

Responding to an incident involving organophosphorus nerve agents

Safety advisory and guidance

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Abstract

The intent of this guide is to provide Department of National Defence (DND) / Canadian Armed Forces (CAF) and First Responder personnel with the required knowledge of organophosphorus nerve agents, including the Fourth Generation Agents (FGA), to inform decision making during the Response Phase of an incident.

Résumé

Le but de ce guide est de fournir au personnel du ministère de la Défense nationale (MDN)/des Forces armées canadiennes et des premiers intervenants l'information requises sur les agent neurotoxiques organophosphorés, y compris les agents de quatrième génération (FGAs) pour éclairer et aider la prise de décision pendant la phase d'intervention d'un incident.

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Introduction

The intent of this guide is to provide Department of National Defence (DND) / Canadian Armed Forces (CAF) and First Responder personnel with the required knowledge of organophosphorus nerve agents, including the Fourth Generation Agents (FGA), to inform decision making during the Response Phase of an incident. Certain aspects may be applicable to the Recovery and Remediation Phase of an incident. This guide includes information on hazard assessment; toxicity, symptoms and health monitoring; protection; detection and identification; contamination control; casualty decontamination and management; medical treatment; and operator/responder decontamination. The Reference Document will assist personnel to manage incidents involving organophosphorus nerve agents in general and explicitly highlights special considerations when FGAs are involved; a Quick Reference Guide (What to consider if you suspect a FGA incident) is provided at **Annex A**. The information herein is based on Canadian government scientists' interpretation of available data on the organophosphorus class of nerve agents.

Background

A range of highly toxic organophosphorus compounds are known: some were developed for military use, the most notable of which are tabun (GA), sarin (GB), soman (GD), cyclosarin (GF) and VX. The newly identified FGAs (also referred to as A-Series agents or Novichok agents) are further examples. Each nerve agent is characterized by specific chemical and physical properties and understanding them is critical to implementing a safe response and management capability for a nerve agent incident. Poisoning from nerve agent exposure can occur through ingestion, inhalation or absorption through skin, eyes, and mucous membranes. Whilst the lethal dose for a given nerve agent varies by the route of exposure, it should be assumed that exposure to any amount in the absence of personal protective equipment (PPE) and without immediate medical support may be fatal.

Recent examples of the use of nerve agents in a civilian environment include the release of GB in Matsumoto and Tokyo in June 1994 and March 1995 respectively, the Syrian chemical attacks in 2013 and 2017, the assassination of Kim Jong-nam in Malaysia with a V-series agent in February 2017, and the attempted assassination of Sergei Skripal¹ in the UK in 2018 and Alexei Navalny in Russia in 2020 with a FGA. The last suspected use of nerve agent in a military conflict was during the Iran-Iraq war in March 1988 as part of the Halabja chemical attack.

As of 07 June 2020 FGAs are now included in the Chemical Weapons Convention list of Schedule 1 chemicals, along with the classical nerve agents in the G- and V-series.

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¹ Three other individuals in the UK were also exposed, one of whom died.

Nerve agent properties and hazards

The information presented in Table 1 is most relevant to post agent release, i.e., the start of the Response Phase when DND/CAF and/or qualified First Responder entry teams are preparing to move into the hot (initial isolation) zone. The table identifies key agent properties and physical hazards of most concern for each nerve agent that should be considered when determining how to manage the incident.

The chemical/physical properties of nerve agents vary considerably. All agents are liquid at room temperature. Some agents will evaporate quickly forming a toxic vapour whilst a few will remain in the liquid phase due to their extremely low volatility. Others will exist as both liquids and vapours for varying periods of time, again dependent on their volatility. For the most part, the nerve agent's volatility determines the most likely expected hazard to be encountered at an incident, ground/surface contamination and or vapour, and its persistence in the environment.

Table 1: Key agent properties and physical hazards.

Nerve agents may be disseminated (spread) as bulk liquid, droplets, aerosol, or as a vapour. Bulk liquid may be disseminated by pouring it from a container, using a mister or other device that releases liquid. All of the nerve agents could be disseminated readily on to the ground, surfaces, objects or people in this manner. The extent of the hazard would depend on the nerve agent, its volatility and the quantity released. Lower volatility agents such as GF, VX and FGAs will be more persistent; VX and FGAs may remain on surfaces for many months if not exposed to adverse weather. The more volatile agents (GA, GB and GD) would also present a secondary vapour inhalation and ocular hazard due to evaporation from bulk liquid and droplets on surfaces. GB, because of its very high volatility, may become a significant vapour hazard following bulk liquid dispersal. The severity of the exposure for any of the volatile agents will increase with the amount of agent disseminated in the environment, the ambient temperature and the agent's toxicity. At temperatures in excess of 25 \degree C, particularly in confined spaces or areas with minimal ventilation, vapour from VX and FGAs may be of concern.

GF, VX and FGAs released in bulk form will pose a dermal contact hazard, with the FGAs of particular concern. FGAs easily absorb into skin and readily wick into engineering and other materials and objects commonly found in public places (concrete, asphalt, brick, ceramic, carpet, fabric, plastics, polymers, etc.). Visually detecting the presence of a FGA may be virtually impossible even minutes after being released. Accordingly, a lethal dose of a FGA may be present even if the agent is not visible on the surface, which creates a high risk of dermal exposure through contact transfer. This risk is acute for CAF operators and First Responders attending to victims, contacting surfaces or handling objects where a FGA was released, and extends to the general public. In a bulk liquid release of VX or a FGA individuals would most likely be exposed to agent on their skin. Although dose dependent, there may be a delay in the onset of symptoms following a dermal exposure. This, and the likelihood of contamination transfer between individuals, may give rise to "hot spots" of individuals manifesting symptoms hundreds of metres to kilometres from the site of the release. Dermal exposure should be assumed to lead to secondary ingestion and ocular exposure by self-touch, exacerbating the physiological effects of the nerve agent poisoning.

Dissemination of GB, GA, GD and GF as a spray of fine droplets or aerosol would produce a vapour hazard as they evaporated in the air and may lead to a combined vapour and aerosol exposure hazard extending downwind from the release point dependent on the ambient temperature, volatility of the agent and distance downwind. GB would rapidly form a vapour "cloud" whilst GA, GD and GF would occur as both droplets and vapour, where the droplet fraction would decrease and the vapour fraction increase downwind. The possibility of liquid contamination on surfaces downwind from a spray release should not be discounted. Casualties may be expected in this downwind area.

