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RESPONSE TO THE DIRECTOR-GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD TO PROVIDE CONSIDERATION ON WHICH RIOT CONTROL AGENTS ARE SUBJECT TO DECLARATION UNDER THE CHEMICAL WEAPONS CONVENTION

1. Response to the Director-General's Request to the Scientific Advisory Board to Consider Which Riot Control Agents are Subject to Declaration Under the Chemical Weapons Convention (hereinafter "the Convention").

Annex:

Response to the Director-General's Request to the Scientific Advisory Board to Consider Which Riot Control Agents are Subject to Declaration Under the Chemical Weapons Convention.

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Annex

RESPONSE TO THE DIRECTOR-GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD TO CONSIDER WHICH RIOT CONTROL AGENTS ARE SUBJECT TO DECLARATION UNDER THE CHEMICAL WEAPONS CONVENTION

1. EXECUTIVE SUMMARY

1.1 This report provides advice from the Scientific Advisory Board (SAB) on which riot control agents (RCAs) would be subject to declaration under the Convention in response to a request by the Director-General at the Board's Twentieth Session in June 2013 [1]. The request appears in Appendix 1.

1.2 The SAB considered a list of 59 chemicals that included the 14 chemicals declared as RCAs since entry into force of the Convention; chemicals identified as potential RCAs from a list of "riot control agents and old/abandoned chemical weapons" to be considered for inclusion in the OPCW Chemical Agent Database (OCAD) that had been drafted by the SAB's Temporary Working Group (TWG) on Analytical Procedures in 2001 (Appendix 2) [2]; an initial survey conducted by the Technical Secretariat in 2013 of RCAs that have been researched or are available for purchase, beyond those that are already declared; and 12 additional chemicals recognised by the SAB as having potential RCA applications.

1.3 The SAB found that 17 out of the 59 chemicals meet the definition of an RCA as defined by Article II(7) of the Convention. Adamsite was not one of these, consistent with earlier SAB advice (Appendix 3). Those chemicals that met the definition of an RCA were: 2-chloroacetophenone, 2-chlorobenzylidenemalononitrile, dibenzo[*b*,*f*][1,4]oxazepine, oleoresin capsicum, capsaicin, dihydrocapsaicin, pseudocapsaicin, homocapsaicin, homodihydrocapsaicin, nordihydrocapsaicin, 4-nonanolylmorpholine, 2'-chloroacetophenone, 3'-chloroacetophenone, α-chlorobenzylidenemalononitrile, *cis*-4-acetylaminodicyclohexylmethane, *N*,*N*'-bis(isopropyl)ethylenediimine, and *N*,*N*'-bis(*tert*-butyl)ethylenediimine. Their chemical properties and Chemical Abstracts Service (CAS) numbers appear in Appendix 4.

1.4 The list of 17 RCAs (Appendix 4) has previously been provided to States Parties as a point of reference in support of their declarations (see S/1177/2014, dated 1 May 2014[1]). The additional 42 additional chemicals considered by the SAB (Appendix 5) might also be provided as a reference list of substances that do not meet the criteria of an RCA (and thus should not be declared as such) but have historically been considered for use as an RCA.

1.5 This original list of 59 has been reviewed and an additional chemical (piperine) that meets the inclusion criteria was identified. This chemical does not meet the definition of an RCA and is included at the end of the table of Appendix 5.

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[1] Available at www.opcw.org/fileadmin/OPCW/S_series/2014/en/s-1177-2014_e_.pdf.

2. OBJECTIVE

2.1 At the Twentieth Session of the SAB in June 2013 [1], the Technical Secretariat introduced a request from the Director-General to consider an indicative list of substances that could potentially be considered as RCAs (including 14 chemicals that have been declared as RCAs since the Convention entered into force), and to provide advice on:

(a) Whether the list reflects the current RCAs that could be considered as declarable in accordance with Article III(1)(e) of the Convention; and, in particular:

(i) the soundness of the criteria used by the Secretariat in drawing up the initial list;

(ii) which other considerations or criteria, if any, should be used in developing the list;

(iii) which chemicals, if any, should be deleted from the list; and

(iv) which chemicals, if any, should be added to the list.

2.2 The SAB noted that this request is specific to RCAs and is intended to identify chemicals on the list that meet criteria specific to RCAs as defined by Article II(7) of the Convention.

2.3 Article III(1)(e) provides that, with respect to RCAs, States Parties shall "specify the chemical name, structural formula and Chemical Abstracts Service (CAS) registry number, if assigned, of each chemical it holds for riot control purposes. This declaration shall be updated not later than 30 days after any change becomes effective."

2.4 Relevant SAB reports relating to RCAs are reproduced herein in Appendices 2 and 3.

3. DEFINING A RIOT CONTROL AGENT

3.1 Article II(7) of the Convention defines RCAs as "[a]ny chemical not listed in a Schedule, which can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure".

3.2 The definition of a prospective RCA hinges on whether it causes reversible irritation or disabling physical effects that disappear shortly after exposure. A chemical that does not do this, but is significantly harmful and deleterious to humans, is excluded by Article II(7) from being categorised as an RCA.

3.3 In assessing the indicative list, the literature describing the toxicology of each chemical was weighed carefully.

3.4 The term "can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure" in Article II(7) is not defined absolutely and implies a statistical probability of response. Toxicities of chemicals vary in different animal species and under different conditions. Therefore, it

is not always possible in the absence of human data to predict accurately from animal data the effects on humans. The Himsworth report [3] into toxicological aspects of CS (one of the most common chemicals to be used as a tear gas) and its use for civil purposes noted that the effects of any chemical intended for use in internal security operations should be studied in a manner 'more akin to that in which we regard the effects of a new drug.' Unfortunately toxicological studies on many of the chemicals on the initial list have not been performed to the level of scrutiny a new drug receives. In assessing the suitability of each chemical for consistency with the RCA definition in Article II(7) the scientific literature was reviewed and recommendations were made based on its analysis.

4. FINDINGS

4.1 In response to the Director-General's specific questions:

(a) The list does reflect the current RCAs that could be considered declarable in accordance with Article III(1)(e).

(b) The criteria used by the Technical Secretariat to draw up the list are judged sound. These criteria are (see also Appendix 1):

(i) All the RCAs that have been declared since entry into force of the Convention.

(ii) Previous advice by the SAB: in 2001 the SAB's TWG on Analytical Procedures drew up a list of "riot control agents and old/abandoned chemical weapons" to be considered for inclusion in the OCAD, which the SAB in principle endorsed (cf. Paragraphs 2.4-2.5 in Appendices 3 and 4 of SABIV/1, in which the SAB focused on the compounds that the Board thought should be incorporated into the OCAD with the highest priority [4]); and

(iii) An initial survey conducted by the Technical Secretariat in 2013 of RCAs that have been researched or are available for purchase, beyond those that are already declared.

(c) The main point in considering the list, as discussed in Section 3, is whether the toxicity profile of each chemical matches the definition of an RCA in Article II(7).

(d) No chemicals should be deleted from the list and those which do not match the definition of an RCA in Article II(7) have been identified.

(e) The chemicals that should be added to the list are those linked in the scientific literature to riot control, and therein their physiological action compared to RCAs, or those having physiological properties that could favour their research or potential use in this respect.

4.2 An analysis of each chemical was performed by consulting previous SAB reports (Appendices 2 and 3) and the scientific literature (Appendices 4 and 5). A judgement on whether each chemical met the criteria of an RCA was then made.

4.3 The scientific literature reviewed [1 – 145] revealed the majority of the 17 chemicals found to meet the definition of an RCA act by activating Transient Receptor Potential Ankyrin 1 (TRPA1) or Vanilloid 1 (TRPV1) receptors in the peripheral nervous system (PNS) [48,145]. It is this action that triggers in humans "sensory irritation or disabling physical effects which disappear within a short time following termination of exposure". The remainder of the 17 chemicals remain to be proved to activate TRPA1 or TRPV1 receptors, but it is likely that they also target these receptors; their sensory irritant action is also consistent with a specific temporary effect on the PNS.

5. CONCLUSIONS

5.1 In this Section, an asterisk signifies a chemical added to the initial list because it fitted the criteria used by the Technical Secretariat and those in Section 4.1(e) of this report.

