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HI-6 DMS safety and pharmacokinetics study in healthy volunteers

Submission date 12/11/2025	**Recruitment status** Recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 13/11/2025	**Overall study status** Ongoing	
Last Edited 20/04/2026	**Condition category** Other	

Plain English summary of protocol

Background and study aims
The study is testing a drug called HI-6 DMS, which is being developed to treat poisoning from nerve agents (highly toxic chemicals). These agents block an important enzyme, causing severe symptoms and even death if untreated. HI-6 DMS works by reactivating this enzyme. The goal of this study is to see if the drug is safe, well-tolerated, and how it behaves in the body when given as an intravenous (IV) infusion. This research will help prepare for emergencies involving nerve agent exposure.

Who can participate?
Healthy adults aged 18 to 50 years can join. They must have a normal medical history, lab results, and electrocardiogram (ECG), and agree to use effective birth control for 1 month before and after the study. People who smoke, have certain health conditions, or take specific medications cannot participate.

What does the study involve?
The study uses a dose escalation design, meaning different groups will receive increasing doses to find the highest dose that is considered safe.

Participants will:
- Get either the study drug or a placebo through an IV line.
- Stay in a clinic for monitoring before, during, and after dosing.
- Undergo blood and urine tests, ECGs, check for vital signs, and physical exams.
- Provide blood and urine samples at planned times during the study.

What are the possible benefits and risks of participating?
Benefits: There is no direct health benefit since participants are healthy volunteers, but the study helps to develop treatments for nerve agent poisoning.
Risks: Unknown side effects from the drug. Based on animal studies, possible risks include kidney issues and heart rhythm changes. Common side effects associated with the administration of HI-6 DMS based on past clinical experience include pain at injection site, dry

mouth, face numbness, fatigue, light-headedness, drowsiness, nausea, and headache. Safety measures include close monitoring and stopping the dosing or the entire study based on stopping criteria if problems occur.

Where is the study run from?
The study will take place at BioPharma Services Inc., Toronto, Ontario, Canada.

When is the study starting and how long is it expected to run for?
April 2026 to January 2027

Who is funding the study?
The study is funded by the Department of National Defence (Canada).

Who is the main contact?
BioPharma Services Inc., 4000 Weston Road, Toronto, Ontario M9L 3A2, Canada
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Contact information

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Additional identifiers

Protocol serial number
W3931-150027

Study information

Scientific Title
A randomized, placebo-controlled, double-blind, sequential, dose escalation study assessing the safety, tolerability, and pharmacokinetics of HI-6 DMS intravenous infusion in healthy volunteers

Study objectives
1a. To assess the safety and tolerability of an intravenous (IV) loading dose followed by continuous IV infusion of HI-6 DMS for 24 hours in healthy volunteers.
1b. To identify the no-adverse effect and maximum tolerated dose (MTD) of continuous IV infusion of HI-6 DMS following a fixed IV loading dose.
2. To determine the pharmacokinetic (PK) parameters of HI-6 DMS in plasma and urine following:
-An IV loading dose (15-minute infusion).
-A continuous IV infusion over 24 hours.
-Combination of an IV loading dose (15-minute infusion) followed by a continuous IV infusion over 24 hours.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 10/11/2025, Veritas IRB Inc. (3551 St. Charles Blvd., Suite 501, Kirkland, H9H 3C4, Canada; +1 (0)514-337-0442; infoirb@veritasirb.com), ref: 025-3856-23136-2

2. Approved 12/02/2026, Veritas IRB Inc. ((3551 St. Charles Blvd., Suite 501, Kirkland, H9H 3C4, Canada; +1 (0)514-337-0442; infoirb@veritasirb.com), ref: 2026-3856-23848-1

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Blinded (masking used)

Control
Dose comparison

Assignment
Sequential

Purpose
Treatment

Study type(s)
Safety

Health condition(s) or problem(s) studied
Safety and pharmacokinetics in healthy volunteers

Interventions
The study uses a dose escalation design and seven sequential dosing cohorts are included.