Dissemination of VX or a FGA as a spray of fine droplets would, due their low volatility, result in a "hanging" mixed droplet and vapour cloud that may deposit liquid on surfaces at significant distances from the release point. Accordingly, there may be an inhalation and dermal exposure hazard at the time of release, as well as a secondary dermal contact and contamination transfer hazard during the response phase, which would present many of the challenges associated with bulk liquid contamination discussed above. Casualties may be expected in this downwind area. Note, VX or FGAs could be impregnated on fine solid particulates and disseminated dry. Evidence of dust or powder on surfaces along with chemical casualties may indicate a release of this type. The principal hazards of concern in this case would be direct contact, contact transfer and secondary re-aerosolization of agent impregnated particulates from surfaces and clothing of casualties. A final

note, particulates less than 0.1 millimetre in size are near impossible to see with the naked eye. A lack of evidence of the presence of aerosol or particulates does not imply that they are absent. See the advice in the Personnel and Victim Emergency Decontamination and Casualty Management Section below.

A certain level of sophistication would be required to disseminate the higher volatility nerve agents in a pure vapour state. Whilst such an attack would certainly cause many casualties, the vapour cloud would be expected to move downwind from the release point and the concentration diminish due to dilution as it did so. Thus, in such a scenario the presence of vapour is unlikely to be a factor in the response phase.

Toxicity

Nerve agent toxicity varies from agent to agent: all are highly toxic, and irrespective of the quantity, without immediate medical treatment the consequences may result in a fatal outcome. Route of exposure, whether dermal or inhalation, is a more relevant factor to consider. There is limited dermal liquid exposure toxicity data available for the classical nerve agents, although it is well understood that VX is the most toxic of the group by this route. Of note, FGAs are considered to be somewhat more toxic than VX. The skin will act as a barrier to a liquid nerve agent (assuming no trauma) by delaying the entry of the chemical into the blood system. The time to onset of an adverse physiological response resulting from a dermal liquid exposure is variable (minutes to several days) and depends on many factors including the chemical/physical properties of the nerve agent, the amount of agent to contaminate the skin, the location on the body, the moisture level of the skin, the ambient temperature and the age and health of the victim. The volatility of the nerve agent also will dictate its persistence on the skin. GB will evaporate quickly reducing the exposure time whilst VX and FGAs, due to their low volatility, will remain on the skin, and over the course of minutes to hours, diffuse through and collect in the fatty sub-dermal layer from which they will slowly enter the systemic blood circulation. In the Salisbury incident, exposure to an unknown quantity of liquid FGA on the palm of the hands resulted in the onset of visible symptoms of severe poisoning in 2 to 3 h.

Although dermal vapour exposure to nerve agent (non-inhalational) should in no way be downplayed, the time needed to cause the same adverse effect as a liquid dermal exposure dose is likely to be markedly longer, with low vapour concentrations requiring a much longer time than high vapour concentrations. GA is considered to have the lowest dermal vapour exposure toxicity.

All nerve agents are extremely toxic via the inhalational route and many factors affect the physiological response and outcome to an exposure, such as the vapour concentration (related to the mass released and the volume of the space into which it was released), whether fine droplets are also present in the air, cloud inhomogeneity, breathing rate, physiological sensitivity, etc. Practically speaking it is the vapour concentration that is of most concern, as a high concentration of a nerve agent of lower toxicity may cause equivalent or more significant adverse effects than exposure to a low concentration of a nerve agent with a higher toxicity. Increased exposure time elevates the effects. Inhalation of aerosolized nerve agent (as fine droplets or impregnated on fine solid particulates) may be equally as toxic as vapour. It must be stressed that any exposure to nerve agent via the inhalational route will cause rapid onset of nerve agent poisoning, and in the absence of medical treatment, may be fatal.

Nerve agent symptoms

Upon entering the body, organophosporus nerve agents bind and inhibit acetylcholinesterase (AChE), a critical enzyme that terminates synaptic transmission, preventing continuous nerve firings at nerve endings, and necessary for healthy neural and muscular function. Indicator signs and symptoms from nerve agent poisoning are well described and are a direct result of AChE inhibition. They include copious secretions from the mouth and nose, wet or noisy breathing caused by fluid collecting in the lungs, vomiting, muscle twitching, seizures and coma. While some of these signs and symptoms may bear similarity to a drug overdose, it is unlikely that all would be observed in an unconscious person suffering from an opioid overdose. Furthermore, other evidence (drug paraphernalia) present at the scene may indicate opioid or drug related incapacitation and provide discrimination from a nerve agent incident. It should be recognized that the ongoing problem with novel preparations of illicit street drugs may make an on-scene assessment based on signs and symptoms difficult. Laboratory based testing of blood samples from casualties will often be required to confirm a nerve agent exposure, characterized by significantly depressed levels of AChE.

Nerve agent symptoms of exposure may include:

- SLUDGEM (*S*alivation—drooling or foaming at the mouth; *L*acrimation—tearing of eyes; *U*rination; *Diarrhea; Gastrointestinal upset; <i>Emesis—vomiting and excessive secretions; M*iosis—typically vapour exposure causing the pupil of the eye to contract).
- Other notable symptoms include muscle twitching, tremors and seizures, tightness in the chest; and sudden collapse to an unconscious state, convulsions, paralysis, and respiratory failure leading to death.

Health monitoring of DND/CAF and First Responder Personnel and other specialist support teams

As soon as possible following a confirmed nerve agent incident a process should be implemented during the Response Phase to perform on-scene, rapid AChE testing to monitor and track over time blood AChE levels in personnel entering and exiting from the hot (initial isolation) zone. Health monitoring must extend to the Recovery and Remediation Phase and include the collection of blood samples for more intensive laboratory-based analytical assessment of possible nerve agent exposure.

Protection

The PPE requirements specified herein are for Response Phase operations only, and assume the presence of liquid nerve agent and or vapour due to evaporation, or possibly agent impregnated solid particulates.

In almost all situations, at the outset of a response to an incident, personnel will not know the identity of the chemical(s) present, and they will not have a complete understanding of the type and extent of the hazard. Thus, PPE selection will typically default to the worst-case and or all-hazard requirement. The preferred option for first time entry into the hot (initial isolation) zone requires body protection constructed from liquid impermeable materials in conjunction with either a self-contained breathing apparatus or powered air purifying respirator with chemical, biological, radiological and nuclear (CBRN) filtration canister. The presence of liquid and vapour due to evaporation would dictate the use of an encapsulated protective system.

Upon completing a hazard assessment, including establishing the boundaries of the warm and cold zones, more options for PPE may be considered. Suitable choices may include impermeable, hazardous liquid splash apparel, combined with an air purifying respirator with CBRN filtration canister. Note, these systems are not designed to be vapour proof and should not be worn where a vapour hazard exists, or is suspected to exist, without wearing a carbon adsorbent undergarment. DND/CAF operators have in-service PPE designed for use in environments where nerve agents may have been used. This includes the Horizon 1 (H1) coverall or the Chemical/Biological Protective Combat Uniform (CPCU), butyl rubber overboots, butyl rubber gloves, C4 respirator/C7A canister, other certified military respirators/canisters, and the new C5 respirator/C8 canister. Commercially available variants of military style suits that use adsorbent carbon materials are available, as are approved respirators, gloves and overboots. First responders are referred to CAN/CGSB/CSA-Z1610-11, Protection of First Responders from Chemical, Biological, Radiological, and Nuclear (CBRN) Events, for specific guidance and requirements for PPE selection for CBRN release events. A list of PPE configurations is found at **Annex B**. Disposable protective apparel (such as dust avoidance and non-hazardous liquid splash suits) are not viable protection options for the Response Phase.

