



European Monitoring Centre
for Drugs and Drug Addiction

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EMCDDA

RISK ASSESSMENTS

Report on the risk assessment of
2C-I, 2C-T-2 and 2C-T-7 in the framework
of the joint action on new synthetic drugs

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European Monitoring Centre
for Drugs and Drug Addiction

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Information on the EMCDDA can be found on its website (<http://www.emcdda.eu.int>).

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Foreword

It gives me particular pleasure to present the results of the risk assessment undertaken by the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) on three substances: 2C-I (2,5-dimethoxy-4-iodophenethylamine), 2C-T-2 (2,5-dimethoxy-4-ethylthiophenethylamine) and 2C-T-7 (2,5-dimethoxy-4-(n)-propylthiophenethylamine). The risk assessment was carried out under the terms of a joint action adopted on 16 June 1997 by the Council of the European Union (1).

The meeting to assess the risks of 2C-I, 2C-T-2, 2C-T-7 was convened under the auspices of the Scientific Committee of the EMCDDA and was held on 31 March and 1 April 2003 at the Centre's headquarters in Lisbon. The meeting produced formal reports on the risk assessments, which were adopted the same day. As foreseen in the joint action, the reports were submitted without delay to the European Commission and to the Greek Presidency of the horizontal working party on drugs (HWPDP) of the Council of the EU for further action.

As a result, on 27 November 2003, the Council adopted the decision (2) to submit 2C-I, 2C-T-2 and 2C-T-7 to control measures and criminal penalties in the 15 EU countries. The Council decision stipulates that, within three months, Member States shall introduce the necessary measures into their national law, in compliance with their obligations under the 1971 United Nations Convention on Psychotropic Substances.

Such a concrete result at a political level confirms the effectiveness of the rapid-response mechanism provided by the joint action on new synthetic drugs. It is also encouraging to see the strong cooperation that has developed over the last years between the EMCDDA and its institutional partners involved in the risk assessment process, including the European Police Office (Europol), the European Agency for the Evaluation of Medicinal Products (EMA) and the European Commission. In particular, I would like to underline the excellent work done by the EMCDDA's early-warning system via the Reitox network of national focal points and through Europol's national units. The dedication of all partners will be crucial in the

(1) Joint action concerning the 'information exchange, risk assessment and the control of new synthetic drugs' (OJ L 167, 25.6.1997). A joint action is a decision adopted unanimously by the EU Member States within the framework of the third pillar of the Treaty on European Union (cooperation in the field of justice and home affairs). Synthetic drugs are psychoactive substances produced in laboratories and not derived from natural products. They include 3,4-methylenedioxy-N-methylamphetamine (MDMA, 'ecstasy'), other amphetamines and lysergic acid diethylamide (LSD).

(2) OJ L 321, 6.12.2003, pp. 64–65.

successful implementation of the new Council decision proposed by the Commission to replace the 1997 joint action on new synthetic drugs. This initiative is directly related to the outcome of the external evaluation of the joint action undertaken by the Commission as stipulated by the European Union action plan on drugs 2000–04. The new legal instrument aims to clarify the definitions and procedures and extend the scope to all new synthetic drugs and all new narcotic drugs alike.

I would like to thank all those who participated in the risk assessment process for 2C-1, 2C-T-2 and 2C-T-7 for the high quality of the work carried out. This makes a valuable scientific contribution, validated at a European level, and, as such, gives proven support to political decision-making.

Georges Estievenart

Executive Director, EMCDDA

Abbreviations

2C-B	2,5-dimethoxy-4-bromophenethylamine
2C-H	2,5-dimethoxyphenethylamine
2C-I	2,5-dimethoxy-4-iodophenethylamine
2C-T	2,5-dimethoxy-4-methylthiophenethylamine
2C-T-2	2,5-dimethoxy-4-ethylthiophenethylamine
2C-T-7	2,5-dimethoxy-4-(n)-propylthiophenethylamine
ACTH	adrenocorticotrophic hormone
ALEPH-2	2,5-dimethoxy-4-ethylthioamphetamine
bpm	beats per minute
DOB	2,5-dimethoxy-4-bromoamphetamine
DOM	2,5-dimethoxy-4-methylamphetamine
GHB	gamma-hydroxybutyrate
5-HT	5-hydroxytryptamine (serotonin)
i.p.	intraperitoneal
i.m.	intramuscular
i.v.	intravenous
LSD	lysergic acid diethylamide
MAO	monoamine oxidase
Mescaline	3,4,5-trimethoxyphenethylamine
MDMA	3,4-methylenedioxy-N-methylamphetamine
4-MTA	4-methylthioamphetamine
SSRI	selective serotonin reuptake inhibitor
TMA-2	2,4,5-trimethoxyamphetamine



Introduction

Since the adoption by the Council in June 1997 of the joint action on the information exchange, risk assessment and control of new synthetic drugs, 2C-I (2,5-dimethoxy-4-iodophenethylamine), 2C-T-2 (2,5-dimethoxy-4-ethylthiophenethylamine) and 2C-T-7 (2,5-dimethoxy-4-(n)-propylthiophenethylamine) are the sixth, seventh and eighth substances to be subjected to risk assessment.

2C-I, 2C-T-2 and 2C-T-7 are among the numerous 'new synthetic drugs' with no legitimate therapeutic use that are described in Shulgin's *Pihkal* (Shulgin and Shulgin, 1991). All three compounds have the structural characteristics of phenethylamines, which are associated with stimulant and hallucinogenic actions and, therefore, seem to be comparable to substances already classified in the schedules of the 1971 United Nations Convention on Psychotropic Substances, such as 2C-B (4-bromo-2,5-dimethoxyphenethylamine, as listed in Schedule II).

The specific scientific risk assessments of 2C-I, 2C-T-2 and 2C-T-7 have been extremely difficult due to the lack of peer-reviewed scientific data. However, information based on analogy to partially related compounds such as 2C-B (phenethylamine-based) and DOB (amphetamine-based), both involving bromine as opposed to sulphur, as well as evidence from other information sources such as individual user reports, provided the basis for the assessments. It is worth noting that it was deemed inappropriate to compare data derived from MDMA, PMA and 4-MTA studies, because of the absence of 2,5-dimethoxy substituent groups in these compounds.

An overview of the pharmacology, toxicology, clinical experience and individual health and psychological risks of 2C-I, 2C-T-2 and 2C-T-7 use was compiled by Simon Elliott, Senior Clinical Scientist at the Regional Laboratory for Toxicology, Birmingham. This overview was further extended by a review, completed by the EMCDDA and Europol, on the pharmacotoxicological, sociological and criminological information available about the three substances.

The members of the Scientific Committee of the EMCDDA, extended with experts nominated by the Member States and representatives of the European Commission, Europol and the EMEA, met in Lisbon on 31 March 2003 to examine the health

and social risks of 2C-I, 2C-T-2 and 2C-T-7 as well as the possible consequences of prohibition. The conclusions and recommendations of the risk assessment reports were prepared and adopted on 1 April 2003. Based on the conclusions of the reports, the Council decided to adopt a decision making 2C-I, 2C-T-2 and 2C-T-7 the subject of control measures in the EU Member States, as provided for under Schedules I and II of the 1971 UN Convention on Psychotropic Substances.

In the light of the risk assessments carried out since 1998, the Scientific Committee's sub-committee on synthetic drugs came to the following conclusions: the decision to have a molecule assessed often implies a lack of scientific data about its toxicity as well as its dependence potential or its implication in social disturbances; however, lack of scientific data does not guarantee that the molecule is not harmful. A principle of precaution should therefore be the rule when only limited data are available.

The Scientific Committee of the EMCDDA is aware of how difficult it is to obtain scientific data on a new drug and is currently reflecting, in the framework of its sub-committee on synthetic drugs, on the possibility of proposing an emergency temporary scheduling of the identified substance in order to allow time for collecting sufficient scientific information. However, such a proposal could only be discussed within the perspective of a new Council decision modifying the current joint action on new synthetic drugs. Meanwhile, despite its limitations, the provisions of Article 4 of the joint action have been implemented for the risk assessment of 2C-I, 2C-T-2 and 2C-T-7.

As Chairperson and Vice-Chairperson of the Scientific Committee, we would like to express our gratitude to our colleagues on the Scientific Committee as well as to the staff of the EMCDDA, in particular Alain Wallon, Lena Westberg, Deborah Olszewski and Roumen Sedefov, who worked hard before, during and after the meetings to finalise the reports in order to provide detailed and precise conclusions and ensure a speedy completion of the project. We hope that all these efforts will be appreciated by those to whom this report is addressed.

Salme Ahlström and Jean-Pol Tassin

Chairperson and Vice-Chairperson, Scientific Committee of the EMCDDA

Council decision

Council Decision 2003/847/JHA of 27 November 2003 concerning control measures and criminal sanctions in respect of the new synthetic drugs 2C-I, 2C-T-2, 2C-T-7 and TMA-2

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty of the European Union,

Having regard to Council Joint Action 97/396/JHA of 16 June 1997 concerning the information exchange, risk assessment and the control of new synthetic drugs ⁽¹⁾, and in particular Article 5(1) thereof,

Having regard to the initiative of the Italian Republic,

Whereas:

- (1) Risk assessment reports on 2C-I (2,5-dimethoxy-4-iodophenethylamine), 2C-T-2 (2,5-dimethoxy-4-ethylthiophenethylamine), 2C-T-7 (2,5-dimethoxy-4-(n)-propylthiophenethylamine) and TMA-2 (2,4,5-trimethoxyamphetamine) were drawn up on the basis of Article 4(3) of Joint Action 97/396/JHA at a meeting convened under the auspices of the Scientific Committee of the European Monitoring Centre for Drugs and Drug Addiction.
- (2) 2C-I, 2C-T-2, 2C-T-7 and TMA-2 are amphetamine derivatives having structural features of phenethylamines, which are associated with hallucinogenic and stimulant activity. 2C-I, 2C-T-2, 2C-T-7 and TMA-2 have not been reported to be associated with fatal or non-fatal intoxication within the Community. However, 2C-I, 2C-T-2, 2C-T-7 and TMA-2 are hallucinogenic drugs that carry potential risks common to other hallucinogenic substances such as 2C-B, DOB, TMA and DOM, already classified in Schedules I or II to the 1971 United Nations Convention on Psychotropic Substances. Therefore a risk of acute or chronic toxicity cannot be excluded.
- (3) 2C-I, 2C-T-2, 2C-T-7 and TMA-2 are not currently listed in any of the schedules to the 1971 United Nations Convention on Psychotropic Substances.

⁽¹⁾ OJ L 167, 25.6.1997, p. 1.

- (4) At present, 2C-I and 2C-T-2 are controlled under the national drugs legislation in five Member States; 2C-T-7 and TMA-2 are controlled in four Member States.
- (5) 2C-I, 2C-T-2, 2C-T-7 and TMA-2 have no therapeutic value or industrial use.
- (6) 2C-I has been identified in four Member States; 2C-T-2 and 2C-T-7 have been identified in six Member States; TMA-2 has been identified in five Member States. At present one Member State has reported one case of international trafficking of 2C-T-2 involving two Member States; no international trafficking of 2C-I, 2C-T-2 and TMA-2 has been reported. Laboratories involving the production of 2C-I, 2C-T-2, 2C-T-7 and TMA-2 have been seized in three Member States. In one of these Member States, the seizure of a large amount of the intermediate precursor 2C-H and documentation suggests the production of 2C-I. The major chemical precursors of 2C-I, 2C-T-2, 2C-T-7 and TMA-2 are commercially available.
- (7) 2C-I, 2C-T-2, 2C-T-7 and TMA-2 should be subjected by the Member States to control measures and criminal penalties, as provided for under their legislation complying with their obligations under the 1971 United Nations Convention on Psychotropic Substances with respect to substances listed in Schedules I or II thereto,

HAS DECIDED AS FOLLOWS:

Article 1

Member States shall take the necessary measures, in accordance with their national law, to submit 2C-I (2,5-dimethoxy-4-iodophenethylamine), 2C-T-2 (2,5-dimethoxy-4-ethylthiophenethylamine), 2C-T-7 (2,5-dimethoxy-4-(n)propylthiophenethylamine) and TMA-2 (2,4,5-trimethoxyamphetamine) to control measures and criminal penalties, as provided for under their legislation complying with their obligations under the 1971 United Nations Convention on Psychotropic Substances with respect to substances listed in Schedules I or II thereto.

Article 2

Member States shall, in accordance with the third subparagraph of Article 5(1) of Joint Action 97/396/JHA, take the measures referred to in Article 1 within three months of the date on which this decision takes effect.

Within six months of the date on which this decision takes effect Member States shall inform the Secretariat General of the Council and the Commission of the measures they have taken.

Article 3

This decision shall be published in the *Official Journal of the European Union*. It shall take effect on the day following that of its publication.

Done at Brussels, 27 November 2003.

For the Council
The President
R. Castelli

Chapter 1

Report on the risk assessment of 2C-I in the framework of the joint action on new synthetic drugs

On 12 December 2002, the horizontal working party on drugs of the Council of the European Union decided that risk assessment of four new synthetic drugs, 2C-T-2, 2C-T-7, 2C-I and TMA-2, should be initiated. On 20 December 2002, in accordance with practice under the 1997 joint action, the Danish Presidency formally notified the EMCDDA of the decision of the HWPD to submit 2C-T-2, 2C-T-7, 2C-I and TMA-2 for risk assessment under Article 4 of the joint action on new synthetic drugs of 16 June 1997.

A meeting of the Scientific Committee of the EMCDDA, extended with experts nominated by the Member States and representatives of the European Commission, Europol and the EMEA, was held on 31 March to 1 April 2003 to assess the health and social risks of 2C-I as well as the possible consequences of its prohibition.

The meeting considered the following documents:

- i. Review of the pharmacotoxicological data for the risk assessment of 2C-I; report to the EMCDDA
- ii. Public health risks: epidemiological evidence; EMCDDA
- iii. Sociological/criminological evidence; EMCDDA
- iv. Europol contribution to the risk assessment on 2C-I

In conjunction with further information and comments from the expert participants, these documents formed the basis of the risk assessment which is reported below.

Chemical description

2C-I is 2,5-dimethoxy-4-iodophenethylamine. Other chemical names include: 4-iodo-2,5-dimethoxyphenethylamine, (2,5-dimethoxy-4-iodophenyl)-2-aminoethane and 4-iod-2,5-dimethoxyphenethylazan.

The synthesis of 2C-I is described in *Pihkal* (Shulgin and Shulgin, 1991), based on the initial use of 2,5-dimethoxybenzaldehyde to eventually produce a preliminary precursor, 2,5-dimethoxyphenethylamine (2C-H). The former compound 2,5-dimethoxybenzaldehyde is available commercially. The method is extensive, requiring specialist equipment and an appropriate environment. The exact method of synthesis used by clandestine laboratories is not known.

At present, 2C-I has no medical or industrial use.

Pharmaceutical description

2C-I is typically available in powder or tablet form, although 2C-I in liquid form has also been noted by the Danish focal point. A seized tablet was white in appearance, had an 'i' logo and was approximately 6.1 mm x 2.7 mm in size, weighing 120 mg (Denmark, 2002).

As 2C-I comes in powder or tablet form, the primary route of administration is oral. Neither insufflation (snorting) nor any other routes (e.g. intravenous administration) are mentioned in 2C-I user reports. Original studies by Shulgin involved oral administration of doses of 2C-I of 15 to 20 mg. User reports have mentioned oral doses of 3 to 25 mg (typically 20 mg).

Health risks

Individual health risks

Acute effects

Little scientific evidence related to the action of 2C-I on neurotransmitter systems has been published to date, so discussion of the neuropharmacological aspects at the risk assessment meeting was based on speculative comparison with partially related compounds such as 2C-B (based on phenethylamine) and DOB (based on amphetamine), both involving bromine as opposed to iodine.

Studies involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also

acted as a competitive 5-HT antagonist, but, at higher concentrations ($2.8 \times 10^{-5}M$), it acted as a non-competitive 5-HT antagonist. In addition, DOB (4-bromo-2,5-dimethoxyamphetamine) was found to have a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB.

A recent study found 2C-I to have higher agonistic efficacy at 5-HT_{2C} receptors compared to 5-HT_{2A} receptors. However, further studies will be required before definitive conclusions can be drawn.

There has been no other specific research conducted on 2C-I. Serotonin agonists stimulate hypothalamic neurons involved in ACTH and cortisol secretion, in addition to stimulating growth hormones and prolactin secretion (as evidenced by mescaline and DOM). It is possible, therefore, that 2C-I may produce similar effects on hormonal secretion.

There is also a small amount of subjective evidence available on the Internet regarding cardiovascular and thermoregulatory responses. However, these user surveys record a variety of responses to 2C-I use.

At present there are no animal or human data concerning general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-I. Only subjective evidence is available from limited user self-reports involving observations of some adverse effects and toxic symptoms. In general, although users have described 2C-I as 'powerful' and a 'strong stimulant' with hallucinogenic properties, there is virtually no mention of adverse effects such as nausea, vomiting or muscle cramps (as reported for 2C-T-2 and 2C-T-7) in users purporting to have taken only 2C-I. However, the nature of the reports suggests that this may be due to selective reporting rather than absence of such symptoms. However, some users report stomach tension, nausea, vomiting and jaw tension in instances of combining 2C-I with one or more of the following: 5-methoxy-dipropyltryptamine, cannabis, alcohol, caffeine, tryptophan, alprazolam and clonazepam. It has been noted by users of 2C-I that the desired effect may be delayed, sometimes resulting in users taking additional (sometimes higher) doses.

It appears that, unlike other phenethylamine derivatives (including 2C-B), 2C-I tablets do not usually contain other phenethylamines or stimulants, thus reducing the possibility of concomitant ingestion of other drugs in such illicit preparations. However, as the pharmacology of 2C-I is largely unknown, it is difficult to predict with accuracy any potential drug interactions or contraindications. Winter et al. studied the acute effects of monoamine reuptake inhibitors (SSRIs such as fluvoxamine, fluoxetine and venlafaxine) on the stimulatory effects of hallucinogens (including DOM) and observed an additivity of effects rather than a potentiation. It is possible, therefore, that similar effects may occur with 2C-I. Various users report concomitant use with other drugs but specific evidence is unclear. However, in some cases this has produced toxic effects (see above).

Anecdotal user evidence indicates the onset of initial action as being one to two hours after ingestion. However, some users report this as being longer compared to related drugs (e.g. 2C-B or MDMA). Effects are typically described as lasting for up to 10 hours post oral dose. This compares to eight to 12 hours for orally ingested LSD and 10 to 12 hours for mescaline, as reported by Shulgin.

Clinical effects

There have been no reported deaths or instances of non-fatal intoxication involving 2C-I. However, as with clinical toxicological investigations, the lack of reference material may compromise the analysis of post-mortem cases.

There have been no scientific studies involving 2C-I users. Limited subjective user reports indicate that 2C-I produces various psychedelic effects (generally comparable to other hallucinogens, particularly 2C-B) and feelings of empathy (similar to MDMA).

Isolated user reports compare 2C-I to 2C-B, due to an apparent similarity in their effects. However, some users describe the effects of 2C-I as being 'deeper, more purely psychedelic and less sensory' and, in some cases, less intense. As mentioned above, various users have reported delayed onset of the desired effects compared to related drugs (e.g. 2C-B or MDMA), which may result in additional doses or other drugs being taken, thus increasing the risk of toxicity or accidental overdose.

Dependence

No specific research has been performed to evaluate the potential of 2C-I to induce dependency in animals or humans. Although the exact pharmacology of 2C-I is unknown, speculative comparison with related compounds suggests it is unlikely to produce physical dependence or addiction. However, without any specific studies, definitive conclusions cannot be drawn.

Psychological effects

There are no published data on the specific psychological effects, acute or chronic, of 2C-I. As mentioned above, limited anecdotal reports describe the psychological effects of 2C-I experienced by users. Such reports mention a general clarity of thought, with little or no 'psychological after-effects'. However, some introspection and 'negative thought-loops' were described by a number of users.

Public health risks

Availability and quality of 2C-I on the market

2C-I has been identified in four Member States: Denmark, Germany, Sweden and the United Kingdom.

Information based on early-warning databases suggests that 2C-I is very rare. One tablet of 2C-I was seized in Denmark. This had an 'i' logo and so was probably not sold to users as ecstasy (MDMA).

Knowledge and perception of 2C-I among users

The level of awareness about 2C-I is generally negligible, except among small subgroups of experimenters who may use mescaline, DOB or 2C-B for particular effects. Due to the lack of research studies, the level of knowledge among these particular consumer subgroups (as can be seen on the Internet) appears to be more detailed than in the general scientific community. In the absence of accurate and regulated chemical analysis, objective scientific knowledge remains extremely limited. Major information sources are Internet sites and 'dance floor pharmacology' (an informal network whereby information passes from friend to friend). Despite warnings about the potential harm associated with using health information from the Internet, a systematic search of peer-reviewed literature found few reported cases of harm. This

may be due to an actual low risk for harm associated with the use of information available on the Internet, or to under-reporting of cases, or to bias.

Prevalence and patterns of use

Evidence of 2C-I use in the EU is very limited. Population surveys of young adults in the EU show that a range of 1 % in Finland to 12 % in the United Kingdom have 'lifetime prevalence' of hallucinogenic substances, most commonly 'magic mushrooms'. School surveys of 15- to 16-year-olds in the EU show that 1 to 5 % of this age group have used LSD or other hallucinogens, compared to 10 % in the USA (EMCDDA and ESPAD).

Characteristics and behaviour of users

2C-I users may belong to a very small group of people with a pseudo-scientific interest in experimenting with hallucinogenic substances, often referred to as 'psychonauts'. There appears to be a trend among a small but significant minority of users towards broadening their repertoire of drug experiences, involving a wider range of drugs and combinations. Special concerns relate to the lack of knowledge about the drug contents and the specific harmful effects of 2C-I, either alone or in combination with other drugs.

Indicators of health consequences

Information on the health consequences is limited to an apparently very small population of users. There is no information available on the long-term consequences for health of 2C-I use.

Context of use

There is no scientific evidence about the risk factors linked to the circumstances and consumption practices of 2C-I use.

Social risks

Sociological aspects

Young people outside of the ecstasy-using population are relatively unlikely to come into contact with 2C-I under present conditions.