Participants will be randomized using a computer-generated schedule to receive either HI-6 Dimethanesulfonate (HI-6 DMS) or placebo (0.9% Sodium Chloride Injection).

Cohort 1 will receive an IV Loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (placebo).

Cohort 2 will receive an IV loading dose over 15 minutes (placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 1.0 µg/mL.

Cohort 3 will receive an IV loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 1.0 µg/mL.

Cohort 4 will receive an IV loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 2.5 µg/mL.

Cohort 5 will receive an IV loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 5.0 µg/mL.

Cohort 6 will receive an IV loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 8.4 µg/mL.

Cohort 7 will receive an IV loading dose over 15 minutes (400 mg HI-6 DMS or placebo) followed by continuous IV infusion over 24 hours (HI-6 DMS or placebo) to achieve a targeted steady-state plasma concentration of 12.5 µg/mL.

Following the end of dosing, all participants will be followed up for another 24 hours.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
HI-6 Dimethanesulfonate

Primary outcome(s)
Safety is measured using the following assessments at specified timepoints between study entry (-10 hours, Evening Prior to Dosing) to 48 hours 15 minutes after the start of dosing:
1. Frequency, severity, and type of adverse events (including infusion site reactions and predefined dose-limiting toxicities)
2. Clinically significant changes in laboratory parameters (hematology, biochemistry, and urinalysis)
3. Vital signs (heart rate, blood pressure, venous oxygen saturation, body temperature, respiratory rate)
4. Electrocardiogram findings and physical examinations

Key secondary outcome(s)
Pharmacokinetic parameters are measured by analyzing HI-6 DMS in plasma and urine samples at specified timepoints between 1 hour before dosing to 48 hours 15 minutes after the start of dosing.

Completion date
31/01/2027

Eligibility

Key inclusion criteria
Current inclusion criteria as of 19/02/2026:
1. Healthy volunteers between 18 and 50 years inclusive, at the time of signing the informed consent.
2. Women of childbearing potential (WOCBP) and male participants with partners of childbearing potential must agree to use highly effective methods of contraception (described below) for at least 30 days (1 month) before trial intervention administration and for (1) month after completion of trial intervention administration. WOCBP are defined as females who have not been surgically sterilized or who are not postmenopausal. A woman is considered not of childbearing potential if she meets the following criteria:
• Has been postmenopausal for at least 12 consecutive months prior to study drug administration
• Has undergone surgical sterilization (bilateral oophorectomy, bilateral salpingectomy, or hysterectomy) at least 6 months prior to study drug administration, or
• Has medically documented ovarian failure
The following are adequate methods of contraception:
• The consistent use of an approved hormonal contraception (birth control pill/patches, rings)
• An intrauterine device (IUD)
• Contraceptive injection (Depo-Provera)

• Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam)
• Sexual abstinence (no sexual intercourse) or
• Sterilization
3. Non-surgically sterile male participants or male participants with female partners of childbearing potential (including pregnant or breastfeeding) must use a highly effective method of contraception during the study and for one (1) month after completion of trial intervention administration, or ensure that their partner(s) will use a highly effective method of contraception for the same time duration. Male participants must use a condom and spermicide and the adequate methods of contraception for their female partners of childbearing potential are described above.
4. WOCBP must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction for one (1) month after completion of trial intervention administration.
5. Male participants must be willing to refrain from sperm donation for one (1) month after completion of trial intervention administration.
6. BMI range of 18.0 - 30.0 kg/m2.
7. Findings within the range of clinical acceptability in medical history, physical examination, 12-lead ECG, vital signs, and laboratory results within the “normal ranges” for the relevant laboratory tests (unless the investigator considers the deviation to be irrelevant for the purpose of the study).
8. Non-smoking (i.e., having no history of tobacco, or other substance or no smoking for greater than or equal to 12 months and not having smoked within the past year by self-report).
9. Negative for hepatitis B surface antigen, hepatitis C antibody, human immunodeficiency virus (HIV), and tuberculosis at screening.
10. Negative urine screen for drugs of abuse and negative urine cotinine test to confirm absence of recent tobacco use.
11. Breath alcohol concentration no greater than 0.0%.
12. Able to understand the requirements of the study and sign Informed Consent Form (ICF).

