Quantity/unit |
|----------|------------------------------|---|---------------|
| 460-73-1 | 1,1,1,3,3-Pentafluoropropane | HFC-245fa: C ₃ H ₃ F ₅ | 95% |
| 811-97-2 | 1,1,1,2-Tetrafluoroethane | HFC-134a: C ₂ H ₂ F ₄ | 5% |

Classification:

| Risk Phrases: | Symbol Letter: |
|---------------|----------------|
| 66 | None |

Description:

A gas at room temperature with a faint, sweetish ether-like odour, and a clear colourless, volatile liquid when compressed, or at lower temperatures.

3. Hazard Identification

Designation of hazard: Aerosol package

Special information on hazard to man and environment: In use ensure good ventilation.

4. First Aid Measures

General information:

There are no serious health hazards in connection with the clinical use of Dermogesic® non-flammable cold spray as a vapo-coolant, provided it is used in a well-ventilated area. The skin and lungs can absorb Dermogesic® non-flammable cold spray. A single prolonged skin exposure is not likely to result in absorption of harmful amounts. Over-exposure to Dermogesic® non-flammable cold spray is unlikely to occur given the quantity of Dermogesic® non-flammable cold spray in any single 100ml package. However, when Oxygen levels in air are reduced to 12-14% by displacement, symptoms of asphyxiation, loss of coordination, increased pulse rate and deeper respiration will occur. At high levels cardiac arrhythmia may occur. Contact with the

Dermogestic® non-flammable cold spray liquid is unlikely at room temperature but may cause frostbite

Inhalation:

Immediately remove to fresh air. If breathing has stopped, or is impaired, give artificial respiration and supplemental oxygen as required. Keep victim warm and quiet. Seek medical attention immediately. DO NOT give adrenaline (epinephrine)

Unintentional skin contact:

Rinse with water. In rare cases cutaneous sensitisation may occur. Rapid evaporation of Dermogestic® non-flammable cold spray may cause frostbite. If unintentional freezing occurs, flood or soak with tepid water. Do not use hot water. Seek medical attention.

Eye contact:

Liquid contact may cause frostbite. Rinse thoroughly with tepid water for at least 15 minutes. Do not use hot water. Seek medical attention.

Ingestion:

Ingestion is unlikely at room temperatures. Do not induce vomiting. Do not give stimulants. Seek medical attention immediately

Information for the doctor: see above

5. Fire Fighting Measures

Extinguishing media:

Use media appropriate to surrounding fire. The material itself is not flammable. Water spray may be used to cool aerosol containers.

Special risks posed by the substance, its combustion products or reaction products:

Dermogestic® non-flammable cold spray is not flammable at ambient temperatures and atmospheric pressure. However this material may become combustible when mixed with air under pressure and exposed to strong ignition sources. Contact with certain reactive metals may result in the formation of explosive or exothermic reactions at very high temperatures and/or pressures. Hazardous decomposition products may include Halogens, Halogen Acids and possibly Carbonyl Halides.

Fire Fighting Protective Equipment:

Fire fighters should wear appropriate self-contained breathing apparatus for protection against possible decomposition products. Appropriate eye and skin protection should be provided.

6. Accidental Release Measures

Personal protective measures:

In cases of large spill use full-vision safety glasses and insulated safety gloves constructed of PVA, neoprene, or butyl rubber. Use breathing apparatus in cases of large spill in poorly ventilated area.

Environmental control measures:

Do not discharge into drains/surface water/groundwater.

Cleaning/adsorption procedures:

Take up with non-combustible absorbent material such as sand.

Additional information:

Allow spilled Dermogestic® non-flammable cold spray to evaporate. Ventilate enclosed areas. In cases of large spill, evacuate all personnel from area. Eliminate sources of ignition.

7. Handling and Storage

Safe Handling:

Do not heat over 50°C. Do not spray into eyes. In clinical use minimise inhalation of vapours by the patient, especially when applying to head and/or neck.

Specific uses

For external topical use as a vapo-coolant and cryo-analgesic. Briefly spray area requiring analgesia until a thin snow film forms. Do not spray on open wounds. Do not over-cool skin as this may cause frostbite. Repeated exposure may cause skin dryness or cracking. In clinical use minimise inhalation of vapours by the patient, especially when applying to head and/or neck. Do not spray into eyes.

