AH-7921

Critical Review Report

Agenda item 4.21

Expert Committee on Drug Dependence

Thirty-sixth Meeting

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World Health Organization

Acknowledgments

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Contents

Summary

AH-7921 is a synthetic opioid. It has been available particularly in Europe since mid-2012 via websites selling "research chemicals" predominantly in powder form. There have been limited published studies but in animals it has been shown to be generally equi-potent to morphine exhibiting a steep dose response curve for respiratory depression. Over a short period of time it has been associated with six non-fatal intoxications and sixteen deaths in four countries. Although other drugs were involved in the majority of cases, AH-7921 was determined to be contributory. Animal studies have indicated both an abuse and dependence potential for AH-7921 but no human data are available.

1. Substance identification

A. International Nonproprietary Name (INN)

Not applicable

B. Chemical Abstract Service (CAS) Registry Number

Free base: 55154-30-8

Hydrochloride salt: 41804-96-0

C. Other Names

AH-7921

3,4-dichloro-N-{[1-(dimethylamino)cyclohexyl]methyl}benzamide

1-(3,4-dichlorobenzamidomethyl)cyclohexyldimethylamine

Doxylam

D. Trade Names

None

E. Street Names

AH-7921 ('AH' refers to 'Allen & Hanburys', the company patenting

the drug); doxylam; doxylan.

AH-7921 is seemingly not associated with any street names but is referred to as AH-7921 on the internet "legal high" websites.

F. Physical properties

AH-7921 is a powder.

G. WHO Review History

AH-7921 was not previously pre-reviewed or critically reviewed. A direct critical review is proposed based on information brought to WHO's attention that AH-7921 is clandestinely manufactured, of especially serious risk to public health and society, and of no recognized therapeutic use by any party. Preliminary data collected from literature and different countries indicated that this substance may cause substantial harm and that it has no medical use.

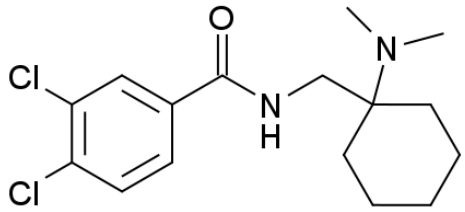
2. Chemistry

A. Chemical Name

IUPAC Name: 3,4-dichloro-N-{[1-(dimethylamino)cyclohexyl]methyl}benzamide.
CA Index Name: Not applicable

B. Chemical Structure

Free base:



Molecular Formula:	$C_{16}H_{22}Cl_2N_2O$
Molecular Weight:	Free base = 329.26
Melting point:	215–216°C (HCl salt); free base melting point is unknown
Boiling point:	not known
Fusion point:	not known

C. Stereoisomers

AH-7921 has no chiral centres and therefore no stereoisomers.

D. Synthesis

The synthesis of AH-7921 has been published (Harper *et al.,* 1974). The reaction of cyclohexanone, potassium cyanide and dimethylamine hydrochloride in aqueous ethanol provides the corresponding α-aminonitrile. This is reduced by $LiAlH_4$ to form the corresponding primary amine which is acylated with 3,4-dichlorobenzoyl chloride in pyridine to form AH-7921.

E. Chemical description

Researchers at the University of Aston in Birmingham and the pharmaceutical company Allen & Hanburys Ltd developed and patented a series of benzamide derivatives with an aminocyclohexane moiety (Harper and Veitch, 1976; Harper *et al.*, 1974). The most active compound in the series was AH-7921. AH-7921 is an N-substituted cyclohexylmethylbenzamide, where the benzamide moiety is dichlorinated at positions 3 and 4 of the ring and the aminocyclohexane moiety is N, N-dimethylated.

F. Chemical properties

See Section B and G.

