

Sorafenib Tosylate

sc-357801



The Power to Question

Material Safety Data Sheet

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

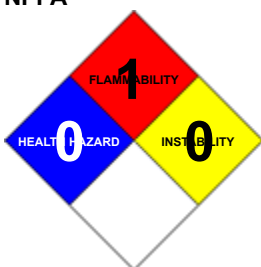
PRODUCT NAME

Sorafenib Tosylate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
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EMERGENCY

ChemWatch

Within the US & Canada: 877-715-9305

Outside the US & Canada: +800 2436 2255

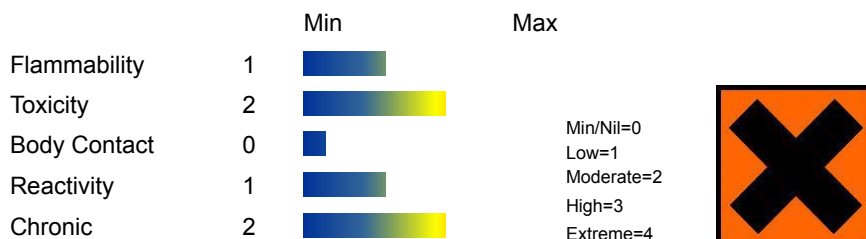
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C21-H16-Cl-F3-N4-O3.C7-H8-S-O3, 4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoylamino]phenoxy]-N-,methyl-pyridine-2-carboxamide, 4-toluenesulfonate, 4-methyl-3-((4-(3-pyridinyl)-2-pyrimidinyl)amino)-N-(5-(4-methyl-1H-, "imidazol-1-yl)-3-(trifluoromethyl)phenyl)benzamide monomethanesulfonate", "2-pyridinecarboxamide, 4-[4-[[[4-chloro-3-(trifluoromethyl)phenyl]amino]-, "carbonyl]amino]phenoxy]-N-methyl-, 4-methylbenzenesulfonate (11)", 4-[4-[[4-chloro-3-(trifluoromethyl)phenyl]carbamoylamino]phenoxy]-N-, "methylpyridine-2-carboxamide; 4-methylbenzenesulfonic acid", 4-[4-(((4-chloro-3-(trifluoromethyl)phenyl)amino)carbonyl)amino]phenoxy]-, "N-methyl-, mono(4-methylbenzenesulfonate)", "4-{4-[3-(4-chloro-3-trifluoromethyl-phenyl)ureido]-phenoxy}-pyridine-", "2-carboxylic acid methylamide-4-methylbenzenesulfonate", "sorafenib tosylate", "sorafenib mesylate", Nexavar, Xarelto, "Bay 43-9006 tosylate", "BAY 54-9085", LS-186598, D06272, "antineoplastic/ cytotoxic"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Limited evidence of a carcinogenic effect.
Possible risk of impaired fertility.
Possible risk of harm to the unborn child.
Harmful to aquatic organisms.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.
 - The killing action of antineoplastic drugs used for cancer chemotherapy is not selective for cancerous cells alone but affect all dividing cells.
- Acute side effects include loss of appetite, nausea and vomiting, allergic reaction (skin rash, itch, redness, low blood pressure, unwellness and anaphylactic shock) and local irritation.

EYE

- Although the material is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may cause transient discomfort characterised by tearing or conjunctival redness (as with windburn).
- Slight abrasive damage may also result.

SKIN

- The material is not thought to produce adverse health effects or skin irritation following contact (as classified by EC Directives using animal models).
- Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
- Open cuts, abraded or irritated skin should not be exposed to this material.
 - Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects.
- Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

- The material is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified by EC Directives using animal models).
- Nevertheless, adverse systemic effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.
- If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of

the material result in excessive exposures.

CHRONIC HEALTH EFFECTS

■ There has been concern that this material can cause cancer or mutations, but there is not enough data to make an assessment.

Ample evidence from experiments exists that there is a suspicion this material directly reduces fertility.

Based on experience with animal studies, exposure to the material may result in toxic effects to the development of the foetus, at levels which do not cause significant toxic effects to the mother.

Substance accumulation, in the human body, may occur and may cause some concern following repeated or long-term occupational exposure.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung. Prime symptom is breathlessness; lung shadows show on X-ray.

Anti-cancer drugs used for chemotherapy can depress the bone marrow with reduction in the number of white blood cells and platelets and bleeding. Susceptibility to infections and bleeding is increased, which can be life-threatening. Digestive system effects may include inflammation of the mouth cavity, mouth ulcers, oesophagus inflammation, abdominal pain and bleeds, diarrhoea, bowel ulcers and perforation. Reversible hair loss can result and wound healing may be delayed. Long-term effects on the gonads may cause periods to stop and inhibit sperm production. Most anti-cancer drugs can potentially cause mutations and birth defects, and coupled with the effects of the suppression of the immune system, may also cause cancer.

The material may inhibit protein kinase. This may suppress cell or tissue growth or development.

