

**THE UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND****THE TREATMENT OF SALTS OF SCHEDULED CHEMICALS WITHIN THE SCHEDULES TO THE CHEMICAL WEAPONS CONVENTION****1. Executive Summary**

- 1.1 Salts are chemical compounds produced by the action of an acid on a free base (a neutral, uncharged form of a chemical). For example, the nitrogen mustard HN2 is a free base, whereas HN2 hydrochloride is a salt of this compound. A number of salts are specifically included within the Schedules to the Chemical Weapons Convention (hereinafter “the Schedules”), and are therefore liable for declaration or verification under the terms of the Verification Annex to the Chemical Weapons Convention (hereinafter, “the Verification Annex”). No other salts of scheduled chemicals are subject to the provisions of the Verification Annex. However, a number of chemicals included within the Schedules are unstable: many of these chemicals are not usually manufactured, traded or stored as the free base (that is, the form listed within the Schedules), but as the salt form. In these cases, where the salts of the scheduled chemical are not scheduled themselves, significant amounts of such chemicals could be produced and retained, including for misuse as chemical weapons, without any requirement for declaration or inspection under the Chemical Weapons Convention (hereinafter “the Convention”).
- 1.2 We believe that consideration should now be given, on a case by case basis, to salts of particular scheduled chemicals, to determine whether further action needs to be taken to include any of them within the Schedules. It is now timely for States Parties to work together to agree a common approach which reflects the realities of the chemical industry and provides the best practical means to ensure appropriate transparency for additional salts of scheduled chemicals, where this is justified.
- 1.3 We propose that States Parties work together to develop methods to provide transparency of activities relating to such salts under the provisions of the Verification Annex, where no transparency currently exists. Any potential solutions must ensure that legitimate usage of such compounds is not hindered. It is recommended that the first task should be to examine the salts of the Schedule 1 A chemicals saxitoxin and the nitrogen mustards, because – unlike most other unscheduled salts of Schedule 1 chemicals - they are a potential threat to the object and purpose of Article VI and Part VI of the Verification Annex, and they are legitimately produced and traded.



The nitrogen mustards were historically produced in large quantities and subsequently weaponised by a number of nations during World War II, whilst saxitoxin has been in the past weaponised (albeit in small quantities for covert use) by at least one nation. The salts of both chemicals are used for medical applications, albeit in small amounts.

## 2. Preface

- 2.1 Salts of organic compounds are discrete chemicals in their own right, and thus can be assigned separate Chemical Abstract Service (hereinafter “CAS”) numbers from their free base (that is, neutral) forms. Salt forms may be produced in preference to the free base because of their increased stability, enabling long-term storage to take place, or because of their increased solubility in specific (polar) solvents. They can be readily converted back to the free base form as required. The salt of a free base of a chemical can often be readily generated through the reaction of the free base with an acid.
- 2.2 A number of salts are specifically identified within the Schedules for declaration and verification purposes, along with their corresponding free bases.<sup>1</sup> However, in many entries, only the free base form of a chemical is listed. The misuse of any unlisted salts of scheduled chemicals (or indeed any other toxic chemical or precursor) is of course prohibited by the Convention. But, in our view, such salts would not be liable to declaration or verification under the provisions of the Verification Annex.
- 2.3 This paper discusses whether the exclusion of certain salts of scheduled chemicals from verification may reduce confidence in the verification regime under Article VI of the Convention. We propose that States Parties carry out a detailed technical study of salts of relevance to the Convention as a matter of priority, to enable potential ways forward to be formulated and agreed.

## 3. Salts and schedules

- 3.1 Schedules 1 and 2 contain specific reference both to the free bases of certain chemicals, and also to their protonated<sup>2</sup> and/or alkylated<sup>3</sup> salts. It is therefore clear that these particular salts are included within the Schedules, and must be subject to verification in the same way as their free bases. However, there are other instances in the Schedules where only the free base of a particular chemical is included. Because some Schedule entries explicitly cover particular salts, the assumption could be made that all other salts of scheduled chemicals were considered and intentionally omitted by the negotiators. However, it is not certain that this was the case: although we are