Previous inclusion criteria:
1. Healthy volunteers between 18 and 50 years inclusive, at the time of signing the informed consent.
2. Women of childbearing potential (WOCBP) and male participants with partners of childbearing potential must agree to use highly effective methods of contraception (described below) for (1) month after completion of trial intervention administration. WOCBP are all those except participants who are surgically sterile, who have medically documented ovarian failure, or who are at least 1 year postmenopausal.
The following are adequate methods of contraception:
• The consistent use of an approved hormonal contraception (birth control pill/patches, rings)
• An intrauterine device (IUD)
• Contraceptive injection (Depo-Provera)
• Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam)
• Sexual abstinence (no sexual intercourse) or
• Sterilization.
3. Non-surgically sterile male participants or male participants with female partners of childbearing potential (including pregnant or breastfeeding) must use a highly effective method of contraception during the study and for one (1) month after completion of trial intervention administration, or ensure that their partner(s) will use a highly effective method of contraception for the same time duration. Male participants must use a condom and spermicide and the adequate methods of contraception for their female partners of childbearing potential are described above.
4. WOCBP must agree not to donate eggs (ova, oocytes) for the purposes of assisted reproduction for one (1) month after completion of trial intervention administration.

5. Male participants must be willing to refrain from sperm donation for one (1) month after completion of trial intervention administration.
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7. Findings within the range of clinical acceptability in medical history, physical examination, 12-lead ECG, vital signs, and laboratory results within the “normal ranges” for the relevant laboratory tests (unless the investigator considers the deviation to be irrelevant for the purpose of the study).
8. Non-smoking (i.e., having no history of tobacco, or other substance or no smoking for greater than or equal to 12 months and not having smoked within the past year by self-report).
9. Negative for hepatitis B surface antigen, hepatitis C antibody, human immunodeficiency virus (HIV), and tuberculin skin-prick test at screening.
10. Negative urine screen for drugs of abuse.
11. Able to understand the requirements of the study and sign Informed Consent Form (ICF).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
Yes

Age group
Adult

Lower age limit
18 Years

Upper age limit
50 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
Current exclusion criteria as of 19/02/2026:
1. Any condition or therapy that, in the opinion of the investigator, may be significantly worsened by the administration of HI-6 DMS or is likely to interfere with the successful collection of the measures required.
2. Clinically significant illnesses or surgery within 4 weeks prior to trial intervention administration.
3. Any clinically significant history or presence of clinically significant neurological, endocrinal, cardiovascular, pulmonary, hematologic, immunologic, psychiatric, or metabolic disease or any medical history or condition associated with impaired cyanide detoxification or sulfurtransferase (rhodanese, thiosulfate sulfurtransferase) activity (e.g., history of hypersensitivity or adverse reaction to cyanide or cyanide-releasing compounds such as nitroprusside, Leber's Hereditary Optic Neuropathy), as determined by the investigator.
4. Any known impairment in renal drug clearance, including but not limited to reduced estimated glomerular filtration rate (eGFR) below 90 ml/min/1.73 m2 (National Kidney Foundation, 2022), tubular dysfunction, or genetic polymorphisms affecting renal transporters (e.g., MATE1, MATE2-