As with all illicit drug use, lack of scientific and objective information contributes towards increased risk. Firstly, inaccurate media coverage and overestimation of prevalence may promote diffusion by encouraging young people to try it. Secondly, official dissemination of inaccurate information is counterproductive, as it can undermine credibility.

A few more experimental drug users appear to be motivated to use 2C-I by a desire to experience a wide range of sensations.

Social consequences

There is currently no scientific evidence of negative social consequences. However, 2C-I carries potential risks common to other hallucinogenic substances.

Consequences for the social behaviour of the user

There is no specific evidence to link the use of 2C-I to disorderly conduct, acquisitive crime or violence. However, the delayed action described by users may have implications for driving a vehicle and using machinery.

Other social consequences

There is no indication that 2C-I is particularly associated with any major value conflicts or has any important implications for social institutions beyond those described for similar compounds.

Criminological aspects

The law enforcement agencies of all 15 Member States reported to Europol that there is no information available to suggest that there is large-scale production and distribution of and/or trafficking in 2C-I or that organised crime has any role in these activities. Belgium and Italy reported that the main reason for the lack of information is that the substance is not controlled in those countries and, therefore, no records are kept by the law enforcement agencies.

Germany and Sweden reported that limited quantities of 2C-I were produced in 1999. This related, in both countries, to one case only, involving small 'kitchen-type' laboratories.

Three Member States reported seizures of 2C-I. These were small, both in terms of numbers and the quantities seized. Denmark reported a seizure, in April 2002, of one 2C-I tablet, which was sent to a forensic laboratory by a psychiatrist working in the drug field. Germany reported a seizure, in 1999, of 0.3 gm of 2C-I from a kitchen-type laboratory in Brannenburg, Bavaria. Sweden reported one seizure, in 1999, of a small amount of 2C-I that was also produced in a kitchen-type laboratory. No link to organised crime was established.

In 1999, the United Kingdom Reitox focal point reported a small seizure of 2C-I to the EMCDDA.

Prohibition

Legal status

An analysis of the legal status of 2C-I shows that the drug is controlled in five Member States. 2C-I is not controlled in the USA.

In Germany, 2C-I was placed under permanent control on 19 June 2001. The substance had already been controlled on a temporary basis since 1999. The arguments (outlined in the legal text 'Fünfzehnte Betäubungsmittelrechts-Änderungsverordnung-15. BtMÄndV', of 19 June 2001) for placing these kinds of drugs under permanent control are as follows: (i) these substances are being used as ecstasy-type drugs; and (ii) they are produced by illegal laboratories that modify the chemical structure of illegal drugs in order to avoid the law ('designer drugs').

In the United Kingdom, 2C-I comes under the definition of a controlled substance (Class A) by virtue of a generic description set out in the Misuse of Drugs Act (1977).

In Ireland, 2C-I is a controlled drug under Schedule 1 of the Misuse of Drugs Act, as a result of the generic control approach.

In Denmark, 2C-I has been controlled since May 2002 ('Bekendtgørelse nr. 305 af 16. maj 2002 om ændring af bekendtgørelse om euforiserende stoffer').

In Greece, the drug is controlled under Table A of Law 1729/87.

Possible consequences of prohibition

The meeting acknowledged that 2C-I is already controlled in five Member States. It was noted that, structurally, 2C-I seems to be comparable to substances already classified under Schedules I or II of the 1971 United Nations Convention on Psychotropic Substances. It was also noted that 2C-I has no medical or industrial use.

Arising from the above, it was felt that there is no real alternative to prohibition as a control measure. It was widely agreed that such measures would enhance the capacity for detection and monitoring of the drug on the market and limit the potential for expansion of the supply and use of 2C-I. Another supporting argument was that exempting 2C-I from legal controls would send an inaccurate message about the comparative safety of the substance. Increased availability of information about the drug would also stimulate the gathering and dissemination of analytical information for public health purposes.

The meeting was also of the opinion that prohibition could engender stigmatisation of the small self-limiting groups of 2C-I users. It was also felt that the lack of scientific evidence makes it very difficult to determine the possible consequences of legal controls on 2C-I.

There was a consensus of opinion that control measures should not prevent the dissemination of accurate information on 2C-I to users and to relevant professionals for preventive and harm reduction measures. Marginalisation of 2C-I users should be avoided.

Conclusions

The Scientific Committee of the EMCDDA, extended with experts from the Member States and representatives of the Commission, Europol and the EMEA, have considered the health and social risks as well as the possible consequences of prohibition of 2C-I and, in accordance with Article 4 of the joint action, submit the following conclusions.

- 2C-I has the structural characteristics of phenethylamines, which are associated with stimulant and hallucinogenic activity. This would appear to make it comparable to

substances already classified in the schedules of the 1971 United Nations Convention on Psychotropic Substances, such as 2C-B (listed in Schedule II as 4-bromo-2,5-dimethoxyphenethylamine).

Specific scientific risk assessment of 2C-I is extremely difficult, due to the lack of peer-reviewed scientific data. However, information based on analogy to 2C-B and DOB and evidence classified to evidence level IV ⁽⁴⁾ indicate the following.

- 2C-I is a synthetic drug that was first synthesised by Shulgin.
- Seized/available material includes powder, tablets (white, 'i' logo) and liquid preparations.
- 2C-I has no current medical or industrial use.
- There is confirmed 5-HT_{2C} and 5-HT_{2A} serotonergic receptor agonistic activity and potential 5-HT₁ and α_1 -adrenergic receptor agonistic activity.
- Users report hallucinogenic/visual effects (similar to 2C-B, LSD and mescaline) and feelings of empathy (similar to MDMA); however, no scientific data are available.
- Self-reporting users have only mentioned oral ingestion of 2C-I.
- Due to the lack of specific scientific evidence, acute or chronic toxicity has not been confirmed in humans, but toxic effects cannot be excluded.
- Anecdotal reports from users suggest that 2C-I may have a slower onset of action than related drugs (e.g. 2C-B or MDMA). This could result in some users taking additional doses or other drugs, thus increasing the risk of toxicity or overdose.
- There have been no reported cases of fatal or non-fatal intoxication.
- There is currently no scientific evidence of negative social consequences. However, 2C-I carries risks common to other hallucinogenic substances that are already controlled.
- There is no evidence to suggest that there is large-scale manufacture and trafficking of 2C-I or that organised crime is implicated.
- 2C-I has been identified in four EU Member States and it is controlled in five.

(4) Refers to the classification of information sources in *Guidelines for risk assessment of new synthetic drugs*, adopted by the EMCDDA's Scientific Committee.

Recommendations

- The meeting was strongly of the opinion that, due to its hallucinogenic/stimulant properties and its potential risk to health, 2C-I should be a controlled substance. However, there were some experts who felt that there was insufficient scientific evidence to make such a recommendation.
- The meeting also recommended that any decision to place 2C-I under control should not inhibit the gathering of information about drugs on the market and the dissemination of accurate information on 2C-I to users and relevant professionals.
- The major chemical precursor of 2C-I, namely 2,5-dimethoxybenzaldehyde, is available commercially. Should the substance be controlled, the meeting recommended that the Drug Precursors Committee (set up under Article 10 of Regulation (EEC) No 3677/90 and Directive 92/109/EEC) should closely examine the situation regarding this precursor chemical, which is involved in the synthesis of 2C-I and is not yet subject to any surveillance measures.
- The meeting reiterated its earlier recommendation that, when a new synthetic drug is notified for risk assessment, arrangements be made for the provision of standard reference materials and associated analytical data to forensic and toxicology laboratories within the European Union. The meeting further recommended that 2C-I be included in the UNDCP proficiency-testing programme.

Lisbon, 31 March to 1 April 2003

Report on the risk assessment of 2C-T-2 in the framework of the joint action on new synthetic drugs

On 12 December 2002, the horizontal working party on drugs of the Council of the European Union decided that risk assessment of four new synthetic drugs, 2C-T-2, 2C-T-7, 2C-I and TMA-2, should be initiated. On 20 December 2002, in accordance with practice under the 1997 joint action, the Danish Presidency formally notified the EMCDDA of the decision of the HWPD to submit 2C-T-2, 2C-T-7, 2C-I and TMA-2 for risk assessment under Article 4 of the joint action on new synthetic drugs of 16 June 1997.

A meeting of the Scientific Committee of the EMCDDA, extended with experts nominated by the Member States and representatives of the European Commission, Europol and the EMEA, was held on 31 March 2003 to assess the health and social risks of 2C-T-2 as well as the possible consequences of prohibition.

The meeting considered the following documents.

- i. Review of the pharmacotoxicological data for the risk assessment of 2C-T-2; report to the EMCDDA
- ii. Public health risks: epidemiological evidence; EMCDDA
- iii. Sociological/criminological evidence; EMCDDA
- iv. Europol contribution to the risk assessment on 2C-T-2

In conjunction with further information and comments from the expert participants, these documents formed the basis of the risk assessment which is reported below.

Chemical description

2C-T-2 is 2,5-dimethoxy-4-ethylthiophenethylamine. Other chemical names include: 4-ethylthio-2,5-dimethoxyphenethylamine and 4-ethylsulfanyl-2,5-dimethoxyphenethylazan. The abbreviation '2C-T-2' is derived from the nomenclature according to Shulgin. Although this compound has less carbons than 2C-T-7, the '-2'

part of the abbreviation has no structural significance. 2C-T-2 hydrochloride is a white crystalline solid. The synthesis protocol described in *Pihkal* (Shulgin and Shulgin) is based on initial use of 1,4-dimethoxybenzene to eventually produce a preliminary precursor, 2,5-dimethoxythiophenol. Shulgin describes the latter compound as a 'valuable precursor to all members of the 2C-T family' and it is now commercially available. The abovementioned method requires specialist equipment and an appropriate environment. Intermediate substances and the final product according to the Shulgin synthetic methodology for 2C-T-2 were identified in chemicals/material seized from a clandestine laboratory.

2C-T-2 exhibits a slightly more orange colour using the Marquis reagent assay compared to a slightly more red colour with 2C-T-7.

At present, 2C-T-2 has no medical or industrial use.

Pharmaceutical description

2C-T-2 is typically available in powder or tablet form. No associated 'street names' have been reported specifically relating to 2C-T-2. 2C-T-2 was previously (1997–99) sold in Dutch smartshops as 2C-T-7 or 'S5' (4-MTA). It was also apparently sold in similar shops in Sweden in 1998–99. More recently, information from Reitox national focal points has indicated that tablets had been seized which were white in appearance, had no logo and were approximately 8.5 to 8.8 mm x 3.4 to 3.7 mm, weighing 247 to 249 mg (in France and Denmark, respectively).

As 2C-T-2 comes in powder or tablet form, the primary route of administration is oral. However, insufflation (snorting) is also commonly mentioned in user reports. In a survey of 43 self-reporting 2C-T-2 users, the following percentages of respondents indicated their usual routes of administration: oral (83.7 %) and insufflation (16.3 %). Unlike 2C-T-7, smoking and rectal or intravenous/intramuscular administration were not mentioned. Original studies by Shulgin involved oral administration of 2C-T-2 in doses of between 12 and 25 mg. This is compared to *Pihkal* 'recommended' doses of 80 to 150 mg for MDMA, 178 to 256 mg for mescaline (hydrochloride), 12 to 24 mg for 2C-B, 60 to 100 mg for 2C-T, 10 to 30 mg for 2C-T-7, 1 to 3 mg for DOB and 3 to 10 mg for DOM. Respondents in a user survey mentioned oral doses of between 5 and 40 mg (average 21 mg) and intranasal doses of between 2.5 and

35 mg (average 13 mg). Compared to the wide-ranging doses mentioned for 2C-T-7, by inference this may indicate that there is less individual sensitivity to 2C-T-2.

Health risks

Individual health risks

Acute effects

No scientific evidence related to the action of 2C-T-2 on neurotransmitter systems has been published to date, so discussion of the neuropharmacological aspects of 2C-T-2 at the risk assessment meeting was based on speculative comparison with partially related compounds such as 2C-B (based on phenethylamine) and DOB (based on amphetamine), both involving bromine as opposed to sulphur.

Studies involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also acted as a competitive 5-HT antagonist, but, at higher concentrations (2.8 x 10⁻⁵M), it acted as a non-competitive 5-HT antagonist. In addition, DOB (4-bromo-2,5-dimethoxyamphetamine) was found to have a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB.

As 2C-T-2 is phenethylamine based, it is possible it may have serotonergic receptor affinity similar to 2C-B (i.e. binding to 5-HT₂ and, to some degree, 5-HT₁ receptors). Researchers have already provided evidence of the involvement of 5-HT₂ serotonergic receptors (in particular 5-HT_{2A}) in the action of hallucinogenic agents. It is conceivable, therefore, that the apparent hallucinogenic effects of 2C-T-2 may be related to similar receptor affinities. However, such conjecture is only based on limited information on related compounds, and further specific studies of 2C-T-2 will be required before definitive conclusions can be drawn.

Subjective evidence from user surveys indicates variable observations regarding cardiovascular and thermoregulatory responses. However, the sample size of these surveys was 10 times smaller than for 2C-T-7. Compared to 2C-T-7, where 31.9 % of

users noted headaches (suggesting the possibility of raised blood pressure), only 9.3 % reported headaches with 2C-T-2. Although inconsistent observations regarding its effect on body temperature were described for 2C-T-7, this information appears to be associated with 2C-T-7, not 2C-T-2.

No metabolic studies have been performed for 2C-T-2. However, it is likely that its metabolism proceeds via similar pathways to 2C-B, possibly with additional metabolic reactions. Anecdotal evidence from user self-reports indicates an onset of action of between one and two hours, with effects lasting up to 6 to 8 hours. However, these data typically refer to oral ingestion, and users report more rapid onset and shorter duration of effects following insufflation. This compares to 8 to 12 hours for orally ingested LSD and 10 to 12 hours for mescaline, as described by Shulgin.

At present there are no animal or human data concerning general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-T-2. Only subjective evidence is available from user surveys involving observations of apparent adverse effects and toxic symptoms. A study of self-reporting 2C-T-2 users indicated that side-effects of varying degrees were noted in the majority of users, but none were prolonged or severe. The most common side-effect was nausea, followed by muscle tension, vomiting, diarrhoea, tachycardia, dehydration, headaches, hypertension and, to a lesser degree, stomach ache and confusion. It should be noted that, overall, there were fewer instances of adverse effects with 2C-T-2 compared to 2C-T-7. However, the 2C-T-2 population surveyed only numbered 43, far less than the 423 surveyed for 2C-T-7.

Unlike other phenethylamine derivatives (including 2C-B), 2C-T-2 is not usually present in tablets containing other phenethylamines or stimulants, which reduces the possibility of concomitant ingestion of other drugs. However, as the pharmacology of 2C-T-2 is largely unknown, it is difficult to predict with accuracy any potential drug interaction or contraindication. Acute effects of monoamine reuptake inhibitors (SSRIs) on the stimulatory effects of hallucinogens have been observed in one study, showing an additivity of effects rather than a potentiation. Similar effects could possibly occur with 2C-T-2. There have also been various reports of potential adverse interaction with monoamine oxidase inhibitors (MAOIs) (Murple, 2001). However, specific studies of such drugs in combination with 2C-T-2 have not been performed, so the potential interactions described above have not been confirmed.

Clinical effects

There have been no reported deaths or instances of non-fatal intoxication involving 2C-T-2. As it has not undergone any clinical or pre-clinical evaluation studies, the majority of data on 2C-T-2 is based on self-reporting by users. In general, users reported strong visual effects, emotional responses (similar to MDMA) and some negative psychedelic mental effects such as anxiety, paranoia and panic attacks. Adverse effects such as nausea, muscle tension and vomiting were also noted.

Dependence

No specific research has been performed to evaluate the dependence potential of 2C-T-2 in animals or humans. Anecdotal user reports suggest that tolerance to the effects of 2C-T-2 can occur in some instances. If tolerance does occur, it is possible that there may also be cross-tolerance between other related psychedelic phenethylamines such as 2C-T-7, 2C-B and mescaline. Although the specific pharmacology of 2C-T-2 is unknown, speculative comparison with related compounds suggests it is unlikely to produce physical dependence or addiction. However, without any specific studies, definitive conclusions cannot be drawn.

Psychological effects

There are no published data on the specific psychological effects, acute or chronic, of 2C-T-2. Some of the 43 respondents providing self-reports for the survey mentioned above reported experiencing feelings of wellbeing and mental clarity a day after ingestion, but others described feeling mentally drained and emotionally unbalanced.

Public health risks

Availability and quality of 2C-T-2 on the market

2C-T-2 has been identified in six Member States: Denmark, Germany, France, the Netherlands, Finland and Sweden.

Information based on early-warning databases suggests that 2C-T-2 is very rare. However, it was found in the EU between 1998 and mid-2002 (France, August 2002). Denmark reported a case of international trafficking (2 038 tablets seized on 26 January 2001).

From 1997, 2C-T-2 was sold in smartshops in the Netherlands. In 1998, 'Conscious dreams' began to market 2C-T-2, whilst De Sjamaan Internet suppliers were independently obtaining and selling 2C-T-2. In 1998, a 'smart' drugstore in Sweden was also selling 2C-T-2. Smartshops stopped selling 2C-T-2 as a result of controls introduced in April 1999 in the Netherlands and Sweden. In April 2000, 2C-T-2 was available on the international market in a pure powder form from a handful of chemical supply companies, though these companies explicitly forbade human use in their customer agreements. An Internet search using the Google search engine in March 2003 did not find online sales of 2C-T-2.

On the basis of limited information, it is possible to state that tablets typically contain 10 mg of 2C-T-2. In the Netherlands, white tablets containing 2C-T-2 were sold as 2C-T-7 in 1997. In France, white tablets containing 2C-T-2 were sold as 'mescaline' in August 2002. The fact that a significant amount of 2C-T-2 tablets with no logo has been seized in Denmark could be a matter for serious concern, because of the risk of confusion with MDMA among the wider population of ecstasy users.

According to Internet sources, in 1998 the estimated price of 2C-T-2 was between EUR 3 and 4 per tablet.

Knowledge and perception of 2C-T-2 among users

Level of awareness about 2C-T-2 is generally negligible, except among small subgroups of experimenters who may use 2C-T-7, mescaline, DOB or 2C-B for particular effects. Due to the lack of research studies, the level of knowledge among these particular consumer subgroups (as can be seen on the Internet) appears to be more detailed than in the general scientific community. However, perceptions among consumers about the contents of products sold as 2C-T-2 are usually based on the information provided by suppliers and the beliefs of consumers. In the absence of accurate and regulated chemical analysis, objective scientific knowledge remains extremely limited. Major information sources are Internet sites and 'dance floor pharmacology' (an informal network whereby information passes from friend to friend). Despite warnings about the potential harm associated with using health information from the Internet, a systematic search of peer-reviewed literature found few reported cases of harm. This may be due to an actual low risk for harm associated with the use of information available on the Internet, or to under-reporting of such cases, or to bias.

Prevalence and patterns of use

Scientific evidence of 2C-T-2 use within the EU is very limited. In the Netherlands, targeted surveys conducted by the Amsterdam Antennae project in different settings found lifetime prevalence of 2C-T-2 of around 2 %, compared to over 50 % for ecstasy. An Internet survey obtained 43 valid responses from people who had taken 2C-T-2; however, their country of residence is unknown. According to the same survey, use ranged from 1 to 20 times, with an average of 3.69 times; doses ranged from 5 to 40 mg, with the average being 21 mg. The reported administration routes were oral (84 %) and by insufflation (16 %). Participants in Internet surveys and newsgroups report combined use with other drugs, but not as much as with 2C-T-7.

Population surveys of young adults in the EU show that a range of from 1 % in Finland to 12 % in the United Kingdom have lifetime prevalence of using hallucinogenic substances, most commonly 'magic' mushrooms. School surveys of 15- to 16-year-olds in the EU show that 1 to 5 % of this age group have used LSD or other hallucinogens, compared to 10 % in the USA (EMCDDA and ESPAD).

Characteristics and behaviour of users

An Internet survey of 43 respondents shows that 91 % of respondents were male and the age of those who had tried 2C-T-2 ranged from 16 to 47 years.

2C-T-2 users may belong to a small group of people with a pseudo-scientific interest in experimenting with hallucinogenic substances, often referred to as 'psychonauts'. There appears to be a trend among a small but significant minority towards broadening their repertoire of drug experiences, involving a wider range of drugs and combinations. Special concerns relate to the lack of knowledge about the drug contents and the specific harmful effects of 2C-T-2, either alone or combined with other drugs.

Indicators of health consequences

Information on the health consequences of 2C-T-2 use is limited. The section on 'Clinical effects' describes information gathered from what appears to be a very small population of users. There is no information available on the long-term consequences of 2C-T-2 use.

Context of use

There is no scientific evidence about risk factors linked to the circumstances and consumption practices associated with 2C-T-2 use.

Social risks

Sociological aspects

Young people outside of the ecstasy-using population are relatively unlikely to come into contact with 2C-T-2 under present conditions. However, the seizure in Denmark in 2001 of 2 038 tablets with no logo indicates that such a possibility cannot be excluded.

As with all illicit drug use, lack of scientific and objective information contributes towards increased risk. Firstly, inaccurate media coverage and overestimation of prevalence may promote diffusion by encouraging young people to try it. Secondly, official dissemination of inaccurate information is counterproductive, as it can undermine credibility.

A few more experimental drug users appear to be motivated by a desire to experience a wide range of sensations. The number is not known, but they are not an insignificant group. However, the erratic and highly dose-sensitive nature of 2C-T-2 and negative adverse effects such as nausea, muscle tension and vomiting suggest that there may be little likelihood that 2C-T-2 will grow in popularity or become widely used.

Social consequences

There is currently no scientific evidence of negative social consequences. However, 2C-T-2 carries potential risks common to other hallucinogenic substances that are already controlled.

Consequences for the social behaviour of the user

There is no specific evidence to link the use of 2C-T-2 to disorderly conduct, acquisitive crime or violence. However, the long duration of action with 2C-T-2 may have implications for driving a vehicle and using machinery.

Other social consequences

There is no indication that 2C-T-2 is particularly associated with any major value conflicts or has any important implications for social institutions beyond those described for similar compounds, such as 2C-B or DOB.

