Draft bill

of the Federal Ministry of Health

Ordinance amending Annexes to the Narcotics Act and the New Psychoactive Substances Act

A. Problem and objective

For the new drug zuranolone, current scientific findings indicate that a potential for dependence and abuse cannot be ruled out. Therefore, monitoring under narcotics law is required for zuranolone.

The emergence and spread of ever new chemical variants of new psychoactive substances (NPS) on the drug market directly or indirectly poses a threat to the health of individuals and the population. Due to the diversity in molecular structure and complexity of NPS, some of the new variants of these substances are not covered by the existing substance groups in the New Psychoactive Substances Act (NpSG). In order to cover all variants which, according to new scientific findings, present a risk comparable to those already covered by the existing substance groups, a continuous update of the substance groups in the Annex to the NpSG is needed. This is intended to curtail the spread and abuse of these new, harmful variants and enable or facilitate criminal prosecution.

B. Solution

On the basis of §1(2)(1)(3) BtMG, the medicinal product zuranolone is included in Annex III to the Narcotics Act (BtMG) with Article 1. Due to their lower potency, preparations of the substance zuranolone that contain up to a maximum of 50 mg of the active substance per divided form are exempt.

On the basis of § 7 NpSG, the Annex to the NpSG is adapted to the current state of scientific knowledge by updating certain substance groups to include further NPS. The expansion concerns the substance groups of ‘compounds derived from 2-phenethylamine’, ‘cannabimimetics/synthetic cannabinoids’, ‘benzodiazepines’, ‘compounds derived from N-(2-aminocyclohexyl)amide’, ‘compounds derived from tryptamine’, ‘compounds derived from arylcyclohexyl(methyl)amine’ and ‘compounds derived from benzimidazole’. In addition, the Annex to the NpSG is expanded by the addition of two substance groups. The necessary revision of the Annex to the NpSG is also taken as an opportunity to recast and clarify it.

C. Alternatives

None.

D. Budgetary expenditure without compliance costs

Additional requirements due to compliance costs at federal level are to be covered both financially and in terms of staffing plans in the respective sections of the budget.

E. Compliance costs

E.1 Compliance costs for citizens

There are no added compliance costs for citizens.

E.2 Compliance costs for businesses

There are no added compliance costs for businesses.

E.3 Compliance costs for the authorities

There are no added compliance costs for the administration.

F. Other costs

None.

Draft bill of the Federal Ministry of Health

Ordinance amending Annexes to the Narcotics Act and the New Psychoactive Substances Act*

of ...

On the basis of § 1(2) of the Narcotics Act, in the version published on 1 March 1994 (Federal Law Gazette I p. 358), last amended by Article 1 of the Ordinance of 29 November 2024 (Federal Law Gazette 2024 I No 379), the Federal Government, and on the basis of § 7 of the New Psychoactive Substances Act (Neue-psychoaktive-Stoffe-Gesetz), amended by Article 93 of the Ordinance of 19 June 2020 (Federal Law Gazette I No 1328) in conjunction with § 1(2) of the Competences (Amendment) Act of 16 August 2002 (Federal Law Gazette I p. 3165) and the organisational decree of 8 December 2021 (Federal Law Gazette I p. 5176), the Federal Ministry of Health, in agreement with the Federal Ministry of the Interior, the Federal Ministry of Justice and Consumer Protection and the Federal Ministry of Finance, and after consulting experts, hereby lays down:

Artikel 1

Amendment to Annex III of the Narcotics Act

Annex III to the Narcotics Act in the version published on 1 March 1994 (Federal Law Gazette I p. 358), last amended by Article 1 of the Ordinance of 29 November 2024 (Federal Law Gazette 2024 I No 379), the following heading is inserted alphabetically in the existing order:

INN	**Other non-proprietary or common names**	**chemical names (IUPAC)**
‘— zuranolone	—	1-[(3α,5β)-3-hydroxy-3-methyl-20-oxo-19-norpregnan-21-yl]-1*H*-pyrazole-4-carbonitrile
— except in preparations containing up to 50 mg of zuranolone per separate form, without any of the substances listed in Annexes I-III.’.		

Artikel 2

The Annex to the New Psychoactive Substances Act of 21 November 2016 (Federal Law Gazette I p. 2615), last amended by Article 1 of the Ordinance of 21 June 2024 (Federal Law Gazette 2024 I p. 210), shall be replaced by the text set out in the Annex to this Ordinance.

* Notified in accordance with Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services (OJ L 241, 17/9/2015, p. 1).

Artikel 3

This Ordinance shall enter into force on the day following its promulgation.

The Federal Council has granted approval.