5.2 The following chemicals meet the criteria of a Riot Control Agent as defined by Article II(7):

(a) 2-Chloroacetophenone (CN)

(b) 2-Chlorobenzylidenemalonitrile (CS)

(c) Dibenzo[*b,f*][1,4]oxazepine (CR)

(d) Oleoresin capsicum (OC)

(e) 8-Methyl-*N*-vanillyl-*trans*-6-nonenamide (capsaicin)

(f) 8-Methyl-*N*-vanillylnonamide (dihydrocapsaicin)

(g) *N*-Vanillylnonamide (pseudocapsaicin, PAVA)

(h) *N*-Vanillyl-9-methyldec-7-(*E*)-enamide (homocapsaicin)

(i) *N*-Vanillyl-9-methyldecanamide (homodihydrocapsaicin)

(j) *N*-Vanillyl-7-methyloctanamide (nordihydrocapsaicin)

(k) 4-Nonanolylmorpholine (MPA)

(l) 2'-Chloroacetophenone

(m) 3'-Chloroacetophenone

(n) α-Chlorobenzylidenemalononitrile

(o) *Cis*-4-acetylaminodicyclohexylmethane *

(p) *N*,*N*'-Bis(isopropyl)ethylenediimine *

(q) *N*,*N*'-Bis(*tert*-butyl)ethylenediimine *

5.3 The following chemicals do not meet the criteria of a Riot Control Agent as defined by Article II(7):

(a) Acrolein

(b) 4'-Chloroacetophenone

(c) 2-Bromoacetophenone *

(d) 2-Bromoethyl acetate

(e) Ethyl chloroacetate *

(f) Ethyl bromoacetate

(g) Ethyl iodoacetate

(h) Chloroacetone

(i) Bromoacetone

(j) Iodoacetone

(k) 1,1-Dichloroacetone *

(l) 1-Bromo-2-butanone (bromomethyl ethyl ketone)

(m) Bromobenzyl cyanide (CA)

(n) Benzyl chloride

(o) Benzyl bromide

(p) Benzyl iodide

(q) 2-Methylbenzyl bromide (*o*-xylyl bromide)

(r) 3-Methylbenzyl bromide (*m*-xylyl bromide)

(s) 4-Methylbenzyl bromide (*p*-xylyl bromide)

(t) 2-Nitrobenzyl chloride *

(u) 1,2-Bis(bromomethyl)benzene (*o*-xylylene dibromide) *

(v) 1-Methoxy-1,3,5-cycloheptatriene (CHT)

(w) (*Z*,*E*)-Propanethial *S*-oxide

(x) Trichloronitromethane (chloropicrin)

(y) Tribromonitromethane (bromopicrin) *

(z) 1,1,2,2-Tetrachloro-1,2-dinitroethane *

(aa) Phenylimidocarbonyl chloride

(bb) Phosgene oxime (CX)

(cc) Methyl chloroformate *

(dd) Chloromethyl chloroformate

(ee) Dichloromethyl chloroformate *

(ff) Trichloromethyl chloroformate (diphosgene)

(gg) Bis(trichloromethyl) carbonate (triphosgene)

(hh) Methyldichloroarsine (MD)

(ii) Ethyldichloroarsine (ED)

(jj) Phenyldichloroarsine (PD)

(kk) Diphenylchloroarsine (DA)

(ll) Diphenylcyanoarsine (DC)

(mm) 10-Chloro-5,10-dihydrophenarsazine (Adamsite, DM)

(nn) 10-Chloro-5,10-acridarsine (Excelsior) *

(oo) 5(10*H*)Acridarsinecarbonitrile *

(pp) Trialkyl-lead salts *

(qq) Piperine *

5.4 Three of the fourteen chemicals declared as RCAs since the Convention entered into force have properties that exclude their definition as an RCA under Article II(7). They are 10-chloro-5,10-dihydrophenarsazine (Adamsite), 2-bromoethyl acetate, and 4'-chloroacetophenone. The impact of these chemicals on life processes was considered to have a high probability of causing death or permanent harm.

5.5 The conclusion that Adamsite does not meet the criteria of an RCA is consistent with the conclusion reached by the SAB in 1999, in that “it should no longer be used as an RCA, as it fails to meet today’s concerns for safety” (Appendix 3) [5,6].

5.6 *Cis*-4-acetylaminodicyclohexylmethane, *N*,*N*'-bis(isopropyl)ethylenediimine, and *N*,*N*'-bis(*tert*-butyl)ethylenediimine were considered in addition to the initial list. They met the criteria used by the Secretariat and those given in Section 4.1(e) of this report, and were found to meet the definition of an RCA under Article II(7).

5.7 Forty-three other chemicals, comprising those on the initial list supplemented by 13 additions considered for reasons given in Section 4.1(e) herein, do not fit the definition of an RCA.

5.8 Trichloronitromethane (chloropicrin) appears on Schedule 3A(4) and is thus excluded as the Article II(7) definition states that RCAs are not listed on any Schedules.

6. RECOMMENDATIONS

6.1 The list of 17 RCAs (Appendix 4) has previously been provided to States Parties as a point of reference in support of their declarations (see S/1177/2014). The additional 43 additional chemicals considered by the SAB (Appendix 5) might also be provided as a reference list of substances that do not meet the criteria of an RCA (and thus should not be declared as such) but have historically been considered for use as an RCA.

6.2 Inclusion of data for the 60 chemicals considered in this report into the OCAD should be considered, in line with the SAB 2001 recommendation [2].

Appendix 1

DIRECTOR GENERAL'S REQUEST TO THE SCIENTIFIC ADVISORY BOARD [1]

1. States Parties are required to declare riot control agents (RCAs) in accordance with Article III(1)(e) of the Convention.

2. The Director-General wishes to assemble an indicative list of substances that the Secretariat currently considers as RCAs. Such a list, which would not be exhaustive, will be made available to States Parties as a point of reference in support of their declarations.

3. The Convention provides that "riot control agent" means "any chemical not listed in a Schedule, which can produce rapidly in humans sensory irritation or disabling physical effects which disappear within a short time following termination of exposure" (Article II(7)). However, the definition of RCAs in the Convention leaves some room for interpretation as to which chemicals can be considered as meeting the requirement specified in Article II(7).

4. An initial list has been developed by the Technical Secretariat, based on the following criteria:

   (a) All the RCAs that have been declared since entry-into-force of the Convention:

   (b) Previous advice by the Scientific Advisory Board (SAB): in 2001 the SAB's (TWG on Analytical Procedures drew up a list of "riot control agents and old/abandoned chemical weapons" to be considered for inclusion in the OCAD, which the SAB in principle endorsed (cf. Paragraphs 2.4-2.5 in Appendices 3 and 4 of SABIV/1, in which the SAB focused on the compounds that the Board thought should be incorporated into the OCAD with the highest priority); and

   (c) An initial survey conducted by the Technical Secretariat in 2013 of RCAs that have been researched or are available for purchase, beyond those that are already declared.

5. The Director-General requests the Scientific Advisory Board to consider the attached initial list of riot-control agents that have been declared by States Parties, researched, or that are available for purchase, and requests the Board to provide technical advice on:

   (a) Whether that list reflects the current riot-control agents that could be considered as declarable in accordance with Article III(1)(e); and, in particular

   (b) The soundness of the criteria used by the Secretariat in drawing up the initial list;

(c) Which other considerations or criteria, if any, should be used in developing the list;

(d) Which chemicals, if any, should be deleted from the list; and

(e) Which chemicals, if any, should be added to the list.

Technical Secretariat
June 2013

Appendix 2

FINDINGS ON RCAS FROM THE TWG ON ANALYTICAL PROCEDURES (TEXT FROM SAB IV/1)

1. From 28-29 August 2000, the Board's Temporary Working Group (TWG) on Analytical Procedures met to discuss the possible inclusion of unscheduled chemicals in the OPCW Central Analytical Database (OCAD) as requested by the Director-General [4].

2. The Board reviewed these recommendations and endorsed in principle the inclusion of the spectra of certain unscheduled chemicals. The Board submitted the following conclusions to the Director-General:[2]

   (a) The spectra of certain non-scheduled chemicals should be incorporated into the OCAD, primarily to assist in challenge inspections or for investigations of alleged use. The selection of data for on-site analysis should be done in accordance with the purpose of sampling and analysis during an inspection. The addition of such data could also expand the analytical capabilities of the designated laboratories. The following groups of non-scheduled chemicals, prioritised in the following sequence, should be considered for inclusion:

      (i) non-scheduled degradation products of scheduled chemicals;

      (ii) riot control agents and old/abandoned chemical weapons;

      (iii) salts of scheduled chemicals; and

      (iv) non-scheduled precursors and by-products of the synthesis of scheduled chemicals;

   (b) The general principles for the possible inclusion of non-scheduled chemicals in the OCAD for the various groups of non-scheduled chemicals and riot control agents should be those contained in paragraphs 5 and 6 of the report of the TWG. In addition, the Board recommended that only spectra of unscheduled chemicals that are not widely used in the chemical industry should be incorporated, in order to facilitate the protection of confidentiality, and also in order to avoid false-positive detection; and

   (c) The lists of chemicals proposed by the TWG were reviewed. The Board endorsed them in principle, and identified those compounds that should be incorporated into the OCAD with the highest priority. These compounds are contained in Appendix 4 of this report.

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2 SAB IV/1, paragraph 2.5

3. The TWG on Analytical Procedures of the SAB met in The Hague on the 28 and 29 August 2000 to develop a list of non-scheduled chemicals whose spectra should be incorporated into the OCAD [4].