Criminological aspects

The law enforcement agencies of all 15 Member States reported to Europol that there is no information available to suggest that there is large-scale production, distribution and/or trafficking in 2C-T-2 or that organised crime has a role in these activities. Belgium and Italy reported that the main reason for the lack of information is that the substance is not controlled in those countries and, therefore, no records are kept by the law enforcement agencies.

Germany reported that a limited quantity of 2C-T-2 was produced in 1999. This related to one case only, involving a small 'kitchen-type' laboratory in Brannenburg, Bavaria.

Five Member States reported seizures of 2C-T-2. These were small, both in terms of numbers and quantities seized. One of these, Denmark, reported a case of international trafficking involving a seizure of 2C-T-2 in November 2000. This resulted from a criminal investigation which had revealed that a suspect was to receive drugs by mail from the Netherlands. The package, which was intercepted, contained 2 038 tablets of 2C-T-2 in two cans carrying the words 'Think fast, Hedoné 1 000 tablets'. Finland reported a seizure of four tablets of 2C-T-2 in 2001. France reported a seizure of one tablet of 2C-T-2 in 1998. Germany reported a seizure, in 1999, of 5.3 gm of 2C-T-2 from the laboratory in Brannenburg, and, in Sweden, six seizures of 2C-T-2 occurred in 1998, three in 1999, two in 2000 and one in 2001. In all the Swedish cases, the amounts seized were small and occurred at street level. In the Netherlands, DIMS reported two cases of 2C-T-2: one in a tablet in April 2000 and one in powder form in June 2001.

Prohibition

Legal status

An analysis of the legal status of 2C-T-2 in the 15 Member States shows that the drug is controlled in five Member States. In Germany, 2C-T-2 was placed under Schedule I on 7 October 1998 (listed as 4-Ethylsulfanyl-2,5-dimethoxyphenethylazan). In Sweden, 2C-T-2 was placed under 'emergency scheduling' on 1 April 1999. In the United Kingdom, 2C-T-2 is a Class A drug. In Ireland, 2C-T-2 comes under Schedule I and it is a controlled drug in Greece.

2C-T-2 is not controlled in the USA.

Possible consequences of prohibition

The meeting noted that 2C-T-2 is already controlled in five Member States. It was also noted that, structurally, 2C-T-2 is a potent hallucinogen comparable to substances already classified under Schedules I or II of the 1971 United Nations Convention on Psychotropic Substances. The meeting also noted that 2C-T-2 has no medical or industrial use.

Arising from the above, it was felt that there is no real alternative to prohibition as a control measure. It was widely agreed that this would enhance the capacity for detection and monitoring of the drug on the market and limit the potential for expansion in the supply and use of 2C-T-2. Another supporting argument was that exempting 2C-T-2 from legal control would send an inaccurate message about the comparative safety of the substance. Increased availability of information about the drug would also stimulate the gathering and dissemination of analytical information for public health purposes.

The meeting feared that prohibition could engender stigmatisation of the small self-limiting groups of 2C-T-2 users. It was also felt that the lack of scientific evidence makes it very difficult to determine the possible consequences of legal controls.

There was a consensus of opinion that control measures should not prevent the dissemination of accurate information about 2C-T-2 to users and to relevant professionals for preventive and harm reduction measures. Marginalisation of 2C-T-2 users should be avoided.

Conclusions

The Scientific Committee of the EMCDDA, extended with experts from the Member States and representatives of the Commission, Europol and the EMEA, has considered the health and social risks as well as the possible consequences of prohibition of 2C-T-2 and, in accordance with Article 4 of the joint action, submits the following conclusions.

- 2C-T-2 has the structural characteristics of phenethylamines, which are associated with stimulant and hallucinogenic activity. This would appear to make it comparable to substances already classified in the schedules of the 1971 United Nations Convention on Psychotropic Substances, such as 2C-B (listed in Schedule II as 4-bromo-2,5-dimethoxyphenethylamine).

Specific scientific risk assessment of 2C-T-2 is extremely difficult due to the lack of peer-reviewed scientific data. However, information based on analogy with 2C-B and DOB and evidence classified to evidence level IV ⁽⁵⁾ indicate the following.

- 2C-T-2 is a synthetic drug that was first synthesised in 1981 by Shulgin.
- Seized/available material includes powder and tablets (white, no logo).
- 2C-T-2 has no current medical or industrial use.
- It is a potential 5-HT_{2C}, 5-HT_{2A} and 5-HT₁ serotonergic and α_1 -adrenergic receptor agonist.
- Users report hallucinogenic/visual effects similar to 2C-B, LSD and mescaline and feelings of empathy similar to MDMA. There may be side-effects such as nausea, muscle tension, vomiting, anxiety and some confusion/disorientation; however, no scientific data are available.
- Self-reporting users have only mentioned oral ingestion and insufflation (snorting) of 2C-T-2.
- Due to the lack of specific scientific evidence, acute or chronic toxicity has not been confirmed in humans, but toxic effects cannot be excluded.

(5) Refers to the classification of information sources in *Guidelines for risk assessment of new synthetic drugs*, adopted by the EMCDDA's Scientific Committee.

- There have been no reported cases of fatal or non-fatal intoxication.
- There is currently no scientific evidence of negative social consequences. However, 2C-T-2 carries risks common to other hallucinogenic substances that are already controlled.
- There has been one reported case of international trafficking of 2C-T-2 in November 2000, involving two EU Member States.
- 2C-T-2 has been identified in six Member States and it is controlled in five.

Recommendations

- The meeting was strongly of the opinion that, due to its hallucinogenic/stimulant properties and potential serious risk for health, 2C-T-2 should be a controlled substance. However, there were some experts who felt that there was insufficient scientific evidence to make such a recommendation.
- The meeting also recommended that any decision to place 2C-T-2 under legal control should not inhibit the gathering of information about drugs on the market and the dissemination of accurate information on 2C-T-2 to users and relevant professionals.
- The major chemical precursor of 2C-T-2, namely 2,5-dimethoxythiophenol, is commercially available. Should the substance be controlled, the meeting recommended that the Drug Precursors Committee (set up under Article 10 of Regulation (EEC) No 3677/90 and Directive 92/109/EEC) closely examine the situation of this precursor chemical, which is involved in the synthesis of 2C-T-2 and is not yet subject to any surveillance measures.
- The meeting reiterated its earlier recommendation that, when a new synthetic drug is notified for risk assessment, arrangements be made for the provision of standard reference materials and associated analytical data to forensic and toxicology laboratories within the European Union. The meeting further recommended that 2C-T-2 be included within the UNDCP proficiency-testing programme.

Lisbon, 31 March 2003

Report on the risk assessment of 2C-T-7 in the framework of the joint action on new synthetic drugs

On 12 December 2002, the horizontal working party on drugs of the Council of the European Union decided that risk assessment of four new synthetic drugs, 2C-T-2, 2C-T-7, 2C-I and TMA-2, should be initiated. On 20 December 2002, in accordance with practice under the 1997 joint action, the Danish Presidency formally notified the EMCDDA of the decision of the HWPD to submit 2C-T-2, 2C-T-7, 2C-I and TMA-2 for risk assessment under Article 4 of the joint action on new synthetic drugs of 16 June 1997.

A meeting of the Scientific Committee of the EMCDDA, extended with experts nominated by the Member States and representatives of the European Commission, Europol and the EMEA, was held on 31 March 2003 to assess the health and social risks of 2C-T-7, as well as the possible consequences of prohibition.

The meeting considered the following documents.

- i. Review of the pharmacotoxicological data for the risk assessment of 2C-T-7; report to the EMCDDA
- ii. Public health risks: epidemiological evidence; EMCDDA
- iii. Sociological/criminological evidence; EMCDDA
- iv. Europol contribution to the risk assessment on 2C-T-7

In conjunction with further information and comments from the expert participants, these documents formed the basis of the risk assessment which is reported below.

Chemical description

2C-T-7 is 2,5-dimethoxy-4-(n)-propylthiophenethylamine. Other chemical names are rearrangements of the different elements of this name, such as 4-propylthio-2,5-dimethoxy-phenethylamine (or PT-DM-PEA). The synthesis protocol described in *Pihkal*

by Shulgin and Shulgin (1991), who are thought to have first synthesised 2C-T-7 in 1986, is based on the initial use of 1,4-dimethoxybenzene to eventually produce a preliminary precursor, 2,5-dimethoxythiophenol. Described by Shulgin as a 'valuable precursor to all members of the 2C-T family', the latter compound is now commercially available. The abovementioned method requires specialist equipment and an appropriate environment. The exact method of synthesis used by clandestine laboratories is not known.

2C-T-7 exhibits a slow/weak 'salmon orange' (pink, orange-red) colour using the Marquis reagent assay.

At present, 2C-T-7 has no medical or industrial use.

Pharmaceutical description

2C-T-7 is typically available in powder or tablet form, but may also be found in capsules or liquid form. It appears to have various 'street names', including 'T-seven', 'Beautiful', 'Lucky seven', 'Seven-up', 'Seventh heaven', 'Red raspberry', 'Tweety bird mescaline' and 'Tripstacy'. 2C-T-7 used to be commercially available in the EU (1999–2001) as 'Blue mystic'. It was available from Dutch smartshops as a blue tablet with a 'Yin-yang' logo.

As 2C-T-7 comes in powder or tablet form, the primary route of administration is oral. However, insufflation (snorting) is also commonly mentioned in user reports. Some less common routes of administration include smoking, rectal administration and intravenous or intramuscular administration. Original studies by Shulgin involved oral administration of 2C-T-7 in doses of between 20 and 30 mg, but the study indicated that around 10 mg may be sufficient for some users. The very few self-reports from intravenous/intramuscular users mentioned doses of between 1 and 3 mg.

Health risks

Individual health risks

Acute effects

No evidence related to the action of 2C-T-7 on neurotransmitter systems has, as yet, been published in peer-reviewed scientific journals, so discussion of the neuropharmacological aspects of 2C-T-7 at the risk assessment meeting was based on speculative comparison with partially related compounds such as 2C-B (which is based on phenethylamine) and DOB (which is based on amphetamine), both involving bromine as opposed to sulphur. 2C-B and DOB are already classified in Schedules II and I, respectively, of the 1971 UN Convention.

Studies involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also acted as a competitive 5-HT antagonist, but, at higher concentrations (2.8 x 10⁻⁵M), it acted as a non-competitive 5-HT antagonist. In addition, DOB (4-bromo-2,5-dimethoxyamphetamine) was found to have a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB.

As 2C-T-7 is phenethylamine based, it is possible that it may have serotonergic receptor affinity similar to 2C-B (i.e. binding to 5-HT₂ and, to some degree, 5-HT₁ receptors). Researchers have already provided evidence of the involvement of 5-HT₂ serotonergic receptors (in particular 5-HT_{2A}) in the action of hallucinogenic agents. It is conceivable, therefore, that the apparent hallucinogenic effects of 2C-T-7 may be related to similar receptor affinities. However, such conjecture is only based on limited information on related compounds and further specific studies of 2C-T-7 will be required before definitive conclusions can be drawn.

Subjective evidence from user surveys indicates variable observations regarding cardiovascular and thermoregulatory responses. The tachycardia and/or headaches reported by a number of users were thought to indicate the possibility of increased blood pressure. However, the value of such reports is seriously limited by the lack of

medical confirmation and the inconsistency of observations regarding effects on body temperature.

No metabolic studies have been conducted for 2C-T-7. However, it is likely that its metabolism may proceed via similar pathways as 2C-B, possibly with additional metabolic reactions. Anecdotal evidence indicates an onset of action of between one and two and a half hours, particularly if the substance is taken on an empty stomach, with effects lasting up to 15 hours. However, these data typically refer to oral ingestion and users report more rapid onset and shorter duration of effects following insufflation.

At present, there are no animal or human data concerning general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-T-7. Only subjective evidence is available from user surveys involving observations of apparent adverse effects and toxic symptoms. According to user self-reports, 2C-T-7 use involving intranasal administration appeared to result in a greater number of references to adverse effects than with oral administration. The most common side-effect was nausea, followed by headaches, vomiting, tachycardia, dehydration, diarrhoea, hypertension and, to a lesser degree, gastrointestinal effects, confusion or delirium (at high doses), dizziness and muscle spasms.

Unlike other phenethylamine derivatives (including 2C-B), 2C-T-7 tablets do not usually contain other phenethylamines or stimulants, thus reducing the possibility of concomitant ingestion of other drugs in such illicit preparations. However, as the pharmacology of 2C-T-7 is largely unknown, it is difficult to predict with accuracy any potential drug interaction or contraindication. Acute effects of monoamine reuptake inhibitors (SSRIs) on the stimulatory effects of hallucinogens have been observed in one study, showing an additivity of effects rather than a potentiation. Similar effects could possibly occur with 2C-T-7. Potential adverse interaction with monoamine oxidase inhibitors (MAOIs) has been mentioned in various user reports and by Shulgin. However, specific studies of such drugs in combination with 2C-T-7 have not been conducted, so the potential interactions described above have not been confirmed.

Clinical effects

2C-T-7 has been implicated in three deaths in the USA. Of these, the presence of 2C-T-7 was confirmed in one case following specific toxicological analysis.

Preliminary information on this case suggests that only 2C-T-7 was taken: 35 mg intranasally (snorting).

No deaths have been linked to 2C-T-7 within Europe. However, the lack of reference material may compromise the analysis of post-mortem cases.

There have been no confirmed cases of non-fatal intoxication. 2C-T-7 is not usually detected during routine toxicological analysis. As for post-mortem toxicological investigations, the lack of reference material may compromise clinical toxicological analysis in hospital settings. Anecdotal cases included in the user survey responses published on the Internet occurred in the USA, Mexico, Finland and the Netherlands.

Further data are required before the involvement of 2C-T-7 can be established and accurate mortality and morbidity figures produced.

Dependence

There have been no systematic studies of the tolerance or dependence potential of 2C-T-7. If tolerance does occur, it is possible that cross-tolerance may occur between other related psychedelic phenethylamines such as 2C-T-2, 2C-B and mescaline. Although the specific pharmacology of 2C-T-7 is unknown, speculative comparison with related compounds suggests it is unlikely to produce physical dependence or addiction. However, without any specific studies, definitive conclusions cannot be drawn.

Psychological effects

There are no published data on the specific psychological effects, acute or chronic, of 2C-T-7. The available data are essentially based on self-reporting by users. Users describe the psychological effects of 2C-T-7 as similar to other hallucinogens such as 2C-B, LSD and mescaline. A large number of specific effects are reported on the Internet, but the most common are: strong visual effects, emotional responses (similar to MDMA), some negative psychedelic mental effects (anxiety, paranoia, panic

attacks), delirium (at high doses), increased suppleness and enhancement of the senses. The effects are typically described as being intense and may also include severe disorientation/disassociation at high doses, particularly following insufflation. Reported after-effects include euphoria or, conversely, 'mental sluggishness', including impaired memory recall, mild confusion/disorientation and difficulty in concentrating.

Public health risks

Availability and quality of the product on the market

Between 1998 and 2001, 2C-T-7 has been identified in six Member States: Germany, France, the Netherlands, Finland, Sweden and the United Kingdom. Four of these reported small seizures were at street level. In early 2000, 2C-T-7 began to be sold in smartshops in the Netherlands by De Sjamaan Internet suppliers under the brand name of 'Blue mystic'. This took the form of blue tablets with a 'Yin-yang' logo. Distribution stopped in May 2001. In 2000, a seizure of four 'Blue mystic' 2C-T-7 tablets was recorded by DIMS and a small amount of 2C-B was also found. In January 2000, 2C-T-7 was available on the international market in pure powder form from a handful of chemical supply companies, though these companies explicitly forbade human use in their customer agreements. From summer 2000 onwards, discussion of 2C-T-7 on the Internet between groups of 'experimental' users has significantly grown. However, the availability of this drug at street level seems to be currently very low, especially in Europe. In 2001, DIMS recorded finding a small amount of 2C-T-7 in powder form. According to a project report by Amsterdam Antennae, 2C-T-7 has not been available in Amsterdam for nearly two years. An Internet Google search in March 2003 did not find online sales of 2C-T-7.

2C-T-7 was also detected in 2000 in Canada (with the street name 'Red raspberry') and has been reported sporadically in the United States (with various street names), where three deaths apparently involving this compound in high doses have been reported.

On the basis of limited information, tablets/capsules typically contain 10 mg of the active compound (one sample of 20 mg was seized in Germany). According to Internet sources, in 2000 the estimated price of 2C-T-7 ranged between EUR 2 and 5 per tablet.

Knowledge and perception of 2C-T-7 among users

The level of awareness about 2C-T-7 amongst drug consumers is generally negligible, except among small subgroups of experimenters who may use mescaline, DOB or 2C-B for particular effects. Due to the lack of research studies, the level of knowledge among these particular consumer subgroups (as can be seen on the Internet) appears to be more detailed than in the general scientific community. However, perceptions among consumers about the contents of products sold as 2C-T-7 are usually based on the information provided by suppliers and the beliefs of consumers. In the absence of accurate and regulated chemical analysis, objective scientific knowledge remains extremely limited. Major information sources are Internet sites and 'dance floor pharmacology' (an informal network whereby information passes from friend to friend). Despite warnings about the potential harm associated with using health information from the Internet, a systematic search of peer-reviewed literature found few reported cases of harm. This may be due to an actual low risk for harm associated with the use of information available on the Internet, or to under-reporting of such cases, or to bias.

In 1997, white tablets containing 2C-T-2 were sold as 2C-T-7 in Dutch smartshops. In 2000, a small amount of 2C-B was found in one of the four tablets of 2C-T-7 recorded by DIMS in the Netherlands. Since 2C-T-7 has been available in pure powder form, a small number of severe panic reactions have been reported on Internet forums. This appears to have been due to the drug ketamine being confused with 2C-T-7 by users snorting ketamine-sized doses of 2C-T-7. Moreover, participants in Internet surveys and newsgroups have reported an extensive range of combinations with other drugs.

Prevalence and patterns of use

Scientific evidence of 2C-T-7 use within the EU is very limited. In the Netherlands, targeted surveys conducted by the Amsterdam Antennae project in different settings found lifetime prevalence of 2C-T-7 use to be less than 1 %, compared to over 50 % for ecstasy. In the United Kingdom, a dance music magazine survey of nearly 500 respondents in 2002 found that none of them had ever tried 2C-T-7. An Internet survey of 2C-T-7 users obtained 423 valid responses from people who had taken 2C-T-7. However, the countries of residence of these respondents are unknown, although it is probable that many were from the USA. In this Internet survey from a

non-representative sample of the general population, prevalence of use ranged from 1 to 200 times, with an average of 4.78 times. Doses ranged from 1 to 125 mg, with the average being 27 mg. The administration routes for 2C-T-7 were usually oral (69 %) or intranasal (28 %). Very low levels of use by smoking, rectal insertion and injecting were also reported.

Two major factors that affect trends are availability and reliability of effects. 2C-T-7 is less available now than in 1999–2001 and people looking for new experiences may have moved on to other products. The author of the Internet survey cited above suggests that the effects of 2C-T-7 are erratic and highly dose-sensitive, making it unlikely to become very popular.

Population surveys in the EU show that a range of 1 % of young adults in Finland to 12 % in the United Kingdom have had 'lifetime prevalence' of using hallucinogenic substances, most commonly 'magic' mushrooms. School surveys of 15- to 16-year-olds in the EU show that 1 to 5 % of this age group have used LSD or other hallucinogens, compared to 10 % in the USA (EMCDDA and ESPAD).

Characteristics and behaviour of users

An Internet survey of 423 respondents shows that 89.4 % of respondents were male and 9.9 % were female (0.7 % did not specify), with an age range of 14 to 64 (average 27 years old).

2C-T-7 users may belong to a small group of people with a pseudo-scientific interest in experimenting with hallucinogenic substances, often referred to as 'psychonauts'. There appears to be a trend among a small but significant minority towards broadening their repertoire of drug experiences, involving a wider range of drugs and combinations of drugs.

Indicators of health consequences

Information on the health consequences in the population is limited to an apparently very small population of users. There is no information available on the long-term consequences of 2C-T-7 use.

Context of use

There is no scientific evidence about risk factors linked to the circumstances and consumption practices associated with 2C-T-7 use. However, anecdotal user reports mention an apparent increased prevalence and duration of side-effects following insufflation, indicating a potential harm/toxicity risk. Two of the three fatalities implicating 2C-T-7 involved this route of administration.

Social risks

Sociological aspects

Young people outside of the ecstasy-using population are relatively unlikely to come into contact with 2C-T-7 under present conditions.

As with all illicit drug use, lack of scientific and objective information contributes towards increased risk. Firstly, inaccurate media coverage and overestimates of use may promote diffusion by encouraging young people to try it. Secondly, official dissemination of inaccurate information is counterproductive, as it can undermine credibility.

A few more experimental drug users appear to be motivated by a desire to experience a wide range of sensations. The number is not known, but they are not an insignificant group. However, the erratic and highly dose-sensitive nature of 2C-T-7 and negative adverse effects such as nausea, headaches, intoxication and instances of death described on the Internet suggest that there may be little likelihood that 2C-T-7 will grow in popularity or become widely used.

Social consequences

There is currently no scientific evidence of negative social consequences. However, 2C-T-7 carries potential risks common to other hallucinogenic substances.

Consequences for the social behaviour of the user

There is no specific evidence to link the use of 2C-T-7 to disorderly conduct, acquisitive crime or violence. However, the long duration of its action may have implications for driving and using machinery.

Other social consequences

There is no indication that 2C-T-7 is particularly associated with any major value conflicts or has any important implications for social institutions beyond those described for similar compounds, such as 2C-B or DOB.

Criminological aspects

Between 1998 and 2001, 2C-T-7 was identified in Germany, France, the Netherlands, Finland, Sweden and the United Kingdom. The law enforcement agencies of all 15 Member States reported to Europol that there is no information available that would suggest large-scale production, distribution and/or trafficking of 2C-T-7 or that organised crime has a role in these activities. Belgium and Italy reported that the main reason for the lack of information is that the substance is not controlled in those countries and, therefore, no records are kept by the law enforcement agencies.