G. Chemical identification

Extraction and analysis of AH-7921 is relatively straightforward given its chemically basic nature and structure making it amenable to a number of techniques. Detection methods such as gas chromatography with mass-spectrometry (GC-MS), high performance liquid chromatography with diode-array detection (HPLC-DAD) and/or mass-spectrometry (LC-MS) and accurate mass spectrometry have been published as part of case studies (Soh and Elliott 2013, Vorce *et al.,* 2014). The detection outputs depend on the technique used

but for AH-7921, the underivatised GC-electron impact mass spectrum has ion peaks at (m/z) = 126 (base peak); 175 and 173, 147, 145, 109, 84, 58 and 44 (Uchiyama *et al.* 2013 and Vorce *et al.,* 2014). Similarly, with LC-MS, the pronated molecular ion [M+H] of 329.3 m/z is observed with fragmentation resulting in ion peaks at 95, 145, 173, 190 and 284 m/z depending on the collision energy used. No presumptive test data (including Marquis field tests) exist. There is no apparent cross-reactivity with commercially-available urine immunoassay tests for opiates (Elliott 2014).

3. Ease of convertibility into controlled substances

No information available.

4. General pharmacology

4.1. Pharmacodynamics

Animal studies

Researchers at the University of Aston in Birmingham and the pharmaceutical company Allen & Hanburys Ltd developed and patented a series of benzamide derivatives as potential analgesic agents (Harper and Veitch, 1976; Harper *et al.,* 1974). The most active compound in the series was AH-7921 was shown to produce significant analgesic properties in the mouse being equally or slightly more active than morphine both in inhibiting writhing induced by phenylquinone upon oral administration and in reducing nociceptive responses in the hot-plate test upon subcutaneous (s.c.) administration. The antinociceptive potencies (ED50) found in the initial studies by Harper *et al.,* (1974) and Brittain *et al.,* (1973) with mice for morphine and AH-7921 are given in Table 1. (Conversion of the weight-based ED50 values into molar values for the HCl salts of morphine and AH-7921, gives respective ED50 values as 8.7 and 6.8 micromol/kg in the mouse hot-plate test and 3.7 and 2.3 micromol/kg in the phenylquinone test.)

Comparative pharmacological evaluation with rodents indicated that AH-7921, like morphine, is a μ-opioid receptor agonist though its analgesic activity may also involve k-opioid receptors (Tyers, 1980)[6]. Pain sensation provoked by either heat or non-heat (e.g., chemical writhing and pressure) noxious stimuli was inhibited by AH-7921 as effectively as by morphine (Table 1).

Table 1. Antinociceptive potencies (ED50 values in mg/kg) of morphine and AH-7921 (95% confidence limit)

Compound	Hot-plate test mouse (s.c.)	Tail-flick test 55oC, rat, (s.c.)	Phenylquinone test, mouse (oral)	Acetylcholine-induced writhing, mouse (s.c.)	Inflamed paw pressure, rat (s.c.)
Morphine	2.8 (1.1–4.8) [(1)] 1.7 (1.1–2.2) [(2)]	0.6 (0.3–1.2) [(2)]	1.1 (0.7–1.8)[(1)]	0.45 (0.2–0.9)[(2)]	0.43 (0.3–0.5)[(2)]
AH-7921	2.5 (1.2–6.4) [(1)] 1.8 (1.4–2.1) [(2)]	0.8 (0.3–1.6) [(2)]	0.85 (1.4–1.7)[(1)]	0.59 (0.5–0.8)[(2)]	0.57 (0.5–0.7)[(2)]

[(1)] Brittain et al., 1973; Harper et al, 1974
[(2)] Tyers, 1980

In the dog, the minimal effective doses of morphine and AH-7921 to suppress pain evoked by electric stimulation of the dental pulp were 1.25±0.3 and 1.25±0.8 mg/kg, respectively, while in a similar test with rhesus monkeys the minimal antinociceptive doses of morphine and AH-7921 were <5.0 and 13.8±1.2 mg/kg, respectively (Brittain *et al.,* 1973).