4. Riot control agents[3]

(a) The following principles are recommended for adding RCAs (as defined in the Convention):

(i) The chemicals must have been used as riot control agents; or

(ii) Have been declared by a State Party as a riot control agent.

(iii) In addition to the riot control agent its analytical derivatives, if applicable, should be added.

(iv) Based on these principles a number of chemicals is recommended which are contained in Appendix 5 to this report. The list should not be considered as exhaustive and should be expanded when new riot agents are declared.

5. Riot control agents and old/abandoned chemical weapons: from Appendices 3-5 of [4]

Methyldichloroarsine (MD)	CAS 593-89-5
Ethyldichloroarsine (ED)	CAS 598-14-1
Phenyldichloroarsine (PD)	CAS 696-28-6
Diphenylchloroarsine (Clark I)	CAS 712-48-1
Diphenylcyanoarsine (Clark II)	CAS 23525-22-6
10-Chloro-5,10-dihydrophenarsazine (Adamsite)	CAS 578-94-9
Alpha-bromobenzyl cyanide (CA)	CAS 5798-79-8
Omega-chloroacetophenone (CN)	CAS 532-27-4
2-Chlorobenzylidenemalononitrile (CS)	CAS 2698-41-1
Dibenzoxazepine (CR)	CAS 257-07-8
Capsaicin	CAS 404-86-4
4-Nonanoylmorpholine	CAS 5299-64-9
Pelargonic acid vanillylamide	CAS 2444-46-4
Ethyl iodoacetate	CAS 623-48-3
Ethyl bromoacetate	CAS 105-36-2
Phosgene oxime (CX)	CAS 1794-86-1
Ortho-xylyl bromide	CAS 89-92-9
Meta-xylyl bromide	CAS 620-13-3
Para-xylyl bromide	CAS 104-81-4
Benzyl bromide	CAS 100-39-0
Diphosgene	CAS 503-38-8
Triphosgene	CAS 32315-10-9

[3] SAB IV/1, paragraph 6

Appendix 3

PREVIOUS SAB FINDINGS ON ADAMSITE IN 1999-2000 [6]

1. Following a request by the Director-General the Board conducted during its second session an initial discussion of technical criteria that should be taken into account when declaring holdings of Adamsite [5]. The issue was brought to the attention of the Board because of the divergence in the ways in which different States Parties have declared such holdings. The Board recommended that this issue be discussed by a TWG and that a technical seminar be convened to study the scientific aspects relevant to declarations of such holdings.

2. The relevant sections from the aforementioned report are:

   (a) The Board received and discussed the draft report of the TWG on Adamsite (DM) dated 7 October 1999 at its third session.[4]

   (b) On the basis of the conclusions of the TWG, the Board reached the following conclusions:[5]

      (i) although DM is not listed in the Schedules of Chemicals appendixed to the Convention, it has a history as a chemical weapon, albeit as one which is inferior in effectiveness if compared to other agents. It has also been used for riot control purposes;

      (ii) at present DM has no medical, industrial or other legitimate uses, except for research;

      (iii) it is not contested that, when DM is used as an RCA with restraint, and in the open, the occurrence of deaths or permanent damage is unlikely. However, some fatalities have nevertheless been reported (presumably as a result of the dissemination of excessive quantities of DM); and

      (iv) DM should accordingly no longer be used as an RCA, as it fails to meet today's concerns for safety. In addition, it also does not meet today's concerns with respect to environmental protection (in particular in relation to arsenic contamination). Should a country decide to maintain the option of retaining DM as an RCA, its holdings should be consistent with such intended uses (the quantities should not exceed a few tonnes, and any holdings should not be in a weaponised[6] form).

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4 SAB-III/1, paragraph 2.1. Report available at: https://www.opcw.org/fileadmin/OPCW/SAB/en/sab-iii-01.pdf

5 SAB-III/1, paragraph 2.5

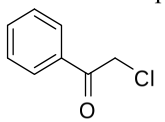
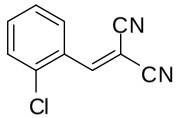
6 It may be kept in smoke candles, smoke grenades and similar devices, or in bulk, for use in suspensions.

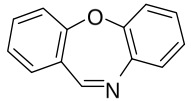
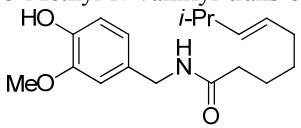
(c) The Board did not consider it appropriate to address the legal implications of its findings on Adamsite. Given that Adamsite is not listed in the Schedules to the Convention, the Board recommended that the conclusions contained in subparagraphs (a)-(b) above be used as a basis for defining the legal status of Adamsite in relation to the Convention.[7]

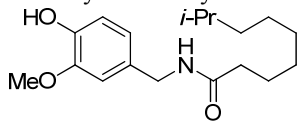
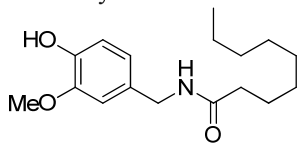
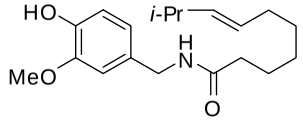
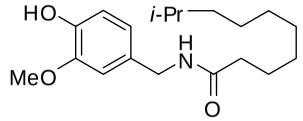
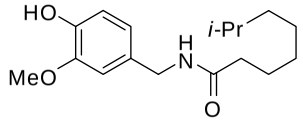
[7] SAB-III/1, paragraph 2.6

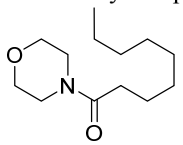
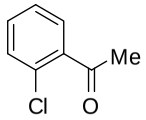
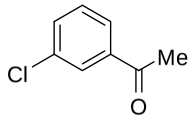
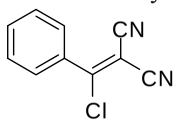
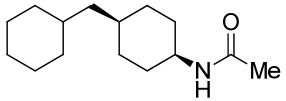
Appendix 4

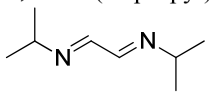
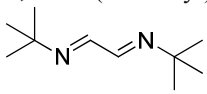
LIST OF CHEMICALS THAT MEET THE DEFINITION OF RIOT CONTROL AGENTS

Chemical name and CAS number	Physical state	Notes	Physiological effect
2-Chloroacetophenone (CN)  *Synonyms*: Mace, CAP, KhAf CNB (10% CN, 45% benzene, 40% carbon tetrachloride), CNC (30% CN, 70% chloroform), and CNS (23% CN, 38.4% chloropicrin, 38.4% chloroform) CAS 532-27-4	White solid with odour of apple blossom Mp 54-56 °C Bp 245 °C	Sparingly soluble in water, dissolves in chloroform and other organic solvents. Stable and does not decompose on heating or detonation; its lachrymatory effects are soon lost by condensation to the solid state soon after dispersion: non-persistent and not hydrolysed readily [7].	Immediately irritates eyes (at 0.3 mg/m³) and upper respiratory passages [8-28]. High concentrations cause tears, irritation, tingling and pain in the nose and throat; and burning and itching of tender skin, especially areas wet by perspiration. High concentrations cause blisters with effects similar to sunburn – blisters are harmless and disappear in a few hours. Some individuals experience nausea after exposure. ICt_{50} 80 mg/m³ [8]. LCt_{50} 7000 mg min/m³ from solvent and 14,000 mg min/m³ from a thermal grenade. Rapid detoxification – effects disappear in minutes. Limit of supportability is 4.5 mg/m³ of air [9]. Animal studies show that toxic effects are more severe than those of CS [28]. CN has been superseded as an RCA by CS which is safer to use.
2-Chlorobenzylidenemalonitrile (CS)  *Synonyms*: 2-Chlorbenzalmalononitrile, *o*-chlorobenzylidene malononitrile, K62 CS (pure), CS1 (95% CS, 5% silica aerogel), CS2 (CS and silica aerogel), CSX (1 g CS, 99 g tri-*n*-octyl phosphite). CS dissolved in methyl ethyl ketone is used in spray devices CAS 2698-41-1	White solid with pungent peppery odour Mp 93-95 °C Bp 310-315 °C dec.	CS is the most common RCA, known as "tear gas" [29-34]. Different forms have different persistency. CS is sparingly soluble in water (~0.008 wt % at 25 °C). Dispersed as a solid aerosol [35]. Thermal breakdown products have been studied [36-39].	CS aerosol irritates eyes, nose, and throat within 20-60 s. Causes temporary disablement: tears, coughing, breathing difficulty, chest tightness, involuntary closing of eyes, stinging of moist skin, mucous formation in nose, and dizziness [18,19,26,40-65]. Eye effects at 1-5 mg/m³. LCt_{50} 61,000 mg min/m³ and ICt_{50} 10-20 mg/m³ [8]. Exposure to fresh air dissipates effects in 5-10 min, with skin rash persisting ~1 day after heavy exposures. No lasting health effects when used in open areas at high dilution. Rarely, high concentrations reduce lung function temporarily [66] or burn skin that heals rapidly [67-68]. CS is metabolised in animals [69-74] and humans [75] to products of low toxicity. Some analogues of CS also cause sensory irritation [76-77].

