Critical Review Report:

Spirochlorphine

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Expert Committee on Drug Dependence

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Executive Summary

Spirochlorphine [IUPAC name: 8-[1-(4-Chlorophenyl)ethyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one), belongs to the orphine analogue subclass, comprising a family of piperidine benzimidazolone opioids whose synthesis was originally described in a 1967 patent. However, no medical use of spirochlorphine was identified. Spirochlorphine is structurally related to brorphine and bezitramide, both of which are controlled under Schedule I of the United Nations 1961 Single Convention on Narcotic Drugs. Spirochlorphine has not been reviewed previously by the WHO Expert Committee on Drug Dependence.

Spirochlorphine has been detected in seized material, typically of unknown purity or concentration. Spirochlorphine sold as a reference material has been described as a white solid. In seizures, it has been identified in white powders and liquids, although packaging of one seizure indicates that spirochlorphine is available on the market as blotters or e-liquids.

No reports on the main route used for its administration could be found. However, a notice of intent to control four orphine analogues as Schedule I substances (including spirochlorphine) published by the Federal Register (United States) suggests that the common routes of administration for such substances include oral consumption, inhalation (including vaping), and injection.

In vitro pharmacological studies showed that spirochlorphine is an opioid agonist, with higher binding affinity to μ-, δ- and κ-opioid receptors than that of fentanyl and morphine. Different in vivo assays also showed that spirochlorphine produces analgesic effects with a potency higher or comparable to that of fentanyl.

According to the UNODC Early Warning Advisory (EWA), spirochlorphine was reported in a total of 2 post-mortem cases in 2025, but its potential contribution to the cause of death was not determined.

No animal or human studies have examined its dependence or abuse potential.

There are no known therapeutic or industrial uses of spirochlorphine and no marketing authorisations. It is used as a reference material in scientific research and forensic applications. Spirochlorphine was formally notified for the first time to the European Union Drugs Agency (EUDA) in April 2025, and up to September 2025, 19 seizures of this substance were reported to the EUDA. The Center for Forensic Science Research and Education (CFSRE) first identified it in May 2025, having detected spirochlorphine in 15 drug samples up to October 2025. Spirochlorphine has also been seized in mixtures with other opioids, including nitazenes.

Spirochlorphine is not controlled under the 1961, 1971, or 1988 United Nations Conventions.

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1. Substance identification

A. International Nonproprietary Name (INN)

Not assigned.

B. Chemical Abstract Service (CAS) Registry Number

3222-88-6 (*free base, unspecified stereochemistry*).

C. Other Chemical Names

R-6890
R6890
8-(*p*-chloro-α-methylbenzyl)-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one
1-phenyl-4-oxo-8-[1-(4-chlorophenyl)ethyl]-1,3,8-triazaspiro[4.5]decane
8-[1-(4-chlorophenyl)ethyl]-4-oxo-1-phenyl-1,3,8-triazaspiro[4.5]decane
1,3,8-triazaspiro[4.5]decan-4-one, 8-[1-(4-chlorophenyl)ethyl]-1-phenyl-
1-phenyl-8-[1-(p-chlorophenyl)ethyl]-1,3,8-triazaspiro[4.5]decan-4-one
8-[1-(*RS*)-(4-chlorophenyl)ethyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one.

D. Trade Names

No recognized trade names were identified. Spirochlorphine is commercially available as an analytical reference standard under the product designation R-6890 (Spirochlorphine) [1].

E. Street Names

No established street names were identified. Available information indicates that the substance may be marketed using its common name, spirochlorphine, or the research codes R-6890 and R6890.

F. Physical Appearance

Spirochlorphine free base is reported to be a solid [1].

Seized spirochlorphine-containing materials have been reported as white powders, crystalline material and liquid preparations. Notably, the packaging of one seizure may indicate that spirochlorphine is available on the market as blotters and vegetable glycerine- or propylene glycol-based liquids intended for vaping (e-liquid). Most identifications of spirochlorphine reported to the EUDA do not specify whether the substance was detected as the free base or a salt form. However, in one case, the hydrochloride salt form of spirochlorphine was identified in a powder sample [2].