Germany reported that a limited quantity of 2C-T-7 was produced in 1999. This related to one case only, involving a small 'kitchen-type' laboratory in Brannenburg, Bavaria.

Four Member States reported seizures of 2C-T-7, but these were small, both in terms of numbers and quantities seized. Finland reported a seizure of 0.06 gm of 2C-T-7 in 2001. France reported a seizure of three tablets of 2C-T-7 in 2001. Germany reported a seizure of 7.7 gm of 2C-T-7 in 1999 from the laboratory in Brannenburg and another seizure in Berlin, between 1996 and 1998 (no further details are available). In Sweden, one seizure of 2C-T-7 occurred in 1998, one in 1999, one in 2000 and one in 2001. In all the Swedish cases, the amounts seized were small and occurred at street level.

In the United Kingdom, the Reitox national focal point reported to the EMCDDA on the discovery of three tablets of 2C-T-7 in an amnesty bin in a London club in 2000. In the Netherlands, 2C-T-7 was distributed in smartshops between 1999 and 2000.

The total amount of 2C-T-7 seized in the Member States is very small when compared to ecstasy seizures in the European Union (over 15 million tablets annually in recent

years). Member States' law enforcement agencies did not provide data on violence in connection with the production, distribution and trafficking of 2C-T-7.

Possible consequences of prohibition

Legal status

An analysis of the legal status of 2C-T-7 in the 15 Member States shows that the drug is controlled in four. In Germany, 2C-T-7 was placed under control on 20 January 1998. In Sweden, it is controlled under the emergency list. In the United Kingdom, it is a Class A drug and it is also a controlled drug in Greece.

In the USA, in September 2002, the DEA issued a final order to place 2C-T-7 temporarily under Schedule I. This temporary scheduling will last for up to 18 months or until the drug is permanently scheduled. 2C-T-7 is also controlled in Canada.

Prohibition

The meeting acknowledged that 2C-T-7 is already controlled in four Member States. It noted that, structurally, 2C-T-7 is a potent hallucinogen comparable to substances already classified under Schedules I or II of the 1971 United Nations Convention on Psychotropic Substances. It was also noted that 2C-T-7 has no medical or industrial use.

Arising from the above, it was felt that there is no real alternative to prohibition as a control measure. It was widely agreed that such measures would enhance the capacity for detection and monitoring of the drug on the market and limit the potential for expansion of the supply and use of 2C-T-7. Another supporting argument was that exempting 2C-T-7 from legal control would send an inaccurate message about the comparative safety of the substance. Increased availability of information about the drug would also stimulate the gathering and dissemination of analytical information for public health purposes.

The meeting feared that prohibition could engender stigmatisation of the small self-limiting groups of 2C-T-7 users. It was also felt that the lack of scientific evidence makes it very difficult to determine the possible consequences of legal controls on 2C-T-7.

There was a consensus of opinion that control measures should not prevent the dissemination of accurate information on 2C-T-7 to users and to relevant professionals for preventive and harm reduction measures. Marginalisation of 2C-T-7 users should be avoided.

Conclusions

The Scientific Committee of the EMCDDA, extended with experts from the Member States and representatives of the Commission, Europol and the EMEA, has considered the health and social risks as well as the possible consequences of prohibition of 2C-T-7 and, in accordance with Article 4 of the joint action, submits the following conclusions.

- 2C-T-7 has the structural characteristics of phenethylamines, which are associated with stimulant and hallucinogenic activity. This would appear to make it comparable to substances already classified in the schedules of the 1971 United Nations Convention on Psychotropic Substances, such as 2C-B (listed in Schedule II as 4-bromo-2,5-dimethoxyphenethylamine).

Specific scientific risk assessment of 2C-T-7 is extremely difficult, due to the lack of peer-reviewed scientific data. However, information based on analogy with 2C-B and DOB and evidence classified to evidence level IV ⁽⁶⁾ indicate the following.

- 2C-T-7 is a synthetic drug that was first synthesised in 1986 by Shulgin.
- Seized/available material includes powder, tablets (blue, 'Yin-yang' logo), capsules or liquid preparations.
- 2C-T-7 has no current medical or industrial use.
- It is a potential 5-HT_{2C}, 5-HT_{2A} and 5-HT₁ serotonergic and α_1 -adrenergic receptor agonist.
- Users report hallucinogenic/visual effects similar to 2C-B, LSD and mescaline and emotional responses similar to MDMA. There may be effects such as nausea,

(⁶) Refers to the classification of information sources in *Guidelines for risk assessment of new synthetic drugs*, adopted by the EMCDDA's Scientific Committee.

headaches, vomiting, anxiety, confusion/disorientation, agitation, aggression and violent behaviour; however, no scientific data are available.

- Both oral ingestion and insufflation (snorting) of 2C-T-7 have been reported. However, self-reporting users have also mentioned rectal administration and injecting.
- Due to the lack of specific scientific evidence, acute or chronic toxicity has not been confirmed in humans, but toxic effects cannot be excluded.
- There has been one death in which the involvement of 2C-T-7 has been confirmed in the USA; no fatalities have been reported in Europe. There have been no confirmed reports of non-fatal intoxication.
- There is currently no scientific evidence of negative social consequences. However, 2C-T-7 carries risks common to other hallucinogenic substances that are already under control.
- There is no evidence to suggest that there is large-scale production and trafficking of 2C-T-7 or any involvement of organised crime.
- 2C-T-7 has been identified in six Member States and it is controlled in four.

Recommendations

- The meeting was strongly of the opinion that, due to its hallucinogenic/stimulant properties and potential serious risk for health, 2C-T-7 should be a controlled substance. However, there were some experts who felt that there was insufficient scientific evidence to make such a recommendation.
- The meeting also recommended that any decision to place 2C-T-7 under control should not inhibit the gathering of information about drugs on the market and the dissemination of accurate information on 2C-T-7 to users and relevant professionals.
- The major chemical precursor of 2C-T-7, namely 2,5-dimethoxythiophenol, is commercially available. Should the substance be controlled, the meeting recommended that the Drug Precursors Committee (set up under Article 10 of Regulation (EEC) No 3677/90 and Directive 92/109/EEC) closely examine the

situation of this precursor chemical, which is involved in the synthesis of 2C-T-7 and is not yet subject to any surveillance measures.

- The meeting reiterated its earlier recommendation that, when a new synthetic drug is notified for risk assessment, arrangements be made for the provision of standard reference materials and associated analytical data to forensic and toxicology laboratories within the European Union. The meeting further recommended that 2C-T-7 be included within the UNDCP proficiency-testing programme.

Lisbon, 31 March 2003

Chapter 2

Europol–EMCDDA progress report on 2C-I, 2C-T-2 and 2C-T-7

Joint EMCDDA–Europol progress report on 2C-I, 2C-T-2 and 2C-T-7 to the horizontal working party on drugs of the Council of the European Union in the framework of the joint action on new synthetic drugs

1. Since the adoption of the joint action on new synthetic drugs in June 1997 and the setting-up of the early warning system, a number of synthetic substances have been detected and monitored.
2. Depending on different variables, such as the gravity of the consequences of using a substance, the nature of the evidence, the frequency of its detection and the scale of its presence on the market (notifications and seizures), the EMCDDA and Europol:
 - (a) have produced joint reports for some of these substances (when the initial estimation of risks has required it); and
 - (b) have continued to collect information on the others (those with less evident risks), in order to build up a complete picture.
3. On the basis of the EMCDDA–Europol joint reports, the EMCDDA's enlarged Scientific Committee was requested to carry out risk assessments on selected substances. Thus, risk assessment reports have been produced for the following substances: MBDB, 4-MTA, GHB, ketamine and PMMA.
4. Following the normal risk assessment exercises and procedures, decisions were taken to put some of these substances (4-MTA, PMMA) under control and to continue to monitor the others (MBDB, GHB, ketamine).
5. In the meantime, the EMCDDA and Europol have obtained more information on a number of other substances. These are: 2C-T-2, 2C-T-7, 2C-I, TMA-2, BZP, TFMP, PMEA, DOC, 5-MeO-DMT, 5-MeO-DIPT, DXM, DPT, A-MT and ALEPH-7.
6. This report presents the current information on 2C-I, 2C-T-2 and 2C-T-7.
7. The horizontal working party on drugs is requested to take note of this information and to give instructions if the substance should undergo a risk assessment.

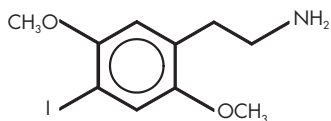
2C-I

Chemical and physical description

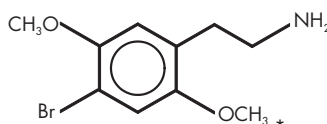
Chemical name: 2,5-dimethoxy-4-iodo-phenethylamine

Chemical structure:

2C-I



2C-B



Molecular formula: $C_{10}H_{14}INO_2$

Synonyms: 4-Iodo-2,5-dimethoxy-phenethylamine
(2,5-dimethoxy-4-iodophenyl)-2-aminoethane
4-Iod-2,5-dimethoxyphenethylazan (Germany)

Street name: '2C-I' (seized tablets often have an 'i' logo)

Pharmaceutical form: tablet or powder

Route of administration, dose and duration

Route of administration: oral

Common dose range: 10 to 20 mg

Duration: 6 to 10 hours

Effects

2C-I is frequently compared to the controlled drug 2C-B (UN Schedule II), because of the analogous chemical structures and subjective effects of the two drugs. With regard to the latter, the entactogen (producing feelings of empathy) and energetic properties of the two drugs are described by Shulgin as quite similar.

Health risks

The delayed onset of action (up to 90 minutes) of 2C-I could potentially lead users to take too much of the drug if they become impatient (topping up before the effects hit) and provoke adverse effects.

There have been no reported fatalities in the EU.

Legal status

2C-I is a ring-substituted phenethylamine, which is currently not listed under any of the schedules of the 1971 UN Convention on Psychotropic Substances.

In Germany, 2C-I was put under permanent control on 19 June 2001. The substance was already under control on a temporary basis from 1999. The arguments for placing these kinds of drugs under permanent control can be found in the legal text 'Fünfzehnte Betäubungsmittelrechts-Änderungsverordnung-15. BtMÄndV' (19 June 2001). The substances covered are: (i) those that are used as 'ecstasy' drugs; and (ii) those that are produced by illegal laboratories, which modify the chemical structure of illegal drugs in order that they should not come under the law ('designer drugs').

In the United Kingdom, 2C-I comes within the definition of a controlled substance by virtue of a generic description as set out in paragraph (i)(c) of the Misuse of Drugs Act, 1977 (Controlled Drugs) (Declaration) Order, 1987.

In Denmark, 2C-I has been controlled since May 2002 ('Bekendtgørelse nr. 305 af 16. maj 2002 om ændring af bekendtgørelse om euforiserende stoffer').

2C-I is not controlled in the USA.

Reports to the EMCDDA ⁽⁵⁾

(A = reporting form; B = other)

Denmark (A): notification on 14 May 2002 of a seizure (in May 2002) of one white pill containing 120 mg 2C-I and bearing an 'i' logo and of 2 ml in liquid form.

⁽⁵⁾ Since the finalisation of this report, more information about 2C-I seizures in the EU has been accumulated: in the first half of 2003 there were seven 2C-I seizures in the United Kingdom, two in Finland and six in Sweden. All the seizures in the United Kingdom and one of those in Sweden were in tablet form with an 'i' logo; one of the seizures in Finland was of tablets but no information is available about the logo. The remaining seizures in Sweden and one of the Finnish seizures were in the form of a white powder. In October 2003, the EMCDDA received an official notification (A) of the first identification of 2C-I in France, where six tablets were seized in Marseille. Furthermore, 2C-H (a compound that is non-active in man), which is a precursor to 2C-I, 2C-C and 2C-B, was seized in relatively large quantities in Finland and the Netherlands and there is evidence that, in the latter seizure, the 2C-H was intended as a precursor for the production of 2C-I.

United Kingdom (B): one case of a seizure in 1999.

Sweden (B): one seizure in 1999.

Reports to Europol

Two Member States, Germany and Sweden, reported incidental, small-scale production, in 1999, of 2C-I in kitchen-type facilities.

Three Member States, Denmark, Germany and Sweden, reported seizures of 2C-I. The German and Swedish seizures related to the seized kitchen-type facilities.

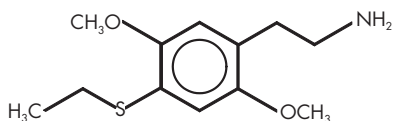
2C-T-2

Chemical and physical description

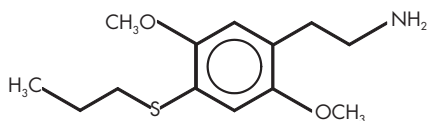
Chemical name: 4-ethylthio-2,5-dimethoxyphenethylamine

Chemical structure:

2C-T-2



2C-T-7



Molecular formula: C₁₂H₁₉NO₂S

Synonyms: 4-ethylthio-2,5-dimethoxyphenethylamine

4-ethylsulfanyl-2,5-dimethoxyphenethylazan (Germany)

Street name: '2C-T-2'

Pharmaceutical form: mostly tablet form; sometimes powder form (hydrochloride salt)

Identification: slightly more orange colour using the Marquis reagent assay compared to a slightly more red colour with 2C-T-7 (Erowid, 2001)

Routes of administration, dose and duration

Routes of administration: oral or intranasal (insufflation/snorting)

Common dose range: 10 to 35 mg (average = 20 mg orally; 13 mg intranasally)

Duration: 6 to 8 hours

Effects

The effects of 2C-T-2 are very similar to 2C-T-7. The effects of 2C-T-2 seem to share some general similarities with mescaline or 2C-B.

‘There is a considerable parallel between 2C-T-2 and 2C-T-7... With 2C-T-2, there is more of a tendency to have physical disturbances such as nausea and diarrhoea. And the experience is distinctly shorter.’ (A. Shulgin)

Health risks

As with the other 24 drugs of the 2C-T family, 2C-T-2’s clinical safety profile is not well known nor has it been adequately researched. The most severe side-effects, according to user reports, are nausea, vomiting, delirium, dissociation, loss of memory, panic attacks and a strong depression of CNS, which could induce convulsions or suffocation or lead to physical injury. Combining 2C-T-2 with MDMA increases the risk to health.

Similarly to 2C-T-7, ‘snorting’ the drug in powder form increases the secondary effects and the risk of overdose. Combining 2C-T-2 with MAOIs (commonly found in a number of antidepressants) is potentially dangerous (risk of serotonergic syndrome).

There have been no reported fatalities in the EU.

Legitimate uses for 2C-T-2

There are no known licensed therapeutic uses for 2C-T-2.

Legal status (*)

2C-T-2 is a ring-substituted phenethylamine, which is currently not listed under any of the schedules of the 1971 UN Convention on Psychotropic Substances.

In Germany, 2C-T-2 was placed under Schedule I on 7 October 1998 (listed as 4-ethylsulfanyl-2,5-dimethoxyphenethylazan).

In Sweden, 2C-T-2 was placed under 'emergency scheduling' on 1 April 1999.

In the Netherlands, 2C-T-2 has been classified as an unregistered pharmaceutical since 12 April 1999. The unlicensed manufacture, sale, import, trade and possession of this substance is liable for prosecution.

2C-T-2 is not controlled in the USA.

Reports to the EMCDDA

(A = reporting form; B = other)

France (A): notification on 23 September 2002 (seizure of one white tablet, no logo, sold as 'mescaline'), collected by Sintes (the national poison/substance identification system) in August 2002.

Germany (A): notification in March 1998 of several seizures reported by BKA in February 1998 of a total of 20 tablets (170 mg) with an 'X' logo.

Sweden (A): notification on 15 January 1999 of one seizure of 0.07 gm of powder on 10 July 1998.

Sweden (B): six seizures in 1998, three seizures in 1999, two in 2000, one in 2001.

(*) Since the finalisation of this report, 2C-T-2 has been made a subject of control in France (Judgment, 13 October 2003, OJ 246, 23.10.2003, p. 18032, Annex 4).

Denmark (B): a seizure of 2 000 tablets on 26 January 2001.

The Netherlands (B): mentioned in the DIMS report in 1998.

Spain (B): one mention in 1998.

Reports to Europol

One Member State, Germany, reported incidental, small-scale production, in 1999, of 2C-T-2 in a kitchen-type facility.

Five Member States, Denmark, Germany, France, Finland and Sweden, reported small seizures of 2C-T-2. The German seizure related to the seized kitchen-type facility.

One Member State, Denmark, reported on a case of international trafficking of 2C-T-2 through the mail system. The drugs originated in the Netherlands.

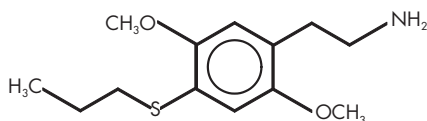
2C-T-7

Chemical and physical description

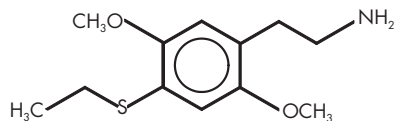
Chemical name: 2,5-dimethoxy-4-(n)-propylthiophenethylamine

Chemical structure:

2C-T-7



2C-T-2



Molecular formula: C₁₃H₂₁NO₂S

Synonyms: 4-propylthio-2,5-dimethoxy-phenethylamine (PT-DM-PEA)

Street names: 'T-seven', 'Beautiful', 'Lucky seven', 'Seven-up', 'Seventh heaven', 'Tweety bird mescaline', 'Tripstasy' (US), 'Red raspberry' (Canada), 'Blue mystic' (brand name in the Netherlands; has 'Yin-yang' logo)

Pharmaceutical form: powder form (hydrochloride salt) or capsule/tablet

Identification: slow/weak 'salmon orange' (pink, orange-red) colour using the Marquis reagent assay (Erowid)

Routes of administration, dose and duration

Routes of administration: oral (most common route) or intranasal (insufflation/snorting)

Dose range: 10 to 30 mg orally; 2.5 to 35 mg intranasally

Duration of action: 5 to 12 hours

Effects

As with 2C-T-2 and 2C-1, the effects of 2C-T-7 are described as classically psychedelic, sharing some of the characteristics of mescaline and 2C-B.

'Individual sensitivities seem to vary greatly with 2C-T-7, in sharp contrast to 2C-T-2'. (synthesis of user reports by Murple/Erowid, February 2001)

Health risks

2C-T-7's clinical safety profile has not been adequately researched and is not well known. User reports exhibit a lot of conflicting and confusing information, including about the duration of action, physical stimulation, dose, etc. Because this drug appears to be highly dose-sensitive, users should be extremely careful with dosage. 2C-T-7 can cause unexpected side-effects and this increases with high doses: nausea, diarrhoea, vomiting, delirium, dissociation, loss of memory, panic attacks and a strong depression of CNS, which could induce convulsions or suffocation or lead to physical injury. Combining 2C-T-7 with MDMA may pose a significant health risk.

Snorting the drug in powder form is recognised as being the most dangerous route, as it increases the secondary effects and the risk of severe (even lethal) overdose. Combining 2C-T-7 with MAOIs is potentially dangerous (MAOIs are commonly found in antidepressants such as phenelzine, tranylcypromine, isocarboxazid, l-deprenyl and moclobemide). As with other psychedelics, 2C-T-7 may trigger latent psychological and mental problems.

There have been no reported fatalities in the EU.

In the USA, three deaths involving 2C-T-7 have been reported: one in October 2000 (35 mg, snorted) and two in April 2001 (2C-T-7 combined with MDMA).

Legitimate uses for 2C-T-7

There are no known licensed therapeutic uses for 2C-T-7.

Legal status ⁽¹⁰⁾

2C-T-7 is a ring-substituted phenethylamine, which is currently not listed under any of the schedules of the 1971 UN Convention on Psychotropic Substances.

In Germany, 2C-T-7 was placed under control on 20 January 1998.

In Sweden, this drug is controlled under the emergency list.

In the United Kingdom and Ireland, 2C-T-7 is a Class A drug.

In the USA, in September 2002, the DEA issued a final order to place 2C-T-7 temporarily under Schedule I. This temporary scheduling will last up to 18 months or until the drug is permanently scheduled. 2C-T-7 is also controlled in Canada.

Reports to the EMCDDA

(A = reporting form; B = other)

France (A): notification on 21 February 2001 of one seizure (on 12 February 2001) of three blue tablets ('Blue mystic', with 'Yin-yang' logo) weighing 256 mg each, with 10 mg of the active compound.

Finland (B): one case of seven blue tablets ('Blue mystic', with 'Yin-yang' logo) in 2002.

⁽¹⁰⁾ Since the finalisation of this report, 2C-T-7 has been made a subject of control in France (Judgment, 13 October 2003, OJ 246, 23.10.2003, p. 18032, Annex 4).

United Kingdom (B): report in January 2002 of one case of three tablets collected in a London club amnesty bin in January 2001 (first case in the United Kingdom).

Germany (B): one seizure in 2001 of one 2C-T-7 pill (20 mg).

Sweden (B): one seizure in 1999, one seizure in 2000, one in 2001.

Reports to Europol

One Member State, Germany, reported incidental, small-scale production, in 1999, of 2C-T-7 in a kitchen-type facility.

Four Member States, Germany, France, Finland and Sweden, reported on small seizures of 2C-T-7. The German seizure related to the seized kitchen-type facility.

Chapter 3

Review of the pharmacotoxicological data on 2C-I ⁽¹⁾

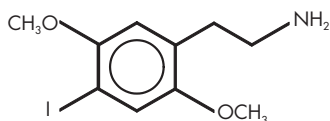
Very limited data for 2C-I have been published in peer-reviewed scientific journals. The following information includes studies involving structurally related compounds and user-based evidence (Information Classification IV, EMCDDA, 1999).

Chemical and pharmaceutical information

Chemical description

The chemical structure of 2,5-dimethoxy-4-iodophenethylamine (2C-I) is shown in Figure 1. Other chemical names include 4-iodo-2,5-dimethoxyphenethylamine, (2,5-dimethoxy-4-iodophenyl)-2-aminoethane and 4-iod-2,5-dimethoxyphenethylazan. The abbreviation '2C-I' is derived from the nomenclature according to Shulgin and Shulgin (1991), with the '-I' referring to the presence of an iodine atom that has no additional branching, unlike the 2C-Ts (Pihkal No 33).