Sewell and Spencer (1974) studied the action of intracerebroventricularly (ICV) injected serotonin and noradrenaline on the analgesics effect of several drugs in the mouse tail-flick test. It was found that serotonin increased (prolonged) the antinociceptive effects of both morphine and AH-7921. However, ICV administration of noradrenaline had opposite effects and attenuated the antinociceptive effects of these analgesics.

Hayes and Tyers (1983) studied in the mouse the role of opioid receptor types in the various side effects produced by selected opioid receptor agonists, including AH-7921, applied subcutaneously. Among the several parameters estimated were drug-induced body temperature decrease and respiratory rate (Table 2). The ED50 value for the former was defined as the dose of the test drug capable of reducing body temperature to 2^{o}C below to that of saline-treated animals. The ED50 value for the latter was defined as the dose of the test drug capable of depressing the respiratory rate of the control group by 25%. It is noteworthy, that for respiratory depression, the dose response curve for AH-7921 was steep: doses that produced side effects were similar to those producing analgesia in the chemically induced pain. All the effects produced by the drugs were reduced significantly by simultaneous administration of the opioid receptor antagonist naloxone (1 mg/kg s.c.).

Table 2. Antinociceptive and side-effect potencies (ED50 values in mg/kg) of morphine and AH-7921 in the mouse upon subcutaneous administration (95% confidence limit)(1)

Compound	Acetylcholine-induced writhing	Body temperature decrease	Respiratory rate decrease
Morphine	0.45 (0.21–0.91)	20.9 (10.3–66.5)	4.2 (1.8–7.7)
AH-7921	0.55 (0.27–0.94)	11.4 (7.7–18.3)	2.5 (2.0–3.0)

(1) Hayes and Tyers, 1983

During a study on the relationship between the chemical structure of a homologous series of aminocyclohexane derivatives and their affinity to opioid receptor preparations from guinea pig brain, AH-7921 showed moderate selectivity towards μ -opioid receptors over k-opioid receptors (Ki = 10 nM versus 150 nM) (Loew et al., 1988). The development of this structurally simple compound was not pursued further and, since 1988, no other pharmacological studies with AH-7921 or its close analogues have appeared in the scientific literature.

Human data

Although tested in animals, there are no reported human clinical trials with AH-7921 in the scientific literature. Information on the use and effects of the drug is scarce and originate from Internet discussion forums and, to an even more limited extent, some recent poisoning cases.

Internet drug forums started to discuss the psychoactivity of the drug from early 2012, but there are only a few experience reports posted on such forums.

The first detailed experience reports on AH-7921 appeared in early 2013 on the Erowid website. In one of the reports, the vapours of a total of 40 mg of the free amine (powdery crystal) were inhaled during a 30 min period. The peak-effects lasted for 1.5 h and were described as "like a relaxed morphine effect mixed with a medium oxycodone/hydrocodone buzz". Another report described the experiences of two users who sublingually applied a solution made from 1 g of the powdery crystal (the CAS registration number provided by the vendor indicated the HCl salt form), lemon juice (10 ml) and warm water (40 ml). After the initial sublingual doses of 2 ml of the solution (containing 40 mg of the drug), total amounts of about 145 and 155 mg of the drug were consumed during an 11 h session by the users (redosing was done in 60 to 120 minutes intervals).

In addition to analgesia, relaxation, euphoria, "opiate glow" and alertness, occasional itching, nausea and, toward the end of the session, tremors were experienced. Slight myosis was noted three hours after the first dose. No serious adverse effects were mentioned in any of these reports.

Another report is by an ex-heroin user who injected 100–150 mg of a solution of the drug. The effects were described as "a lovely smack-like high… complete with nod, decent euphoria and the hallmarks of a quality Morphine/bordering Diamorphine high". Also mentioned were the development of tolerance after repeated use of the drug and combined use ('speedballing') of AH-7921 with ethylphenidate (~80 mg).