Drug materials analysed in the United States were described as white solid material and purple solid powder [3]. However, the purple colour cannot be attributed specifically to spirochlorphine because some samples contained additional substances. In most reported cases, it was not established whether the substance was present as the free base or as a salt.

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G. WHO Review History

Spirochlorphine has not been formally reviewed by WHO and is not currently under international control.

2. Chemistry

A. Chemical Name

IUPAC Name: 8-[1-(4-chlorophenyl)ethyl]-1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one

CA Index Name: 1,3,8-Triazaspiro[4.5]decan-4-one, 8-[1-(4-chlorophenyl)ethyl]-1-phenyl-

SMILES

CC(N1CCC2(CC1)N(CNC2=O)c3ccccc3)c4ccc(Cl)cc4 (*free base, unspecified stereochemistry*)

Cl.CC(N1CCC2(CC1)N(CNC2=O)c3ccccc3)c4ccc(Cl)cc4 (*hydrochloride salt, unspecified stereochemistry*)

C[C@H](N1CCC2(CC1)N(CNC2=O)c3ccccc3)c4ccc(Cl)cc4 (*S-isomer*)

C[C@@H](N1CCC2(CC1)N(CNC2=O)c3ccccc3)c4ccc(Cl)cc4 (*R-isomer*)

InChI

InChI=1S/C21H24ClN3O/c1-16(17-7-9-18(22)10-8-17)24-13-11-21(12-14-24)20(26)23-15-25(21)19-5-3-2-4-6-19/h2-10,16H,11-15H2,1H3,(H,23,26) (*free base, unspecified stereochemistry*)

InChI=1S/C21H24ClN3O.ClH/c1-16(17-7-9-18(22)10-8-17)24-13-11-21(12-14-24)20(26)23-15-25(21)19-5-3-2-4-6-19;/h2-10,16H,11-15H2,1H3,(H,23,26);1H (*hydrochloride salt, unspecified stereochemistry*)

InChI=1S/C21H24ClN3O/c1-16(17-7-9-18(22)10-8-17)24-13-11-21(12-14-24)20(26)23-15-25(21)19-5-3-2-4-6-19/h2-10,16H,11-15H2,1H3,(H,23,26)/t16-/m0/s1 (*S-isomer*)

InChI=1S/C21H24ClN3O/c1-16(17-7-9-18(22)10-8-17)24-13-11-21(12-14-24)20(26)23-15-25(21)19-5-3-2-4-6-19/h2-10,16H,11-15H2,1H3,(H,23,26)/t16-/m1/s1 (*R-isomer*)

InChIKey

KFEYPBZJPJJRFX-UHFFFAOYSA-N (*free base, unspecified stereochemistry*)

JQFOIWRYMOKZQC-UHFFFAOYSA-N (*hydrochloride salt, unspecified stereochemistry*)

KFEYPBZJPJJRFX-INIZCTEOSA-N (*S-isomer*)

KFEYPBZJPJJRFX-MRXNPFEDSA-N (*R-isomer*)

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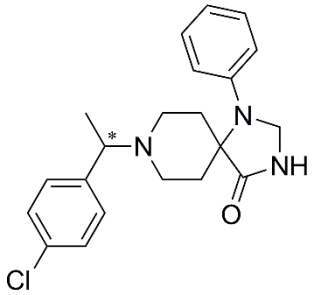
B. Chemical Structure

Free base:



Molecular Formula: $C_{21}H_{24}ClN_3O$
Molecular Weight: 369.89 g/mol

C. Stereoisomers

Spirochlorphine contains one stereogenic centre in the 1-(4-chlorophenyl)ethyl substituent and may therefore exist as two enantiomers, the *R*-enantiomer and the *S*-enantiomer. No information was identified on the enantiomeric composition of spirochlorphine detected in seized, collected or biological samples. Unless stereochemistry is specifically determined, reported material should therefore be considered to have unspecified stereochemical composition and may be racemic [2].