Protection against fire and explosion:

Propellant and solvent vapours can form explosive mixtures with air under extreme conditions.

Storage:

Store at room temperature in a dry well-ventilated area only.

Standards of storage rooms and containers:

While Dermogestic® non-flammable cold spray is not flammable, it should be stored in an area of low fire risk and out of direct sunlight.

Information on storing different substances together: None

Further information on storage conditions: None

Storage classification: None

8. Exposure Controls/Personal Protection

The UK's Health and Safety Commission's Advisory Committee on Toxic Substances has set no Maximum Exposure Limit for either HFC-245fa or HFC-134a. The American Industrial Hygiene Association has set Workplace Environmental Exposure Limits (WEEL) for HFC-245a of 300 parts per million (ppm) of air based on the 8-hour Time Weighted Average reference period and of 1000 ppm for HFC-134a for the same period. In the UK, an Occupational Exposure Limit (OEL) for HFC134a of 1000ppm has been set.

Employers should prevent, or if this is not reasonably practicable, adequately control, employees' exposure as far below these limits as is reasonably practicable.

Personal protection:

General protective and hygienic measures:

When using, do not eat, drink or smoke. Always use in a well-ventilated environment.

Respiratory protection:

Not essential for small spills. For large spills use full-face positive pressure, self-contained breathing apparatus. In clinical use minimise inhalation of vapours by patient, especially when applying to head and/or neck.

Hand protection:

Not necessary during normal clinical use unless user has known sensitivity to HFC-245fa and/or HFC-134a in which case hand protection is recommended.

Eye protection:

Not essential during normal clinical use, otherwise recommended. In clinical use around face or neck, cover patient's eyes in order to minimise risk of inadvertent exposure

Body protection: Not essential

Additional Information: No data are available on the air odour threshold concentration.

9. Physical and Chemical Properties

HFC-245fa

Appearance:

| | |
|--------------------|---------------------------------|
| Presentation form: | Aerosol can |
| Contents colour: | Clear, colourless liquid |
| Contents odour: | Faint sweetish ether-like odour |

Change in physical state

| | |
|------------------------------|---------------------|
| Melting point/melting range: | -160 °C |
| Boiling point/boiling range: | 15.3 °C at 1013 hPa |
| Flash point: | None |
| Ignition temperature: | 412°C |
| Auto-ignition: | 412°C |

Explosion danger

| | |
|---------------------------------|---|
| Lower explosion limit UEG: | None at 1013hPa at ambient temperatures |
| Upper explosion limit OEG: | None at 1013hPa at ambient temperatures |
| Vapour pressure (at 20°C): | 1227hPa |
| Density (at 4°C): | 1.32g/ml |
| Specific gravity (at 4°C): | 1.32 |
| Solubility in water (at 21°C): | 7.18g/l |
| pH-value: | |
| Partition coefficient at 21.5°C | 1.35 (Log K octanol/water) |
| Viscosity (at 20°C): | |
| Content of solvent: | 0% |

HFC-134a

Appearance:

| | |
|--------------------|---------------------------------|
| Presentation form: | Aerosol can |
| Contents colour: | Clear, colourless liquid |
| Contents odour: | Faint sweetish ether-like odour |

Change in physical state

| | |
|------------------------------|---------------|
| Melting point/melting range: | -108 °C |
| Boiling point/boiling range: | -26 °C |
| Flash point: | Non-Flammable |
| Ignition temperature: | Non-Flammable |
| Auto-ignition: | Non-Flammable |

Explosion danger

| | |
|--------------------------------|---|
| Lower explosion limit UEG: | None at 1013hPa at ambient temperatures |
| Upper explosion limit OEG: | None at 1013hPa at ambient temperatures |
| Vapour pressure (at 20°C): | 5.7 bar |
| Density (at 4°C): | 1.207g/ml |
| Specific gravity (at 0°C): | |
| Solubility in water (at 25°C): | 1g/l |
| pH-value: | |
| Partition coefficient: | 1.35 (Log K octanol/water) |
| Viscosity (at 20°C): | |
| Content of solvent: | 0% |

10. Stability and Reactivity

Conditions to avoid:

Sources of high temperature such as flames, hot spots or welding. Do not mix with Oxygen or air above atmospheric pressure

Materials to avoid:

Contact between Dermogesic® non-flammable cold spray and strong acids, alkalis or chemically reactive metals such as potassium, calcium, powdered aluminium, zinc, and magnesium may

cause fires and explosions. Contact with flames may produce toxic and corrosive fumes containing halogens, halogen acids and possibly carbonyl halides.