Chemical structure of 2C-I



Molecular formula: $C_{10}H_{14}INO_2$
 Molecular weight: 307

There is no chemical abstracts registration (CAS) number for 2C-I. 2C-I hydrochloride is a white microcrystalline solid.

⁽¹⁾ This report was written by S. P. Elliott of the Regional Laboratory for Toxicology (City Hospital, Birmingham, United Kingdom) for the risk assessment meeting on 2C-I held in Lisbon on 31 March and 1 April 2003. Help and information was provided by: S. Ahlstrom, D. Corrigan, C. Furnari, J. Idanpaa-Heikkila, M. Mallaret, C. Poethko-Muller, J-P. Tassin, A. Wallon, R. Wennig, L. Westberg. The report was commissioned by the EMCDDA as a background paper for the risk assessment of the compound 2C-I. The report follows the structure of Annexes A and B of the risk assessment guidelines developed by the Scientific Committee of the EMCDDA.

Methods of synthesis

The synthesis of 2C-I is described in *Pihkal*, based on the initial use of 2,5-dimethoxybenzaldehyde to produce a preliminary precursor, 2,5-dimethoxyphenethylamine (2C-H) (Shulgin and Shulgin, 1991). The former compound, 2,5-dimethoxybenzaldehyde, is commercially available. The method is extensive, requiring specialist equipment and an appropriate environment. There is no information available about the exact method of synthesis used by clandestine laboratories.

Identification

There is no published information regarding the analytical profile of 2C-I. However, data pertaining to gas chromatography with mass spectrometry (GC-MS), high performance liquid chromatography with mass spectrometry (HPLC-MS), nuclear magnetic resonance (NMR) and Fourier transform infrared spectroscopy (FTIR) have been obtained (Bernhard, 2002). Like 2C-T compounds, 2C-I would not be expected to be detected by commonly used immunoassay procedures for the preliminary identification of amphetamines in urine (particularly based on monoclonal antibodies).

Legitimate uses of 2C-I

There are no known licensed therapeutic uses for 2C-I.

Pharmaceutical form

2C-I is typically available in powder or tablet form, although 2C-I in liquid form has also been noted by the Danish focal point. A tablet seized in Denmark in 2002 was white in appearance, had an 'i' logo and was approximately 6.1 x 2.7 mm, weighing 120 mg.

Routes of administration and dosage

As 2C-I is obtained in powder or tablet form, the primary route of administration is oral. Insufflation (snorting) and other routes (e.g. intravenous administration) associated with 2C-T-2 and 2C-T-7 (Murple, 2001) are not mentioned in 2C-I user reports (Erowid, 2001–03).

Original studies by Shulgin and Shulgin (1991) involved oral administration of 2C-I in doses of between 15 and 20 mg. This is compared to a Pihkal 'recommended' dose of 80 to 150 mg for MDMA, 178 to 256 mg for mescaline (hydrochloride), 12 to 24 mg for 2C-B, 60 to 100 mg for 2C-T, 10 to 30 mg for 2C-T-7, 1 to 3 mg for DOB and 3 to 10 mg for DOM (Shulgin and Shulgin, 1991) and a Tihkal 'recommended' dose of 0.06 to 0.2 mg for LSD (Shulgin and Shulgin, 1997). User reports have mentioned oral doses of between 3 and 25 mg (typically 20 mg) (Erowid, 2001–03). It should be noted, however, that the accuracy of such reports are dependent on user honesty and accurate weighing of the compound or knowledge of the actual content/weight of the tablet/powder's constituents.

Toxicology and pharmacology in animals and humans

Very limited data for 2C-I have been published in peer-reviewed scientific journals. Consequently, the following information includes speculative comparison with partially related compounds such as 2C-B (which is phenethylamine based) and DOB (which is amphetamine based), both involving bromine as opposed to iodine. It is inappropriate to compare data derived from MDMA, PMA and 4-MTA studies, due to the absence of 2,5-dimethoxy substituent groups in such compounds.

Neuropharmacology

Previous studies by Lobos et al. (1992) involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also acted as a competitive 5-HT antagonist but, at higher concentrations (2.8 × 10⁻⁵M), it acted as a non-competitive 5-HT antagonist (Lobos et al., 1992). In addition, Glennon et al. (1988) found that DOB (4-bromo-2,5-dimethoxyamphetamine) had a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB. Therefore, as 2C-I is more structurally related to 2C-B, it is possible it may have a similar serotonergic receptor affinity (i.e. binding to 5-HT₂ and, to some degree, 5-HT₁ receptors). Recently, Acuna-Castillo et al. (2002) found that 2C-I had higher agonistic efficacy at 5-HT_{2C} receptors compared to 5-HT_{2A} receptors. However, the relative efficacy was lower than the phenylisopropylamines also studied (including

2,5-dimethoxy-4-iodophenylisopropylamine). Previously, researchers have provided evidence for the involvement of 5-HT₂ serotonergic receptors (in particular 5-HT_{2A}) in the action of hallucinogenic agents (Glennon et al., 1984). In particular, using radio-labelled (125I)-2C-I, Johnson et al. (1990) showed that the 5-HT receptor is significantly linked to hallucinogenic activity (Johnson et al.). Despite the initial information for 2C-I indicating it to be a potential 5-HT_{2C} (and, to a lower extent, 5-HT_{2A}) receptor agonist, further studies are required before definitive conclusions can be drawn.

Neuroendocrinology

No specific research has been conducted on 2C-I. Serotonin agonists stimulate hypothalamic neurons involved in ACTH and cortisol secretion (Fuller, 1981), in addition to stimulating growth hormone and prolactin secretion (as evidenced by mescaline and DOM) (Demisch and Neubauer, 1979; Meltzer et al., 1978). It is possible, therefore, that 2C-I may produce similar effects on hormonal secretion.

Cardiovascular and thermoregulatory responses

No specific research has been conducted on 2C-I. There is also only very limited subjective evidence available from user surveys, which indicates varying observations for these clinical features.

Toxicology

At present there are no animal or human data concerning the general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-I.

Toxicity in animals

Shulgin and Shulgin (1991) reported on studies on mice involving intraperitoneal (i.p.) administration of DOB and found the LD50 to be between 100 and 125 mg/kg. Administration of 50 mg/kg (i.p.) resulted in twitching, 100 mg/kg produced shaking, and mice receiving >125 mg/kg exhibited convulsions and eventually died. No such studies have been performed for 2C-I and, due to the structural differences between DOB and 2C-I (which is likely to alter the toxicity of the respective compounds), such data are not directly comparable. In particular, Shulgin describes

2 mg as an effective dose for DOB but suggests that 14 to 22 mg may be required using 2C-I.

Toxicity in humans

As mentioned above, only subjective evidence is available from a small number of user reports on the apparent adverse effects and toxic symptoms of 2C-I.

In general, although users have described 2C-I as a 'powerful' and 'strong stimulant' with hallucinogenic properties (Erowid, 2001–03), users purporting to have taken only 2C-I make virtually no mention of adverse effects such as nausea, vomiting and muscle cramps, as reported for 2C-T-2 and 2C-T-7 (Erowid, 2001–03; Murple, 2001). However, this may be due to selective reporting rather than absence of such symptoms. Nevertheless, some users reported stomach tension, nausea, vomiting and jaw tension when combining 2C-I with one or more of the following: 5-methoxy-dipropyltryptamine, cannabis, alcohol, caffeine, tryptophan, alprazolam and clonazepam.

Users have noted that the desired effect of 2C-I may be delayed, with the result that a user may take additional (sometimes higher) doses, which could result in accidental overdose.

Interactions with other drugs or medicines

Unlike other phenethylamine derivatives, including 2C-B (De Boer et al., 1999), it appears that 2C-I is not usually present in tablets containing other phenethylamines or stimulants. This therefore reduces the possibility of concomitant ingestion of other drugs in illicit preparations. However, as the pharmacology of 2C-I is largely unknown, it is difficult to predict with accuracy any particular potential drug interactions or contraindications. Winter et al. (1999) studied the acute effects of monoamine reuptake inhibitors (SSRIs such as fluvoxamine, fluoxetine and venlafaxine) on the stimulus effects of hallucinogens (including DOM) and observed an additivity of effects rather than a potentiation. It is possible, therefore, that similar effects may occur with 2C-I. Some users report concomitant use with other drugs (e.g. 5-methoxy-dipropyltryptamine, cannabis, alcohol, caffeine, tryptophan, alprazolam and clonazepam), but there is a lack of specific evidence. However, in some cases this did result in toxic effects (see the section entitled 'Toxicity in humans').

Non-fatal cases of 2C-I intoxication in humans

Like the 2C-Ts, 2C-I is not usually detected during routine toxicological analysis (this is typically due to the lack of any reference material). The evidence for use is usually based on anecdotal or circumstantial evidence (if any information is available to medical staff at all). There have been no reported instances of non-fatal intoxication involving the use of 2C-I.

Fatal cases of 2C-I intoxication in humans

Unlike 2C-T-7, there have been no reported fatalities implicating 2C-I. However, the lack of reference material may compromise clinical toxicological investigations during post-mortems.

Pharmacokinetics and metabolism

No specific research has been conducted on 2C-I. However, metabolic studies of 2C-B have been performed on rats and by analysis of human urine (De Boer et al., 1998; Kanamori et al., 2002). Kanamori et al. identified two pathways in the rat involving (a) initial deamination followed by reduction or oxidation; and (b) 2- or 5-position O-desmethylation followed by amino acetylation (Kanamori et al., 2002). De Boer et al. (1998) identified unchanged parent compound (i.e. 2C-B) in addition to 4-bromo-2,5-dimethoxyphenylacetic acid, 4-bromo-2,5-dimethoxybenzoic acid and 4-bromo-5-hydroxy-2-methoxyphenethylamine in the urine of 2C-B users. It is likely that metabolism of 2C-I may proceed via similar pathways, probably involving oxidative deamination (I, II) and O-desmethylation of the aromatic methoxy groups (III) in addition to excretion of unchanged drug (the possibility of species-dependent metabolism notwithstanding). This would lead to the corresponding compounds:

- I = 2,5-dimethoxy-4-iodophenylacetic acid
- II = 2,5-dimethoxy-4-iodobenzoic acid
- III = 4-iodo-5-hydroxy-2-methoxyphenethylamine

However, additional metabolic reactions are a possibility, particularly potential N-acetylation (as observed in rats by Kanamori et al., 2002).

Anecdotal evidence from users indicates an onset of initial action of one to two hours. However, some users report slower desired effects compared to related drugs (e.g. 2C-B) or MDMA. The effects are typically described as lasting for up to 10 hours post-oral dose (Shulgin and Shulgin, 1991; Erowid, 2001–03). This compares to a duration of action of 8 to 12 hours for orally ingested LSD and 10 to 12 hours for mescaline (Shulgin and Shulgin, 1991).

Clinical experience

2C-I has not undergone any clinical or pre-clinical evaluation studies. The majority of data is based on self-reporting by users.

Studies on street users

Unlike 2C-T-2 and 2C-T-7, there have been no studies involving 2C-I users. There have been a small number of isolated user reports, which, in general, compare 2C-I to 2C-B due to an apparent similarity in their effects, although some users describe 2C-I as being 'deeper, more purely psychedelic and less sensory' and, in some cases, less intense (Shulgin and Shulgin, 1991; Erowid, 2001–03). Hallucinogenic and visual responses have been reported, in addition to feelings of empathy described as similar to those produced by MDMA. As mentioned above, various users report delayed desired effects compared to related drugs (e.g. 2C-B) or MDMA (Erowid, 2001–03).

Overall, the small number of subjective user reports available indicate that 2C-I produces various psychedelic effects (comparable to other hallucinogens, particularly 2C-B) and feelings of empathy (similar to MDMA). A delayed onset of effects has been described.

Dependence potential in humans

Tolerance

No specific research has been conducted on 2C-I. In addition, no user reports appear to have mentioned the occurrence or absence of tolerance to the effects of 2C-I (Erowid, 2001–03). If tolerance does occur, it is possible that cross-tolerance could occur between other related psychedelic phenethylamines such as 2C-T-2, 2C-T-7, 2C-B and mescaline.

Dependence potential

No specific research has been conducted on 2C-I. Although the specific pharmacology of 2C-I is unknown, speculative comparison with related compounds suggests that it is unlikely to produce physical dependence or addiction such as that which occurs with opiate use. However, without specific study, definitive conclusions cannot be drawn.

Psychological risk assessment (cognition, mood and mental functioning)

Acute and chronic effects

There are no published data on the specific psychological effects of 2C-I, acute or chronic. As described in the pharmacological report, limited anecdotal user reports describe a few subjective psychological effects that occur with 2C-I use (Erowid, 2001–03). Such reports mention a general clarity of thought with little or no ‘psychological after-effects’. However, some introspection and ‘negative thought-loops’ were described by some users.

Conclusions

- 2C-I is a synthetic drug which was first synthesised by Shulgin.
- Seized/available material includes powder, tablets (white, ‘i’ logo) and liquid preparations.
- 2C-I has no licensed therapeutic or industrial use.
- 2C-I is a confirmed 5-HT_{2C} and 5-HT_{2A} receptor agonist, in addition to potential 5-HT₁ and α_1 -adrenergic receptor affinity.
- Users report stimulant effects, hallucinogenic/visual effects (similar to 2C-B) and emotional/empathetic responses (similar to MDMA). There is very little information regarding adverse effects.
- Due to the lack of specific scientific evidence, acute or chronic toxicity of 2C-I has not been confirmed in humans, but toxic effects cannot be excluded.
- Anecdotal reports from users suggest that 2C-I might have an unexpected slower onset of desired effects compared to related drugs (e.g. 2C-B) or MDMA. This may

result in some users taking additional doses or other drugs, which may increase the risk of toxicity or overdose.

- There have been no reported cases of fatal or non-fatal intoxication.

Review of the pharmacotoxicological data on 2C-T-2 ⁽¹²⁾

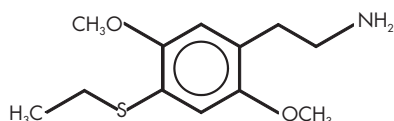
Very limited data for 2C-T-2 have been published in peer-reviewed scientific journals. The following information includes studies involving structurally related compounds and user-based evidence (Information Classification IV, EMCDDA, 1999).

Chemical and pharmaceutical information

Chemical description

The chemical structure of 2,5-dimethoxy-4-ethylthiophenethylamine (2C-T-2) is shown in Figure 1. Other chemical names include 4-ethylthio-2,5-dimethoxyphenethylamine and 4-ethylsulfanyl-2,5-dimethoxyphenethylazan. The abbreviation '2C-T-2' is derived from the nomenclature according to Shulgin and Shulgin (1991), and, although this compound has less carbons than 2C-T-7, the '-2' part of the abbreviation has no structural significance but refers only to the historical order of study/discovery (Pihkal No 40).

Chemical structure of 2C-T-2



Molecular formula: $C_{12}H_{19}NO_2S$
Molecular weight: 241.35

There is no chemical abstracts registration (CAS) number for 2C-T-2. 2C-T-2 hydrochloride is a white crystalline solid.

⁽¹²⁾ This report was written by S. P. Elliott of the Regional Laboratory for Toxicology (City Hospital, Birmingham, United Kingdom) for the risk assessment meeting on 2C-T-2 held in Lisbon on 31 March and 1 April 2003. Help and information was provided by: S. Ahlstrom, D. Corrigan, C. Furnari, J. Idanpää-Heikkilä, M. Mallaret, C. Poethko-Müller, J-P. Tassin, A. Wallon, R. Wennig, L. Westberg. The report was commissioned by the EMCDDA as a background paper for the risk assessment of the compound 2C-T-2. The report follows the structure of Annexes A and B of the risk assessment guidelines developed by the Scientific Committee of the EMCDDA.

Methods of synthesis

It is thought that 2C-T-2 was first synthesised in 1981 by Shulgin (Erowid, 2001). A synthesis protocol was later described in *Pihkal* based on initial use of 1,4-dimethoxybenzene to produce a preliminary precursor, 2,5-dimethoxythiophenol (Shulgin and Shulgin, 1991). Shulgin describes the latter compound as a 'valuable precursor to all members of the 2C-T family' and this is now commercially available (Poortman, 1999). The method is extensive, requiring specialist equipment and an appropriate environment. Poortman analysed chemicals/material seized from a clandestine laboratory where the intermediate substances and final product pertaining to the Shulgin synthetic methodology for 2C-T-2 were identified (Poortman, 1999).

Identification

2C-T-2 apparently exhibits a slightly more orange colour using the Marquis reagent assay compared to the slightly more red colour obtained with 2C-T-7 (Erowid, 2001). There is minimal information regarding the analytical profile of 2C-T-2 using common methods such as gas chromatography with mass spectrometry (GC-MS), or nitrogen-phosphorus detection (GC-NPD), or high-performance liquid chromatography with diode-array detection (HPLC-DAD). Electron impact (EI) mass spectral data (without any chemical derivatisation) has indicated major abundant ions of 212, 183, 241 (molecular ion), 153 and 197 (in order of abundance) (Poortman, 1999). Bosman et al. (1998) also presented GC-MS data. In addition, Fourier transform infrared spectroscopy (FTIR) data have been described (Poortman, 1999). Like 2C-T-7, 2C-T-2 would not be expected to be detected by commonly used immunoassay procedures for the preliminary identification of amphetamines in urine (particularly based on monoclonal antibodies).

Legitimate uses of 2C-T-2

There are no known licensed therapeutic or industrial uses for 2C-T-2. However, there is some information indicating its use in 'psychedelic therapy' (Shulgin and Shulgin, 1991; Stolaroff and Wells, 1993; Murple, 2001).

Pharmaceutical form

2C-T-2 is typically available in powder or tablet form. No associated 'street names' have been reported specifically relating to 2C-T-2. Between 1997 and 1999, 2C-T-2

was sold in Dutch smartshops purporting to be 2C-T-7 or 'S5' (4-MTA). It is also believed that it was sold in similar shops in Sweden in 1999. More recently, information from national Reitox centres has indicated that tablets have been seized which are white in appearance, have no logo and are approximately 8.5 to 8.8 mm x 3.4 to 3.7 mm, weighing 247 to 249 mg (France and Denmark).

The purchase price varies but is largely comparable to other phenethylamine derivatives such as MDMA (typically EUR 5 to 20) (Erowid, 2002).

Routes of administration and dosage

As 2C-T-2 is obtained in powder or tablet form, the primary route of administration is oral, but insufflation (snorting) is also frequently mentioned in user reports (Murple, 2001). In the Murple survey of 43 self-reporting 2C-T-2 users, respondents indicated that their usual routes of administration were oral (83.7 %) and intranasal (16.3 %). Unlike 2C-T-7, smoking, rectal and intravenous/intramuscular administration were not mentioned.

Original studies by Shulgin and Shulgin (1991) involved oral administration of doses of 2C-T-2 of 12 to 25 mg (Shulgin and Shulgin, 1991). This is compared to a Pihkal 'recommended' dose of 80 to 150 mg for MDMA, 178 to 256 mg for mescaline (hydrochloride), 12 to 24 mg for 2C-B, 60 to 100 mg for 2C-T, 10 to 30 mg for 2C-T-7, 1 to 3 mg for DOB and 3 to 10 mg for DOM (Shulgin and Shulgin, 1991) and a Tihkal 'recommended' dose of 0.06 to 0.2 mg for LSD (Shulgin and Shulgin, 1997). Respondents in a user survey mentioned oral doses of 5 to 40 mg (average 21 mg) and intranasal doses of 2.5 to 35 mg (average 13 mg) (Murple, 2001). By implication, the wide-ranging doses mentioned for 2C-T-7 may indicate that there is less individual sensitivity to 2C-T-2. It should be noted, however, that the accuracy of the statements about dosage collated by Murple is dependent on user honesty and accurate weighing of the compound or knowledge of the actual content/weight of the tablet/powder's constituents.

Toxicology and pharmacology in animals and humans

No data for 2C-T-2 have been published in peer-reviewed scientific journals. The following information is based on speculative comparison with partially related

compounds such as 2C-B (which is phenethylamine based) and DOB (which is amphetamine based), both involving bromine as opposed to sulphur. It is inappropriate to compare data derived from MDMA, PMA and 4-MTA studies, due to the absence of 2,5-dimethoxy substituent groups in such compounds.

Neuropharmacology

No specific research has been conducted on 2C-T-2. Studies by Lobos et al. (1992) involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also acted as a competitive 5-HT antagonist, but, at higher concentrations (2.8 x 10⁻⁵M), it acted as a non-competitive 5-HT antagonist (Lobos et al., 1992). An amphetamine-based analogue of 2C-T-2, ALEPH-2 (2,5-dimethoxy-4-ethylthioamphetamine), was also found to be a partial agonist of 5-HT_{2A} and a full agonist of 5-HT_{2C} (Acuna-Castillo et al., 2000). In addition, Glennon et al. (1988) found that DOB (4-bromo-2,5-dimethoxyamphetamine) had a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB. Therefore, as 2C-T-2 is phenethylamine based, it is possible it may have serotonergic receptor affinity similar to 2C-B (i.e. binding to 5-HT₂ and, to some degree, 5-HT₁ receptors). Researchers have already provided evidence of the involvement of 5-HT₂ serotonergic receptors (in particular 5-HT_{2A}) in the action of hallucinogenic agents (Glennon et al., 1984). It is conceivable, therefore, that the apparent hallucinogenic effects of 2C-T-2 may be related to similar receptor affinities. However, such conjecture is only based on limited information on related compounds and further studies of 2C-T-2 are required before definitive conclusions can be drawn.

Neuroendocrinology

No specific research has been conducted on 2C-T-2. Serotonin agonists stimulate hypothalamic neurons involved in ACTH and cortisol secretion (Fuller, 1981), in addition to stimulating growth hormone and prolactin secretion (as evidenced by mescaline and DOM) (Meltzer et al., 1978, 1981; Demisch and Neubauer, 1979). It is possible, therefore, that 2C-T-2 may produce similar effects on hormonal secretion.

Cardiovascular and thermoregulatory responses

No specific research has been conducted on 2C-T-2. Only subjective evidence is available from user surveys, showing a variety of observations on cardiovascular and thermoregulatory responses. However, the sample size of the Murple survey was smaller than the one for 2C-T-7.