4.2. Routes of administration and dosage

As AH-7921 is typically obtained in the form of a powder, tablet or capsule, the primary route of administration is oral consumption. However, according to user reports, the routes of administration of the drug may be oral, nasal insufflation, sublingual, rectal and injection (Erowid and The Lycaeum). Specifically for dosage, other, less detailed Internet reports than those stated above mention nasal insufflation (60 mg), sublingual application (50 mg), a combination of insufflation (10mg) plus oral (60 mg) consumption, as well as injection (70 mg) and rectal administration (40 mg).

4.3. Pharmacokinetics

Animal studies
There do not appear to be any published pharmacokinetic data for AH-7921 in animals.

Human studies
Whilst there do not appear to be any published pharmacokinetic data for AH-7921 in humans, Soh and Elliott (2013) published the presumed detection of desmethyl- and didesmethyl- metabolites of AH-7921 (through demethylation of the N,N-dimethylcyclohexanamine group). This was further reported by Vorce *et al.,* (2014).

5. Toxicology

There are no published pre-clinical safety data available concerning the toxicity, reproductive impact and mutagenic/carcinogenic potential of AH-7921. However, the study by Harper *et al.;* (1974) implies that the LD50 of AH-7921 is greater than 10/mg/kg upon intravenous (i.v.) administration in the rat.

Overall, there is insufficient clinical information to determine typical toxic effects of AH-7921, however the opioid nature of the drug would likely result in morphine-like toxicity (e.g. sedation and respiratory depression).

6. Adverse reactions in humans

A total of 6 non-fatal intoxications and 16 deaths associated with AH-7921 were reported by Sweden, the United Kingdom, Norway and the USA. Not all of these cases have been analytically confirmed but importantly for those that were, AH-7921 was considered to be a contributing factor in the cause of death. See below and Table 3 for further details of the deaths.

Non-fatal cases

Six non-fatal intoxications associated with AH-7921 were reported by the Swedish Poison Information Centre between December 2012 and March 2013. The presence of AH-7921 was analytically confirmed in five of the six cases. No information was provided on whether the AH-7921 was quantified in these five cases. No further details are currently available on these cases, including clinical symptoms.

Fatal cases

10 deaths associated with AH-7921 occurring between January 2013 and September 2013 were reported in Sweden. All of these cases were analytically confirmed. In nine of the cases, the concentration of AH-7921 in post-mortem femoral blood ranged from 0.03 to 0.99 μg/g (roughly equivalent to 0.03-0.99 mg/L); in the remaining case AH-7921 was detected in post-mortem hair but was not quantified. In all 10 cases AH-7921 was found in combination with at least one other psychoactive substance. These included: amphetamine (2 cases); 3-methylmethcathinone (2); a metabolite of ketamine; alcohol; buprenorphine; benzodiazepines (alprazolam, diazepam, nordiazepam, pyrazolam) and other medicines (zopiclone, paroxetine, bupropion, mirtazapine, pregabalin, gabapentin, aripiprazole). For six cases the stated cause of death was: 'toxic effect of AH-7921'; 'overdose of AH-7921'; 'unintentional overdose', 'overdose of benzodiazepines and opiates', 'intoxication with opioids among others' and 'pneumonia caused by aspiration'. In one case the cause of death was reported as 'unclear'. In two cases the cause of death remains to be determined. In one death no further information was provided.

Norway reported two deaths associated with AH-7921. The first death occurred in December 2012, the second in August 2013. In the first case AH-7921 was not analytically confirmed but was suspected due to the circumstances of the death. During the investigation the police found a bag with small amounts of white powder and a used syringe close to the deceased. AH-7921 was detected in both the powder and a sample taken from the syringe. Etizolam and phenazepam were also found at the scene. In the second case the presence of AH-7921 was analytically confirmed. The level of AH-7921 was quantified at 1.3 μmol/L (= 0.43 mg/L). Other substances were also present 2-fluoromethamphetamine (0.041 μmol/L), 3-methylmethcathinone (0.012 μmol/L),

codeine (1.4 μmol/L) and paracetamol (124 μmol/L). There was information that the deceased had bought drugs on the Internet.
A further death occurring in Norway (analysed in Sweden) detected AH-7921 in femoral blood and quantified at a concentration of 0.34 μg/g (~ 0.34 mg/L); etizolam was also detected and quantified at 0.27 μg. At this time it is not clear if this case relates to the first case reported by Norway (above) or is an additional death. As such it has not been included in the total number of deaths.