D. *Methods and Ease of Illicit Manufacturing*

No information is currently available on the specific precursors, synthetic procedures, production sites, equipment, yields, scale, or purity associated with spirochlorphine encountered on the illicit drug market. No clandestine laboratory producing spirochlorphine has been reported, and the synthetic routes actually used for products circulating on the drug market remain unknown [2].

Published patent and scientific literature provide information on possible methods of manufacture. The key intermediate 1-phenyl-1,3,8-triazaspiro[4.5]decan-4-one, commonly referred to as spirodecanone, and 4′-chloroacetophenone [1-(4-chlorophenyl)ethanone] have been reported as possible precursors for the preparation of spirochlorphine. The process has been described as similar to that used for the synthesis of carfentanyl [2; 4]. General synthetic routes and precursors for triaza-spirodecanones were disclosed in a Janssen Pharmaceutica patent [5]. According to the EUDA, the spirocyclic ring system may be prepared by conversion of a benzylpiperidinone into an anilinocyanohydrin derivative, followed by cyclisation [2].

The available literature indicates that the preparation of spirochlorphine involves multiple chemical transformations and access to a relatively specialised spirodecanone intermediate, rather than a simple one-step process. However, no information is available to reliably assess the practical ease of illicit manufacture, including precursor accessibility, production requirements, yields, scalability, purification procedures or the purity of products encountered on the illicit drug market [2].

Notably, the synthesis of spirochlorphine has been discussed in the BlueLight online forum [6].

E. Chemical Properties

Melting point
206.5-208.5 °C [5].

Boiling point
Not found.

Solubility
Spirochlorphine free base is reported to be soluble at concentrations of at least 10 mg/mL in acetone and DMSO [1]

F. Identification and Analysis

Spirochlorphine has been identified in physical samples using gas chromatography–mass spectrometry (GC–MS), liquid chromatography–quadrupole time-of-flight mass spectrometry (LC–QTOF-MS), and nuclear magnetic resonance spectroscopy (NMR) [2; 3].

An HPLC method with photodiode-array detection (HPLC-PDA) has also been described for the chromatographic separation of a mixture of 13 orphine opioid reference standards, including spirochlorphine (R-6890) [7]. However, this method was demonstrated using analytical standards and was not reported as a validated method for seized materials or biological samples.

No published analytical method specifically validated for the quantitative determination of spirochlorphine in biological matrices was identified. Methods developed for the structurally related opioid brorphine, including LC–QTOF-MS and targeted LC–MS/MS, may be adaptable, but compound-specific validation would be required. Because expected concentrations in biological samples may be in the low-nanogram or sub-nanogram range, highly sensitive analytical instrumentation and low limits of detection may be necessary [2; 8; 9].

3. Ease of Convertibility Into Controlled Substances

At the time of writing this report, no documented, straightforward or synthetically advantageous conversion of spirochlorphine into substances currently under international control was identified.

4. General Pharmacology

A. Routes of administration and dosage

No reports from participants in online discussion forums could be identified that provided information on the preferred routes of administration or dosage of spirochlorphine.

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A notice of intent to control four orphine analogues as Schedule I substances (including spirochlorphine) published by the Federal Register (United States) suggests that the common routes of administration for those four substances include oral consumption, inhalation (including vaping), and injection [10].

Reports from two European Union (EU) Member States (Estonia and Latvia), which include findings from syringe residue analysis, suggest injection as a route of administration for spirochlorphine [2].

Discussions in the BlueLight online forum suggest making a stock solution of 20 drops of water per mL of water [6]. In Drugs Forum, an entry suggests using 200 μg spirochlorphine, as it would "equal a 100 mg morphine dose" [11].

B. Pharmacokinetics

No data on the absorption, distribution, metabolism and excretion of spirochlorphine were found.