User comments collated by Murple (2001) indicated that 16.3 % experienced tachycardia and 2.3 % experienced hypertension (both largely route independent). It is doubtful, however, that users had access to blood pressure and heart rate monitors for medical confirmation of these symptoms. Compared to 2C-T-7, where 31.9 % of users noted headaches (indicating possible increased blood pressure), only 9.3 % reported headaches with 2C-T-2 (Murple, 2001).

Although various (inconsistent) observations regarding effects on body temperature were described by Murple, this information appears to be associated with 2C-T-7, not 2C-T-2.

Toxicology

At present, there are no animal or human data concerning the general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-T-2.

Toxicity in animals

Shulgin and Shulgin (1991) reported on studies on mice involving intraperitoneal (i.p.) administration of DOB and found the LD50 to be between 100 and 125 mg/kg. Administration of 50 mg/kg (i.p.) resulted in twitching, 100 mg/kg produced shaking, and mice receiving >125 mg/kg exhibited convulsions and eventually died. No such studies have been performed for 2C-T-2 and, due to the significant structural differences between DOB and 2C-T-2 (which is likely to alter the toxicity of the respective compounds), such data are not directly comparable. In particular, Shulgin describes 2 mg as an effective dose for DOB but suggests that 12 to 25 mg may be required using 2C-T-2.

Toxicity in humans

As mentioned above, only subjective evidence is available from user surveys on the apparent adverse effects and toxic symptoms of 2C-T-2. In a study of 43 self-reporting 2C-T-2 users described by Murple (2001), side-effects of varying degrees were noted in approximately 81 % of users. Of these, none was prolonged or severe, compared to 3 % with 2C-T-7. The most common side-effect was nausea (60.5 %), followed by muscle tension (32.6 %), vomiting (23.3 %), diarrhoea (18.6 %), tachycardia (16.3 %), dehydration (16.3 %; probably related to diarrhoea/vomiting or the administration situation/environment), headaches (9.3 %), hypertension (2.3 %) and, to a smaller extent, some stomach ache and confusion. It should be noted that, overall, there were less adverse effects with 2C-T-2 compared to 2C-T-7. However, the 2C-T-2 study was far smaller (43 respondents) than the 2C-T-7 study (423 respondents). Similar adverse symptoms were reported in a study by Stolaroff and Wells (1993), particularly nausea, vomiting and muscle tension/spasms, but there were less cardiac effects.

Interactions with other drugs or medicines

Unlike other phenethylamine derivatives, including 2C-B, it appears that 2C-T-2 is not usually present in tablets containing other phenethylamines or stimulants (De Boer et al., 1999; Erowid, 2000). This therefore reduces the possibility of concomitant ingestion of other drugs in such illicit preparations. However, as the pharmacology of 2C-T-2 is largely unknown, it is difficult to predict with accuracy any particular potential drug interactions or contraindications. Winter et al. (1999) studied the acute effects of monoamine reuptake inhibitors (SSRIs such as fluvoxamine, fluoxetine and venlafaxine) on the stimulus effects of hallucinogens (including DOM) and observed an additivity of effects rather than a potentiation. It is possible, therefore, that similar effects may occur with 2C-T-2. Some user reports collated by Murple have mentioned the concurrent use of other drugs (Murple, 2001). Other psychedelic drugs apparently produced synergistic effects, whereas benzodiazepines and GHB produced anxiolytic and sedative effects. Like 2C-T-7, stimulants appeared to be potentiated by 2C-T-2. There were a number of individual comments made by users regarding single drugs, but these have not been included in this report. Despite the concomitant use of MDMA by some users, there was no information indicating enhanced MDMA toxicity due to direct (e.g. synergistic) or indirect (e.g. metabolic) effects. In addition, potential adverse interaction with monoamine oxidase inhibitors (MAOIs) has been mentioned

(Murple, 2001). However, no specific studies have been conducted on the effects of such drugs when administered with 2C-T-2, so these and the other potential interactions described above have not been confirmed.

Non-fatal cases of 2C-T-2 intoxication in humans

There have been no reported instances of non-fatal intoxication involving the use of 2C-T-2. It is not usually detected during routine toxicological analysis (typically due to the lack of any reference material), and the indication of use is usually based on anecdotal or circumstantial evidence (if any information is available to medical staff at all).

Fatal cases of 2C-T-2 intoxication in humans

There have been no reported fatalities implicating 2C-T-2. However, the lack of reference material may compromise the analysis of post-mortem cases when conducting clinical toxicological investigations.

Pharmacokinetics and metabolism

No specific research has been conducted on 2C-T-2. However, metabolic studies using 2C-B have been conducted on rats and on human urine (De Boer et al., 1998; Kanamori et al., 2002). Kanamori et al. (2002) identified two pathways in the rat involving (a) initial deamination followed by reduction or oxidation; and (b) 2- or 5-position O-desmethylation followed by amino acetylation. De Boer et al. (1998) identified the unchanged parent compound (i.e. 2C-B) and 4-bromo-2,5-dimethoxyphenylacetic acid, 4-bromo-2,5-dimethoxybenzoic acid and 4-bromo-5-hydroxy-2-methoxyphenethylamine in the urine of 2C-B users. It is likely that metabolism of 2C-T-2 may proceed via similar pathways, probably involving oxidative deamination (I, II) and O-desmethylation of the aromatic methoxy groups (III), in addition to excretion of unchanged drug (the possibility of species-dependent metabolism notwithstanding). This would lead to the corresponding compounds:

- I = 2,5-dimethoxy-4-ethylthiophenylacetic acid
- II = 2,5-dimethoxy-4-ethylthiobenzoic acid
- III = 4-ethylthio-5-hydroxy-2-methoxyphenethylamine

However, additional metabolic reactions are a possibility, particularly involving the ethylthio moiety at the 4-position or (as observed in rats by Kanamori et al., 2002) potential N-acetylation.

Anecdotal evidence from users indicates an onset of action of one to two hours, with effects lasting up to 6 to 8 hours (Murple, 2001). However, these data typically refer to oral ingestion and user comments indicate more rapid onset and shorter duration of effects following insufflation (Murple, 2001). This compares to a duration of action of 8 to 12 hours for orally ingested LSD and 10 to 12 hours for mescaline, as described by Shulgin and Shulgin (1991).

Clinical experience

2C-T-2 has not undergone any clinical or pre-clinical evaluation studies. The majority of data is based on self-reporting by users.

Studies on street users

There have been two studies on 2C-T-2 use (Stolaroff and Wells, 1993; Murple, 2001). Stolaroff and Wells chose subjects who had 'stable personalities' and had 'had no previous experience' of the drugs tested (however, the majority of users had used psychedelic drugs). The 63 subjects were divided into three groups: one group of seven were given MDMA, a group of eight were given 2C-T-7 and the remainder were given 2C-T-2. The drug doses were decided by the individuals (for 2C-T-2, between 10 and 30 mg) and were administered in the morning on an empty stomach, with supplementary doses after two hours if requested (11 of the 2C-T-2 users requested supplementary doses). Subjects were requested to complete a questionnaire within a few days of the experiment. Participants were aged between 18 and 67 (the people in the 2C-T-2 group were also between 18 and 67). The following subjective responses were evaluated: visual activity, clarity of thought, flow of insights, increased sense of a higher meaning, feeling of wellbeing and improved communication, energy levels and overall functioning. In general, the 2C-T-2 sample size was larger than for the other drugs evaluated, but, overall, 2C-T-2 was found to produce similar effects to those of 2C-T-7, though shorter and less intense/euphoric.

The study by Murple (2001) involved collating information from 43 respondents in an Internet-based survey presented on the Erowid website (2001). Of the respondents, 90.7 % were male and 9.3 % were female, with an age range of 16 to 47 (average age 27). Many of the users reported pre-existing medical conditions ranging from asthma to bipolar disorder. Data on the route of administration and dose are presented above. However, doses of between 2.5 and 40 mg of 2C-T-2 for both oral and intranasal administration have been reported, which may indicate that insufflation of 2C-T-2 represents a lower risk than insufflation of 2C-T-7. Respondents reported having used 2C-T-2 an average of 3.69 times, but with a variable frequency of use. Of all the users, 55.8 % indicated they would be willing to use 2C-T-2 again at the same dose, 25.6 % indicated they would like to take a higher dose and 7.0 % reported they would not wish to use it again (of these, six individuals cited non-specific side-effects as the reason). A number of specific comments are presented on the website, but many users reported experiencing strong visual effects, emotional responses similar to MDMA and some negative psychedelic mental effects (anxiety, paranoia, panic attacks). Adverse effects such as nausea, muscle tension and vomiting have been reported in other studies (as described in the 'Toxicology' section above).

Overall, subjective user reports indicate that 2C-T-2 produces various psychedelic effects (generally comparable to other hallucinogens such as mescaline, LSD and 2C-B) along with nausea, muscle tension, vomiting and sometimes 'negative' mental effects (e.g. anxiety). The effects are typically described as being less intense than with 2C-T-7.

Dependence potential in humans

Tolerance

No specific research has been conducted on 2C-T-2. Based on anecdotal user reports, the occurrence of tolerance to the effects of 2C-T-2 appears to be variable (Murple, 2001). If tolerance does occur, it is possible that cross-tolerance may occur between other related psychedelic phenethylamines such as 2C-T-7, 2C-B and mescaline.

Dependence potential

No specific research has been conducted on 2C-T-2. Although the specific pharmacology of 2C-T-2 is unknown, speculative comparison with related compounds suggests that it is unlikely to produce physical dependence or addiction. However, without specific studies, definitive conclusions cannot be drawn.

Psychological risk assessment (cognition, mood and mental functioning)

Acute and chronic effects

There are no published data on the specific psychological effects, acute or chronic, of 2C-T-2. As described in the pharmacological report, anecdotal reports from users describe various subjective psychological effects that occur with 2C-T-2 use.

In a study by Stolaroff and Wells (1993), 75 % of users reported enhanced clarity of thought and 5 % described a loss of clarity; 77.5 % of users reported an improvement in the 'flow of insights', with only 2.5 % reporting that this worsened; 82.5 % described an increase in the perception of a higher meaning (compared to 62.5 % for 2C-T-7); 80 % of users reported an improvement in their sense of wellbeing (compared to 100 % for MDMA). Finally, 62.5 % of users also described an improvement in communication skills and 17.5 % reported a deterioration in such skills.

Reports from 43 users collated by Murple (2001) mentioned various feelings of wellbeing and mental clarity a day after ingestion, whereas some users described being mentally drained and emotionally disturbed. When questioned about the possible long-term effects, 46.5 % of users failed to answer, 18.6 % felt they had benefited psychologically, no users felt they had been psychologically harmed and 34.9 % felt there were no long-term psychological effects. However, such responses are purely speculative in terms of the potential chronic effects of 2C-T-2.

Conclusions

- 2C-T-2 is a synthetic drug which was first synthesised in 1981 by Shulgin.
- Seized/available material includes white powder or white tablets.
- 2C-T-2 has no licensed therapeutic or industrial use.
- 2C-T-2 is a potential 5-HT_{2C}, 5-HT_{2A}, 5-HT₁ and α_1 -adrenergic receptor agonist.
- Users report hallucinogenic/visual effects similar to 2C-B, LSD and mescaline, and feelings of empathy similar to MDMA. Other effects reported are nausea, muscle tension, vomiting, anxiety and some confusion/disorientation.
- Self-reporting users have only mentioned oral ingestion and insufflation (snorting) of 2C-T-2.
- Due to the lack of specific scientific evidence, acute or chronic toxicity of 2C-T-2 has not been confirmed in humans, but toxic effects cannot be excluded.
- There have been no reported cases of fatal or non-fatal intoxication.

Review of the pharmacotoxicological data on 2C-T-7 ⁽¹³⁾

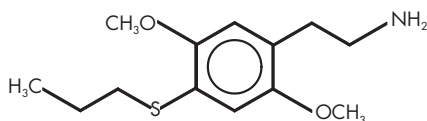
Very limited data for 2C-T-7 have been published in peer-reviewed scientific journals. The following information includes studies involving structurally related compounds and user-based evidence (Information Classification IV, EMCDDA, 1999). Studies are ongoing to obtain further scientific data on this compound.

Chemical and pharmaceutical information

Chemical description

The chemical structure of 2,5-dimethoxy-4-(n)-propylthiophenethylamine (2C-T-7) is shown below (Figure 1). The abbreviation '2C-T-7' is derived from the nomenclature according to Shulgin and Shulgin (1991), and, although this compound has more carbons than 2C-T-2, the '-7' part of the abbreviation has no structural significance but simply refers to the historical order of study/discovery (Pihkal No 43). Other chemical names are rearrangements of the name shown above (such as 4-propylthio-2,5-dimethoxy-phenethylamine, or PT-DM-PEA).

Chemical structure of 2C-T-7



Molecular formula: $C_{13}H_{21}NO_2S$
Molecular weight: 255.37

There is no chemical abstracts registration (CAS) number for 2C-T-7. 2C-T-7 base is an oil, whereas 2C-T-7 hydrochloride is a white crystalline solid.

⁽¹³⁾ This report was written by S. P. Elliott of the Regional Laboratory for Toxicology (City Hospital, Birmingham, United Kingdom) for the risk assessment meeting on 2C-T-7 held in Lisbon on 31 March and 1 April 2003. Help and information was provided by: S. Ahlstrom, D. Corrigan, C. Furnari, J. Idanpää-Heikkilä, M. Mallaret, C. Poethko-Muller, J-P. Tassin, A. Wallon, R. Wennig, L. Westberg. The report was commissioned by the EMCDDA as a background paper for the risk assessment of the compound 2C-T-7. The report follows the structure of Annexes A and B of the risk assessment guidelines developed by the Scientific Committee of the EMCDDA.

Methods of synthesis

It is thought that 2C-T-7 was first synthesised in 1986 by Shulgin (Hardison, 2000; Erowid, 2001). A synthesis protocol was later described in *Pihkal* based on initial use of 1,4-dimethoxybenzene to produce a preliminary precursor, 2,5-dimethoxythiophenol (Shulgin and Shulgin, 1991). Shulgin and Shulgin describe the latter compound as a 'valuable precursor to all members of the 2C-T family' and this is now available commercially (Poortman, 1999). The method is extensive, requiring specialist equipment and an appropriate environment. There is no information about the exact method of synthesis used by clandestine laboratories.

Identification

2C-T-7 exhibits a slow/weak 'salmon orange' (pink, orange-red) colour using the Marquis reagent assay (Erowid, 2000; LTG, 2001; Zimmerman, 2001). A change from dark orange to a dark purplish orange was observed using Mecke's reagent and a cherry-red colour was observed using sodium nitroprusside reagent (Zimmerman, 2001). There is some information regarding the analytical profile of 2C-T-7 using common methods such as gas chromatography with mass spectrometry (GC-MS), or nitrogen-phosphorus detection (GC-NPD), or high performance liquid chromatography with diode-array detection (HPLC-DAD). Curtis et al. (2001) have extracted and identified 2C-T-7 in biological fluids based on GC-NPD with GC-MS confirmatory analysis. Electron impact (EI) mass spectral data have indicated major abundant ions of 226, 183, 255 (molecular ion), 153 and 169 (in order of abundance) (LTG, 2001; Zimmerman, 2001). HPLC-DAD data have shown UV maxima of 206, 253 and 304 nm with a UV spectrum different to that of other phenethylamines, including MDMA, amphetamine and 2C-B (Elliott, 2000). Nuclear magnetic resonance (NMR) and Fourier transform infrared spectroscopy (FTIR) data have also been described (Zimmerman, 2001). 2C-T-7 would not be detected by commonly used immunoassay procedures for the preliminary identification of amphetamines in urine (particularly based on monoclonal antibodies), unless it were present at unusually high concentrations (Elliott, 2001; LTG, 2001).

Legitimate uses of 2C-T-7

There are no known licensed therapeutic uses for 2C-T-7. However, there is some information indicating its use in 'psychedelic therapy' (Shulgin and Shulgin, 1991; Stolaroff and Wells, 1993; Murple, 2001a).

Pharmaceutical form

2C-T-7 is typically available in powder or tablet form, but it may also be found in capsules or liquid form. It has various 'street names', including 'T-seven', 'Beautiful', 'Lucky seven', 'Seven-up', 'Seventh heaven', 'Red raspberry', 'Tweety bird mescaline' and 'Tripstasy' (Murple, 2001a). Tablets referred to as 'Green fish' and 'Number seven' allegedly contained 2C-T-7, but this could not be confirmed by specific analysis (Murple, 2001a). 2C-T-7 may also have been sold as ketamine. However, as with the majority of information regarding the illicit market, evidence is anecdotal at best. Between 1999 and 2001, 2C-T-7 was available commercially as 'Blue mystic' via Dutch smartshops; the presence of the compound was confirmed by laboratory analysis (Niesink, 2000) and was referred to as PT-DM-PEA on the packaging (originally 7.5 mg, then reformulated to 10 mg). Such tablets are blue in colour, with a 'Yin-yang' logo, and are approximately 7.4 x 4.8 mm, weighing 265 mg (LTG, 2001).

The purchase price varies but is largely comparable to other phenethylamine derivatives such as MDMA (typically EUR 5 to 20) (Erowid, 2002).

Routes of administration and dosage

As 2C-T-7 is obtained in powder or tablet form, the primary route of administration is oral, but insufflation (snorting) is also frequently mentioned in user reports (Murple, 2001a). Less common routes of administration include smoking and rectal, intravenous or intramuscular administration (Murple, 2001a). In the Murple survey of 423 self-reporting 2C-T-7 users, respondents indicated that their usual routes of administration were: oral (68.1 %), insufflation (27.9 %), smoking (2.8 %), rectal (1.2 %) and intravenous/intramuscular (0 %).

Original studies by Shulgin and Shulgin (1991) involved oral administration of 2C-T-7 doses of 20 to 30 mg but indicated that around 10 mg may be sufficient for some users. This is compared to a PiHKal 'recommended' dose of 80 to 150 mg for MDMA, 178 to 256 mg for mescaline (hydrochloride), 12 to 24 mg for 2C-B, 60 to 100 mg for 2C-T, 10 to 30 mg for 2C-T-7, 1 to 3 mg for DOB and 3 to 10 mg for DOM (Shulgin and Shulgin, 1991) and a TiHKal 'recommended' dose of 0.06 to 0.2 mg for LSD (Shulgin and Shulgin, 1997). Respondents in a user survey mentioned oral doses of 1 to 125 mg (average 27 mg), intranasal doses of 0.5 to 50 mg (average 15 mg),

rectal doses of 7 to 33 mg (average 15 mg) and smoking doses of 1 to 40 mg (average 12 mg) and the few respondents using the intravenous/intramuscular route mentioned doses of 1 to 3 mg (Murple, 2001a). The wide range of doses mentioned (particularly for oral administration) and some of the respondents' comments suggested that there may be some individual sensitivity to 2C-T-7. It should be noted, however, that the accuracy of the comments collated by Murple is dependent on user honesty and accurate weighing of the compound or knowledge of the actual content/weight of the tablet/powder's constituents.

Toxicology and pharmacology in animals and humans

No data for 2C-T-7 have been published in peer-reviewed scientific journals. The following information is based on speculative comparison with partially related compounds such as 2C-B (which is based on phenethylamine) and DOB (which is based on amphetamine), both involving bromine as opposed to sulphur. It is inappropriate to compare data derived from MDMA, PMA and 4-MTA studies, due to the absence of 2,5-dimethoxy substituent groups in such compounds.

Neuropharmacology

No specific research has been conducted using 2C-T-7. Studies by Lobos et al. (1992) involving a bromine-substituted analogue, 2C-B (4-bromo-2,5-dimethoxyphenethylamine), have shown it to be a partial agonist for 5-HT₂ (5-HT_{2A} and 5-HT_{2C}) serotonergic receptors and α_1 -adrenergic receptors. At 10⁻⁶M, 2C-B also acted as a competitive 5-HT antagonist, but, at higher concentrations (2.8 × 10⁻⁵M), it acted as a non-competitive 5-HT antagonist (Lobos et al., 1992). In addition, Glennon et al. (1988) found that DOB (4-bromo-2,5-dimethoxyamphetamine) had a high affinity for 5-HT₂ receptors, whereas 2C-B was also found to have significant affinity for 5-HT_{1A}, 5-HT_{1B} and 5-HT_{1C} receptors and thus was deemed to be less selective than its amphetamine-based analogue, DOB. Therefore, as 2C-T-7 is phenethylamine based, it is possible it may have serotonergic receptor affinity similar to 2C-B (i.e. binding to 5-HT₂ and, to some degree, 5-HT₁ receptors). Researchers have already provided evidence of the involvement of 5-HT₂ serotonergic receptors (in particular 5-HT_{2A}) in the action of hallucinogenic agents (Glennon et al., 1984). It is conceivable, therefore, that the apparent hallucinogenic effects of 2C-T-7 may be related to similar receptor affinities. However, such conjecture is only based on limited

information on related compounds and further specific studies of 2C-T-7 are required before definitive conclusions can be drawn.

Neuroendocrinology

No specific research has been conducted using 2C-T-7. Serotonin agonists stimulate hypothalamic neurons involved in ACTH and cortisol secretion (Fuller, 1981), in addition to stimulating growth hormone and prolactin secretion (as evidenced by mescaline and DOM) (Meltzer et al., 1978, 1981; Demisch and Neubauer, 1979). It is possible, therefore, that 2C-T-7 may produce similar effects on hormonal secretion.

Cardiovascular and thermoregulatory responses

No specific research has been conducted using 2C-T-7. Only subjective evidence is available from user surveys, which indicates varying observations for these clinical features. User comments compiled by Murple (2001b) indicated that 21.8 % experienced tachycardia and 5.9 % experienced hypertension (both largely route independent). It is doubtful, however, that users had access to blood pressure and heart rate monitors for medical confirmation of these symptoms. Headaches were noted by 31.9 % of users, indicating possible increased blood pressure (Murple, 2001b). Tachycardia was also mentioned in the evaluation conducted by Hardison (2000). The Murple user survey also included inconsistent observations regarding effects on body temperature, with users feeling hot and/or cold. There did not appear to be any obvious consistency between reports.