The need to prevent nerve agent from contacting skin is paramount. Personnel must avoid handling contaminated objects, touching surfaces, touching their clothing or victims clothing with their bare hands. Responders must double glove (don two layers of gloves) as soon as they arrive at a suspected nerve agent incident. Liquid nerve agent, and in particular VX and FGAs, readily absorbs into the skin and may cause delayed onset nerve agent poisoning, and also become an active depot for transferring agent to other surfaces, objects and people. The preferred option is a butyl rubber glove as the primary glove (next to skin) covered with a nitrile rubber glove, which serves as the sacrificial layer. Butyl rubber provides the most effective protection against nerve agent and is typically sufficiently robust to withstand normal wear against tear and puncture. Should the outer sacrificial glove become contaminated or torn, it must be removed as soon as possible and a new outer layer glove donned. Note, nitrile rubber gloves are not an effective barrier to liquid agent, thus they will not protect you from nerve agent poisoning. Make certain all gloves are treated as contaminated waste and isolated in appropriate storage containers following their removal.

For all PPE requirements personnel shall ensure that the PPE configuration is appropriate for the hazard, wear the correct size and confirm that equipment is functional and properly donned, recognize PPE limitations, particularly with respect to limited-protection choices, monitor the scene for changing conditions that can affect the level of PPE required, and re-evaluate incident conditions on a regular basis to ensure the protection provided by the PPE remain appropriate.

Detection

Hand-held chemical agent detectors are available that will readily detect G-series (GA, GB, GD and GF) nerve agent vapour provided that the concentration in the air is within an instrument's detection specifications. Accordingly, vapour detectors should give a positive detection response where nerve agent was released as a vapour or where fine liquid droplets or bulk liquid are present on surfaces and evaporating.

Detecting VX and FGAs with currently fielded hand-held vapour detectors presents a greater challenge because of the low volatility of these agents. If you suspect an incident involves VX or a FGA do not waste time attempting to sample the air above and around surfaces with chemical vapour detectors. Chemical detectors operating in "vapour detection" mode cannot detect these agents. Failure to register a positive response for a nerve agent does not mean that it is not present if other on-site observations suggest the possibility of a nerve agent incident. Some chemical detectors have an optional surface sampler with a built-in heating element. The sampler is used to scrape a surface suspected of being contaminated. When inserted into the nozzle of the detector, the surface sampler tip is heated, vapourizing any agent that is present, which is then drawn into the detector. Agent collected as free liquid, bound to surface material or impregnated on solid particulates may be detectable depending on the mass in the sample. Only hand-held detectors using this sampling technology offer the possibility to detect agents with volatilities as low as VX and FGAs. Note, one cannot assume that the surface sampler will pick up agent from all surfaces, thus there is the potential risk for a false negative result. Further, one may have no indication whether the surface contamination associated with a positive signal is above or below a toxicologically significant level. Some detectors may only identify the chemical family (for example, nerve agent based on the presence of phosphorous), not the specific agent.

Colourimetric detection based on acetylcholinesterase inhibition will produce a response when used for low volatility nerve agents such as VX or Novichoks. These detection devices require a swab sample from a surface and rely on a multi-step reaction process to produce a colour change that the user reads and interprets. Generally, only acetylcholinesterase-inhibiting chemicals such as nerve agents and pesticides will produce a positive response but some detection reactions may be adversely affected if strong acids or bases are also present on the sampled surfaces.

Hand-held spectroscopic detection and identification devices using attenuated total reflectance infra-red (ATR-IR) spectroscopy, Raman spectroscopy or high-pressure mass spectrometry, offer the capability to both detect and identify chemicals based on their chemical structure. Practical and expedient use of these types of instruments necessitates either collecting a sample or locating contamination on surfaces. If the agent's spectra is not present in the device's on-board library to produce a positive match, specialized training is required in spectral interpretation to ascertain the nature of the chemical and its identity. Subject matter experts will be required for advanced chemical identification.

Canadian government CBRN response teams with specialized assets will be required to determine the presence of FGAs at an incident, and to ascertain the possible spread beyond the release site. Furthermore, unambiguous identification will require dedicated scientific resources of the Canadian government. Following an initial evaluation for the presence of suspect chemicals, contact the RCMP-led National CBRN Response Team if you believe an incident may involve FGAs.

Contamination control

Contamination control is critical in the event of a nerve agent attack. As soon as possible establish a cordon around area(s) suspected of nerve agent contamination. Establish strict procedures controlling access to the contaminated area to minimize the potential for spread of contamination through contact transfer, and ensure that decontamination and command locations are upwind of the suspected release site. Instituting a robust contamination control regime for the incident site and all personnel involved is especially critical. Strict observance in the selection and use of PPE, decontamination lines and waste isolation are essential to safely managing a nerve agent incident. In particular, assume FGAs will spread beyond the incident location and increase your diligence accordingly. All potentially contaminated areas should be cordoned off and access restricted until the presence of agent can be confirmed and a plan to remove it is in place, or that the location has been certified "agent free" by government experts according to a defined safe detection limit.

Personnel and victim emergency decontamination and casualty management

- Assess casulaties for signs and symptoms of nerve agent exposure. If they are exhibiting SLUDGEM and/or other notable symptoms (muscle twitching, tremors and seizures, tightness in the chest, convulsions, paralysis, in an unconscious state or respiratory failure)—TREAT FOR NERVE AGENT POISONING;
- Administer auto-injector therapy, if available, for nerve agent poisoning; including an oxime (AChE reactivator), diazepam (anticonvulsant) and atropine (reduce secretions); if available, atropine administration should be continued until secretions have been controlled;
- Establish a functional airway, with intubation if available;
- Carefully remove all clothing and personal effects and isolate as contaminated waste in appropriate containers for later destruction. This step is critical to control agent contamination, secondary exposure and cross-contamination between victims, operators and medical personnel. The most rapid and effective means of controlling contamination may be to cut the clothing off victims;
- If nerve agent contamination is visible on the skin make every effort to dry-blot the liquid using paper towels or other cloth-like material. Double gloves must be worn to do this safely. All waste must be treated as contaminated and isolated in appropriate waste containers;
- Wash victim's skin with copious amounts of soap and water using a sponge/cloth and a pail of water or a low pressure shower;
- DO NOT use high pressure decontamination washing systems on individuals known or suspected to be contaminated;
- DO NOT use alcohol based hand sanitizers for decontamination as they may actually enhance the absorption of agent into the skin;