C. Pharmacodynamics

Studies on the binding and functional activity of spirochlorphine at human δ, κ, and μ opioid receptors transfected into Chinese hamster ovary (CHO) cells [12] showed that spirochlorphine had a higher binding affinity to μ-opioid receptors than morphine and fentanyl. Likewise, the binding affinity of spirochlorphine to δ- and κ-opioid receptors was also higher than that of fentanyl and morphine. Spirochlorphine showed higher potency at μ-opioid receptors compared to δ- and κ-opioid receptors. Spirochlorphine showed a higher agonism to μ-opioid receptors than fentanyl and morphine (about 2.6- and 2-fold, respectively). Spirochlorphine also showed a higher agonism to δ- and κ-opioid receptors than fentanyl and morphine. Further details of the binding and agonism of spirochlorphine at opioid receptors are presented in Annex 3.

Spirochlorphine was tested for its ability to produce analgesic effects in the warm-water tail-flick assay in nine Swiss-Webster mice, using a cumulative-dosing procedure (from 0.0032 to 0.32 mg/kg) followed by a time-course of the peak effect of spirochlorphine [13]. Spirochlorphine increased tail-flick latencies to a maximum possible effect (MPE) of 100 % after administration of 0.32 mg/kg in a dose-dependent manner. Potency ratios (ED_{50} test compound/ED_{50} reference compound) indicated that spirochlorphine was more potent than morphine and fentanyl. Spirochlorphine was considered to be as efficacious as morphine but less efficacious than fentanyl. The peak analgesic effects of spirochlorphine lasted 30 min and decreased to 25.1 ± 6.4 % MPE within 90 min.

Subcutaneous injection of naltrexone (1 mg/kg) before administration of spirochlorphine blocked the analgesic effect of spirochlorphine, supporting the involvement of opioid receptors in the action of spirochlorphine. Further details of the analgesic effects of spirochlorphine are presented in Annex 3.

In vitro functional (focused on μ-opioid receptors) and in vivo behavioural data reported by EUDA further support these findings [14], generally indicating that spirochlorphine has

a broadly comparable potency to fentanyl. Specifically, in vitro binding (using radioactively labelled tyrosyl-3,5-3H(N)-DAMGO) and functional (NanoBiT® β-Arrestin 2 recruitment, homogenous time-resolved fluorescence, and AequoScreen®) assays showed that spirochlorphine binds the μ-opioid receptor with high affinity, being comparable to fentanyl and chlorphine (used as reference opioids). Spirochlorphine was also shown to activate the μ-opioid receptor in vitro, with an efficacy comparable to that of chlorphine, and slightly higher than or comparable to that of fentanyl. Its potency was slightly higher than or comparable to that of chlorphine, and slightly lower or comparable to that of fentanyl. In a battery of behavioural tests that included the assessment of antinociception (tail withdrawal and tail pinch assays), body temperature, motor activity, skeletal muscle strength, and cardiorespiratory analysis (electrocardiogram, plethysmography), spirochlorphine produced dose-dependent antinociception, bradycardia, and respiratory depression with a potency broadly comparable to that of fentanyl [14].

Participant discussions in online forums (BlueLight, Drugs Forum) also mention spirochlorphine to be 2-5 times more potent than fentanyl [6; 11].

5. Toxicology

According to the UNODC Early Warning Advisory (EWA), spirochlorphine was reported for the first time in 2024. Since then, it was detected in a total of 38 drug samples across several different countries (Canada, Czechia, Denmark, Estonia, Finland, Latvia, Netherlands, Sweden, United Kingdom, and United States) and in two post-mortem cases (one in the United Kingdom and another in the United States) [15]. The contribution of spirochlorphine to the cause of death in these two cases was not reported. There are no reports of clinical admissions, drug driving, drug-facilitated crime (DFC), drug-facilitated sexual assault (DFSA) or other toxicological cases associated with spirochlorphine.