Hazardous decomposition products:

Halogens, halogen acids and possibly carbonyl halides

Further information:

Liquid Dermogestic® non-flammable cold spray will attack some forms of plastic, rubber and coatings.

11. Toxicological Information

Dermogestic non-flammable cold spray consists of 95% HFC-245fa and 5% HFC-134a. The components are considered separately under each heading below

Acute toxicity:

HFC-245fa: In rats a 4-hour exposure to HFC-245fa at 203,000 ppm did not cause lethality or clinical signs of toxicity except for transient CNS depression during exposure. In mice a 4-hour exposure to HFC 245fa at 101,000 ppm did not cause lethality or clinical signs of toxicity. No signs of eye or nasal irritation were noted in acute inhalation studies in rats and mice. No signs of skin irritation were seen in rabbits following dermal application under an occlusive dressing for 24 hours. Hydrofluorocarbons are only poorly adsorbed through the skin.

HFC-134a: HFC-134a is of low acute toxicity by the inhalation route. In the rat a 15-minute LC₅₀ of > 800,000 ppm and a 4-hour LC₅₀ of > 500,000 ppm have been reported. A 10-min-EC₅₀ for the anaesthetic effect of HFC-134a, measured by the loss of the righting reflex, was 280,000 ppm in the rat and 270,000 ppm in the mouse. Liquefied HFC-134a placed on scarified and intact skin areas of rabbits caused slight irritation to intact skin, possibly due to local freezing, after 24 hours of contact. No signs of irritation were reported when HFC 134a vapour was applied directly onto guinea pig skin, twice daily, using a metered dose device.

Administration of gaseous HFC-134a to the eyes of rabbits resulted in only very slight irritation which was transient and rapidly reversible.

Specific symptoms shown in experiments with animals:

HFC-245fa The potential of HFC-245fa to sensitise the heart to adrenaline was investigated in dogs. The no-observed effect level (NOEL) was 34,100 ppm for the development of cardiac arrhythmia in the presence of injected adrenaline. At 2,000 ppm, 1 female rat presented with a trace (Grade 1 of 5) of diffuse myocarditis. This observation was not statistically significant and it was concluded by the authors that this single (Grade 1) observation might be unrelated to treatment or at most, represent a threshold for this effect.

HFC-134a: None of the dogs exposed to 50,000 ppm HFC-134a exhibited a cardiac sensitisation response. HFC-134a induced anaesthesia in dogs, cats and monkeys within 1 minute of exposure to 500,000ppm. Emergence from deep anaesthesia generally occurred within 2 minutes post-exposure. No evidence of neurological dysfunction was observed in rats exposed to HFC-134a at concentrations of either 0, 150,000 or 200,000 ppm for between 1 and 2 hours.

Experience in man:

HFC-245fa: Not tested/no data. Given that at 2000ppm one rat presented with a trace of diffuse myocarditis, and while this was not statistically significant and may have been unrelated to treatment, it might represent a threshold for this effect, the American Industrial Hygiene Association has recommended an eight-hour workplace environmental exposure limit of 300ppm.

HFC-134a: No adverse health effects in humans from exposure to HFC-134a have been reported. HFC-134a is used as a replacement for CFCs as a propellant in metered dose inhalers for the treatment of respiratory diseases and has been shown to be safe in clinical trials at the typical inhaled doses. Further studies concluded that exposure to levels of up to 8,000 ppm HFC-134a for 1 hour did not result in any adverse effects on pulse, blood pressure, electrocardiogram or lung function.

Corrosivity/irritation:

Liquid Dermogestic non-flammable cold spray may cause frostbite in the skin or eye. There is no evidence of significant skin or eye irritation from HFC-245fa or HFC 134a

Sensitisation:

HFC-245fa: Not tested/no data

HFC-134a : Studies have failed to demonstrate contact sensitization potential with HFC-134a

Repeated-Dose Toxicity:

HFC-245fa: Rats were exposed for 6 hours per day to levels of 0, 500, 2,000, 10,000, and 50,000 ppm HFC-245fa daily for 28 consecutive days. There were no treatment-related effects on body weight, survival or histological parameters. Urine volume was increased. Increases were seen in BUN levels and alkaline phosphates (AP), glutamic pyruvic transaminase (GPT), glutamic oxaloacetic transaminase (GOT), and creatinine phosphokinase (CPK) activities, primarily in rats exposed at 10,000 and 50,000 ppm. Urinary fluoride levels were also elevated in an exposure-related pattern. Similar results were obtained from a 13 week study in rats with the same daily exposures. Histopathological examination did not show any effects on the kidney, liver, or lungs. There was an increased incidence of myocarditis in all animals exposed at 50,000 ppm and in the majority exposed at 10,000 ppm. It was described as mild. At 2,000 ppm, 1 female rat presented with a trace (Grade 1 of 5) of diffuse myocarditis. This observation was not statistically significant and it was concluded by the authors that this single (Grade 1) observation might be unrelated to treatment or at most, represent a threshold for this effect.

HFC-134a: Several studies in rats, mice and dogs at exposures of up to 120,000ppm HFC 134a for up to 6 hours per day and up to 376 days showed no compound-related pathological changes or effects were observed in any of the exposed rats.

Mutagenicity:

HFC-245fa was not active in either of two Ames assays in *Salmonella typhimurium* and *Escherichia coli*.at airborne concentrations up to 40% v/v or 100% v/v (400,000 or 100,0000 ppm). Weak evidence of clastogenic activity in cultured human lymphocytes was seen in with 24-h exposures to levels of 30 and 40% v/v, but not with 24-h exposures at 10 or 20%, nor with 6-h exposures to any concentration. In all cases where evidence for clastogenicity was seen, there was also a reduction in mean mitotic index suggestive of cytotoxicity.

HFC134a: Studies have shown that there is no evidence of gene mutation by HFC-134a in bacteria or yeast. Further studies with HFC-134a showed no evidence of mutagenicity or chromosomal aberration in cultured mammalian cells or *in vivo*.

Chronic Toxicity/Carcinogenicity:

HFC-245fa: No data were available beyond 13 weeks. There were no data available on carcinogenicity. However, the absence of mutagenic activity in the Ames assay and Mouse Micronucleus Assay and minimal activity seen in the chromosome aberration assay reduce the concern regarding the potential carcinogenicity of HFC-245fa. Furthermore, other similar chemicals such as chlorotetrafluoroethane and tetrafluoroethane have not been carcinogenic in lifetime inhalation studies

HFC-134a: Rats receiving 300 mg/kg body weight HFC-134a 5 days per week for 52 weeks. did not show an increase in the incidence of tumours when compared with control groups. A combined chronic toxicity/carcinogenicity study was conducted in rats at concentrations of 0, 2 500, 10,000 or 50,000 ppm HFC-134a for 6 hours per day, five days per week showed that after 104 weeks there was an increased incidence of Leydig cell hyperplasia and benign Leydig cell tumours. The no-effect level was considered to be 10,000 ppm HFC-134a.

Reproductive and Developmental toxicity:

HFC-245fa: In an inhalation, developmental toxicity study, groups of pregnant rats were exposed for 6 hours per day to levels of 0, 500, 2,000, 10,000, and 50,000 ppm HFC-245fa from day 6 to day 15 of gestation. A slight reduction in pup weight was seen at 50,000, but not at 10,000 ppm. There were no developmental effects at any level.

HFC-134a: In mice exposed to concentrations of HFC-134a up to 50,000 ppm for 6 hours per day for 5 days, no effects on fertility were observed. In a multi-generation reproductive toxicity study in rats there were no treatment-related effects on reproductive performance, maturation or development of the offspring. Studies in rats concluded that HFC-134a is neither teratogenic nor embryotoxic at levels up to and including 50,000 ppm, but at this highest level

HFC-134a may be slightly foetotoxic. The minimum maternal effect exposure level was 100,000 ppm, and the minimum embryo/foetal effect exposure level was 300,000 ppm. A study in rabbits showed that exposure to concentrations of 40,000 and 10,000 ppm HFC-134a was associated with slight maternal toxicity manifest as reduced body weight gain and food consumption. There was no evidence for maternal toxicity at the exposure level of 2,500 ppm. There was no evidence of embryotoxicity or foetotoxicity in rabbits at any exposure level.