Dibenzo[*b,f*][1,4]oxazepine (CR)  *Synonyms*: CR CAS 257-07-8	Yellow stable powder [78-85] Mp 72 °C Bp 335 °C	Insoluble in water. Soluble in benzene, chloroform, and carbon tetrachloride. Stable in hot aqueous acid or alkali. CR is dissolved in 80 parts of propylene glycol and 20 parts of water to form a 0.1% CR solution for riot control [8]. CR does not degrade in water and persists for a long time in the environment [84,85].	Exposure causes symptoms similar to CS [20,22-24,26]. CR powerfully irritates the eyes (~10 times that of CS) [86,87] and has low inherent toxicity, giving it a wide safety ratio ($IC_{50}/TC_{50} > 350$). Concentration that irritates the eye is 0.01 mg/m³ but no irritation when concentration falls <0.001 mg/m³. IC_{50} 0.15 mg/m³ and threshold effects on respiratory system at 0.002 mg/m³ and the eyes at 0.004 mg/m³ [8]. CR irritates oral cavity causing burning pains and malaise, and the nose producing nasal discharge and obstruction. Delivered in aerosol form, CR irritates eyes causing stinging, the feeling of a foreign body in the eye, and involuntary spasm of eyelids (blepharospasm). As concentrations increase, severity and duration of symptoms increase; ~0.5 mg CR can immediately irritate the skin and cause it to redden. Blistering is not seen: redness quickly disappears following washing with water. Information on likelihood of long-term effects after exposure is unavailable, but toxicological findings to date give no cause for concern [88-93].
Oleoresin capsicum Resin containing ≥8% capsaicins: capsaicin, dihydrocapsaicin, and nordihydrocapsaicin. Capsaicin is main capsaicinoid in chillis, then dihydrocapsaicin. These two compounds are about twice as potent to sensory nerves as the minor capsaicinoids: homo- and nordihydro-capsaicin, and homocapsaicin. *Synonyms*: OC CAS 8023-77-6	A mixture of products in an organic solvent	Obtained by grinding dried chilli peppers (Capsicum frutescenes), extracting them with an organic solvent, removing the solvent to give the wax-like resin. Pepper spray contains the resin emulsified in aqueous propylene glycol.	In minute quantities, produces intense burning sensation of the eyes and tender skin [25,65]. Considered safe, although concentrates cause some respiratory distress, lachrymation, and mucosal burning [94]. Chemical constituents do not appear to be carcinogenic. Sprays in toxic solvents can cause eye damage [95]. A study of the inhalation toxicity of oleoresin capsicum from Capsicum frutescenes var. Nagahari in mice indicated this mixture, containing 40% capsaicinoids, to be the most suitable and environmentally-friendly compound from a natural source to be used as an ingredient for tear gas munitions [96]. Human volunteer studies have been reported [97,98].
8-Methyl-*N*-vanillyl-trans-6-nonenamide  *Synonyms*: C, capsaicin, Moitin, Zacin CAS 404-86-4	White solid Mp 62-65 °C Bp 210-220 °C at 0.01 mmHg	Active component of cayenne pepper, isolated from Capsicum species. Used in pain management and as a pest deterrent.	Stimulates sensory nerves to effect changes in systemic blood pressure and respiration. On skin it causes irritation and oedema. Repeat applications result in progressively diminished response until the area becomes insensitive. Facial exposure causes a burning sensation, cough, sneezing, and laryngitis, shortness of breath, headache, nausea and vomiting. Toxicology not fully known; no evidence for carcinogenicity or mutagenicity in humans.

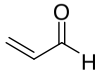
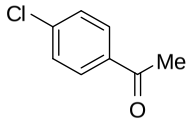
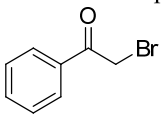
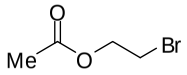
8-Methyl-*N*-vanillylnonanamide  *Synonyms*: Dihydrocapsaicin, DHC CAS 19408-84-5	White solid Physical data unavailable	Isolated from Capsicum species (see the entry on capsicum oleoresin).	Causes eye, skin and respiratory irritation [99]. Prolonged or repeated exposure can cause diarrhoea and/or liver damage. Toxicology in humans has not been fully studied. No evidence for carcinogenicity or mutagenicity in humans.
N-Vanillylnonanamide  *Synonyms*: N-(4-hydroxy-3-methoxy-benzyl)nonanamide, nonivamide, pseudo-capsaicin, pelargonic acid vanillylamide, PAVA CAS 2444-46-4	White solid with stinging odour Mp 57 °C	In chillis but commonly produced commercially by synthesis. More heat stable than capsaicin. Used under name PAVA in pepper sprays and as a food additive in spicy flavourings.	Causes eye, skin and respiratory irritation, skin sensitisation and allergy [99]. Inhalation can cause cough, headache, nausea and vomiting. As with other capsaicinoids, the effects disappear within 15-35 min upon removal to fresh air. Toxicology in humans has not been fully investigated. No evidence for carcinogenicity or mutagenicity in humans.
N-Vanillyl-9-methyldec-7-(E)-enamide  *Synonyms*: homocapsaicin CAS 58493-48-4	Lipophilic colourless odourless crystalline or waxy solid	Accounts for ~1% of the total capsaicinoids in an oleoresin capsicum extract.	Biological action similar to oleoresin capsicum of which it is a constituent. Modest pungency – half that of capsaicin. Causes a burning sensation in the mouth upon swallowing that fades after a short time.
N-Vanillyl-9-methyldecanamide  *Synonyms*: homodihydrocapsaicin CAS 20279-06-5	Lipophilic colourless odourless crystalline or waxy solid	Accounts for ~1% of the total capsaicinoids in an oleoresin capsicum extract.	Biological action similar to oleoresin capsicum of which it is a constituent. High pungency - stronger burning sensation than pepper spray. Causes a burning sensation in the mouth upon swallowing that fades after a short while.
N-Vanillyl-7-methyloctanamide  *Synonyms*: nordihydrocapsaicin CAS 28789-35-7	Lipophilic colourless odourless crystalline or waxy solid	Accounts for ~7% of the total of capsaicinoids in oleoresin capsicum extract.	Biological action similar to oleoresin capsicum of which it is a constituent. High pungency. Causes a burning sensation in the mouth upon swallowing that fades after a short time.

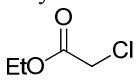
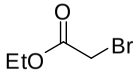
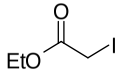
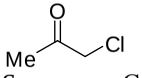
4-Nonanoylmorpholine  *Synonyms*: MPA, MPK, pelargonic acid morpholide CAS 5299-64-9	Liquid Bp 310 °C	Used as solvent and co-irritant in CS and CR mixtures. Used alone - low effectiveness, even at highest permitted concentration. Insoluble in water, but soluble in organic solvents (e.g. acetone).	Mixed with CS or CR it causes sensory irritation for 15-30 min [16,17]. Such mixtures are effective against dogs and people under the influence of alcohol and drugs. Human volunteers exposed to the 4-nonanoylmorpholine experienced a burning sensation of the nose with rhinorrhea, and throat and eyes with lachrymation [17]. All symptoms were relieved immediately by movement to fresh air. Occasional and mild transient conjunctivitis was sometimes observed. Physical examination of the volunteers after exposure revealed no significant changes.
2'-Chloroacetophenone  *Synonyms*: *o*-chloroacetophenone CAS 2142-68-9	Colourless liquid Bp 229 °C	Commercially available. Almost insoluble in water. Soluble in organic solvents.	Inhalation causes eye and skin irritation, cough, shortness of breath, headache, nausea and vomiting [99]. Toxicology in humans has not been fully investigated. No evidence for carcinogenicity or mutagenicity in humans.
3'-Chloroacetophenone  *Synonyms*: *m*-chloroacetophenone CAS 99-02-5	Colourless liquid Bp 228 °C	Commercially available. Almost insoluble in water. Soluble in organic solvents.	Inhalation causes eye and skin irritation, cough, shortness of breath, headache, nausea and vomiting [99]. Toxicology in humans has not been fully investigated. No evidence for carcinogenicity or mutagenicity in humans.
α-Chlorobenzylidenemalononitrile  *Synonyms*: None CAS 18270-61-6	White solid Mp 68-70 °C Bp 126 °C/0.1 mmHg	Commercially available. Very sparingly soluble in water. Soluble in common organic solvents.	Exposure causes a burning sensation, cough, wheezing, laryngitis, shortness of breath, headache, nausea and vomiting [99]. Toxicology in humans has not been fully investigated. No evidence for carcinogenicity or mutagenicity in humans.
Cis-4-Acetylaminodicyclohexylmethane  *Synonyms*: None CAS 37794-87-9 (*trans* CAS 37794-48-2)	White solid Mp 112 °C	"These compounds have two advantages over currently used riot control agents such as CS and CN. One, the compounds are more potent at low concentrations and two, they provide residual activity over a long period of time" [100].	Potent irritant of mucous membranes. In humans produces a running nose, a choking sensation, and uncontrollable coughing (trans isomer is essentially inactive) which disappear within a short time after termination of exposure. Irritant to mice, dogs and guinea pigs, but these tests not configured to reveal if there were other toxic effects that caused permanent harm. *Cis* isomer is 10-30 times more effective an animal irritant than the trans isomer [100].