Two EU Member States reported a total of 3 biological samples in which exposure to spirochlorphine was confirmed between January and December 2025: Czechia reported two acute poisonings. Both poisonings concerned the same individual, involved polysubstance exposure, and were classified as life-threatening. Germany reported one death that occurred in January 2025 and in which exposure to spirochlorphine was confirmed, although the causal role of spirochlorphine in the death was not reported [2].

No reports described the toxic dose of spirochlorphine for humans.

6. Adverse Reactions in Humans

No reports describing the adverse reactions of spirochlorphine could be identified.
However, based on its structural and pharmacological similarity with other orphine opioids, and on in vivo behavioural data (described in section 4), it is likely that spirochlorphine may produce bradycardia and respiratory depression.

Spirochlorphine was detected in two post-mortem cases (one in the United Kingdom and another in the United States). However, the causal contribution of spirochlorphine to the death was not determined [15].

7. Dependence Potential

A. Animal Studies

No studies were identified.

B. Human Studies

No studies were identified.

8. Abuse Potential

A. Animal Studies

No studies that examined the abuse potential of spirochlorphine in animals were identified.

B. Human Studies

No studies that examined the human abuse potential of spirochlorphine were identified.

9. Therapeutic Applications and Extent of Therapeutic Use and Epidemiology of Medical Use

The synthesis of spirochlorphine was reported in a 1967 patent by Janssen Pharmaceutica as part of a series of piperidine benzimidazolones [16]. However, none of those compounds were approved for therapeutic use.

Spirochlorphine is not known to have any therapeutic applications.

10. Listing on the WHO Model List of Essential Medicines

Spirochlorphine is not listed on the 24th WHO List of Essential Medicines or the 10th WHO List of Essential Medicines for Children.

11. Marketing Authorizations (as a Medicinal Product)

Spirochlorphine is not known to be authorized for marketing.

12. Industrial Use

Spirochlorphine is not known to have any industrial use.

13. Non-Medical Use, Abuse and Dependence

While information on patterns of use of spirochlorphine is limited, data available from two EU Member States (Estonia and Latvia) indicates that spirochlorphine is used by people who inject opioids. Specifically, in Latvia, spirochlorphine was identified in 13 of

181 syringes (7 %) collected between November and December 2024. In Estonia, spirochlorphine was identified in 5 of 30 used syringes (17 %) collected in May 2025 and in an additional four syringes collected in September 2025 [2].

The National Crime Agency (NCA) and Office for Health Improvement and Disparities (OHID) have reported that in England alone there have been more than 15 confirmed deaths in which orphines were involved since the spring of 2025. Spirochlorphine was one of the 2 compounds involved (the other one being cychlorphine) [17].

Spirochlorphine has also been seized in mixtures with other opioids, including other orphines, such as nitazenes (e.g., isotonitazepyne) [2].

14. Nature and Magnitude of Public Health Problems Related to Misuse, Abuse and Dependence

As noted in section 13, the nature of public health problems related to spirochlorphine appears to be associated with the injection of this opioid.

No information was found to determine the magnitude of health problems with spirochlorphine. However, the Federal Register (United States) published a notice of intent to control spirochlorphine as a Schedule I substance, considering that, based on the available data about this substance (including its uncontrolled manufacture, distribution, reverse distribution, importation, exportation, conduct of research and chemical analysis, possession, and abuse), spirochlorphine poses imminent hazards to public safety [10].

Information reported to the EUDA by two EU Member States (Estonia and Latvia) suggest that the use of spirochlorphine is occurring within populations already affected by opioid dependence and its associated social harm [2].

15. Licit Production, Consumption and International Trade

Spirochlorphine is used as reference material in scientific research and forensic applications.

16. Illicit Manufacture and Traffic and Related Information

Spirochlorphine was first identified by the Center for Forensic Science Research and Education (CFSRE) in May 2025. Up until October 2025, in addition to one toxicology case, the CFSRE detected spirochlorphine in 15 drug samples [3].