Toxicology

At present, there are no animal or human data concerning the general toxicity, reproductive toxicity, neurotoxicity or the mutagenicity and carcinogenic potential of 2C-T-7.

Toxicity in animals

Shulgin and Shulgin (1991) reported on studies on mice involving intraperitoneal (i.p.) administration of DOB and found the LD₅₀ to be between 100 and 125 mg/kg. Administration of 50 mg/kg (i.p.) resulted in twitching, 100 mg/kg produced shaking, and mice receiving >125 mg/kg exhibited convulsions and eventually died. No such studies have been conducted for 2C-T-7 and, due to the significant structural

differences between DOB and 2C-T-7 (which is likely to alter the toxicity of the respective compounds), such data are not directly comparable. In particular, Shulgin describes 2 mg as an effective dose for DOB but suggests that 10 mg may be required using 2C-T-7.

Toxicity in humans

As mentioned above, only subjective evidence is available from user surveys on the apparent adverse effects and toxic symptoms of 2C-T-7. In a study of 423 self-reporting 2C-T-7 users described by Murple (2001a), side-effects of varying degrees were noted in approximately 85 % of users. Of these, 3 % found them to be prolonged and severe. Intranasal administration appeared to result in a greater number of adverse user reports than oral administration. The most common side-effect was nausea (62.7 %), followed by headaches (31.9 %), vomiting (30.5 %), tachycardia (21.8 %), dehydration (18.0 %; probably related to diarrhoea/vomiting or the administration situation/environment), diarrhoea (6.2 %), hypertension (5.9 %) and, to a smaller extent, some gastrointestinal effects, confusion or delirium (at high doses), dizziness and muscle spasms. It should be noted that, overall, there were more adverse effects with 2C-T-7 compared to 2C-T-2. However, the 2C-T-2 study was far smaller (43 respondents) than the 2C-T-7 study (423 respondents). Similar adverse symptoms were reported in a study by Stolaroff and Wells (1993), in particular nausea, vomiting, muscle tension/spasms and some inconsistent cardiac effects.

Interactions with other drugs or medicines

Unlike other phenethylamine derivatives, including 2C-B, it appears that 2C-T-7 is not usually present in tablets containing other phenethylamines or stimulants (De Boer et al., 1999; Erwid, 2000). This therefore reduces the possibility of concomitant ingestion of other drugs in such illicit preparations. However, as the pharmacology of 2C-T-7 is largely unknown, it is difficult to predict with accuracy any particular potential drug interactions or contraindications. Winter et al. (1999) studied the acute effects of monoamine reuptake inhibitors (SSRIs such as fluvoxamine, fluoxetine and venlafaxine) on the stimulus effects of hallucinogens (including DOM) and observed an additivity of effects rather than a potentiation. It is possible, therefore, that similar effects may occur with 2C-T-7. Some user reports collated by Murple have mentioned the concurrent use of other drugs (Murple, 2001a). Other psychedelic drugs apparently produced synergistic effects, whereas benzodiazepines and GHB

produced anxiolytic and sedative effects. Stimulants, including caffeine and cocaine, appeared to be potentiated by 2C-T-7. Simultaneous use with benzylpiperazine was reported by several users to reduce the physical side-effects, but one user reported a tachycardia with a heart rate of over 160 bpm. There were a number of individual comments made by users regarding single drugs, but these have not been included in this report. Despite the concomitant use of MDMA by some users, there was no information indicating enhanced MDMA toxicity due to direct (e.g. synergistic) or indirect (e.g. metabolic) effects. In addition, potential adverse interaction with monoamine oxidase inhibitors (MAOIs) has been mentioned, including in the product insert provided with 'Blue mystic' (Erowid, 2000; Murple, 2001a). Murple describes two reports of adverse reactions with deprenyl (MAO B reversible inhibitor), including an incident observed by Shulgin. However, specific studies involving such drugs in combination with 2C-T-7 have not been conducted, so these and the other potential interactions described above have not been confirmed.

Non-fatal cases of 2C-T-7 intoxication in humans

As 2C-T-7 is not usually detected during routine toxicological analysis (typically due to the lack of any reference material), the indication of use is usually based on anecdotal or circumstantial evidence (if any information is available to the medical staff at all). Consequently, confirmed cases of 2C-T-7 intoxication are rare, with no published instances. The Erowid website has received a 'handful of reports' within a four-month period from users reporting hospitalisation resulting from 2C-T-7 use alone (Erowid, 2001). Erowid also reported that high doses can result in prolonged effects associated with individuals 'wandering around ... and ... being incapable of taking care of themselves'. The user survey responses received by Murple (2001a) from respondents in the USA, Mexico, Finland and the Netherlands included anecdotal reports. These reports provide some indication of the circumstances of abuse, but, due to the voluntary nature of the evidence, the details remain anecdotal at best. A brief synopsis follows for each case.

- USA (no date): Approximately 10 minutes following intravenous administration of 25 mg of 2C-T-7 the user became very violent, eventually having to be restrained by the police (including the use of a pepper spray). He was taken to hospital, where he briefly stopped breathing and then became comatose for five days, prior to recovery and discharge.

- USA (2000): Following intranasal administration of 25 mg of 2C-T-7 the user vomited and became extremely confused and disorientated, resulting in emergency admission to hospital. He was discharged the following day.
- Mexico (no date): Following oral administration of 30 mg of 2C-T-7, alcohol ingestion and cannabis smoking, the user collapsed in the street, hit his head and suffered convulsions. He was taken to hospital where a 'mild heart attack' was diagnosed along with concussion. He was a young man who also used LSD, psilocybin and MDMA and may have had a pre-existing heart condition.
- Finland (2000): Following intranasal administration of an estimated 10 mg of 2C-T-7 the user vomited and subsequently fell and hit her head. She suffered convulsions and was taken to hospital. It took more than 10 hours for the effects to wear off for 10 other users that used the same 2C-T-7.
- Netherlands (no date): There is very little information available for this. Possible administration of 2C-T-7 (unspecified route and dose) led to two men panicking and becoming entangled in barbed wire. They were freed by police and taken to hospital, where one man lapsed into a coma for a few days and later recovered.

Overall, there are no confirmed reports of 2C-T-7 administration resulting in non-fatal intoxication. Despite the information described above, there is still very little clinical information about the effects of 2C-T-7 following overdose. Consequently, there are no accurate frequency or demographic data for such instances.

Fatal cases of 2C-T-7 intoxication in humans

At present (as of 2003), three deaths potentially involving 2C-T-7 have been reported in the USA (Erowid, 2001; DEA, 2002). Of these, the presence of 2C-T-7 was confirmed in only one case following specific toxicological analysis. No deaths have been linked to 2C-T-7 within Europe. However, the lack of reference material on clinical toxicology may compromise post-mortem cases. A brief synopsis of the reported fatalities follows.

- USA (2000): Following intranasal administration of 35 mg of 2C-T-7, a 20-year-old male began to feel cold and experienced vomiting and hallucinations. An hour after administration, he became agitated and aggressive and suffered convulsions. About 110 minutes after administration, his companions noticed he had turned blue and

conveyed him to hospital, during which time he stopped breathing, suffered cardiac arrest and died (Erowid, 2001; DEA, 2002). Following toxicological analysis, an unidentified compound in the urine was found to be 2C-T-7 (Curtis et al., 2001). Subsequent analysis detected 2C-T-7 at concentrations of 54 $\mu\text{g/L}$ (micrograms per litre) in heart blood, 100 $\mu\text{g/L}$ in femoral blood, less than 26 $\mu\text{g/L}$ in vitreous humour, 340 ng/g in the brain and 440 $\mu\text{g/L}$ in the urine (Curtis et al., 2001).

- USA (2001): A 17-year-old male apparently took two MDMA tablets and possibly also ephedrine 10 hours prior to intranasal administration of 35 mg of 2C-T-7. Shortly after insufflation of 2C-T-7, he began vomiting, which lasted for 30 to 40 minutes. He then became disorientated and violent and was taken outside, where he was later found unconscious in a friend's car. He died in the car on the way to hospital. The post-mortem specimens were not initially analysed for 2C-T-7. Some months later, the stored blood was analysed, but the findings were 'inconclusive' (Erowid, 2001; DEA, 2002).
- USA (2001): Following oral ingestion of a mixture of 200 mg of MDMA and the contents of a black capsule believed to contain 2C-T-7 (dose unknown), a 24-year-old male became agitated and aggressive/violent. He appears to have suffered seizures and his breathing became irregular. An ambulance was called and he was conveyed to hospital but died shortly after admission (Erowid, 2001; DEA, 2002). Toxicological analysis detected MDMA in the post-mortem blood. No 2C-T-7 was detected in the gastric contents or the liver, but it was identified on the plate believed to have been used to mix the drugs (DEA, 2002).

In conclusion, further data concerning both the circumstances of death and the toxicological findings are required before the involvement of 2C-T-7 can be established and accurate mortality and morbidity figures produced.

Pharmacokinetics and metabolism

No specific research has been conducted using 2C-T-7. However, metabolic studies using 2C-B have been conducted on rats and by analysis of human urine (De Boer et al., 1998; Kanamori et al., 2002). Kanamori et al. (2002) identified two pathways in the rat involving (a) initial deamination followed by reduction or oxidation; and (b) 2- or 5-position O-desmethylation followed by amino acetylation. De Boer et al. (1998) identified the unchanged parent compound (i.e. 2C-B) in addition to 4-bromo-2,5-

dimethoxyphenylacetic acid, 4-bromo-2,5-dimethoxybenzoic acid and 4-bromo-5-hydroxy-2-methoxyphenethylamine in the urine of 2C-B users. It is likely that metabolism of 2C-T-7 may proceed via similar pathways, probably involving oxidative deamination (I, II) and O-desmethylation of the aromatic methoxy groups (III) in addition to excretion of unchanged drug (the possibility of species-dependent metabolism notwithstanding). This would lead to the corresponding compounds:

I = 2,5-dimethoxy-4-propylthiophenylacetic acid

II = 2,5-dimethoxy-4-propylthiobenzoic acid

III = 4-propylthio-5-hydroxy-2-methoxyphenethylamine

However, additional metabolic reactions are a possibility, particularly involving the propylthio moiety at the 4-position or (as observed in rats by Kanamori et al., 2002) potential N-acetylation.

Anecdotal evidence from users indicates an onset of action of one to two and a half hours, particularly if taken on an empty stomach, with effects lasting up to 15 hours (Hardison, 2000; Erowid, 2001). However, these data typically refer to oral ingestion and user comments indicate more rapid onset and shorter duration of effects following insufflation (Murple, 2001b). This compares to a duration of action of 8 to 12 hours for orally ingested LSD and 10 to 12 hours for mescaline (Shulgin and Shulgin, 1991).

Clinical experience

2C-T-7 has not undergone any clinical or pre-clinical evaluation studies. The majority of data is based on self-reporting by users.

Studies on street users

There have been three studies on 2C-T-7 use (Stolaroff and Wells, 1993; Hardison, 2000; Murple, 2001a). Stolaroff and Wells chose subjects who had 'stable personalities' and had 'had no previous experience' of the drugs tested (however, the majority of users had used psychedelic drugs). The 63 subjects were divided into three groups: seven were given MDMA, eight were given 2C-T-7 and the remainder were given 2C-T-2. The drug doses were decided by the individuals (for 2C-T-7, between

20 and 25 mg) and were administered in the morning on an empty stomach, with supplementary doses after two hours if requested (six of the eight 2C-T-7 users requested supplementary doses). Subjects were requested to complete a questionnaire within a few days of the experiment. Participants were aged between 18 and 67 (the 2C-T-7 group were aged between 30 and 57). The following subjective responses were evaluated: visual activity, clarity of thought, effects on flow of insights, increased perception of higher meaning, a feeling of wellbeing and improved communication skills, energy level and overall functioning. In general, the 2C-T-7 sample size was fairly limited and so responses require further confirmation. However, overall, 2C-T-7 was found to produce similar effects to those of 2C-T-2, though longer and more intense/euphoric.

Hardison (2000) evaluated retrospectively the subjective reports of 42 2C-T-7 users (13 females and 29 males) aged 24 to 73. Of these, 33 reported having no previous experience of 2C-T-7. Doses of between 25 and 45 mg were voluntarily administered (25 to 45 mg for males and 25 to 33 mg for females). Some users had also used cannabis (11 users), dihydrocodeine and diazepam (2), alcohol (1), cocaine (1) and 'flower essences' (1) at the same time as 2C-T-7. The onset of effects appeared to range from 15 minutes to four hours (typically one to two hours) and peak experiences occurred after one to six hours and lasted a further one to five hours, but the total length of duration was reported to be between eight and 18 hours. Comments relating to the users' mindset, clarity of thought, movement and energy levels were requested. Respondents noted various subjective responses: 'complete and utter bliss, incredible, cosmic and extremely grateful', 'general sense of wellbeing', 'some emotional periods, feeling sad and disorientated' and 'some difficulties in focusing my thoughts, clear but disorientated'. The majority of responses were described as being largely similar for all users. Various adverse effects were noted (described in the section 'Toxicology') and these were similar to those reported in other studies (e.g. headaches and extreme nausea).

The study by Murple (2001a) involved collating information from 423 respondents in an Internet-based survey presented on the Erowid website (Erowid, 2001). Of respondents, 89.4 % were male and 9.9 % were female (0.7 % not specified), with an age range of 14 to 64 (average age 27). Many of the users reported pre-existing medical conditions ranging from asthma to bipolar disorder. Data on the route of

administration and dose are presented above. However, doses of 1 to 125 mg of 2C-T-7 (particularly for oral ingestion) were reported, with lower doses (up to 50 mg) taken via insufflation, intravenous/intramuscular administration, smoking and rectal administration. Respondents reported having used 2C-T-7 an average of 4.78 times, but with a variable frequency of use. Of all users, 48.0 % indicated they would be willing to use 2C-T-7 again at the same dose, but 5.0 % reported they would not wish to use it again (particularly intranasal users), as a number of these individuals had experienced pain following insufflation and the effects were too intense. A large number of specific comments are presented on the website, but many users reported experiencing strong visual effects, emotional responses similar to MDMA, some negative psychedelic mental effects (e.g. anxiety, paranoia, panic attacks), delirium (at high doses), an increased sense of physical fitness and general enhancement of the senses. As with the other studies described here, adverse effects such as headache, nausea and vomiting were noted (described in the section 'Toxicology').

Overall, subjective user reports indicate that 2C-T-7 produces various psychedelic effects (generally comparable to other hallucinogens such as mescaline, LSD and 2C-B), along with vomiting, headaches and sometimes 'negative' mental effects (e.g. anxiety). The effects are typically described as being intense, often causing severe disorientation/disassociation at high doses, particularly following insufflation.

Dependence potential in humans

Tolerance

No specific research has been conducted using 2C-T-7. Based on anecdotal user reports, the occurrence of tolerance to the effects of 2C-T-7 appears to be variable (Murple, 2001a). Some users report a definite tolerance, whilst some who have regularly used low doses do not. The Erowid website (2001) suggests that using 2C-T-7 two days in a row is likely to lead to a diminished experience on the second day. If tolerance does occur, it is possible that cross-tolerance may occur between other related psychedelic phenethylamines such as 2C-T-2, 2C-B and mescaline.

Dependence potential

No specific research has been conducted using 2C-T-7. Despite this, the Erowid website (2001) states that 2C-T-7 is neither physically addictive nor is it likely to cause psychological dependence. Although the specific pharmacology of 2C-T-7 is

unknown, speculative comparison with related compounds suggests that it is unlikely to produce physical dependence or addiction such as occurs with opiate use. However, without specific studies, definitive conclusions cannot be drawn.

Psychological risk assessment (cognition, mood and mental functioning)

Acute and chronic effects

There are no published data on the specific psychological effects of 2C-T-7, acute or chronic. As described in the pharmacological report, anecdotal reports from users describe various subjective psychological effects that occur with 2C-T-7 use.

In a study by Stolaroff and Wells (1993), 87.5 % of users reported enhanced clarity of thought and 12.5 % described diminished clarity; 50 % of users reported an improvement in the 'flow of insights' and 12.5 % reported that this worsened; 62.5 % described an increase in the perception of a higher meaning (compared to 82.5 % for 2C-T-2); 75 % of users reported an improvement in their sense of wellbeing (compared to 100 % for MDMA). Finally, 75 % of users also described an improvement in their communication skills, but there were no reports of 2C-T-7 impairing communication skills.

A retrospective subjective study of 2C-T-7 users by Hardison (2000) included specific comments such as 'extraordinary free roaming, very lucid and philosophic', 'complete and utter bliss, incredible, cosmic and extremely grateful', 'general sense of wellbeing, I had many insights, catharsis early on', 'some emotional periods, feeling sad and disorientated', 'clarity of thought somewhere between MDMA and LSD', 'some difficulties in focusing my thoughts, clear but disorientated', 'I moved in an easy coordinated manner while hiking and climbing' and 'clarity uncaged, crystalline thoughts, movements like an animal, confident and energetic'.

Reports by 423 users collated by Murple (2001b) also included numerous comments. One user in particular stated, 'I found it to be one of the most powerful cognition enhancers I've ever encountered'. Some users also mentioned experiencing feelings of empathy similar to MDMA. After-effects included euphoria and, conversely, 'mental sluggishness', including impaired memory recall, mild confusion/disorientation and difficulty in concentrating. When questions about the possible long-term effects were posed, 36.9 % of users failed to answer, 29.6 % felt they had benefited

psychologically, 2.1 % felt they had been psychologically harmed and 30.0 % felt there were no long-term psychological effects. However, such responses are purely speculative in terms of the potential chronic effects of 2C-T-7.

Conclusions

- 2C-T-7 is a synthetic drug which was first synthesised in 1986 by Shulgin.
- Seized/available material includes powder, tablets (blue, 'Yin-yang' logo), capsules or liquid preparations.
- 2C-T-7 has no licensed therapeutic or industrial use.
- 2C-T-7 is a potential 5-HT_{2C}, 5-HT_{2A}, 5-HT₁ and α_1 -adrenergic receptor agonist.
- Users report hallucinogenic/visual effects (similar to 2C-B, LSD and mescaline) and emotional/empathetic responses (similar to MDMA). Other effects reported are nausea, headaches, vomiting, anxiety, confusion/disorientation, agitation, aggression and violent behaviour.
- Both oral ingestion and insufflation (snorting) of 2C-T-7 have been reported. However, self-reporting users have also mentioned rectal use and injection.
- Due to the lack of specific scientific evidence, acute or chronic toxicity of 2C-T-7 has not been confirmed in humans, but toxic effects cannot be excluded.
- There has been one death in which the involvement of 2C-T-7 has been confirmed in the USA; and no reported fatalities in Europe. There have been no confirmed reports of non-fatal intoxication.

Table 1: Comparison of pharmacotoxicological data for 2C-I, 2C-T-2 and 2C-T-7

	2C-I	2C-T-2	2C-T-7
Synthesis (precursors)	2,5-dimethoxybenzaldehyde, used to form 2,5-dimethoxyphenethylamine	1,4-dimethoxybenzene, used to form 2,5-dimethoxythiophenol	1,4-dimethoxybenzene, used to form 2,5-dimethoxythiophenol
Identification (reported techniques)	No information	Marquis (red orange) GC-MS and FTIR	Marquis (pink orange) HPLC, GC-NPD, GC-MS, NMR and FTIR
Form	Powder, tablet (white, 'i' logo) and liquid	Powder, tablet (white)	Powder, tablet ('Blue mystic'), capsules and liquid
Dose	oral 15–20 mg (<i>Pihkal</i>) 3–25 mg (<i>users</i>)	12–25 mg (<i>Pihkal</i>) 5–40 mg (<i>users</i>)	10–30 mg (<i>Pihkal</i>) 1–125 mg (<i>users</i>)
	insufflation <i>No information</i>	2.5–35 mg (average 13 mg)	0.5–50 mg (average 15 mg)
Route	Oral	Oral (83.7%) and insufflation (16.3%)	Oral (68.1%), insufflation (27.9%), smoking (2.8%), rectal (1.2%) and i.v./i.m. (0%)
Metabolism (based on 2C-B data)	Oxidative deamination O-desmethylation N-acetylation	Oxidative deamination O-desmethylation N-acetylation Sulphoxidation	Oxidative deamination O-desmethylation N-acetylation Sulphoxidation
Neuropharmacology	5-HT _{2C} , 5-HT _{2A} and serotonergic receptors (published data)	5-HT _{2C} , 5-HT _{2A} , 5-HT ₁ serotonergic and α_1 -adrenergic receptors (based on 2C-B and DOB data)	5-HT _{2C} , 5-HT _{2A} , 5-HT ₁ serotonergic and α_1 -adrenergic receptors (based on 2C-B and DOB data)

	2C-1	2C-T-2	2C-T-7
Cardiac effects	No information	<i>Tachycardia (16.3 %)</i> <i>Hypertension (2.3 %)</i>	<i>Tachycardia (21.8 %)</i> <i>Hypertension (5.9 %)</i>
Thermoregulatory response	No information	<i>Inconclusive</i>	<i>Inconclusive</i>
Toxicity (in humans)	<i>Delayed effects (possible additional dosage)</i> <i>No adverse effects reported</i>	1. <i>Nausea (60.5 %)</i> 2. <i>Muscle tension (32.6 %)</i> 3. <i>Vomiting (23.3 %)</i> 4. <i>Diarrhoea (18.6 %)</i> 5. <i>Tachycardia/dehydration (16 %)</i>	1. <i>Nausea (62.7 %)</i> 2. <i>Headaches (31.9 %)</i> 3. <i>Vomiting (30.5 %)</i> 4. <i>Tachycardia (21.8 %)</i> 5. <i>Dehydration (18 %)</i>
Interactions	SSRIs: additive effect with DOM	SSRIs: additive effect with DOM <i>Stimulants: potentiated</i> <i>Psychedelics: synergistic</i> <i>Sedatives: no potentiation/synergy</i> <i>MAOIs: inconclusive</i>	SSRIs: additive effect with DOM <i>Stimulants: potentiated</i> <i>Psychedelics: synergistic</i> <i>Sedatives: no potentiation/synergy</i> <i>MAOIs: inconclusive</i>
Non-fatal cases (reported effects/toxicity)	No reported cases	No reported cases	<i>Violence, agitation, vomiting, confusion, disorientation, coma</i>
Fatal cases (reported effects/toxicity)	No reported cases	No reported cases	<i>Violence, agitation, vomiting, convulsions, coma, respiratory depression</i>

	2C-1	2C-T-2	2C-T-7
Onset (oral)	<i>Initial effects 1 to 2 hours, but some users report very slow initial effects or delayed peak effects</i>	1 to 2 hours	1 to 2.5 hours
Duration (oral)	Up to 10 hours	Up to 6 to 8 hours	Up to 15 hours
Effects	<i>Hallucinogenic/visual effects Effects similar to or less intense than 2C-B Strong stimulant Emotional effects/feelings of empathy</i>	<i>Hallucinogenic/visual effects Effects less intense and shorter than 2C-T-7 Emotional effects/feelings of empathy Anxiety</i>	<i>Hallucinogenic/visual effects Effects more intense and prolonged than 2C-T-2 Emotional effects/feelings of empathy Anxiety</i>
Dependence/Tolerance	No information	Inconclusive	Inconclusive
Psychological effects (*)	<i>Improved clarity of thought Little/no psychological effects Feelings of empathy</i>	<i>Improved clarity of thought (75 %) Impaired clarity of thought (5 %) Increased perception (82.5 %) Increased feeling of wellbeing (80 %) Improved powers of communication (62.5 %) Psychological benefit (18.6 %) Feelings of empathy</i>	<i>Improved clarity of thought (87.5 %) Impaired clarity of thought (12.5 %) Increased perception (62.5 %) Increased feeling of wellbeing (75 %) Improved powers of communication (75 %) Psychological benefit (29.6 %) Feelings of empathy Confusion/disorientation</i>

Data in *italics* are based on uncontrolled, subjective, self-reporting user studies/reports (EMCDDA, Information Classification IV). Percentage values relate to the survey findings of Murple (2001).