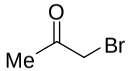
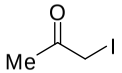
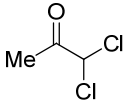
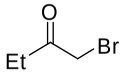
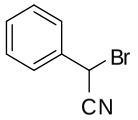
N,*N*'-Bis(isopropyl)ethylenediimine  *Synonyms*: Diimine CAS *E*,*E* 28227-41-0 CAS *Z*,*Z* 185245-09-4 CAS *E*,*Z* 185245-08-3 CAS undefined stereochemistry 57029-91-1	Volatile tan-coloured solid Mp 48-50 °C	Soluble in organic solvents. Environmental persistence is poor. Disseminated by smoke or explosive munitions [101].	Compound is a "fast acting riot control agent capable of irritating exposed personnel within minutes of dissemination. Inhalation of as little as 5 mg can lead to irritation and congestion. Diimine is not considered to be a skin irritant, but eye exposure to as little as 15 mg can lead to watering and irritation. The lethal dose to the average man is unknown, but is calculated to be very high; diimine is regarded as non-toxic" [101]. The effects last from 5 min to 1 h, and there is little effect on the skin [102].
N,*N*'-Bis(*tert*-butyl)ethylenediimine  *Synonyms*: None CAS 30834-74-3 CAS *E*,*E* 28227-42-1	White solid Mp 39-43 °C	Mentioned in a patent: "excellent utility in inducing non-lethal physiological action on people subjected to its vapours" [102].	"During the course of handling this chemical during filtration from ether its lachrymatory powers were noted. The experimenter was overcome with severe lachrymation, coughing and discharges from the nose and mouth, along with stomach cramps. The attack occurred even though the reaction and recovery of the product were being carried out in a well ventilated hood. The attack symptoms subsided in about 5 min, and the experimenter proceeded with the rest of the experiment. The experimenter has not observed any side effects from this exposure once the effects of the initial exposure had subsided" [102].

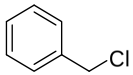
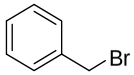
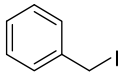
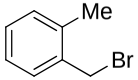
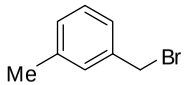
Appendix 5

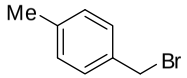
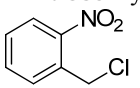
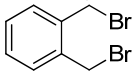
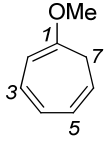
A LIST OF CHEMICALS RESEARCHED WHICH DO NOT MEET THE CRITERIA OF A RIOT CONTROL AGENT

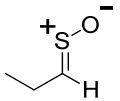
Name and CAS number	Physical state	Notes	Physiological effect
Acrolein  *Synonyms*: Papite, 2-propenal CAS 107-02-8	Colourless or yellow liquid with a pungent odour. Partly miscible with water but miscible with organic solvents. Bp 53 °C	Used in 1916 in World War I. Readily polymerises to an amorphous resin that lacks irritancy. Produced during overcooking of food and is the component in barbecue smoke that has a piercing disagreeable acrid smell and irritates the eyes [103].	Minimum concentration causing lachrymation is 7 mg/m³ of air. Limit of insupportability 50 mg/m³ [9]. Mortality product 2000-7000. Humans cannot tolerate concentrations in air of 5 mg/m³ or higher for > 2 min, while > 20 mg/m³ may be lethal [104]. Low concentrations irritate eyes, skin, mucous membranes; and cause delayed lung damage [105]. Acrolein reacts avidly with proteins [106].
4'-Chloroacetophenone  *Synonyms*: *p*-chloroacetophenone CAS 99-91-2	Colourless liquid. Bp 232 °C	Commercially available. Practically insoluble in water, soluble in organic solvents.	Highly irritating to eyes and mucous membranes [105]. Toxicological profile the same as for 2- and 3-chloroacetophenone except this isomer may be fatal if inhaled [99].
2-Bromoacetophenone  *Synonyms*: ω-bromoaceto-phenone CAS 70-11-1	White solid with an irritating odour that decomposes on exposure to light. Mp 50 °C Bp 260 °C dec.	Commercially available with similar physiological properties to 2-chloroacetophenone.	Lachrymatory power of 2-bromoacetophenone is less than that of 2-chloroacetophenone; however it is still a potent lachrymator [9,105]. It is highly irritating to the skin, eyes and mucous membranes, and can cause severe eye damage and skin burns [99].
2-Bromoethyl acetate  *Synonyms*: Bromoethyl acetate CAS 927-68-4	Colourless liquid Bp 159 °C	Available commercially containing <3% acetic anhydride. Combustible and emits toxic fumes when on fire.	Extremely destructive to tissue of the mucous membranes and upper respiratory tract, eyes, and skin, causing burns [99]. Inhalation causes cough, shortness of breath, and headache. No evidence of a carcinogenic effect; a possible human mutagen, but relevant information is scarce.

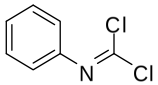
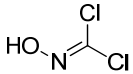
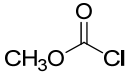
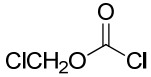
Name and CAS number	Physical state	Notes	Physiological effect
Ethyl chloroacetate  *Synonyms*: ethyl 2-chloroacetate CAS 105-39-5	Colourless liquid having a fruity odour Bp 144 °C	Available commercially. Used to a limited extent in World War I [9]. Manufactured for the preparation of two other substances with increased aggressiveness: ethyl bromoacetate and ethyl iodoacetate.	Lachrymator. Toxic in contact with skin and if inhaled or swallowed. Liquid or vapour can cause serious eye damage [99].
Ethyl bromoacetate  *Synonyms*: Weisskreuz, White Cross CAS 105-36-2	Colourless flammable liquid with a fruity odour Bp 159 °C	Ethyl bromoacetate was the first chemical employed in warfare as a vapour (end of 1914 during World War I) [9]. Used in hand grenades and shells. Because of its relatively high boiling point and low volatility, it could be used in shells without producing a visible cloud on bursting. Once used in joke-type toys before it was banned for this purpose and has also been used illicitly as a preservative in alcoholic beverages.	Extremely destructive to mucous membranes and upper respiratory tract, eyes, and skin; the neat liquid can cause eye and skin burns. Inhalation of vapour can cause coughing, wheezing, inflammation and oedema of respiratory passages, a burning sensation, shortness of breath, headache, nausea and vomiting. Limit of insupportability for a human is 40 mg/m³ of air [9]. Minimum concentration capable of irritating the eyes is 10 mg/m³. Mortality product is 3000. The compound is a toxic alkylating agent and may be fatal if inhaled in sufficient quantity.
Ethyl iodoacetate  *Synonyms*: KSK CAS 623-48-3	Dark brown liquid and invisible vapour with a fruity smell resembling “pear drops” Bp 179-180 °C	Ethyl iodoacetate was used in World War I in shells, especially mixed with chloropicrin (10%) [9].	Stinging of eyes: immediate lachrymation and blepharospasm. Irritates nasal mucosa but not skin [7]. Limit of insupportability is 15 mg/m³ of air [9]. Minimum concentration that irritates the eyes is 1.4 mg/m³. Mortality product is 1500. Toxic alkylating agent. May be fatal if inhaled in sufficient quantity.
Chloroacetone  *Synonyms*: CA, A-Stoff, Tonite CAS 78-95-5	Liquid with a very pungent odour Mp -45 °C Bp 120 °C dec.	Used in World War I mixed with bromoacetone (1:4, viz Martonite). Prepared by the action of chlorine on diketene or acetone [105]. Darkens and resinifies on prolonged exposure to light. May be stabilised by addition of 0.1% water or 1.0% calcium carbonate.	Intensely irritating to eyes, skin, and mucous membranes. Eye contact with ~1 mg can cause pain and irritation [101]. Lowest concentration irritating the eyes is 18 mg/m³ of air [9]. Skin contact with 15-50 mg can produce redness, rash, itching, and/or local discomfort [101]. Lethal dose by inhalation can be ~10,000 mg. It is however a toxic alkylating agent and may be fatal if inhaled in sufficient quantity.