K).
5. Currently taking medications known to significantly induce or inhibit renal drug elimination pathways, such as cimetidine.
6. Blood urea nitrogen (BUN) or serum creatinine (sCr) outside of normal range, or any other abnormal laboratory tests judged by the investigator to be clinically significant.
7. Positive testing for hepatitis B, hepatitis C, HIV, or tuberculosis at screening.
8. ECG abnormalities (clinically significant) or vital sign abnormalities (systolic blood pressure that remains lower than 90 or over 140 mmHg, diastolic blood pressure that remains lower than 50 or over 90 mmHg, or heart rate that remains lower than 50 or over 100 bpm) at screening.
9. History of allergic reactions to heparin or other related drugs.
10. Cancer within the previous 5 years, other than squamous cell or basal cell carcinoma of the skin.
11. History of serious adverse reaction or hypersensitivity to any drug.
12. Known prolonged bleeding times resulting from disease or ongoing regimen use of anticoagulant medication (e.g., warfarin). If participants are on a drug or supplement that prolongs bleeding times (e.g., non-steroidal anti-inflammatory, anticoagulant, high dose vitamin E, fish oil, corticosteroids), they must discontinue use at least 7 days prior to trial intervention. Warfarin use is not permitted within this 14-day window before or after trial intervention administration.
13. Donation of plasma (500 ml) within 7 days prior to trial intervention administration. Donation or loss of whole blood (excluding the volume of blood that will be drawn during the screening procedures of this study) permitted prior to trial intervention administration as follows: 50 ml to 300 ml of whole blood within 30 days, 301 ml to 500 ml of whole blood within 45 days, or more than 500 ml of whole blood within 56 days prior to trial intervention administration.
14. Any known or suspected allergy to any constituent of HI-6 DMS.
15. Any food allergy, intolerance, restriction or special diet that, in the opinion of the investigator, could contraindicate the participant's participation in this study.
16. A depot injection or an implant of any drug within 3 months prior to trial intervention administration (contraceptive injections/implants are exempted).
17. Use of any drugs known to induce or inhibit hepatic drug metabolism (examples of inducers: barbiturates, carbamazepine, phenytoin, glucocorticoids, omeprazole; examples of inhibitors: selective serotonin reuptake inhibitors (SSRI) antidepressants, cimetidine, diltiazem, macrolides, imidazoles, neuroleptics, verapamil, fluoroquinolones, antihistamines) within 30 days prior to trial intervention administration.
18. History of significant alcohol abuse or drug abuse within 1 year prior to the screening visit.
19. Regular use of alcohol within 6 months prior to the screening visit (more than 14 units of alcohol per week [1 unit = 150 ml of wine, 360 ml of beer, or 45 ml of 40% alcohol]).
20. Use of soft drugs (such as marijuana) within 3 months prior to the screening visit or hard drugs (such as cocaine, phencyclidine [PCP] and crack) within 1 year prior to the screening visit or positive urine drug screen at screening.
21. Use of any investigational or non-registered drug or participation in an investigational study within 30 days or 5 half-lives if known, whichever is longer, prior to administration of study drug.
22. Receipt of vaccine within 30 days prior to trial intervention administration.
23. Participants who would require dosing above 15 g/day of HI-6 DMS.
24. Any reason which, in the opinion of the investigator, would prevent the participant from participating in the study.

Previous exclusion criteria:
1. Any condition or therapy that, in the opinion of the investigator, may be significantly worsened by the administration of HI-6 DMS or is likely to interfere with the successful collection of the measures required.
2. Clinically significant illnesses or surgery within 4 weeks prior to trial intervention