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<sup>1</sup> Those entries within the Schedules specifically noting salts are as follows: Sch. 1 A (3) O-Alkyl (H or  $\leq C_{10}$ , incl. cycloalkyl) S-2-dialkyl (Me, Et, n-Pr or i-Pr)-aminoethyl alkyl (Me, Et, n-Pr or i-Pr) phosphonothiolates and corresponding alkylated or protonated salts, Sch. 1 B (10) O-Alkyl (H or  $\leq C_{10}$ , incl. cycloalkyl) O-2-dialkyl (Me, Et, n-Pr or i-Pr)-aminoethyl alkyl (Me, Et, n-Pr or i-Pr) phosphonites and corresponding alkylated or protonated salts, Sch. 2 A (1) Amiton: O,O-Diethyl S-[2-(diethylamino)ethyl]phosphorothiolate and corresponding alkylated or protonated salts, Sch. 2 (B) 10 N,N-Dialkyl (Me, Et, n-Pr or i-Pr) aminoethyl chlorides and corresponding protonated salts, Sch. 2 B (11) N,N-Dialkyl (Me, Et, n-Pr or i-Pr) aminoethane-2-ols and corresponding protonated salts (with the exemptions of N,N-Dimethylaminoethanol and corresponding protonated salts, and N,N-Diethylaminoethanol and corresponding protonated salts), Sch. 2 B (12) N,N-Dialkyl (Me, Et, n-Pr or i-Pr) aminoethane-2-thiols and corresponding protonated salts.

<sup>2</sup> A protonated salt is the product of a reaction of a free base with an acid, resulting in the addition of a hydrogen atom and an associated negatively-charged ion to the free base, e.g. the hydrochloride salt of nitrogen mustard. Such reactions are easily reversible.

<sup>3</sup> An alkylated salt is the product of a reaction of a free base with an organic compound, resulting in the addition of an alkyl group (a group that contains a carbon atom) and its associated negatively-charged ion to the free base, e.g. the methyl iodide salt of nitrogen mustard. Such reactions are easily reversible.

aware that specific salts of certain chemicals were discussed, it is not clear that such consideration was made for all salts of all scheduled chemicals. The majority of States Parties, including the United Kingdom, have based their implementation of the Verification Annex on the premise that the verification regimes for scheduled chemicals should not be assumed to apply to their corresponding salts when these are neither explicitly listed within the Schedules as discrete chemicals, nor included within the generic descriptors of scheduled ‘families’ of chemicals.

- 3.2 Salts are in general very stable, easily stored, and easily converted to the free base. For example, the free base of the nitrogen mustard HN2 can be simply regenerated from the hydrochloride salt through addition of an alkali such as sodium carbonate. Equally simply, the hydrochloride salt of HN2 can be produced by adding hydrochloric acid to a solution of the HN2 free base. Because of this ease of conversion, salts could thus be regarded as ‘precursors’ to their free bases.
- 3.3 Salts also often retain many of the key characteristics of the free base, with broadly similar toxicities and chemical properties. For some scheduled chemicals with a commercial application, it is the salt form of the chemical that is traded and stored because the free base is relatively unstable. If there was an intention to misuse one of the relatively unstable scheduled chemicals for offensive purposes, then it would most likely be in the salt form; even if the salt was not used directly for weapons purposes, then at least it would be used for acquisition, transfer and/or storage, prior to regeneration and use of the free base as a weapon.
- 3.4 It can therefore be argued that it would be prudent to treat automatically all salts of scheduled chemicals in the same fashion as the free bases – i.e. to apply the same restrictions, declaration and verification protocols to them as to those salts explicitly included within the Schedules. Indeed, the Scientific Advisory Board has taken the view that “*there should be no differentiation in the treatment under the Convention of a free base and its corresponding salts*”.<sup>4</sup> We do not agree with this view: because the circumstances surrounding each salt are particular to that chemical, such a generalisation should not be made. However, we believe that salts of scheduled chemicals should be addressed on a case-by-case basis to determine whether further action needs to be taken to bring any additional specified salts unequivocally within the ambit of the Verification Annex.
- 3.5 It is now timely for States Parties to work together to agree a common approach which reflects the realities of the chemical industry and public health concerns, and provides the best practical means to ensure appropriate transparency for additional salts of scheduled chemicals which represent a potential risk to the verification regime. It is important to avoid States Parties taking an uneven approach to the verification of salts under the Verification Annex because this reduces confidence in the Convention. Because, unlike most other unscheduled salts of scheduled chemicals, they represent a potential threat to the object and purpose of Article VI of the Convention and Part VI of the Verification Annex, and because they are legitimately produced and traded, it is proposed to deal first with the salts of the nitrogen mustards and saxitoxin, which are Schedule 1 A chemicals. These are discussed below.