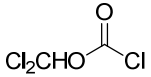
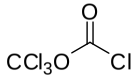
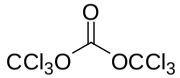
Name and CAS number	Physical state	Notes	Physiological effect
Bromoacetone  *Synonyms*: BA, BC, B-Stoff CAS 598-31-2	Liquid with a pungent odour Bp 137 °C	Used in World War I in shells and hand-bombs and prepared by bromination of acetone [105]. Turns violet rapidly even in absence of air. Sparingly soluble in water, soluble in many organic solvents.	Violent lachrymator. Lowest concentration irritating eyes is 1 mg/m³ [9]. Inhalation of 2-5 mg can cause coughing, nose and throat irritation [101]. Skin contact with 20-30 mg can produce irritation, itching, swelling and discomfort. Skin exposure to 50-100 mg may lead to blisters. Lethal dose through inhalation is 2000-5000 mg. An alkylating agent that may be fatal if inhaled in sufficient quantity.
Iodoacetone  *Synonyms*: 2-iodo-2-propanone CAS 3019-04-3	Pale yellow liquid Bp 163 °C	Used to produce other organic chemicals.	Potent lachrymator and strong irritant that is toxic by inhalation and skin absorption. An alkylating agent that may be fatal if inhaled in sufficient quantity.
1,1-Dichloroacetone  *Synonyms*: DCA, 1,1-dichloro-2-propanone CAS 513-88-2	Colourless liquid Bp 117-118 °C	Commercially available.	Fast-acting irritant capable of causing casualties within minutes [101]. Eye contact with ~3 mg can cause pain. Skin contact with 12-50 mg can cause redness, rash, itching, and/or local discomfort. Inhalation of ~5 mg can cause severe nose and throat irritation and discomfort. Lethal dose through inhalation can be ~10,000 mg. A toxic alkylating agent that may be fatal if inhaled in sufficient quantity [99].
1-Bromo-2-butanone  *Synonyms*: bromomethyl ethyl ketone CAS 816-40-4	Colourless liquid Bp 145-146 °C	Employed in World War I in place of bromoacetone whose production during the war was limited by need to reserve acetone for the explosives industry [9].	Causes burning sensation, cough, wheezing, laryngitis, shortness of breath, headache, nausea, and vomiting. Harmful by inhalation, in contact with skin, and if swallowed. Minimum concentration irritating eyes is 1.6 mg/m³ [9]. Limit of insupportability 11 mg/m³. Mortality product 6000. Alkylating agent that may be fatal if inhaled in sufficient quantity.
Bromobenzyl cyanide  *Synonyms*: BBC, CA, Calmite Larmine, and (R,S)-2-bromo-2-phenylacetonitrileCAS 5798-79-8	Yellow solid; crude material used in World War I was a heavy yellow liquid with a penetrating bitter-sweet smell of rotting fruit Mp 25 °C Bp 242 °C dec.	One of first tear agents used in World War I. Less effective than CN and viewed as obsolete. Decomposes when heated, does not burn; at >242 °C it gives PhCH(CN)=CH(CN)Ph and hydrobromic acid. Insoluble in water, soluble in organic liquids; slow rate of hydrolysis, giving complex products.	Irritating to skin and eyes, and relatively non-toxic. Estimated LCt_{50} is 8000-11,000 mg min/m³ and ICt_{50} ~30 mg min/m³. Detoxified rapidly at low doses. Minimum concentration causing lachrymation is 0.3 mg/m³ of air and the limit of insupportability is 30 mg/m³ [9,101]. Inhalation of 15-30 mg can cause severe irritation, coughing, sore throat, congestion, and nasal discharges within minutes. Lethal dose through inhalation ranges from 2000-6000 mg. Inhalation of ~900 mg per litre of air over 30 min can result in death.

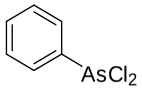
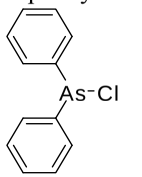
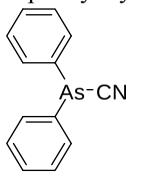
Name and CAS number	Physical state	Notes	Physiological effect
Benzyl chloride  *Synonyms*: α-chlorotoluene CAS 100-44-7	Colourless liquid with an unpleasant odour Bp 179 °C	Used in World War I. Made by chlorination of toluene. Soluble in and fairly stable to water; it is decomposed by prolonged boiling in water (to benzyl alcohol and hydrochloric acid).	Intensely irritating to skin, eyes and mucous membranes. Limit of insupportability: 85 mg/m³ of air [9]. Overexposure causes irritation (eyes, skin, and nose), weakness, irritability, headache, skin damage, and lung damage [105]. Toxic alkylating agent: may cause permanent injury or death after short exposures. Can cause nerve damage and is carcinogenic.
Benzyl bromide  *Synonyms*: Cyclite, T-Stoff CAS 100-39-0	Colourless liquid with an aromatic odour Mp -3 to -1 °C Bp 198-199 °C	Used in World War I. Made from bromine, toluene and ultraviolet light, or bromine and dibenzyl ether. Insoluble in, and slowly decomposed, by water but soluble in organic solvents.	Intensely irritating to skin, eyes, and mucous membranes. Minimum concentration irritating the eyes is 4 mg/m³ [9]. Limit of insupportability is 60 mg/m³ of air. Mortality product is 6000. Large doses depress the central nervous system [105]. Can damage permanently lungs, liver, kidneys and nervous system through its alkylating action, and may be fatal if inhaled in sufficient quantity.
Benzyl iodide  *Synonyms*: Fraisinite CAS 620-05-3	White solid Mp 24 °C Bp 226 °C dec.	One of the most potent lachrymators. Allegedly used in 1915 in World War I. Insoluble in water, soluble in organic solvents. Barely decomposed by water.	Irritates skin, eyes, nose and throat, causing coughing and wheezing. Minimum concentration irritating eyes is 2 mg/m³ in air [9]. Maximum concentration supportable for not more than 1 min is 25-30 mg/m³ in air. Mortality product is 3000. An alkylating agent that may be fatal if inhaled in sufficient quantity.
2-Methylbenzyl bromide  *Synonyms*: *o*-xylyl bromide CAS 89-92-9	White solid with odour when dilute of elder blossom Mp 21 °C Bp 223-234 °C	Commercially available. Mixture with 3- and 4-isomers used in World War I and known as "T-Stoff". Practically insoluble in water, soluble in organic solvents [105].	Powerful lachrymator. Minimum concentration capable of irritating is 1.8 mg/m³ of air. Limit of insupportability is 15 mg/m³ [9]. May be fatal if inhaled, swallowed, or absorbed through the skin, principally through its alkylating action.
3-Methylbenzyl bromide  *Synonyms*: *m*-xylyl bromide CAS 620-13-3	Colourless liquid Mp not available Bp 212-215 °C dec.	Commercially available. Mixture with 3- and 4-isomers used in World War I and known as T-Stoff. Practically insoluble in water, soluble in organic solvents [105].	Powerful lachrymator. Minimum concentration capable of irritating is 1.8 mg/m³ of air. Limit of insupportability is 15 mg/m³ [9]. May be fatal if inhaled, swallowed, or absorbed through the skin, principally through its toxic alkylating action.

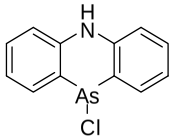
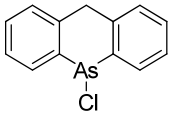
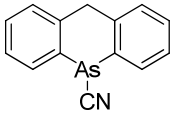
Name and CAS number	Physical state	Notes	Physiological effect
4-Methylbenzyl bromide  *Synonyms*: *p*-xylyl bromide CAS 104-81-4	Colourless liquid Mp 38 °C Bp 218-220 °C	Commercially available. Mixture with 3- and 4-isomers used in World War I and known as T-Stoff. Practically insoluble in water, soluble in organic solvents [105].	Same as above. May be fatal if inhaled, swallowed, or absorbed through the skin, principally through its toxic alkylating action.
2-Nitrobenzyl chloride  *Synonyms*: Cedenite CAS 612-23-7	White solid Bp 48-49 °C	Commercially available. Used in World War I mixed with the isomer 4-nitrobenzyl chloride under the name of "Cedenite".	More powerful irritant than benzyl chloride [9]. Lower limit of irritation is 1.8 mg/m³ of air. The compound is vesicant and can cause severe skin burns.
1,2-Bis(bromomethyl)benzene  CAS 91-13-4	White solid Mp 91-94 °C	Commercially available. Impurity in methylbenzyl bromide (xylyl bromide) mixture (*o*, *m*, and *p*) used for chemical warfare during World War I [9].	Causes severe skin burns and eye damage [99]. A potent alkylating agent that can cause death if inhaled in sufficient quantity.
1-Methoxy-1,3,5-cycloheptatriene  *Synonyms*: CH, CHT, GG, MCHT, tropilidene CAS 1728-32-1	Colourless mobile liquid with an irritating odour Bp 44 °C/10 mmHg	Researched in the 1980s as a sensory irritant. Formed by heating the 7-methoxy isomer, with the 3-methoxy isomer being an intermediate, and usually not obtained pure, but as a mixture with these isomers [107-112]. The 1-methoxy isomer predominates as it is the most stable [113]. Miscible with organic solvents and in water (0.6 mg/ml at 16 °C). Dispersal device for forcing egress of humans from spaces has been patented [114].	1-Methoxy compound is a potent lachrymator - other isomers considerably less active - and at 20 mg/m³ causes powerful irritation within 1 min sufficient to cause flight from contaminated area [114]. Two subjects exposed to 100 mg m³ wearing clothes and a gas mask reported a strong burning sensation under the arms, in the crotch and other sweaty parts of the body. Both subjects were forced to leave the zone within 20 min. When the subjects were exposed to fresh air, the compound evaporated from clothing within minutes and the skin condition abated within 20 min. Slight reddening of the skin disappeared within 1 h. No apparent effect on urine and blood, and study of 1-methoxy-1,3,5-cycloheptatriene on human cells indicated no evidence for a carcinogenic or mutagenic effect. Studies on small mammals indicate some carcinogenic potential [115,116].