administration.
3. Any clinically significant history or presence of clinically significant neurological, endocrinal, cardiovascular, pulmonary, hematologic, immunologic, psychiatric, or metabolic disease.
4. Any known impairment in renal drug clearance, including but not limited to reduced estimated glomerular filtration rate (eGFR) below 90 mL/min/1.73 m2 (National Kidney Foundation, 2022), tubular dysfunction, or genetic polymorphisms affecting renal transporters (e.g., MATE1, MATE2-K).
5. Currently taking medications known to significantly induce or inhibit renal drug elimination pathways, such as cimetidine.
6. Blood urea nitrogen (BUN) or serum creatinine (sCr) outside of normal range, or any other abnormal laboratory tests judged by the investigator to be clinically significant.
7. Positive testing for hepatitis B, hepatitis C, HIV, or tuberculosis at screening.
8. ECG abnormalities (clinically significant) or vital sign abnormalities (systolic blood pressure that remains lower than 90 or over 140 mmHg, diastolic blood pressure that remains lower than 50 or over 90 mmHg, or heart rate that remains lower than 50 or over 100 bpm) at screening.
9. History of allergic reactions to heparin or other related drugs.
10. Cancer within the previous five (5) years, other than squamous cell or basal cell carcinoma of the skin.
11. History of serious adverse reaction or hypersensitivity to any drug.
12. Known prolonged bleeding times resulting from disease or ongoing regimen use of anticoagulant medication (e.g., warfarin). If participants are on a drug or supplement that prolongs bleeding times (e.g., non-steroidal anti-inflammatory, anticoagulant, high dose vitamin E, fish oil, corticosteroids), they must discontinue use at least seven (7) days prior to trial intervention. Warfarin use is not permitted within this 14-day window before or after trial intervention administration.
13. Donation of plasma (500 mL) within 7 days prior to trial intervention administration. Donation or loss of whole blood (excluding the volume of blood that will be drawn during the screening procedures of this study) permitted prior to trial intervention administration as follows: 50 mL to 300 mL of whole blood within 30 days, 301 mL to 500 mL of whole blood within 45 days, or more than 500 mL of whole blood within 56 days prior to trial intervention administration.
14. Any known or suspected allergy to any constituent of HI-6 DMS.
15. Any food allergy, intolerance, restriction or special diet that, in the opinion of the investigator, could contraindicate the participant's participation in this study.
16. A depot injection or an implant of any drug within three (3) months prior to trial intervention administration (contraceptive injections/implants are exempted).
17. Use of any drugs known to induce or inhibit hepatic drug metabolism (examples of inducers: barbiturates, carbamazepine, phenytoin, glucocorticoids, omeprazole; examples of inhibitors: selective serotonin reuptake inhibitors (SSRI) antidepressants, cimetidine, diltiazem, macrolides, imidazoles, neuroleptics, verapamil, fluoroquinolones, antihistamines) within 30 days prior to trial intervention administration.
18. History of significant alcohol abuse or drug abuse within one (1) year prior to the screening visit.
19. Regular use of alcohol within six (6) months prior to the screening visit (more than fourteen units of alcohol per week [1 Unit = 150 mL of wine, 360 mL of beer, or 45 mL of 40% alcohol]).
20. Use of soft drugs (such as marijuana) within three (3) months prior to the screening visit or hard drugs (such as cocaine, phencyclidine [PCP] and crack) within one (1) year prior to the screening visit or positive urine drug screen at screening.
21. Use of any investigational or non-registered drug or participation in an investigational study within four (4) months prior to administration of study drug.
22. Receipt of vaccine within 30 days prior to trial intervention administration.
23. Participants who would require dosing above 15 g/day of HI-6 DMS.

24. Any reason which, in the opinion of the investigator, would prevent the participant from participating in the study.

Date of first enrolment
09/04/2026

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
Canada

Study participating centre
BioPharma Services Inc.
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Sponsor information

Organisation
Department of National Defence

ROR
https://ror.org/035rreb34

Funder(s)

Funder type
Not defined

Funder Name
Ministère de la Défense Nationale

Alternative Name(s)
Ministry of National Defence, Department of National Defence, Department of National Defence of Canada, Department of National Defence (Canada), Canada's Department of National Defence, Canadian Department of National Defence, DND

Funding Body Type
Government organisation

Funding Body Subtype
Local government

Location
Canada

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available