In the USA, it was reported by Vorce et al. (2014) that a 19-year old male was found dead in bed by a friend. The friend indicated that the deceased had purchased two vials and reportedly used it on the nights of and prior to his death (one vial was found to contain AH-7921, the other vial contained MPHP). Dextromethorphan, MPHP (4-methyl-□-pyrrolidinohexiophenone) and AH-7921 were found in the post-mortem urine, with only AH-7921 found in the post-mortem blood. AH-7921 was measured in various fluids and organs; heart blood 3.9 mg/L, "peripheral" blood 9.1 mg/L, urine 6.0 mg/L, liver 26 mg/kg, kidney 7.2 mg/kg, spleen 8.0 mg/kg, heart 5.1 mg/kg, lung 21 mg/kg, brain 7.7 mg/kg, bile 17 mg/L and stomach contents 120 mg (in 125 mL). The cause of death was attributed to AH-7921.

Three analytically confirmed deaths associated with AH-7921 were reported in the United Kingdom (Soh and Elliott 2013, Elliott 2014 and Elliott and Evans 2014).

Case 1 (February 2013): AH-7921 was detected in post-mortem femoral blood with a concentration of 0.58 mg/L. The deceased was found dead at home along with various packets of labelled powders (analytically found to be 5F-AKB48 synthetic cannabinoid, AH-7921, 3,4-dichloromethylphenidate, 2,5-dimethoxy-4-iodoamphetamine (DOI) and etaqualone). However, in addition to AH-7921, 4-methylethcathinone (4-MEC), pentedrone, mephedrone, diphenylpropinol (D2PM), etizolam and etaqualone were also detected in post-mortem urine. Only a low concentration of 4-MEC and/or pentedrone metabolites was detected in the femoral blood, therefore AH-7921 was the predominant compound present in the blood.

Case 2 (July 2013): AH-7921 was detected in post-mortem femoral blood with a concentration of 0.05 mg/L. The deceased was found dead with a bag over the head containing chloroform. Chloroform and ethanol were also detected in the blood.

Case 3 (August 2013): AH-7921 was detected in post-mortem femoral blood with a concentration of 4.46 mg/L. The victim was found unresponsive at home and died later in hospital. Clobazam and a codeine metabolite were detected in the urine along with doxylamine and mirtazapine which were both also detected in the blood at a low concentration.

Table 3. Summary of fatalities where AH-7921 was detected.

	Country	Date of death (gender, age)	Biological sample	AH-7921 conc.	Other drugs	Comments
1	Sweden	Jan 2013 (M, 28)	Femoral blood	0.81 µg/g	10 µg/g gabapentin	Cause of death reported as 'unintentional overdose'
2	Sweden	Feb 2013 (M, 25)	Femoral blood	0.99 µg/g	4.7 µg/g amphetamine, aripiprazole	Cause of death reported as 'pneumonia caused by aspiration'
3	Sweden	Feb 2013	Femoral blood	0.03 µg/g	0.03 µg/g paroxetine	Cause of death reported as 'not decided yet'
4	Sweden	Apr 2013	Femoral blood	0.2 µg/g	pyrazolam, diazepam	Cause of death reported as 'overdose of benzodiazepines and opiates'
5	Sweden	Apr 2013	Femoral blood	0.08 µg/g	0.01 µg/g N-ethylnorketamine, alcohol	Cause of death reported as 'unclear'
6	Sweden	May 2013	Femoral blood	0.3 µg/g	pyrazolam, alprazolam, zopiclone	Cause of death reported as 'overdose of AH-7921'
7	Sweden	June 2013	Femoral blood	0.16 µg/g	0.04 µg/g amphetamine	Cause of death reported as 'not decided yet'
8	Sweden	June 2013	Femoral blood	0.35 µg/g	3-methylmethcatinone	Cause of death reported as 'overdose of AH-7921'
9	Sweden	July 2013	Femoral blood	0.43 µg/g	12 µg/g pregabalin, 0.53 µg/g norbupropion, 0.40 µg/g bupropion, 0.17 µg/g nordiazepam, 0.12 µg/g diazepam, mirtazapine, desmethylmirtazapine	Cause of death reported as 'intoxication with opioids among others'
10	Sweden	Sept 2013	Hair	Positive	3-methyl-methcathinone, buprenorphine	Deceased was treated in intensive care
11	United Kingdom	Feb 2013	Femoral blood	0.58 mg/L	4-MEC, pentedrone, mephedrone, D2PM, etizolam, etaqualone – urine only. 4-MEC/pentedrone metabolites in blood.	Deceased was found dead at home with powders
12	United Kingdom	July 2013	Femoral blood	0.05 mg/L	chloroform, alcohol	Deceased was found dead with bag over head