12. Ecological Information

Most of the HFC 245fa and HFC-134a released to the environment vaporises as a gas into the atmosphere where it breaks down by reaction with substances in the air. They are greenhouse gases and may contribute to global warming. Neither HFC-245fa nor HFC-134a have a significant effect on aquatic organisms, however, neither component should be discharged into drains, surface water or groundwater.

13. Disposal Considerations

Product:

Recommendation: Recycling
 Waste disposal code: 150199 D1
 Designation of waste: Metal packaging with residues
 Accountability: Yes

Packaging containing residues:

Recommendation: Special disposal of waste
 Waste disposal code: 150104 (European Waste Catalogue)
 Designation of waste: Metal packaging

Recommended cleaning:

White spirit

14. Transport Information

Rail/Road/Inland Waterways carriage ADR/RID:

| | HFC 134a | HFC 245fa |
|---------------|-----------------|-----------------|
| UN No: | UN 3159 | UN 3163 |
| Class: | 2 | 2 |
| Hazard Label: | None | None |
| PSN: | Aerosol package | Aerosol Package |

Shipment by sea IMDG (Sea):

| | | |
|-------------------|---------|---------|
| UN No | UN 3159 | UN 3163 |
| EMS: | 2-09 | 2-09 |
| Class | 2.2 | 2.2 |
| Marine pollutant: | No | No |
| PSN: | AEROSOL | AEROSOL |
| Label: | | |

Air transport IATA-Dangerous Goods Regulations:

| | | |
|-----------------------|-------------|-------------|
| Class: | 2.2 | 2.2 |
| UN No.: | UN 3159 | UN 3163 |
| Proper Shipping Name: | AEROSOLS | AEROSOLS |
| Label: | None | None |
| Packing Instructions: | Y203 or 203 | Y203 or 203 |

15. **Regulatory Information**

Dermogestic® non-flammable cold spray is intended for clinical use and is to be registered under the Medical Devices Directive 93/42/EEC as Class IIa Medical Devices and marked CE 0473. Whilst the Chemicals (Hazard Information and Packaging of Supply) Regulations 2002 do not apply to a substance that is a medical device (within the meaning of the Medical Devices Regulations 2002), this Safety Data Sheet has been prepared according to these regulations.

During normal clinical use of Dermogestic® non-flammable cold spray, HFC 245fa and HFC 134a are released into the work environment due to the gas evaporating from the patient's skin. Neither Dermogestic® non-flammable cold spray or its components is listed in Part 1 of the Approved Supply List and they are therefore not designated as substance hazardous to health under the Control of Substances Hazardous to Health Regulations 1999. These regulations place a responsibility on employers to make a suitable and sufficient assessment of the risks related to work with a hazardous substance, and to prevent or, where this is not reasonably practicable, adequately control exposure. Further guidance is given in the publication, COSHH *Essentials*.

Labelling according to the Control of Substances Hazardous to Health Regulations 1999:

Symbol

None

Risk phrases:

66: Repeated exposure may cause skin dryness or cracking

Safety phrases:

2: Keep out of the reach of children

9: Keep container in a well-ventilated place

23 Do not breathe vapours

25 Avoid contact with eyes

36/37 Wear suitable protective clothing and gloves*

51 Use only in well-ventilated areas

61 Avoid release to the environment. Refer to special instructions/safety data sheet*

*As Dermogestic® non-flammable cold spray is a medical device and contains 95ml of HFC-245fa and 5ml HFC-134a and is not intended for supply to the general public, CHIPS3 Regulations (section 8;(11)) permit not listing R & S phrases. These phrases have been omitted to avoid causing undue patient concern or because there is no foreseeable risk under the conditions of use with the quantities supplied.

EC Number: . EC label.

Additional labelling for aerosol presentations:

(According to EC Directives 75/324/EEC and 94/1/EC and subsequent amendments)

Pressurised container. Protect from sunlight and do not expose to temperatures exceeding 50°C.

Do not pierce or burn, even after use.

Do not spray on a naked flame or any incandescent material.

Without adequate ventilation formation of explosive mixtures may be possible.

16. **Other Information**

The above information has been compiled from that provided by our suppliers and other sources. None of the original information relating to hazards or potential hazards has been omitted and so the absence of a particular reference merely implies either that such information has not been determined or that it is not applicable. The above information is furnished without warranty of any kind. Users should consider this data only as a supplement to other information gathered by them and make independent determinations of suitability and completeness of information from all sources to ensure proper use and disposal of the product and the safety of employees and customers.