Annex to Article 2

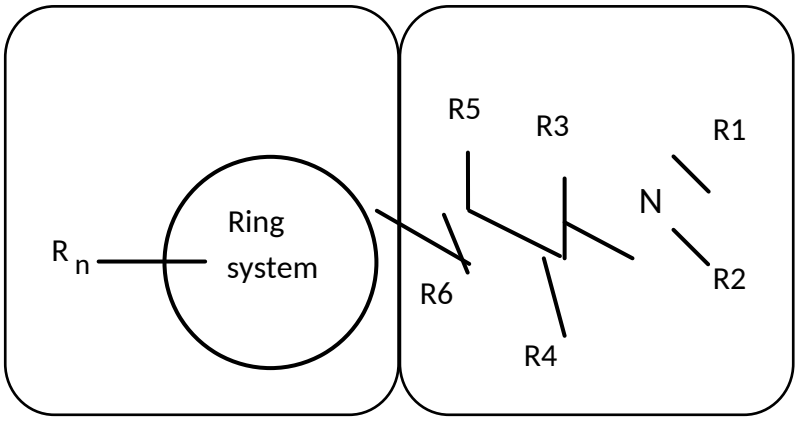
Annex

Preliminary remarks

The substance group definitions in Points 1 to 9 include all possible charged forms, stereoisomers and salts and isotope-substituted compounds of a listed substance. For charged forms and salts, any molecular mass limits apply only to the part of the molecule that excludes the counterion. A hydrogen atom is a possible substituent.

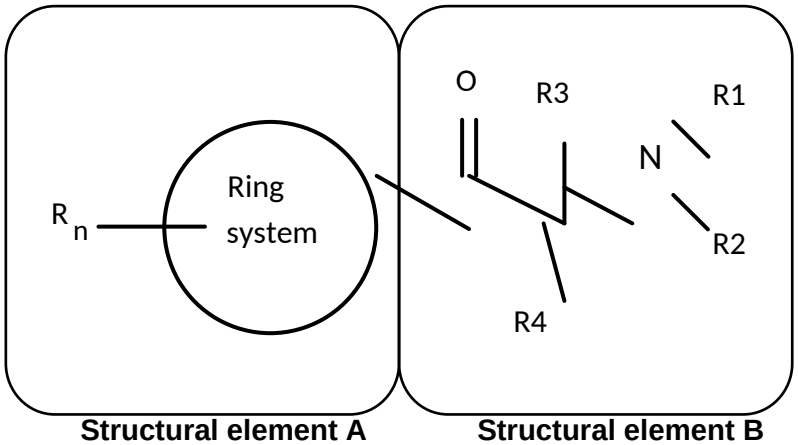
1. Compounds derived from 2-phenethylamine

A compound derived from 2-phenethylamine is any chemical compound which can be derived from a basic 2-phenylethane-1-amine structure (excluding 2-phenethylamine itself), has a maximum molecular mass of 500 u, and corresponds to the modular structure of structural element A and structural element B described below.



Structural element A **Structural element B**

This includes chemical compounds with a cathinone basic structure (2-amino-1-phenyl-1-propanone):

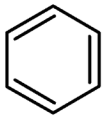


Structural element A **Structural element B**

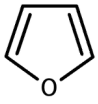
Substances which, while meeting a definition of this substance group, have a core or basic structure specified in the substance group definitions set out in Points 2 to 9 and are not covered by the substance group definition of that point are not included in substance group number 1.

1.1 Structural element A

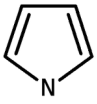
The following ring systems or structures are included for structural element A, where structural element B can be located at any position on structural element A: Phenyl-, furyl-, pyrrolyl-, thienyl-, pyridyl-, cyclopentyl- and cyclohexyl ring.



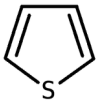
Phenyl



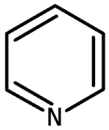
Furanyl



Pyrrolyl

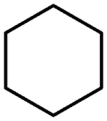


Thienyl



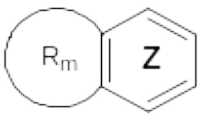
Pyridyl

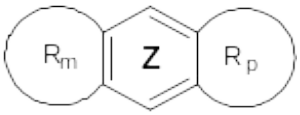
Cyclopentyl



Cyclohexyl

In addition, structural element A may consist of the following bicyclic or tricyclic systems, where structural element B may be located at any position of the bicyclic or tricyclic system:





The anellated rings R_m and R_p may consist of saturated, unsaturated or aromatic ring structures with four to eight ring atoms (including the two carbon atoms of ring Z). These rings R_m and R_p may, in addition to carbon, have a maximum of two atoms from the elements oxygen, nitrogen and sulphur in any combination in the ring. The heteroatom(s) in the rings R_m and$_{R\,p}$ shall be exclusively directly connected to the ring Z. A possible free valence of a nitrogen atom in the rings R_m and R_p can carry a hydrogen atom or a methyl or ethyl residue.

All the aforementioned ring systems of structural element A may be substituted in any position with the following atoms or atom groups (R_n):

hydrogen, fluorine, chlorine, bromine, iodine, alkyl- (up to C_8), alkenyl- (up to C_8), alkinyl- (up to C_8), alkoxy- (up to C_7), carboxy-, alkylsulfanyl- (up to C_7) and nitro groups.