- Use Reactive Skin Decontaminant Lotion (RSDL) if available, according to the instructions of use, on all areas of skin that are suspected of being contaminated. RSDL is highly effective at absorbing G- and V-series nerve agents, as well as FGAs, from the skin. RSDL solvates and neutralizes G- and V-series nerve agents on application and scrubbing. Of special note, RSDL *does not* neutralize FGAs efficiently. Accordingly, it is important that RSDL be removed from the skin using the included sponge, or a cloth/paper towel to "lift and shift" agent and or degradation products off the skin. The lift and shift action of RSDL is especially critical to its efficacy against FGAs;
- Water effluent and any other decontamination formulation including RSDL generated during the decontamination process should be contained and treated as a hazardous waste. FGAs are very stable in water;
- RSDL and RSDL effluent must never be exposed to or come in contact with bleach solution/powder, super tropical bleach (STB) or high-test hypochlorite (HTH), which contain the strong oxidizing chemical calcium hypochlorite. RSDL may become very hot and combust when exposed to these chemicals;
- Casualties must be thoroughly decontaminated prior to relocating them, to avoid secondary contamination of transfer vehicles, medical facilities and critical medical assets; and
- Notify Emergency Medical Facilities or Hospitals that may receive casualties before transfers occur to ensure that medical teams are aware that victims may have been exposed to nerve agent, that a proper triage location has been established and necessary PPE is available.

Medical treatment of casualties at an emergency medical facility or hospital

- Under physician supervision, casualties should be assessed for ongoing signs and symptoms of nerve agent poisoning and treatment administered as necessary;
- Medical teams should be prepared to deliver supportive medical therapy for advanced physiological complications from nerve agent poisoning. Therapy may include aggressive intravenous/intraosseus administration of an oxime reactivator, atropine and diazepam or other anticonvulsants;
- Respiratory failure is a major cause of death from nerve agent poisoning. Acute casualties will need to be intubated and provided with assisted or mechanical ventilation; and
- Institute repeated (daily) application of RSDL on areas of skin suspected of being exposed to nerve agent to aid in the desorption of nerve agent. Treat RSDL waste as containing toxic nerve agent and isolate it in an appropriate waste container.

Decontamination of operator/responder entry teams in a nerve agent incident

- A decontamination line must be established that is capable of processing operators egressing from the hot (initial isolation) zone;
- Organization standard operating procedures (SOPs) should be followed for decontaminating personnel;
- All clothing and equipment should be treated as contaminated and isolated in appropriate waste containers for later destruction; and
- Do not attempt to decontaminate PPE or other equipment used in the hot (initial isolation) zone for re-use if it is known, or suspected of being, contaminated. This is particularly the case for VX and FGAs. PPE and equipment removed from operator entry teams should be considered contaminated, must be isolated in appropriate storage containers, placed under controlled access at the incident site, and disposed of according to an approved plan.

Nerve agent incident response guideline

A Nerve Agent Incident Response Guideline modelled on NATO Civil Emergency Planning, Operations Division, Guidelines for first responders to a CBRN incident, is provided in **Annex C.**

Annex A Quick reference guide

Quick reference—What to consider if you suspect a FGA incident

- FGAs will be encountered as a liquid. They should be considered primarily a dermal contact hazard as they readily penetrate into the skin. They also readily penetrate into many types of engineering and domestic-use materials. FGAs may not be visible on a surface but can still present a significant contact hazard, which can be transferred to other surfaces by touch;
- FGAs are extremely persistent (essentially do not evaporate) and thus extremely difficult to detect with any chemical detector operating in vapour mode. Acetylcholinesterase-based detection, devices with heated samplers/inlets and devices specifically targeting FGAs will have the greatest chance of confirming the presence of these nerve agents;
- Strict contamination control procedures for the incident site and all personnel involved must be implemented to minimize the potential for spread of contamination through contact transfer;
- Only those with proper training and PPE can safely enter the hot (initial isolation) zone. Selection of PPE must be appropriate for the hazard and in accordance with operational training and protocols;
- The need to prevent nerve agent from contacting skin is paramount. Personnel must double glove (don two layers of gloves) as soon as they arrive at a suspected nerve agent incident. The preferred option is a butyl rubber glove as the primary glove (next to skin) covered with a nitrile rubber glove, which serves as the sacrificial layer;
- For personnel decontamination, remove all clothing and personal effects and isolate as contaminated waste in appropriate containers for later destruction. Dry-blot identifiable liquid agent off the skin if possible, wash with copious amounts of warm water and soap, or apply RSDL and scrub to absorb agent from the skin, and importantly, wipe thoroughly to promote "lift and shift". Repeat the use of RSDL multiple times. Note, RSDL *does not* neutralize the FGAs efficiently;
- Water effluent and any other decontamination formulation including RSDL generated during the decontamination process should be contained and treated as a hazardous waste. FGA agents can be very stable in water;
- The onset of symptoms may be immediate or delayed, but prompt casualty management is important for effective medical treatment. Assess casualties for signs and symptoms of nerve agent exposure. If they are exhibiting SLUDGEM and/or other notable symptoms (muscle twitching, tremors and seizures, tightness in the chest, convulsions, paralysis, in an unconscious state or respiratory failure)—TREAT FOR NERVE AGENT POISONING. Treatment must begin as soon as possible following exposure and continue until clinical recovery as determined by a physician;
- Respiratory failure is a major cause of death from nerve agent poisoning. Acute casualties will need to be intubated and provided with assisted or mechanical ventilation;
- Institute repeated (daily) application of RSDL on areas of skin suspected of being exposed to FGAs to aid in the desorption from the skin; and
- All potentially contaminated areas should be cordoned off and access restricted until action can be taken to determine the presence of agent and an associated plan to remove it, or that the location has been certified "agent free" by government experts according to a defined safe detection limit.

Annex B First Responder PPE configurations and options

First responders are referred to CAN/CGSB/CSA-Z1610-11, Protection of First Responders from Chemical, Biological, Radiological, and Nuclear (CBRN) Events, for specific guidance and requirements for personal protective ensemble (PPE) selection for CBRN release events.

Recognized PPE configurations include:

C1S and C1s—provide complete encapsulation of the body and head, use self-contained air and are intended to be worn where the highest actual or potential hazards exist. They provide the highest level of skin, respiratory and ocular protection. The body protection component shall meet the design and performance requirements specified in NFPA 1991 and NFPA 1994. The respiratory protection component shall meet the requirements for NIOSH CBRN SCBA or another SCBA (e.g., as specified in NFPA 1981-02).

C2S—incorporates NIOSH CBRN SCBA but is not a fully encapsulated system. It is intended to be worn where less dermal and respiratory protection are required than are provided by the fully encapsulated C1S or C1s systems, and where an APR is not suitable. The body protection component is similar to and in accordance with NFPA 1994, Class 2. The respiratory component shall meet the requirements for NIOSH CBRN SCBA.