Toxicological data is available and well documented for representative toluene, xylene and cumene sulfonates (including sodium, potassium, ammonium and calcium salts). These data show that hydrotropes have low toxicity for all routes, do not cause genetic damage, show no evidence of causing cancer in long-term skin studies, and have not caused birth defects, developmental defects or reduced fertility.

Adverse effects after repeated long term dosing of hydrotropes to animals included hyperplasia of epithelium at the site of application in skin studies, and decreased relative spleen weight in females. Hydrotropes are classified as a negligible-to-slight irritant to skin and a slight-to-moderate irritant to eyes. The irritation potential of hydrotropes in a water solution depends on concentration, and the irritation is lessened with rinsing. Hydrotropes are not considered to be skin sensitisers.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
sorafenib, p-toluenesulfonate salt	475207-59-1	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- If swallowed do NOT induce vomiting.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- Observe the patient carefully.
- Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious.

EYE

If this product comes in contact with the eyes

- Wash out immediately with fresh running water.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- Seek medical attention without delay; if pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN

If skin or hair contact occurs

- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.

INHALED

- If fumes, aerosols or combustion products are inhaled remove from contaminated area.
- Other measures are usually unnecessary.

NOTES TO PHYSICIAN

- Treat symptomatically.

For employees potentially exposed to antineoplastic and/ or cytotoxic agents on a regular basis, a preplacement physical examination and history (noting risk factors) is recommended. Periodic follow-up examinations should also be undertaken and should be overseen by a physician familiar with the toxic effects of the substance and full details of the nature of work undertaken by the employee.

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Sorafenib is metabolised primarily in the liver, undergoing oxidative metabolism, mediated by CYP3A4, as well as glucuronidation mediated by UGT1A9. Sorafenib accounts for approximately 70-85% of the circulating analytes in plasma at steady- state. Eight metabolites of sorafenib have been identified, of which five have been detected in plasma. The main circulating metabolite of sorafenib in plasma, the pyridine N-oxide, shows in vitro potency similar to that of sorafenib. This metabolite comprises approximately 9-16% of circulating analytes at steady-state.

Section 5 - FIRE FIGHTING MEASURES

Vapor Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available
Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available

EXTINGUISHING MEDIA

- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.

FIRE FIGHTING

- Alert Fire Brigade and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water courses.
- Use water delivered as a fine spray to control fire and cool adjacent area.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty; it is estimated that most organic dusts are combustible (circa 70%) - according to the circumstances under which the combustion process occurs, such materials may cause fires and / or dust explosions.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust (420 micron or less) may burn rapidly and fiercely if ignited - particles exceeding this limit will generally not form flammable dust clouds.; once initiated, however, larger particles up to 1400 microns diameter will contribute to the propagation of an explosion.
- In the same way as gases and vapors, dusts in the form of a cloud are only ignitable over a range of concentrations; in principle, the concepts of lower explosive limit (LEL) and upper explosive limit (UEL).are applicable to dust clouds but only the LEL is of practical use; - this is because of the inherent difficulty of achieving homogeneous dust clouds at high temperatures (for dusts the LEL is often called the "Minimum Explosible Concentration", MEC)
- A dust explosion may release of large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people.

Combustion products include carbon monoxide (CO), carbon dioxide (CO₂), hydrogen chloride, phosgene, hydrogen fluoride, nitrogen oxides (NO_x), sulfur oxides (SO_x), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.

It is recommended that areas handling final finished product have cytotoxic spill kits available.

Spill kits should include

- impermeable body covering,
- shoe covers,
- latex and utility latex gloves,
- goggles,

To avoid accidental exposure due to waste handling of cytotoxics

- Place waste residue in a segregated sealed plastic container.
- Used syringes, needles and sharps should not be crushed, clipped, recapped, but placed directly into an approved sharps container.
- Dispose of any cleanup materials and waste residue according to all applicable laws and regulations e.g, secure chemical landfill disposal.

All personnel likely to involved in a antineoplastic (cytotoxic) spill must receive practical training in

- the correct procedures for handling cytotoxic drugs or waste in order to prevent and minimise the risk of spills
- the location of the spill kit in the area
- the arrangements for medical treatment of any affected personnel
- the procedure for containment of the spill, and decontamination of personnel and the environment, including the different procedures for major and **MINOR SPILLS**

MAJOR SPILLS

Moderate hazard.

- CAUTION Advise personnel in area.
- Alert Emergency Services and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

The National Institute of Health (USA) recommends that the preparation of injectable antineoplastic drugs should be performed in a Class II laminar flow biological safety cabinet and that personnel preparing drugs of this class should wear appropriate personal protective gear. Emphasise controls on containment.

- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers.
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container is suitable for laboratory quantities

- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

Antineoplastics (cytotoxics)

- should be clearly identifiable to all personnel involved in their handling
- should be stored in impervious break-resistant containers
- should be stored in separate, clearly marked storage areas to minimise the risk of breakage, and to limit contamination in the event of leakage.

Spill kits should be available in storage areas.