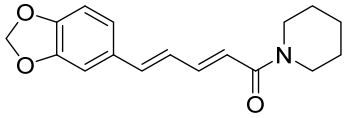
Name and CAS number	Physical state	Notes	Physiological effect
(*Z*,*E*)-Propanethial *S*-oxide  *Synonyms*: *syn*-Propanethial *S*-oxide, thiopropanol *S*-oxide CAS 32157-29-2	Pale yellow unstable liquid	Lachrymator released upon slicing onions (Allium cepa) due to the action of the enzyme allinase on S-(1-propenyl)cysteine sulfoxide present in onions [117]. Can be produced by synthesis but degrades quickly to non-lachrymatory product/s. A related lachrymator, *syn*-butanethiol S-oxide has been found in another onion species (Allium siculum) [118].	Intense and painful lachrymator, but unstable - it decomposes quickly at room temperature [119-121]. Effects are temporarily disabling and rapidly reversible upon entering fresh air. It is unlikely the compound could be isolated in large enough quantities and stabilised sufficiently long enough to constitute a riot control agent, but this possibility in future cannot be discounted based upon an analysis of the scientific literature to date. Toxicity data for it and its decomposition products are unavailable.
Trichloronitromethane CCl_3NO_2 *Synonyms*: Acquinite, chloropicrin, chloropicrine, G8, Klop (mixed with chlorine), klorpikrin, NC, nitrochloroform, PG (mixed with phosgene), picfume, larvicide 100, PS CAS 76-06-2	Colourless volatile liquid with an intense pungent and stinging odour Bp 112 °C	Used extensively as a chemical warfare agent in World War I. Now used as an insecticide and fumigant to disinfect cereal and grain, and in synthesis (especially to make methyl violet dye). First prepared from picric acid and bleach powder and later by addition of sodium hypochlorite to nitromethane [122]. Practically insoluble in water (0.16 g/l at 25 °C) [105]. Miscible with organic solvents. Semi-persistent.	Cumulative toxicity. Causes irritation of eyes, skin, and respiratory system, lachrymation, cough, lung damage, nausea, vomiting [104]. At 0.008 mg/l air, can be detected; at 0.016 mg/l, produces coughing and lachrymation; and at 0.12 mg/l, 30 to 60 min exposure can be fatal [9,123]. Inhalation of ~5 mg can cause irritation and pain to nose and throat [101]. Eye contact with ~3 mg, and skin contact with ~10 mg, can cause irritation and pain. Lethal dose through inhalation is 2000-2500 mg. Lowest irritant concentration is 9 mg/m³ for 10 min and LCt_{50} is 2000 mg min/m³ [8]. Induces sister chromatid exchanges in cultured human lymphocytes but not considered carcinogenic [124]. Convention Schedule 3A(4).
Tribromonitromethane CBr_3NO_2 *Synonyms*: Bromoacquinite, bromopicrin, picfume bromide, nitrobromoform CAS 464-10-8	White solid or semi-liquid with a strong biting odour Mp 10 °C Bp 127 °C/118 mmHg	Patented as a fumigant and soil sterilant [125]. Can persist in the environment for several days to weeks. Disseminated from aerosols, smoke generating or explosive munitions, or sprayed in solvents [101].	One reference states: "bromopicrin is a violent riot control agent, which has been banned by most agencies" [101]. Similar to trichloronitromethane in toxic action. It is a powerful irritant. Eye contact with ~1 mg can irritate. Inhalation of 5-10 mg can cause nose and throat irritation with congestion within minutes [101]. Lethal dose through inhalation is ~1200 mg, but usually ranges from 1500-2200 mg. Skin contact with ~4 mg can irritate, and 10-25 mg can cause sores and lesions.
1,1,2,2-Tetrachloro-1,2-dinitroethane $O_2NCCl_2CCl_2NO_2$ *Synonyms*: None CAS 67226-85-1	White solid Mp 142 °C	Insoluble in water. Soluble in organic solvents (e.g. benzene, ethanol, ether, and ligroin).	One reference states: "tetrachlorodinitroethane is toxic to mice at one-sixth the concentration for chloropicrin. It produces lachrymation in man at one-eighth the concentration that chloropicrin does. It is not stable when exploded in a three-inch shell, but would probably stand up satisfactorily if dissolved in chloropicrin." [126].

Name and CAS number	Physical state	Notes	Physiological effect
Phenylimidocarbonyl chloride  *Synonyms*: Green Cross I, K-Stoff, phenyl carbylamine chloride; phenylimido-phosgene CAS 622-44-6	Pale yellow liquid with onion-like odour. Bp 209-212 °C	From reaction of chlorine with phenyl isothiocyanate; 4- and 2,4-dichlorinated products that co-form have similar properties, but are less irritant. The phenylimidocarbonyl chloride is obtained by distillation. Used during World War I in projectiles with sulfur mustard to mask garlic odour of the latter. Insoluble in water and soluble in most organic solvents. Persistent.	The property of producing in animals corneal ulcers, which do not, however, tend to permanent blindness, undoubtedly identifies the compound as the "blinding gas" of the period. Physiological symptoms mainly those from a mild lung irritant: nausea, sometimes vomiting, throat soreness, chest tightness, and stomach pain [127]. Cough and bronchitis develop later. Lachrymation is not prominent. Irritates the lung, nose, eyes and throat. 0.003 mg/l causes involuntary weeping and ~0.8 mg/l for 1-2 min harms respiratory organs, and 3 mg irritates [9]. Limit of insupportability is 30 mg/m³ in air. Mortality product is 3000-5000 for 10 min exposure.
Phosgene oxime  *Synonyms*: CX, Fosgen oksim, dichloroformoxime CAS 1794-86-1	White solid with a penetrating odour Mp 40 °C Bp 129 °C dec.	From trichloronitromethane and hydrochloric acid. One of the most violent irritants known. Extremely unstable though and unlikely to be used militarily. Soluble in water and only slowly hydrolysed.	Solid or liquid (melted or dissolved in organic solvents) has a severe destructive and burning action on lung, skin and eyes [128]. Inhalation toxicity similar to phosgene. Skin contact causes immediate itching and pain. Vapour in the eye causes immediate lachrymation. Corneal damage develops over 24 h and dims vision. Irritating concentration Ct is 0.17 mg min/m³ and intolerable Ct is 3 mg min/m³. Lowest irritant concentration after a 10 s exposure is 1 mg/m³ [9]. Effects become unbearable after 1 min at 3 mg/m³. Estimated LCt_{50} is 3200 mg min/m³.
Methyl chloroformate  *Synonyms*: none found CAS 79-22-1	Colourless liquid with irritating odour Bp 71 °C	Available commercially. Used in World War I mixed with other chemicals [9]. Because of its strongly irritant properties it has been used in insecticidal preparations, e.g. in "Zyklon B" with hydrocyanic acid. Hydrolysed readily by cold water.	Powerful lachrymator [99]. Causes severe skin burns and eye damage. Harmful if swallowed and in contact with the skin, and fatal if inhaled.
Chloromethyl chloroformate  *Synonyms*: K Stoff, Palite CAS 22128-62-7	Colourless liquid with an irritating odour Bp 107 °C	Commercially available. A mixture with dichloromethyl chloroformate was used in World War I under the name "K Stoff" and "Palite" [9]. Hydrolysed readily by cold water.	Powerful lachrymator [9]. Minimum concentration producing lachrymation is 2 mg/m³ of air. Limit of insupportability is 50 mg/m³ of air. Causes severe skin burns and damage, and toxic if inhaled [99].