C2VP and C2PAPR-VP (C2vP and C2PAPR-vP)—intended to be worn where less dermal and respiratory protection are required than are provided by C1S or C1s and where a multi-hazard APR or PAPR is suitable given the knowledge and understanding of the hazard. The body protection component is similar to and in accordance with NFPA 1994, Class 2. The respiratory component shall meet the requirements for CBRN APR-VP/PAPR-VP as specified in CAN/CGSB/CSA-Z1610-11, clauses B.9.6 and B.9.8. Note, military level respiratory protection that does not meet the full multi-hazard first responder requirement above, designated as vP may also be an option. The vP respirator component shall meet NATO CBRN APR or NIOSH CBRN APR requirements. The vP-PAPR respiratory protection component shall meet the requirements for a NIOSH CBRN PAPR, with an air-purifying element (APE) similar to NATO APE, as specified in CAN/CGSB/CSA-Z1610-11, clauses B.9.7.1 and B.9.9.1.

CFS—intended to be worn by fire service responders requiring protective turnout gear for both fire and CBRN response. The body protection component shall meet the design and performance requirements for turnout gear as specified in NFPA 1971. The respiratory component shall meet the requirements for NIOSH CBRN SCBA.

CMS—"M" refers to military-style body protection (NATO equivalent). It is intended to be worn where agents (if dermally acting) are high-boiling and where less dermal and respiratory protection are required than are provided by configuration C1S or C1s. The body protection component shall include an active carbon layer or garment, or other material or garment, which meets chemical warfare agent (CWA) protection requirements for the body similar to NFPA 1994, Class 2. Note, the CM body protection component may have better physiological burden and comfort characteristics than a C1 or C2 body protection component but less protection against certain types of chemical hazards, particularly low-boiling, dermally active chemicals. Body protection that meets NATO AEP-38 falls within this class.

The respiratory protection component for CMS configurations shall meet the requirements for NIOSH CBRN SCBA.

CMVP, CMvP, CMPAPR-VP, and CMPAPR-vP—"M" reers to military-style body protection (NATO equivalent). They are intended for use where multi-hazard (VP) or limited chemical vapour hazard (vP) respiratory protection are adequate. The body protection component for these configurations shall include an active carbon layer or garment, or other material or garment, which meets CWA protection requirements for the body similar to NFPA 1994, Class 2. The respiratory protection component for VP configurations shall meet the requirements for CBRN APR or PAPR specified in CAN/CGSB/CSA-Z1610-11. The respiratory protection component for vP configurations shall meet the requirements of NATO CBRN APR.

All of the above protective configurations are suitable for at least 1 h of use after exposure, provided that use limitations are respected, and they may be suitable for up to 4 h use depending on how they meet specific requirements as per the appropriate clauses for each configuration in CAN/CGSB/CSA-Z1610-11. Note, the CM class of protective systems are not recommended to be worn at the outset of an incident by first responders for first-time entry into the hot (initial isolation) zone unless they know what the hazard is, its location and amount, and it is known that the CM class of protective systems will provide the appropriate level of protection commensurate with the hazard.

*Gloves—*The need to prevent nerve agent from contacting skin is paramount. First responders must avoid handling contaminated objects, touching surfaces, touching their clothing or victims clothing with their bare hands. First responders must double glove (don two layers of gloves) as soon as they arrive at a suspected nerve agent incident. Liquid nerve agent, and in particular VX and FGAs, readily absorbs into the skin where it may collect and lead to delayed onset poisoning, and also become an active depot for transferring agent to other surfaces, objects and people. The preferred option is a thin (0.22 mm) butyl rubber glove (e.g., North Safety, by Honeywell, part number B074GI) worn as the inner layer next to the skin, and the outer layer a nitrile rubber glove, which serves as the sacrificial layer. The butyl rubber glove is substantially more resistant to tear and punctures than a nitrile rubber glove and will provide more effective protection in a working, operational environment. An acceptable option is two layers of nitrile gloves. In both cases, should the outer sacrificial glove become contaminated or torn, it must be removed and replaced as soon as possible. Note, a single layer of nitrile gloves will not protect you from nerve agents. Once you suspect nerve agent has been released, even with gloves, minimize handling and contact with surfaces, objects and victims. Ensure all used gloves are treated as contaminated waste and isolated in appropriate storage containers.

Selecting less stringent levels of PPE as the response phase progresses should only be considered after completing a full hazard assessment, including knowledge of the type of nerve agent, how it was released, where the contamination is, what form the contamination is in (bulk liquid, vapour or absorbed into material), and the relative amounts present. In addition, the risks and limitations of adopting other PPE must be clearly understood and accounted for.

Annex C Nerve agent incident response guideline

Initial Assessment of Incident

- Approach scene with caution and upwind
- Carry out scene assessment
- Establish incident command (IC)
- Recognise the signs and indicators of a chemical incident and determine whether CBRN or Hazmat
- Estimate number of casualties/victims
- Do not approach or touch casualties, objects/packages
- Identify hazards affecting response and casualty extraction rescue
- Carry out a risk assessment; note that it may not be possible to detect FGAs
- Estimate resource requirements \sim
- Consider specialist advice/resources requirements
- Implement measures to control site access

Immediate Incident Response

- · Estimate/identify location and spread of contamination
- Implement measures to contain/control spread of contamination
- · Establish inner and outer cordon (hot/warm/cold zone)
- · Establish quarantine(holding) area for contaminated victims/casualties
- Establish decontamination and triage areas for contaminated victims/casualties
- \sim Establish decontamination line/area for First Responders returning from hot zone
- Establish location for site waste \sim
- Restrict inner cordon access (protected First Responders only)
- Preserve scene and maintain evidence to the extent possible (criminal investigation)

Equipment

- Personal Protective Equipment (respiratory
- protection, chemical protection suits, gloves, boots) Detection Identification and Monitoring Equipment
- (for personnel, boundary monitoring and analysis)
- Cordon tape, signage, barriers
- Nerve agent medical countermeasures (autoinjectors, RSDL, airway management equipment)
- Medical treatment (trauma, prophylactics, etc)
- Decontamination equipment (emergency, mass, clinical)
	- Soap and water, RSDL
	- Recording system for hot zone personnel Evidence bags
	- Personal property bags (for decontaminated victims)
	- Post decontamination clothing for victims
	- Shelter for victims/casualties form adverse weather
	- Transport (ambulance, bus etc.)
	- Geographical information (maps)
	- Building plans

Nerve Agent Incident Response Guideline*

*Modelled on Guidelines for first responders to a CBRN incident. Civil Emergency Planning, Operations Division -NATO, Updated 1st August 2014.