						and chloroform
13	United Kingdom	Aug 2013	Femoral blood	4.46 mg/L	clobazam, codeine metabolite, doxylamine, mirtazapine – urine doxylamine, mirtazapine – blood	Subject was unresponsive at home and died in hospital
14	Norway	Aug 2013 (M, 23)	Peripheral blood	1.3 µmol/L	2-FMA (0.041 µmol/L), 3-MMC (0.012 µmol/L), codeine (1.4 µmol/L), paracetamol (124 µmol/L)	There was information that the deceased had bought drugs on the internet
15	Norway	Dec 2012	Powder, syringe	-	-	White powder and a used syringe with dried blood close to the deceased.
16	USA	Not known	Peripheral blood Heart blood Other fluids and organs	9.1 mg/L 3.9 mg/L	MPHP, dextromethorphan – urine only	The medical examiner ruled that the cause of death was opioid intoxication and the manner of death was accident.

7. Dependence potential

See 8 (below)

8. Abuse potential

There have been few studies regarding the dependence/abuse potential of AH-7921 with no specific studies in humans. However, the dependence liability of AH-7921 in the rat and rhesus monkey was assessed by Brittain et *al.,* (1973). Naloxone-treatment of rats that had received repeated doses of AH-7921 (5 to 20 mg/kg orally, three times a day for five days) showed 'abstinence syndrome' similar to that observable for morphine using a similar dose schedule. Likewise, nalorphine, also an opioid receptor antagonist, evoked withdrawal symptoms in rhesus monkeys that had received repeated doses of AH-7921 (7.5 to 30 mg/kg s.c., twice daily for 30 days). Furthermore, single doses of AH-7921 (5–10 mg/kg s.c.) completely alleviated the abstinence syndrome in morphine-dependent rhesus monkeys. The study concluded that the drug "would be classified as a narcotic analgesic having high addictive liability".

9. Therapeutic applications and extent of therapeutic use and epidemiology of medical use

Although investigated as an opioid, AH-7921 has no recorded therapeutic applications or medical use.

10. Listing on the WHO Model List of Essential Medicines

AH-7921 is not listed on the WHO Model List of Essential Medicines.

11. Marketing authorizations (as a medicine)

AH-7921 has never been marketed as a medicine.

12. Industrial use

AH-7921 has no industrial use.

13. Non-medical use, abuse and dependence

AH-7921 use and seized material has been reported in Austria, Denmark, Finland, France, Germany, Sweden, the United Kingdom, Norway and USA.

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

14. Nature and magnitude of public health problems related to

misuse, abuse and dependence

AH-7921 use appears to be associated with the purchase of "research chemicals" or equivalent products via the Internet. Therefore, instances of misuse, abuse and dependence would be limited to such individuals rather than the general population. The mode of use may involve the combinational use (intentionally or unintentionally) of other drugs. However, in the fatalities in particular, due to the opioid nature of AH-7921, even in cases where other drugs were involved, AH-7921 was considered to be contributory to the cause of death.