Name and CAS number	Physical state	Notes	Physiological effect
Dichloromethyl chloroformate  *Synonyms*: K Stoff, Palite CAS 22128-63-8	Colourless liquid with an intensely irritating odour Bp 110 °C	Commercially available. Used mixed with chloromethyl chloroformate in World War I under name of "K Stoff" and "Palite" [9]. Hydrolysed readily by cold water.	Less irritating than methyl chloroformate, but more toxic. Limit of insupportability is 75 mg/m³ of air.
Trichloromethyl chloroformate  *Synonyms*: diphosgene, Perstoff CAS 503-38-8	Colourless liquid with a smell of new mown hay Bp 127-128 °C	Not easily hydrolysed by water and therefore semi-persistent.	Action similar to phosgene. Lethal on inhalation, causing cough, lachrymation, chest pain, difficulty breathing, and delayed lung damage. Effects appear in 0-24 h depending on dose. LCt_{50} is 3200 mg min/m³ (same as phosgene). Vapour heavier than air and remains in low-lying areas. Inhalation toxicity is cumulative [9]. No effect on skin.
Bis(trichloromethyl) carbonate  *Synonyms*: triphosgene CAS 32315-10-9	White solid Mp 78-79 °C Bp 205-206 °C	Not easily hydrolysed by cold water and therefore semi-persistent [99].	Irritant vapour but physiological action similar to phosgene. Lethal upon inhalation, causing cough, lachrymation, chest pain, difficulty breathing, and delayed lung damage. Effects appear in 0-24 h depending on dose. LCt_{50} is 3200 mg min/m³ (same as phosgene) [8].
Methyldichloroarsine $MeAsCl_2$ *Synonyms*: methyl dick, MD, Medikus CAS 593-89-5	Colourless volatile liquid with a burning odour Bp 132-133 °C	Probably used in World War I in small quantities [9]. Hydrolysed rapidly by water.	Liquid and vapour irritate eyes, respiratory tract and damage the lung [129]. Exposure of skin to vapour and liquid may produce severe blistering. Inhalation of vapour and liquid may lead to systemic toxicity and death. Can cause irreversible corneal damage. Lower limit of irritation is 2 mg/m³ of air [9]. Maximum concentration a normal person can breathe for no more than 1 min is 25 mg/m³ of air. Vapour has a vesicant action akin to sulfur mustard that presents several hours after exposure.
Ethyldichloroarsine $EtAsCl_2$ *Synonyms*: ethyl dick, ED CAS 598-14-1	Colourless liquid with a fruity but biting and irritating odour Bp 153 °C	Widely used in projectiles in World War I as a volatile agent with a short duration of effectiveness that acted more quickly than diphosgene or sulfur mustard. It was used as a delayed casualty agent that caused vomiting and blistering [9]. Hydrolysed rapidly by water.	Extremely irritating action on nose, eyes, and throat, and causes painful skin wounds [129]. Vapour causes profound respiratory difficulties, faintness, prolonged paralysis, and anaesthesia of extremities. Minimum concentration capable of perceptible irritant action is 1.5 mg/m³ of air [9]. Maximum concentration supportable by a human for ~1 min is 5-10 mg/m³. Vesicant action on skin is perceptible at 1 mg/m³. ICt_{50} and LCt_{50} are 25 and 3000-5000 mg min/m³ [9].

Name and CAS number	Physical state	Notes	Physiological effect
Phenyldichloroarsine  *Synonyms*: dichlorophenylarsine, PD, Pfiffikus, Sternite CAS 696-28-6	Colourless liquid that gradually turns yellow Bp 255 °C	Used in World War II and often found in abandoned "Red Canister" munitions [130].	Instant irritation and pain in eyes, nose, throat and respiratory tract. Effects include sneezing, coughing, salivation, nasal congestion, and suffocation. These persist 5-20 min after retreat. It also produces systemic effects: headache, perspiration, chills, nausea, vomiting, cramps, and depression, malaise and misery. These symptoms appear ~30 min after exposure and persist for several hours. 1.0-2.5 mg/m³ irritates nose and throat; 50 mg/m³ intolerable in 30 s [129]. ICt_{50} is 16 mg min/m³ as vomiting agent and 0 mg min/m³ as vesicant [9]. LCt_{50} is 2600 mg min/m³. Maximum concentration a human can support for ~1 min is 16 mg/m³ of air [9].
Diphenylchloroarsine (DA)  *Synonyms*: Clark I CAS 712-48-1	White solid Mp 41-45 °C Bp 333 °C dec.	Used in World War II and caused surprise as it was able to penetrate the respirators then in use [9]. Nowadays found in abandoned "Red Canister" munitions [130].	Produces irritation, burning and pain in the eye, nose, throat and respiratory tract. Effects include sneezing, coughing, salivation, congestion, and suffocation [9,129]. 1.5-2.5 mg/m³ irritates nose and throat; 50 mg/m³ is intolerable in 30 s. ICt_{50} for man is 22-150 mg min/m³ and LCt_{50} at 13,000 mg min/m³. Also produces systemic effects: headache, perspiration, chills, nausea, vomiting, cramps, depression and malaise. Systemic effects start about 30 min after the beginning of exposure and persist for several hours. Solid and liquid material can cause small blisters on the skin. Ingestion may cause severe injury and death.
Diphenyl cyanoarsine (DC)  *Synonyms*: Clark II CAS 23525-22-6	White solid with odour of garlic/bitter almonds Mp 32-35 °C Bp 377 °C calc. [9]	Used towards the end of World War II alone and mixed with diphenyl chloroarsine [9]. Found in abandoned "Red Canister" munitions [130]. Combustible vapours can form an explosive mixture with air.	Irritates nose and provokes sneezing. Inhalation, ingestion or skin contact may cause severe injury or death. Minimum concentration detectable by odour is 0.005-0.010 mg/m³ of air [9]. A human can tolerate a maximum concentration of 0.25 mg/m³ for no more than 1-2 min. ICt_{50} 30 mg min/m³ for a 30 s exposure and LCt_{50} 10,000 mg min/m³. Nearly impossible to build up a vapour concentration of DC that would be lethal in a short time.

Name and CAS number	Physical state	Notes	Physiological effect
10-Chloro-5,10-dihydrophenarsazine  *Synonyms*: Adamsite, DM CAS 578-94-9	Bright yellow crystalline solid Mp 195 °C Bp 410 °C calc. [9]	Used in World War I [9]. Insoluble in water and difficultly soluble in many organic solvents. When heated it forms an inflammable odourless vapour that is invisible except near the source. Non-persistent [7].	Produces sneezing, burning and aching pain in chest, throat, nose, and gums in 0-5 min [7,16,17]. Recovery usually rapid, but irritant effects may increase for several mins in fresh air. Systemic effects: headache, perspiration, chills, nausea, vomiting, cramps [17]. These start ~30 min after the beginning of exposure and persist for several hours [129]. 0.1-2.5 mg/m³ irritates nose and throat, 50 mg/m³ is intolerable in 30 s. ICt_{50} is estimated as 22-150 mg min/m³ and LCt_{50} as 13,000 mg min/m³. Hydrolyses in body to phenarsazine oxide which is hepatotoxic to rats [131].
10-Chloro-5,10-acridarsine  *Synonyms*: Excelsior CAS 25093-02-1	Pale yellow solid Mp 110 °C	Potent sternutator and analogue of Adamsite developed during World War II and researched afterwards [132].	Potent skin irritant [133] and 10 times as active as diphenylcyanoarsine. 2 mg/m³ is intolerable after 1 min. Human toxicology apparently has not been studied (no information was found); the compound is expected to have systemic toxicity like other arsenicals. Dust in air causes severe irritancy of the face, the lips and the tongue [133-135].
5(10H)Acridarsinecarbonitrile  *Synonyms*: Arsacridine cyanide CAS 23395-81-5	White solid Mp 115 °C	Researched as a sternutator after World War II like Excelsior [132].	A sensory irritant more powerful than its 10-chloro analogue Excelsior.
Trialkyl lead salts $XPbR_3$ R = Me, Et, *n*-Pr X = acid group e.g. $MeC_6H_4SO_2NH$ CAS various numbers	White solids	Study of the sternutatory properties of organolead salts was conducted during World War II [136-142]. Those having the generic structure shown left produced sternutation.	Irritated nose, throat and chest of human volunteers in chamber trials. Activity decreased R = n-Pr > Et > Me and potent compounds were obtained when X was a group derived from an organic acid. Sternutation wore off rapidly on retreating from a contaminated atmosphere. Lead salts cause neurological damage. Triethyl lead fluoroacetate $FCH_2CO_2PbEt_3$ has sternutatory and convulsant action; it is poisonous [136-142].

Name and CAS number	Physical state	Notes	Physiological effect
Piperine  *Synonyms*: (2*E*,4*E*)-5-(benzo[*d*][1,3]di-oxol-5-yl)-1-(piperidin-1-yl)penta-2,4-dien-1-one, piperoylpiperidine, bioperine CAS 94-62-2	Beige-yellow solid Mp 130 °C	Principal irritant occurring naturally in black pepper, used as a spice throughout the world [143,144].	Irritates nose to provoke sneezing and throat to cause coughing. Its irritant action has been linked to its ability to activate both TRPA1 and TRPV1 receptors [143,144]. Although it is a less potent agonist of the human TRPV1 receptor than capsaicin, it has approximately two-fold greater efficacy for this receptor than capsaicin [143]. Toxicology in humans by aerosol route does not appear to have been reported.

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