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry area protected from environmental extremes.
- Store away from incompatible materials and foodstuff containers.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- sorafenib, p-toluenesulfonate salt CAS475207-59-1

PERSONAL PROTECTION



RESPIRATOR

- Particulate. (AS/NZS 1716 & 1715, EN 1432000 & 1492001, ANSI Z88 or national equivalent)

EYE

- Chemical protective goggles with full seal
- Shielded mask (gas-type)
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]

HANDS/FEET

Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity
- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers. [AS/NZS 2210]

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc

OTHER

- When handling antineoplastic materials, it is recommended that a disposal work-uniform (such as Tyvek or closed front surgical-type gown with knit cuffs) is worn.
- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.

ENGINEERING CONTROLS

For potent pharmacological agents

Powders

To prevent contamination and overexposure, no open handling of powder should be allowed.

- Powder handling operations are to be done in a powders weighing hood, a glove box, or other equivalent ventilated containment system.
- In situations where these ventilated containment hoods have not been installed, a non-ventilated enclosed containment hood should be used.
- Pending changes resulting from additional air monitoring data, up to 300 mg can be handled outside of an enclosure provided that no grinding, crushing or other dust-generating process occurs.
- An air-purifying respirator should be worn by all personnel in the immediate area in cases where non-ventilated containment is used, where significant amounts of material (e.g., more than 2 grams) are used, or where the material may become airborne (as through grinding, etc.).

Unless written procedures, specific to the workplace are available, the following is intended as a guide

- For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets *; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems; Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*,
- HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.
- The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated. Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated. When handling Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered; Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered.

Written procedures, specific to a particular work-place, may replace these recommendations

* For Class II Biological Safety Cabinets, Types B2 or B3 should be considered.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

State	Divided Solid	Molecular Weight	637.03
Melting Range (°F)	Not Available	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Partly Miscible
Flash Point (°F)	Not Available	pH (1% solution)	Not Applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not Applicable

Autoignition Temp (°F)	Not Available	Vapor Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

Solid; does not mix well with water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerisation will not occur.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidising agents

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

sorafenib, p-toluenesulfonate salt

TOXICITY AND IRRITATION

unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

SORAFENIB, P-TOLUENESULFONATE SALT

Section 12 - ECOLOGICAL INFORMATION

Harmful to aquatic organisms.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

† Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate. In most instances the supplier of the material should be consulted.

- DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.
- Antineoplastic (cytotoxic) wastes must be packed directly, ready for incineration, into color-coded, secure, labelled, leak-proof containers sufficiently robust to withstand handling without breaking, bursting or leaking.
- Containers of special design are available for particular needs (such as disposal of sharps) and should be

used.

- Once filled and closed, such containers must never be re-opened.
- Immediate containers must bear a nationally accepted symbol or device depicting cytotoxic substances and be labelled with the words: CYTOTOXIC WASTE - INCINERATE in a style of lettering approved by the national/ state authority.
- Where policies and procedures permit the merging of cytotoxic wastes with medical waste in an outer container used for medical waste, cytotoxic waste must first be placed in identifiable color-coded/ labelled cytotoxic containers prior to merging.
- Management procedures must ensure that merged medical and cytotoxic waste is subjected to the incineration requirements appropriate for the total destruction of the cytotoxic waste.

WASTE STORAGE OF CYTOTOXIC WASTES For the storage of cytotoxic waste, segregated or merged with medical waste, provide:

- special storage areas with adequate lighting.
- waste security and restriction of access to authorised persons.
- storage areas designed to facilitate easy routine cleaning and maintenance to hygienic standards, or post-spill decontamination.
- storage of cytotoxic waste in standard, identifying bins or other appropriate containers.

COLLECTION OF CYTOTOXIC WASTES

- Procedures for the collection of cytotoxic wastes, which are compatible with existing operational needs, and which protect workers, other people and the environment, must be developed.
- Waste must be removed from the site by contractors whose workers have been instructed in the protective methods to be used against the hazards involved, and who comply with the safe work practices established by internal and/or national/ state policies. Contractors must instruct, train and direct their personnel in the safe and legal handling of cytotoxic wastes. Contractor's personnel should observe the operating procedures of the waste-generator.
- Transport of cytotoxic wastes, through the community, must comply with the appropriate national/ state codes.

DESTRUCTION OF CYTOTOXIC WASTES

- Destruction of cytotoxic wastes should be carried out in multi-chambered incinerators, licenced for this purpose, operating at 1100 deg. C. or more, with a residence time of at least 1 second.
- Operators must be trained in handling procedures and hazards involved with handling the waste.
- Waste which arrives at the incinerator inappropriately packaged should NOT be returned to the waste generator. An authorised representative of the waste generator must attend the incinerator site to rectify the situation.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

No data for sorafenib, p-toluenesulfonate salt (CAS: , 475207-59-1)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Ingestion may produce health damage*.
 - Cumulative effects may result following exposure*.
- * (limited evidence).

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■ Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references. A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings.

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