Casualty Management

Carry out necessary extractions/rescues

- Assess casualties for signs and symptoms of nerve agent exposure
- Salivation drooling /foaming at the mouth; Lacrimation tearing of eves; Urination; Diarrh Gastrointestinal upset: Emesis - vomiting /secretions: Miosis - pinpoint pupils Other notable symptoms include muscle twitching, tremors and seizures, tightness in the chest unconscious state, convulsions, paralysis, and respiratory failure
- Administer medical countermeasures as necessary
- Auto-injector therapy; Oxime (AChE reactivator), Diazepam (anticonvulsant), Atropine (reduce secretions) - atropine administration continued until secretions have been controlled
- Establish a functional airway, with intubation
- Implement decontamination as appropriate (emergency, mass, clinical) Remove clothing and gross contamination from casualties
- Apply RSDL/wash with warm soapy water (contain waste)
- Implement medical triage and treatment to casualties; continue to assess for signs and symptoms of
- nerve agent poisoning and administer further medical countermeasures as necessary Implement responder/rescuer decontamination

Bibliography

Aas P. The threat of mid-spectrum chemical warfare agents. Prehosp Disaster Med. 2003; 18:3062.

Abou-Donia M.B, Siracuse B., Gupta N., Sobel Sokol A. Sarin (GB, O-isopropyl methylphosphonofluoridate) neurotoxicity: critical review, *Crit Rev Toxicol*. 2016 Nov; 46(10):845–875. (doi: 10.1080/10408444.2016.1220916.)

Amend N., Langgartner J., Siegert M., et al. A case report of cholinesterase inhibitor poisoning: cholinesterase activities and analytical methods for diagnosis and clinical decision making. *Arch Toxicol* 2020; 94:2239–47.

Bajgar J. Organophosphates/nerve agent poisoning: Mechanism of action, diagnosis, prophylaxis, and treatment. *Adv Clin Chem*. 2004; 38:151–216.

Bajgar J. Complex view on poisoning with nerve agents and organophosphates. Acta Medica (Hradec Kralove) 2005; 48:3–21.

Bajgar J., Fusek J., Kassa J., Kuca K., Jun D. Chemical aspects of pharmacological prophylaxis against nerve agent poisoning. *Curr Med Chem*. 2009; 16:2977–86.

Besser R., Gutmann L., Dillmann U., Weilemann L.S., Hopf H.C. End-plate dysfunction in acute organophosphate intoxication. *Neurology* 1989; 39:561–67.

Beste A., Taylor D.E., Shih T-M., Thomas T.P. Mechanisms of acetylcholinesterase protection against sarin and soman by adenosine A1 receptor agonist N6-cyclopentyladenosine. *Comput. Biol. Chem*. 2018; 75:74–81. (doi: 10.1016/j.compbiolchem.2018.04.017.)

Bhattacharjee A.K., Marek E., Le H.T., Gordon R.K. Discovery of non-oxime reactivators using an in silico pharmacophore model of oxime reactivators of OP-inhibited acetylcholinesterase. *Eur. J. Med. Chem*. 2012; 49:229–238. (doi: 10.1016/j.ejmech.2012.01.016.)

Burton D.J., Flynn R.M. Michaelis-arbuzov preparation of halo-F-methylphosphonates. *J. Fluor. Chem*., 10 (1977), pp. 329–332. (doi: 10.1016/S0022-1139(00)83108-5.)

Carlsen L. After Salisbury nerve agents revisited. *Mol. Inform*. 2018; 37:1800106. (doi: 10.1002/minf.201800106.)

Cha Y.S., Kim H., Go J., et al. Features of myocardial injury in severe organophosphate poisoning. *Clin Toxicol* 2014; 52:873–79.

Chai P.R., Hayes B.D., Erickson T.B., Boyer E.W. Novichok agents: a historical, current, and toxicological perspective. *Toxicol. Commun*. 2018; 2:45–48. (doi: 10.1080/24734306.2018.1475151.)

Coleman K.A. History of Chemical Warfare. Palgrave Macmillan UK, London (2005). (doi: 10.1057/9780230501836.)

Colovic M.B., Krstic D.Z., Lazarevic-Pasti T.D., Bondzic A.M., Vasic V.M. Acetylcholinesterase inhibitors: pharmacology and toxicology; *Curr. Neuropharmacol*., 2013; 11(3), 315–335. (doi: 10.2174/1570159x11311030006.)

Costanzi S., Machado J-H., Mitchell M. Nerve agents: what they are, how they work, how to counter them; *ACS Chem. Neurosci*., 2018; 9(5):873–885. (doi: 10.1021/acschemneuro.8b00148.)

Creasy W.R., McGarvey D.J., Brevett C.A.S. Speciation of VX in aqueous solution. *J. Phys. Chem. C* 2013; 117:22 677–22 682. (doi: 10.1021/jp409671y.)

Crowley M., Dando M., Shang L. (eds) Preventing chemical weapons: arms control and disarmament as the sciences converge. Croydon, UK: Royal Society of Chemistry (2018). (doi: 10.1039/9781788010092.)

Darling R.G., Noste E.E. Future Biological and Chemical Weapons; in Ciottone's Disaster Medicine, G.R. Ciottone (Ed); Elsevier, Second Edition, 2016.

Dvir H., Silman I., Harel M., Rosenberry T.L., Sussman J.L. Acetylcholinesterase: from 3D structure to function *Chem. Biol. Interact*., 187 (2010), pp. 10–22. (doi: 10.1016/j.cbi.2010.01.042.)

Ellison D.H. Emergency Action for Chemical and Biological Warfare Agents. (second ed.), CRC Press (2016).

Ellison H.D. Chemical and Biological Warfare Agents, CRC Press, Second Edition, 2008.

Ellison D.H. Handbook of chemical and biological warfare agents, pp. 37–42. Boca Raton, FL: CRC Press, 2007.

Eyer F., Worek F., Eyer P., et al. Obidoxime in acute organophosphate poisoning: 1—clinical effectiveness. *Clin Toxicol* 2009; 47:798–806.

Fact Sheet for First Responders: Organophosphorus Amidine and Guanidine Based New Nerve Agents (in response to OPCW Scientific Advisory Board SAB-28/WP.1, dated 3 July 2018).

Fourth Generation Agents: Reference Guide, January 2019. US Government publication

Ganesan K., Raza S.K., Vijayaraghavan R. Chemical warfare agents, *J Pharm Bioallied Sci*. 2010, Jul–Sep; 2(3): 166–178. (doi: 10.4103/0975-7406.68498.)

Grob D. The manifestations and treatment of poisoning due to nerve gas and other organic phosphate anticholinesterase compounds. *AMA Arch Intern Med* 1956; 98:221–39.

Gupta R.C. Handbook of Toxicology of Chemical Warfare Agents. Academic Press (2015)

Gussow L. Toxicology rounds: the mysteries of novichok and brodifacoum. Emerg. *Med. News,* 2018; 40:30. (doi: 10.1097/01.EEM.0000535030.80353.31.)