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances

15. Licit production, consumption and international trade

Not applicable.

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

16. Illicit manufacture and traffic and related information

No specific data.

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances

17. Current international controls and their impact

Not applicable in relation to affecting impact of medical use.

18. Current and past national controls

AH-7921 is not currently controlled except for Sweden (December 2013) where it is included in the list of substances to be considered as drugs under narcotics law.

Also refer Annex 1: Report on WHO questionnaire for review of psychoactive substances.

19. Other medical and scientific matters relevant for a recommendation on the scheduling of the substance

None.

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This critical review draws information from on the EMCDDA-Europol Joint Report and Technical Annexes of the Risk Assessment of AH-7921 for the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) produced by Dr István Ujváry and Dr Simon Elliott (2014).

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Annex 1:

Report on WHO Questionnaire for Review of Psychoactive Substances for the 36th ECDD: Evaluation of AH-7921

Data were obtained from 72 WHO Member States (18 AFR, 13 AMR, 5 EMR, 29 EUR, 3 SEAR, 4 WPR).

A total of 65 Member States answered the questionnaire for AH-7921. Of these, only 21 respondents (AMR 5, EUR 13, WPR 3) had information on this substance.

LEGITIMATE USE

None reported that AH-7921 was currently authorized or in the process of being authorized/registered as a medical product in their country. However, 1 responded that AH-7921 could be used as an opioid analgesic. Four respondents stated that this substance was used in medical and scientific research including as standards for analyses. There was no use stated for AH-7921 in animal/veterinary care.

HARMFUL USE

Eight respondents confirmed recreational/harmful use of AH-7921; four stated that the common route of administration was oral, one stating this was by oral, inhaling/sniffing and one oral, injection, inhaling/sniffing. Five respondents stated that this substance was obtained only via trafficking, one via diversion and trafficking and another one via clandestine manufacturing. Seven respondents reported on the common formulations of AH-7921 available with six reporting powder and one powder and liquid forms. When asked if AH-7921 was used by any special populations one respondent stated that it was used by the general population and in clubs and two only in the general population. One respondent reported withdrawal, tolerance and other adverse effects or medical illnesses caused by AH-7921. Three deaths were reported by one respondent as well as 1 emergency room visit in another.

In addition one respondent reported several deaths in 2013 as mentioned below - post-mortem femoral blood, 0.81µg/g, unintentional overdose; post-mortem femoral blood, 0.99 µg/g, cause of death pneumonia caused by aspiration; post-mortem femoral blood, 0.03 µg/g, treated in intensive care, cause of death not decided yet; post-mortem femoral blood, 0.20 µg/g, cause of death overdose of benzodiazepines and opiates; post-mortem femoral blood, 0.30µg/g, cause of death overdose of AH-7921; post-mortem femoral blood, 0.08 µg/g, intake of AH-7921 cause of death unclear; post-mortem femoral blood 0.16 µg/g, cause of death not decided yet; post-mortem femoral blood, 0.35µg/g, cause of death toxic effect of AH-7921; post-mortem femoral blood, 0.43µg/g, cause of death intoxication with opioids among others; post mortem femoral blood, 0.34µg/g, not diagnosed

CONTROL

9 reported that AH-7921 was controlled under legislation that was intended to regulate its availability' three under "controlled substance act", four under "medicines law", one under "analogue legislation" and one under "other" laws. Three respondents stated that there were challenges with the implementation of this legislation. On illicit activities related to AH-7921, one respondent reported processing into the consumer product, five reported trafficking, and five an internet market.

Details on seizures are presented below.

	2011 (number of respondents)	**2012 (number of respondents)**
Total number of seizures	No data	5 (5)
Total quantity seized (kg)	No data	0.014

IMPACT OF SCHEDULING

Sixteen respondents reported that if AH-7921 was placed under international control, they would have the laboratory capacity to identify the substance. It has no reported medical use.