(*) Subjective psychological effects for 2C-T-2 and 2C-T-7 are based on a user survey by Murple (2001).

Chapter 4

Sociological and criminological evidence and public health risks of 2C-I, 2C-T-2 and 2C-T-7

Introduction

This chapter summarises the relevant data required by technical annexes C and D of the guidelines for the risk assessment of new synthetic drugs. In the absence of systematic studies of the use of 2C-I, 2C-T-2 and 2C-T-7, the evidence for this report is based on limited information collected from:

1. The Reitox national focal points in the 15 EU Member States
2. Europol's contribution to the risk assessment of 2C-I, 2C-T-2 and 2C-T-7
3. Published research literature
4. Telephone interviews with key experts in the field of drugs research
5. The Internet (English-language searches)
6. Youth media (English-language searches)
7. EMCDDA publications
8. DEA documents

The numbers in the list above are used in this chapter, in square brackets, to code general sources of information. Specific published references are provided at the end of the book.

Sociological and criminological evidence

Social consequences for the user

There is no evidence regarding the social consequences of use of 2C-I, 2C-T-2 and 2C-T-7 or the effects on the social behaviour of users. As with all illicit drug use, lack of scientific and objective information may contribute to harm. Firstly, inaccurate media coverage and overestimates of use may promote diffusion by encouraging young people to try the substance. Secondly, official dissemination of inaccurate information in order to prevent drug use by exaggerating the risks may be counterproductive, as this may result in official sources losing credibility (Farrell, 1989; ESPAD, 1995; EMCDDA, 1999).

Wholesale production and distribution

Law enforcement agencies from all 15 Member States reported to Europol that there is no information available that would suggest large-scale production or distribution of and/or trafficking in 2C-I, 2C-T-2 or 2C-T-7 or that organised crime has a role in these activities. Germany reported incidental, small-scale production, in 1999, of 2C-I, 2C-T-2 and 2C-T-7 in kitchen-type facilities and Sweden reported small-scale production of 2C-I. Belgium and Italy reported that the main reason for their lack of information is the fact that the substance is not controlled in those countries and, therefore, no records are being kept within the law-enforcement system.

Member States' law enforcement agencies had no record of violence in connection with the production and distribution of, and trafficking in, 2C-I, 2C-T-2 or 2C-T-7. No reliable data are available on the extent of money-laundering in relation to such activities.

Public health risks: epidemiological evidence

Availability and quality of product on the market

Information based on early-warning databases suggests that 2C-I, 2C-T-2 and 2C-T-7 are very rare. Research on ecstasy use among recreational drug users in dance and nightlife settings shows that friends are the most usual source for obtaining illicit drugs but they are also available through retail dealers and dealer users (McElrath and McEvoy, 1999; Mixmag study; EMCDDA, 1997).

From 1997, 2C-T-2 was sold in so-called 'smartshops' ⁽¹⁾ in the Netherlands: in 1998, Conscious Dreams began to market 2C-T-2, whilst DeSjamaan ⁽²⁾ were independently obtaining and selling 2C-T-2.

In 1998 a smartshop in Sweden was selling 2C-T-2. However, smartshops stopped selling 2C-T-2 as a result of controls introduced in April 1999 in the Netherlands and Sweden (Murple, 2001) [1]. Since then, there has been no evidence that it has become a black market drug. A reason for this may be that it is more difficult for underground laboratories to manufacture 2C-T-2 than other drugs for which there is

⁽¹⁾ Smartshops usually sell various herbal drugs, nutritional supplements, etc.

⁽²⁾ 'Conscious Dreams' and DeSjamaan are names for smartshops.

more demand. An Internet search using the Google search engine in March 2003 did not find online sales of 2C-T-2.

From 1999, 2C-T-7 was sold in smartshops in the Netherlands. In early 2000, DeSjamaan Internet suppliers began selling 2C-T-7 under the trade name 'Blue Mystic'; this stopped in May 2001. According to the Amsterdam Antennae project, 2C-T-7 has not been available in Amsterdam for the past two years [1]. An Internet search using Google in March 2003 did not find online sales of 2C-T-7.

Reports from the Netherlands [1] indicate that white tablets containing 2C-T-2 were sold as 2C-T-7 in 1997. In August 2002, white tablets containing 2C-T-2 were sold as 'mescaline' in France. In 2000, some Blue Mystic tablets contained a small amount of 2C-B [1].

The total amount of 2C-I, 2C-T-2 and 2C-T-7 seized in the Member States is very small when compared to ecstasy seizures in the European Union (more than 15 million tablets annually in recent years). Denmark, Germany, Sweden and the UK reported seizures of 2C-I (the German and Swedish seizures related to the seized kitchen-type facilities mentioned above). Denmark, Germany, France, Finland and Sweden reported small seizures of 2C-T-2 (the German seizure related to the seized kitchen-type facility). Denmark reported a case of international trafficking of 2C-T-2 through the mail system; the drug originated in the Netherlands. Germany, France, Finland and Sweden reported seizures of 2C-T-7, which were small, both in terms of numbers and the quantities seized. Finland reported a seizure, in 2001, of 0.06 gm of 2C-T-7. France reported a seizure, in 2001, of three tablets of 2C-T-7. Germany reported a seizure (from the laboratory in Brannenburg), in 1999, of 7.7 gm of 2C-T-7, and another in Berlin, between 1996 and 1998, with no further details available. In Sweden, one seizure of 2C-T-7 occurred in 1998, one in 1999, one in 2000 and one in 2001. In all the Swedish cases, the amounts seized were small and occurred at street level [2].

There is little information on the (street) price of 2C-I, 2C-T-2 and 2C-T-7. Purchase prices vary but are largely comparable to other phenethylamine derivatives. Past Internet sales (Murple, 2001) have indicated a price of around EUR5 per tablet of 2C-T-2 or 2C-T-7 (with variations between the different shops). In October 2003, the UK authorities issued an alert stating that a new dance drug (2C-I) 'may appeal to

dealers because – unlike ecstasy, which can now sell for as little as GBP 1 each – 2C-I pills can fetch up to GBP 10 each' [1].

Knowledge, perceptions and availability of information

Availability of information on effects of product

The main information sources are Internet sites and 'dance floor pharmacology', an informal network whereby information passes from friend to friend. The popularity of websites such as www.erowid.org shows the breadth of public interest in drugs. In general, news posted on these sites is acknowledged to be so far ahead of the curve and so readily available that official regulators use the sites to keep abreast of new drug trends [1]. Despite the prevalence of publications warning of the potential harm associated with using health information from the Internet, a systematic search of peer-reviewed literature found that there were few instances of reported harm (Crocco et al., 2000). This may be due to an actual low risk for harm associated with the use of information available on the Internet, or to under-reporting of cases, or to bias.

Level of awareness of product, effects and perceptions among drug consumers

There is a general absence of knowledge about 2C-I, 2C-T-2 and 2C-T-7, even among clubbers with comparatively high prevalence of illicit drug consumption (Mixmag study), with the exception of a very small esoteric subgroup of experimenters who may use mescaline, DOB or 2C-B for experiencing a wider range of effects (Schifano and Martinotti, in preparation). 2C-I has often been seized in tablet form with an 'I' logo which may be to signify to users that it is not ecstasy (MDMA).

Due to a lack of peer-reviewed human research studies, the level of knowledge among consumers, as demonstrated on the Internet, appears to be more comprehensive than it is among the general scientific community. However, perceptions among consumers about the contents of products sold as 2C-I, 2C-T-2 and 2C-T-7 are usually based on the information provided by suppliers and on the typical beliefs of consumers. In the absence of accurate and regulated chemical analysis of the contents, objective scientific knowledge remains extremely limited.

Prevalence and patterns of use

Extent, frequency and routes of use

No reliable evidence exists on the extent and frequency of use of 2C-I, 2C-T-2 and 2C-T-7.

In the Netherlands, targeted surveys conducted by the Amsterdam Antennae project in different settings found lifetime prevalence of 2C-T-2 use of around 2 %, compared to over 50 % for ecstasy (1). An Internet survey of 2C-T-2 users obtained 43 valid responses from people who had taken 2C-T-2. However, their countries of residence are unknown, although many were probably from the USA (Murple, 2001). The same Internet survey showed use of between 1 and 20 times, with 3.69 the average number of times. Doses ranged from 5 mg to 40 mg, with the average being 21 mg. Respondents in neither of the studies are representative of the general population.

In the Netherlands, targeted surveys conducted by the Amsterdam Antennae project in different settings found lifetime prevalence of 2C-T-7 to be less than 1 %, compared to over 50 % for ecstasy [1]. In the UK, a dance music magazine survey of nearly 500 respondents in 2002 found that none of those surveyed had ever tried 2C-T-7 [4]. An Internet survey of 2C-T-7 users obtained 423 valid responses from people who had taken 2C-T-7. However, their countries of residence are unknown, although many were probably from the USA (Murple, 2001). In the same survey, use ranged from 1 to 200 times with 4.78 the average number of times. Doses ranged from 1 mg to 125 mg with the average being 27 mg. The reported routes of administration were oral (69 %) and by insufflation (28 %). However, very low levels of use by smoking, rectal insertion and injecting were also reported (Murple, 2001). As above, the respondents in the studies are not representative of the general population.

The participants in the abovementioned Internet surveys and in newsgroups report a number of combinations of 2C-T-2 use with other drugs, and the 2C-T-7 users reported an extensive range of combinations with other drugs (Murple, 2001). The main purpose of using a combination of drugs is to counteract unwanted side-effects or to enhance the desired effects.

There are no scientific reports on 2C-I use in combination with other drugs. However, on one Internet forum users describe a number of combinations, most frequently with

the related compounds LSD and cannabis. As 2C-I is obtained in the form of a powder or tablet, the primary route of administration seems to be oral. Insufflation (snorting) and other routes (e.g. intravenous administration) associated with 2C-T-2 and 2C-T-7 use (Murple, 2001) are not mentioned in 2C-I user reports (Erowid 2001–03).

Geographical distribution of use

There is some limited evidence for use of 2C-I, 2C-T-2 and 2C-T-7 within the European Union. 2C-I has been identified in Denmark, Spain, Sweden and the United Kingdom. 2C-T-2 has been identified in Denmark, Germany, France, the Netherlands and Sweden. 2C-T-7 has been identified in Germany, France, the Netherlands, Finland, Sweden and the UK [1, 2]. Internet research indicates that Japanese, German and Dutch speakers show particular interest in 2C-T drugs (Schifano and Martinotti, in preparation).

Trends in prevalence and patterns of use

Population surveys of young adults in the EU show that lifetime prevalence of hallucinogenic substances, most commonly 'magic mushrooms', ranges from 1 % in Finland to 12 % in the UK. School surveys of 15- to 16-year-olds show that, in the EU, an average of 2 % of this age group have lifetime experience of LSD or other hallucinogens, compared to 10 % in the USA (ESPAD, 1999; EMCDDA, 2002).

According to various reports, 2C-T-2 is less available now than it was in 1999 [1, 2]. It seems to be relatively obscure and the perception remains that it is seen as an inferior version of 2C-T-7. 2C-T-7 is also less available now than in 1999 [1, 2]; the people looking for new experiences may have moved on to other products [4]. The author of the Internet survey cited above suggests that the effects of 2C-T-7 are erratic and highly dose-sensitive, making it unlikely to become very popular (Murple, 2001).

Research has shown that, in general, people tend to use drugs as long as the positive factors outweigh the negative. Epidemiological evidence suggests that trends in the use of hallucinogens such as LSD and magic mushrooms are self-limiting. Two major factors, which affect trends, are availability and the reliability of pleasant experiences. It has been suggested that the ease with which a drug can be made and its effects are more significant for illicit drug consumers than its illegality (McElrath and McEvoy, 1999).

Characteristics and behaviour of users

There is little evidence about the age, gender or social status of users or about the risk behaviours associated with use. Survey evidence from the Internet suggests that males are more likely to use 2C-T-2 and 2C-T-7 than females (91 % of 2C-T-2 respondents and 89 % of 2C-T-7 respondents were male). The age of people who have tried 2C-T-2 ranges from 16 to 47 years and for 2C-T-7 from 14 to 64 years (Murple, 2001).

Special concerns relate to lack of knowledge about the contents of the drugs and about the specific harmful effects of 2C-T-2 and 2C-T-7 use, either alone or combined with other drugs. The group of young people who are particularly vulnerable are those who are at high risk for a range of problems (Parker and Egginton, 2002).

2C-I, 2C-T-2 and 2C-T-7 are, however, used by a small group of people, often referred to as 'psychonauts', who have a pseudo-scientific interest in experimenting with hallucinogenic substances. There appears to be a trend among a small but significant minority of users towards broadening their repertoire of drug experiences, involving a wider range of drugs and combinations. Following the publication of Shulgin and Perry's (2003) new book on plant isoquinolines, a trend in experimenting with such substances might follow.

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Joint action of 16 June 1997

adopted by the Council on the basis of Article K.3 of the Treaty on European Union, concerning the information exchange, risk assessment and the control of new synthetic drugs (97/396/JHA)

THE COUNCIL OF THE EUROPEAN UNION,

Having regard to the Treaty on European Union, in particular Article K.3(2)(b) thereof,

Having regard to the initiative of the Netherlands,

NOTING that the Dublin European Council welcomed the progress report on drugs on 13 and 14 December 1996 and endorsed the action proposed in that report, including the proposal to tackle the problem of synthetic drugs at three levels, namely, through legislation, practical cooperation against production and trafficking and international cooperation,

REFERRING to the Joint Action 96/750/JHA of 17 December 1996, adopted by the Council on the basis of Article K.3 of the Treaty on European Union, concerning the approximation of the laws and practices of the Member States of the European Union to combat drug addiction and to prevent and combat illegal drug trafficking ⁽¹⁾,

REFERRING in particular to Article 5 of the said joint action, which provides that the Member States shall endeavour to draft convergent legislation to the extent necessary to make up legal ground or fill legal vacuums as regards synthetic drugs. In particular they shall promote the establishment of a rapid information system to enable such drugs to be identified as substances liable to be prohibited as soon as they appear anywhere in a Member State,

(¹) OJ L 342, 31.12.1996, p. 6.

CONSIDERING that the particular dangers inherent in the development of synthetic drugs require rapid action by the Member States,

CONSIDERING that when new synthetic drugs are not brought within the scope of criminal law in all Member States, problems may arise in the international cooperation between the judicial authorities and law enforcement agencies of the Member States owing to the fact that the offence or offences in question are not punishable under the laws of both the requesting and the requested State,

CONSIDERING that from an inventory drawn up since the adoption of the said joint action it can be concluded that new synthetic drugs have appeared within the Member States,

CONSIDERING that common action can be taken only on the basis of reliable information on the emergence of new synthetic drugs and the results of expert assessment of the risks caused by the use of the new synthetic drugs and implications of submitting such drugs under control,

CONSIDERING that it is therefore necessary to set up a common mechanism permitting expeditious action, in taking necessary measures or introducing controls on new synthetic drugs, on the basis of a rapid exchange of information on new synthetic drugs emerging in the Member States and the common assessment of the risks thereof,

WITHOUT PREJUDICE to the powers of the European Community,

HAS ADOPTED THIS JOINT ACTION:

Article 1

Purpose

This joint action aims at the creation of a mechanism for rapid exchange of information on new synthetic drugs and the assessment of their risks in order to permit

the application of the measures of control on psychotropic substances, applicable in the Member States, equally to new synthetic drugs. This mechanism will be jointly implemented in accordance with the procedures established hereunder.

Article 2

Scope

This joint action concerns new synthetic drugs which are not currently listed in any of the schedules to the 1971 United Nations Convention on Psychotropic Substances, and which pose a comparable serious threat to public health as the substances listed in Schedules I or II thereto and which have a limited therapeutic value. It relates to end-products, as distinct from precursors in respect of which Council Regulation (EEC) No 3677/90 of 13 December 1990 laying down measures to be taken to discourage the diversion of certain substances to the illicit manufacture of narcotic drugs and psychotropic substances ⁽²⁾ and Council Directive 92/109/EEC of 14 December 1992 on the manufacture and the placing on the market of certain substances used in the illicit manufacture of narcotic drugs and psychotropic substances ⁽³⁾ provide for a Community regime.

Article 3

Exchange of information

1. Each Member State shall ensure that its Europol national unit and its representative in the Reitox network provide information on the production, traffic and use of new synthetic drugs to the Europol Drugs Unit (EDU) of the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), taking into account the respective mandates of these two bodies. The EDU and the EMCDDA shall collect the information received and communicate this information in an appropriate manner

⁽²⁾ OJ L 357, 20.12.1990, p. 1. Regulation as last amended by Commission Regulation (EEC) No 3769/92 (OJ L 383, 29.12.1992, p. 17).

⁽³⁾ OJ L 370, 19.12.1992, p. 76. Directive as amended by Directive 93/46/EEC (OJ L 159, 1.7.1993, p. 134).

immediately to each other and to the Europol national units and the representatives of the Reitox network of the Member States, to the Commission and the European Agency for the Evaluation of Medicinal Products.

2. The information referred to in paragraph 1 shall include:

- (a) — a chemical and physical description, including the name under which a new synthetic drug is known,
 - information on the frequency, circumstances and/or quantities in which a new synthetic drug is encountered,
 - a first indication of the possible risks associated with the new synthetic drug,and, as far as possible:
- (b) — information on the chemical precursors,
 - information on the mode and scope of the established or expected use of the new synthetic drug as a psychotropic substance,
 - information on other use of the new synthetic drug and the extent of such use,
 - further information on the risks of use of the new synthetic drug, including the health and the social risks.

Article 4

Risk assessment

1. At the request of one of the Member States or the Commission, the EMCDDA shall convene a special meeting under the auspices of the Scientific Committee extended with experts nominated by the Member States and to which representatives of the Commission, the EDU and the European Agency for the Evaluation of Medicinal Products shall be invited.

This committee shall assess the possible risks, including the health and social risks, caused by the use of, and traffic in, new synthetic drugs, and possible consequences of prohibition.

2. The risk assessment shall be carried out on the basis of information provided by the Member States, the Commission, the EMCDDA, the EDU of the European Agency for the Evaluation of Medicinal Products and taking into account all factors which, according to the 1971 United Nations Convention on Psychotropic Substances, would warrant the placing of a substance under international control.
3. On completion of the risk assessment, a report will be drawn up on the findings. In the report all aspects shall be addressed. All opinions on these aspects shall be reflected in the report.

Article 5

Procedure for bringing specific new synthetic drugs under control

1. The Council may, on the basis of an initiative to be presented within a month from the date on which the report of the results of the risk assessment pursuant to Article 4 (1) is established and acting in accordance with Article K.3(2)(b) of the Treaty, adopt unanimously a decision defining the new synthetic drug or drugs which are to be made subject to necessary measures of control.

If the Commission deems it not necessary to present an initiative to have the new synthetic drug or drugs submitted to control measures, it shall present a report to the Council explaining its views.

The Member States undertake, in accordance with the decision taken by the Council, within such delay as that decision may specify, to take the necessary measures in accordance with their national law to submit these new synthetic drugs to control measures and criminal penalties as provided under their legislation complying with their obligations under the 1971 United Nations Convention on Psychotropic Substances with respect to substances listed in Schedules I or II thereto.

2. Nothing in this joint action shall prevent a Member State from maintaining or introducing on its territory any national control measure it deems appropriate once a new synthetic drug has been identified by a Member State.
3. The Presidency shall each year submit a report to the Council on the implementation of the decisions adopted by the Council on the basis of paragraph 1.

Article 6

Publication and entry into force

This joint action shall be published in the Official Journal.
It shall enter into force on the day of its publication.

Done at Luxembourg, 16 June 1997.

For the Council

The President

H. VAN MIERLO

European Monitoring Centre for Drugs and Drug Addiction

Report on the risk assessment of 2C-I, 2C-T-2 and 2C-T-7 in the framework of the joint action on new synthetic drugs

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About the EMCDDA

The European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) is one of the decentralised agencies set up by the European Union to carry out specialised technical or scientific work.

Its role is to gather, analyse and disseminate objective, reliable and comparable information on drugs and drug addiction and, in doing so, provide its audiences with a sound and evidence-based picture of the drug phenomenon at European level.

Among the Centre's target groups are policy-makers who use this information to help formulate coherent national and Community drug strategies. Also served are professionals and researchers working in the drugs field and, more broadly, the European media and general public.

EMCDDA risk assessments are publications examining the health and social risks of individual synthetic drugs on the basis of research carried out by the agency and its partners.