Halámek E., Kobliha Z. Chemicke L., Potential chemical warfare agents; 2011; 105(5):323–333, in Chemical risk and chemical warfare agents: Science and technology against humankind; M. Guidotti, F. Trifirò; *Toxicological & Environmental Chemistry*, 2015, 98(9), 1018–1025. (doi: 10.1080/02772248.2014.996153.)

Heymann W.R. Threats of biological and chemical warfare on civilian populations. *J Am Acad Dermatol*. 2004; 51:452–3.

Hoenig S.L. Compendium of chemical warfare agents; Springer-Verlag, New York, 2007.

Hosseini S.E., Saeidian H., Amozadeh A., Naseri M.T., Babri M. Fragmentation pathways and structural characterization of organophosphorus compounds related to the chemical weapons convention by electron ionization and electrospray ionization tandem mass spectrometry. *Rapid Commun. Mass Spectrom*. 2016; 30:2585–2593. (doi: 10.1002/rcm.7757.)

Hulse E.J., Haslam J.D., Emmett S.R., Woolley T. Organophosphorus nerve agent poisoning: managing the poisoned patient. *Br J Anaesth* 2019; 123:457–63.

John H., van der Schans M.J., Koller M., et al. Fatal sarin poisoning in Syria 2013: forensic verification within an international laboratory network. *Forensic Toxicol* 2018; 36:61–71.

Jokanović M. Medical treatment of acute poisoning with organophosphorus and carbamate pesticides. *Toxicol Lett*. 2009; 190:107.

Khan M.A.S., Lo R., Bandyopadhyay T., Ganguly B. Probing the reactivation process of sarin-inhibited acetylcholinesterase with a-nucleophiles: hydroxylamine anion is predicted to be a better antidote with DFT calculations. *J. Mol. Graph. Model*. 2011; 29:1039–1046. (doi: 10.1016/j.jmgm.2011.04.009.)

Kuca K., Jun D., Musilek K., Pohanka M., Karasova J.Z., Soukup O. Prophylaxis and post-exposure treatment of intoxications caused by nerve agents and organophosphorus pesticides. *Mini Rev. Med. Chem*., 13 (2013), pp. 2102–2115.

López-Muñoz F., Alamo C., Guerra J.A., García-García P. The development of neurotoxic agents as chemical weapons during the National Socialist period in Germany. *Rev Neurol*. 2008; 47:99–106.

Lyagin I., Efremenko E. Theoretical evaluation of suspected enzymatic hydrolysis of novichok agents. *Catal. Commun*. 2019; 120:91–94. (doi: 10.1016/j.catcom.2018.11.019.)

Mandal D., Mondal B., Das A.K. Isomerization and decomposition of a model nerve agent: a computational analysis of the reaction energetics and kinetics of dimethyl ethylphosphonate. *J. Phys. Chem. A* 2010; 114:10 717–10 725. (doi: 10.1021/jp106270d.)

Marrs T.C., Maynard R.L., Sidell F.R. (eds). 2007 Chemical warfare agents: toxicology and treatment, 2nd edn. New York, NY: Wiley.

Marrs T.C., Rice P., Vale J.A. The role of oximes in the treatment of nerve agent poisoning in civilian casualties. *Toxicol Rev*. 2006; 25:297–323.

Maselli R.A., Leung C. Analysis of neuromuscular transmission failure induced by anticholinesterases. *Ann N Y Acad Sci* 1993; 681:402–04.

Mew E.J., Padmanathan P., Konradsen F., et al. The global burden of fatal self-poisoning with pesticides 2006–15: systematic review. *J Affect Disord* 2017; 219:93–104.

Mirzayanov V.S. State Secrets: an Insider's Chronicle of the Russian Chemical Weapons Program. Outskirts Press, Incorporated, 2009.

Moffatt A., Mohammed F., Eddleston M., Azher S., Eyer P., Buckley N.A. Hypothermia and fever after organophosphorus poisoning in humans: a prospective case series. *J Med Toxicol* 2010; 6:379–85.

Mott A.J., Rez P. Calculated infrared spectra of nerve agents and simulants. *Spectrochim. Acta A Mol. Biomol. Spectrosc*. 2012; 91:256–260. (doi: 10.1016/j.saa.2012.02.010.)

Munro N.B., Talmage S.S., Griffin G.D., Waters L.C., Watson A.P., King J.F., Hauschild V. The sources, fate, and toxicity of chemical warfare agent degradation products. *Environ. Health Perspect*. 1999; 107:933–973. (doi: 10.1289/ehp.99107933.)

Nakagawa T., Tu A.T. Murders with VX: Aum Shinrikyo in Japan and the assassination of Kim Jong-Nam in Malaysia; *Forensic Toxicol*., 2018, 1–3. (doi: 10.1007/s11419-018-0426-9.)

Naughton S.X., Terry Jr. A.V. Neurotoxicity in acute and repeated organophosphate exposure. *Toxicology* 2018; 408:101–112. (doi: 10.1016/j.tox.2018.08.011.)

Nepovimova E., Kuca K. The history of poisoning: from ancient times until modern era. *Arch. Toxicol*. 2019; 93:11–24. (doi: 10.1007/s00204-018-2290-0.)

Nepovimova E., Kuca K. Chemical warfare agent novichok—mini-review of available data. *Food Chem. Toxicol*. 2018; 121:343–350. (doi: 10.1016/j.fct.2018.09.015.)

Niven A.S., Roop SA. Inhalational exposure to nerve agents. *Respir. Care Clin N Am*. 2004; 10:59–74.

O'Brien C.J., Greathouse J.A., Tenney C.M. Dissociation of sarin on a cement analogue surface: effects of humidity and confined geometry. *J. Phys. Chem. C*. 2016; 120:28 100–28 109. (doi: 10.1021/acs.jpcc.6b10046.)

Okumura T., Suzuki K., Fukuda A. The Tokyo subwy sarin attack: Disaster management, Part 2: Hospital response. *Acad Emerg Med*. 1998; 5:618–24.

Patocka J., Fusek J. Chemical agents and chemical terrorism. *Cent Eur J Public Health*. 2004; 12:S75–7.

Pitschmann V. Overall view of chemical and biochemical weapons; *Toxins*, 2014; 6(6):1761–1784. (doi: 10.3390/toxins6061761.)

Pope C.N., Brimijoin S. Cholinesterases and the fine line between poison and remedy; *Biochemical Pharmacology*; 2018; 153:205–216. (doi: 10.1016/j.bcp.2018.01.044.)

Prentiss A.M. Chemicals in warfare. New York: McGraw-Hill Book Company; 1937. p. 579.

Prockop L.D. Weapons of mass destruction: Overview of the CBRNEs (Chemical, Biological, Radiological, Nuclear, and Explosives), *Neurol Sci*. 2006 Nov 1; 249(1):50-4. (doi: 10.1016/j.jns.2006.06.017.)