#### **4. Saxitoxin**

- 4.1 Saxitoxin, a Schedule 1A chemical, has in the past been weaponised in small quantities for use in covert operations. However, saxitoxin preparations have legitimate medical and diagnostic uses, including as a test standard during the identification of paralytic shellfish poisoning. This use was recognised by a Technical Amendment to the Convention in 1999. As a special case within Schedule 1, States Parties are permitted to transfer 5 mg or less of saxitoxin to other States Parties for medical/diagnostic purposes, without giving advance notification to the Technical Secretariat (Verification Annex, Part VI, paragraph 5bis).
- 4.2 The entry for saxitoxin in Schedule 1 makes no reference to salt forms: the CAS number provided in fact denotes the free base saxitoxin hydrate, otherwise known as saxitoxin or STX. However, STX itself is unstable, and is rarely traded or used. Because of the inherent instability of STX, many manufacturers trade only in either the dihydrochloride or acetate salts, neither of which are listed within the Schedules, and which are therefore not liable for declaration or routine verification. One manufacturer has publicly stated that it trades in saxitoxin in these salt forms because of the lack of regulations placed upon them, because supply to non-States Parties is then possible and export permits are not required for transfers.<sup>5</sup>
- 4.3 Although the trade in saxitoxin salts is for legitimate research, medical and diagnostic purposes, and involves very small quantities which could not realistically be misused for weapon purposes, this interpretation of the Schedule entry could allow procurement of significant amounts of saxitoxin salts without any requirement for declaration or inspection under the Convention. This is of particular concern since saxitoxin could be used as a weapon in its salt forms, without the need to convert to the free base.
- 4.4 We therefore suggest that potential mechanisms for capturing appropriate salts of saxitoxin within the Schedules should be addressed by States Parties as a matter of priority, with initial focus placed on those salts which have the widest commercial applications (i.e. the hydrochloride and acetate salts). Inclusion of those saxitoxin salts of greatest concern within the Schedules would ensure that further transparency regarding the development, production, acquisition, stockpiling, retention or transfer of an important toxic chemical is provided to States Parties. However, it would also be important in doing so to minimise the potential impact of any action on the public health needs of both States Parties and States not Parties.

#### **5. Nitrogen mustards**

- 5.1 Nitrogen mustards are included in Schedule 1 A (6), with the three chemicals HN1, HN2 and HN3 specifically listed. Each of the nitrogen mustards was investigated as a chemical weapon during World War II by a number of nations: HN1 and HN3 have both been manufactured on a large scale for weapons purposes, and weaponisation of HN3 has been carried out.

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Certified Reference Materials Program of Canada, CRMP Update October 1999, [http://www.imb.nrc.ca/crmp/upoct9\\_f.html](http://www.imb.nrc.ca/crmp/upoct9_f.html)

- 5.2 The Schedules make no mention of the salts of nitrogen mustards: it is thus implicit that the regime for Schedule 1 chemicals (Verification Annex, Part VI) should be applied only to the free bases of the three specified compounds, rather than to their salts. However, the free bases of nitrogen mustards are unstable, and for practical purposes are generally manufactured and stored as the hydrochloride salts, which are relatively stable. Other similarly stable salts can readily be produced. The hydrochloride and other salts have toxic and vesicant properties similar to those of the free bases, and can be readily reconverted to the free base forms. None of the salt forms is likely to be chosen as a weapon fill, because a salt would be more difficult to disseminate than the free base. However, salt forms could be acquired, transferred and/or stored, before conversion to the free base either prior to weaponisation or during delivery of a binary weapon.
- 5.3 As with saxitoxin, certain salts of the nitrogen mustards have legitimate medicinal uses. The hydrochloride salts of both HN2 and HN3 are used as chemotherapy drugs, particularly for the treatment of Hodgkin's disease, non-Hodgkin's lymphoma and some types of chronic leukaemia. Currently, such salts can be freely produced by and transferred between both States Parties and States not Parties perfectly legitimately, outside the provisions of Part VI of the Verification Annex. Thus there are no opportunities to build transparency and confidence in the production and acquisition activities relevant to these salts of a Schedule 1 compound.
- 5.4 Again, we propose that States Parties give particular consideration to how the salts of nitrogen mustards could be brought within the scope of the Schedules. However, any potential solutions must take into account the impact on the small but important trade in, and use of, the hydrochloride salts of HN2 and HN3 in their role as cancer treatments, both for States Parties and for States not Parties.

## 6. Conclusions

We recommend that the States Parties carry out a review of the potential risk posed by non-scheduled salts of scheduled chemicals to confidence in the verification provisions of the Convention. For those salts regarded as being of the highest risk to the object and purpose of the verification regime under Article VI of the Convention, States Parties should work together to propose potential ways to provide transparency of activities with such salts under the provisions of the Verification Annex, where no transparency currently exists, whilst ensuring that legitimate usage is not hindered. It is recommended therefore that the first task should be to examine the salts of the Schedule 1 A chemicals saxitoxin and the nitrogen mustards, with particular emphasis placed upon those salts which are traded world-wide for wholly legitimate pharmaceutical and research purposes. Such salts should be addressed as a priority, both because of the potential threat they pose to the verification regime and to the Convention as a whole, and because they are legitimately produced and traded. Any measures proposed should ensure that their important medical applications are recognised within the Convention and allowed to continue.