Spirochlorphine was formally notified for the first time to the EUDA on behalf of Sweden on April 2025, following the identification of the substance (using GC-MS and NMR) in 0.80 grams of white powder that was seized by police in January 2025 [2]. However, subsequent information reported to EUDA, relating to a case submitted by Latvia, suggests that spirochlorphine may have been present on the European drug market as early as October 2024. In February 2026, the EUDA placed spirochlorphine under intensive monitoring due to concerns about potential public health risks.

On March 10, 2026, the EUDA issued an advisory to its Member States on the increased availability of orphine opioids and associated harms in the European Union (EU), noting that reports from the EU indicated an increase in availability and harms from 2025 onwards, particularly involving cychlorphine and, to a lesser degree, spirochlorphine. This trend was consistent with reports from the United Kingdom, the United States, and Canada [2].

Eight EU Member States (Czechia, Denmark, Estonia, Finland, Germany, Latvia, the Netherlands, and Sweden) reported the first identification of spirochlorphine in their territory between October 2024 and April 2025 [2]. A total of 19 seizures of spirochlorphine were reported to the EUDA between October 2024 and September 2025 by seven EU Member States: Czechia (n=1), Denmark (n=2), Estonia (n=2), Finland (n=1), Germany (n=1), Latvia (n=10), and Sweden (n=2). Of those seizures, 17 (89 %) reported quantities in weight (Kg) and volume (mL), totaling 7.31 kg: 5.57 kg in 4 cases in 2024 and 1.73 kg in 2025. Most of the seized material was reported by Latvia (7.30 kg; >99%). In 2025, a total of 0.28 mL of spirochlorphine was seized in a single case reported by Latvia. In January 2025 and in May 2025, spirochlorphine was detected in two cases involving syringe residues in Estonia. In one case, spirochlorphine was detected alongside diphenhydramine.

Among the 19 cases reported between 2024 and 2025, spirochlorphine was the only substance reported to be present in 9 cases (47%). In seven cases (37%), it was found in combination with one or more other substances, including other opioids (e.g., cychlorphine). In 2026, up to March, no seizures were reported. [2].

Two EU Member States reported a total of 5 collected samples between March 2025 and September 2025: Estonia (4) and Germany (1). In the four cases reported by Estonia spirochlorphine was detected in syringe residues along with carfentanil, diphenhydramine, methadone and xylazine. In the case reported by Germany, spirochlorphine was the only substance reported to be present [2].

17. Current International Controls and Their Impact

Spirochlorphine is not currently controlled under the 1961, 1971, or 1988 United Nations Convention.

18. Current and Past National Controls

A notice of intent to control spirochlorphine as a Schedule I substance was published in the Federal Register (United States) on July 1, 2026 [10].

Seven EU Member States (Czechia, Denmark, Estonia, Italy, Latvia, Lithuania, and Sweden) reported that spirochlorphine is controlled under drug control legislation. Five EU Member States (Finland, Germany, Hungary, Ireland, and Poland) reported that spirochlorphine is controlled under new psychoactive substance legislation. Turkey also reported that spirochlorphine is controlled under New Psychoactive Substance control legislation [2].

Since April 13, 2026, spirochlorphine is monitored by the EUDA as a new psychoactive substance through the European Union Early Warning System (EWS), in accordance with Regulation (EU) 2023/1322. Based on the spirochlorphine's risk assessment, the EUDA determined that spirochlorphine met several criteria (i.e., reports of seized material, pharmacological and toxicological properties and analogy with better-studied substances, and potential for further spread) for it to be considered as posing health risks and consequently determined that an initial report should be produced [2].

Of note, spirochlorphine is structurally related to brorphine and bezitramide, both of which are controlled under Schedule I of the United Nations 1961 Single Convention on Narcotic Drugs.

19. Other Medical and Scientific Matters Relevant for a Recommendation on the Scheduling of the Substance

None.

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