Project on Minimum Standards and Non-Binding Guidelines for First Responders Regarding Planning, Training, Procedure and Equipment for Chemical, Biological, Radiological and Nuclear (CBRN) Incidents: Guidelines for first responders to a CBRN incident. Civil Emergency Planning, Operations Division – NATO, Updated 1st August 2014.

Riley B. The toxicology and treatment of injuries from chemical warfare agents. *Curr Anaesth Crit Care*. 2003; 14:149.

Romano J.A., Salem H., Lukey B.J. Chemical Warfare Agents: Chemistry, Pharmacology, Toxicology, and Therapeutics. (second ed.), CRC Press (2007)

Saeidian H., Mirkhani V., Faraz S.M., Babri M. Unambiguous mass spectral characterization of VX and its six other structural isomers using gas chromatography –mass spectrometry. *Int. J. Mass Spectrom*. 2016; 396:5–12. (doi: 10.1016/j.ijms.2015.12.003.)

Sambrook M.R., Gass I.A., Cragg P.J. Spectroscopic and inclusion properties of G-series chemical warfare agents and their simulants: a DFT study. Supramol. *Chem*. 2018; 30:206–217. (doi: 10.1080/10610278.2017.1401074.)

Schwenk M. Chemical warfare agents. Classes and targets; *Toxicol Lett*., 2018; 293:253–263. (doi: 10.1016/j.toxlet.2017.11.040.)

Schwenk M., Kluge S., Jaroni H. Toxicological aspects of preparedness and aftercare for chemical-incidents. *Toxicology*. 2005; 214:232–48.

Shan X., Vincent J.C., Kirkpatrick S., Walker M.D., Sambrook M.R., Clary D.C. A combined theoretical and experimental study of sarin (GB) decomposition at high temperatures. *J. Phys. Chem. A* 2017; 121:6200–6210. (doi: 10.1021/acs.jpca.7b04282.)

Sharma R., Gupta B., Singh N., Acharya J.R., Musilek K., Kuca K., Ghosh K.K. Development and structural modifications of cholinesterase reactivators against chemical warfare agents in last decade: a review. *Mini Rev. Med. Chem*., 15 (2015), pp. 58–72

Sidell F.R., Borak J. Chemical warfare agents: II. Nerve agents. *Ann Emerg Med*. 1992; 21:865–71.

Sirin G.S., Zhou Y., Lior-Hoffmann L., Wang S., Zhang Y. Aging mechanism of soman inhibited acetylcholinesterase. *J. Phys. Chem. B*, 116 (2012), pp. 12199–12207. (doi: 10.1021/jp307790v.)

Smart J.K. History of Chemical and Biological Warfare: An American Perspective. In: Sidell FR, Takafuji ET, Franz DR, editors. Medical Aspects of Chemical and Biological Warfare. Washington, DC: Office of the Surgeon General; 1997.

Somani S.M. Chemical Warfare Agents. USA: Academic Press Inc; 1992. p. 67.

Steindl D. et al. Novichok nerve agent poisoning. The Lancet. (Published online December 22, 2020.) (doi: 10.1016/S0140-6736(20)32644-1.)

Stone R. U.K. attack puts nerve agent in the spotlight. *Science* 2018; 359:1314–1315. (doi:10.1126/science.359.6382.1314.)

Szinicz L. History of chemical and biological warfare agents. *Toxicology*, 2005; 214:167–181. (doi: 10.1016/j.tox.2005.06.011.)

Thiermann H., Mast U., Klimmek R., et al. Cholinesterase status, pharmacokinetics and laboratory findings during obidoxime therapy in organophosphate poisoned patients. *Hum Exp Toxicol* 1997; 16:473–80.

Thiermann H., Szinicz L., Eyer P., Felgenhauer N., Zilker T., Worek F. Lessons to be learnt from organophosphorus pesticide poisoning for the treatment of nerve agent poisoning. *Toxicology*. 2007; 233:145–54.

Thiermann H., Zilker T., Eyer F., Felgenhauer N., Eyer P., Worek F. Monitoring of neuromuscular transmission in organophosphate pesticide-poisoned patients. *Toxicol Lett* 2009; 191:297–304.

Tokuda 1 Y., Kikuchi M., Takahashi O., Stein G.H. Prehospital management of sarin nerve gas terrorism in urban settings: 10 years of progress after the Tokyo subway sarin attack, *Resuscitation*, 2006 Feb; 68(2):193–202. (doi: 10.1016/j.resuscitation.2005.05.023.)

Tu A.T. Overview of sarin terrorist attacks on Japan. *Am Chem Soc Symp Ser*. 2000; 745:304.

Tucker J.B. War of Nerves: Chemical Warfare from World War I to Al-qaeda. Pantheon Books (2006).

Vale J.A., Marrs T.C., Maynard R.L. Novichok: a murderous nerve agent attack in the *UK. Clin. Toxicol*. 2018; 56:1093–1097. (doi: 10.1080/15563650.2018.1469759.)

Volans G.N, Karalliedde L. Long term effects of chemical weapons. *Lancet*. 2002; 360:S35–6.

Vucinic S et al. Environmental exposure to organophosphorus nerve agents. *Environ. Toxicol. Pharmacol*. 2017; 56:163–171. (doi: 10.1016/j.etap.2017.09.004.)

Wang J., Gu J., Leszczynski J. Phosphonylation mechanisms of sarin and acetylcholinesterase: a model DFT study. *J. Phys. Chem*. *B* 2006; 110:7567–7573. (doi: 10.1021/jp060370v.)

Wiener S.W., Hoffman R.S. Nerve agents: a comprehensive review. *J. Intensive Care Med*., 19 (2004), pp. 22–37. (doi: 10.1177/0885066603258659.)

Worek F., Wille T., Koller M., Thiermann H.. Toxicology of organophosphorus compounds in view of an increasing terrorist threat. *Arch. Toxicol*., 90 (2016), pp. 2131–2145. (doi: 10.1007/s00204-016-1772-1.)

Yu S., Yu S., Zhang L., et al. Efficacy and outcomes of lipid resuscitation on organophosphate poisoning patients: a systematic review and meta-analysis. *Am J Emerg Med* 2019; 37:1611–17.

List of symbols/abbreviations/acronyms/initialisms

13. ABSTRACT (When available in the document, the French version of the abstract must be included here.)

The intent of this guide is to provide Department of National Defence (DND) / Canadian Armed Forces (CAF) and First Responder personnel with the required knowledge of organophosphorus nerve agents, including the Fourth Generation Agents (FGA), to inform decision making during the Response Phase of an incident.

Le but de ce guide est de fournir au personnel du ministère de la Défense nationale (MDN)/des Forces armées canadiennes et des premiers intervenants l'information requises sur les agent neurotoxiques organophosphorés, y compris les agents de quatrième génération (FGAs) pour éclairer et aider la prise de décision pendant la phase d'intervention d'un incident.