The atom groups listed can also be substituted with arbitrary chemically possible combinations of the elements carbon, hydrogen, nitrogen, oxygen, sulphur, fluorine, chlorine, bromine and iodine. The substituents formed in this way may have a continuous chain length of a maximum of eight atoms (not counting hydrogen atoms). Atoms of ring structures are not included in the count.

Molecules in which R_n creates cyclic systems that are annelated to structural element A are not covered by the substance group definition.

1.2 Structural element B

The 2-aminoethyl side chain of structural element B can be substituted with the following atoms, atom groups or ring systems:

a) R_1 and R_2 on the nitrogen atom:

Hydrogen, alkyl (up to C_6), cycloalkyl (ring size up to C_6), benzyl-, alkenyl (up to C_6), alkinyl (up to C_6), alkylcarbonyl (up to C_6), alkyloxycarbonyl (alkyl residue up to C_6), alkylthiocarbonyl (alkyl residue up to C_6), alkylcarbamoyl (alkyl residue up to C_6), arylcarbonyl (arylrest to C_{10}), hydroxy and amino groups. It also includes substances in which the nitrogen atom is part of a non-aromatic saturated or unsaturated cyclic system (e.g. pyrrolidinyl, piperidinyl rings). A ring closure of the nitrogen atom including parts of structural element B (residues R_3 to R_6) is possible. The resulting molecular structure must conform to Point 1.2(a) with regard to the substituents even without the ring closure to structural element B. The resulting ring systems can contain the elements carbon, oxygen, sulphur, nitrogen and hydrogen. These ring systems may contain five to seven atoms. A double bond as a bridge to structural element B is possible. The residues R_1/R_2 can only be present as a double-bonded residue (imine structure) in the ring system resulting from a ring closure with parts of structural element B.

Not included in the substance group of 2-phenethylamine-derived compounds are compounds where the nitrogen atom is integrated directly into a cyclic system that is annelated to structural element A.

The substituents R_1 and R_2 can continue to be substituted (in the case of ring closure only after ring closure) with any chemically possible combinations of the elements carbon, hydrogen, nitrogen, oxygen, sulphur, fluorine, chlorine, bromine and iodine. The resulting substituents R_1/R_2 may have a continuous chain length of a maximum of ten atoms (not counting hydrogen atoms). Atoms of ring structures are not included in the count.

b) R_3 and R_4 on the C_1 atom and R_5 and R_6 on the C_2 atom:

Hydrogen, fluorine, chlorine, bromine, iodine, alkyl- (up to C_{10}), cycloalkyl- (ring size up to C_{10}), benzyl-, phenyl-, alkenyl- (up to C_{10}), alkinyl- (up to C_{10}), hydroxy-, alkoxy- (up to C_{10}), alkylsulfanyl- (up to C_{10}), and alkyloxycarbonyl groups (alkyl residue up to C_{10}), including chemical compounds, where substitutions lead to a ring closure with structural element A or to ring systems containing residues R_3 to R_6 . These ring systems may comprise four to six atoms.

The atom groups and ring systems listed can also be substituted with any chemically possible combinations of the elements carbon, hydrogen, nitrogen, oxygen, sulphur, fluorine, chlorine, bromine and iodine. The resulting substituents R_3 to R_6 may have a continuous chain length of a maximum of twelve atoms (not counting hydrogen atoms). Atoms of ring structures are not included in the count.

Where the residues R_3 to R_6 are part of a ring system containing the nitrogen atom of structural element B, the restrictions referred to in Letter (a) shall apply to other substituents.

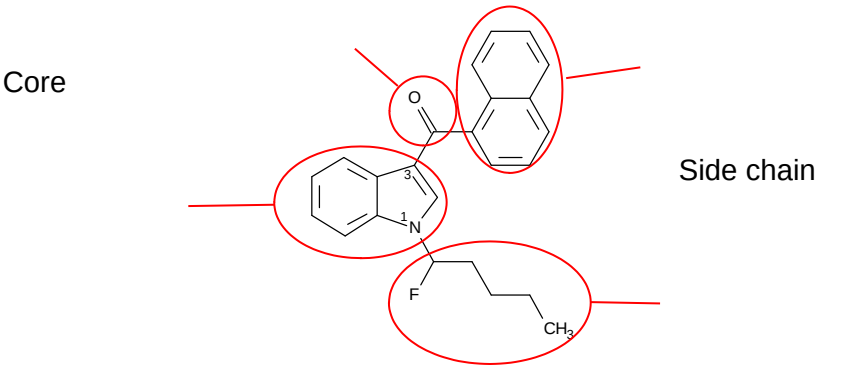
c) Carbonyl group in beta position with respect to the nitrogen atom ('beta-keto derivatives/cathinones', see figure of the cathinone base structure in Paragraph 1: R_5 and R_6 on the C_2 atom: Carbonyl group (C=O)

2. Cannabimimetic agents/synthetic cannabinoids

2.1 Compounds derived from indol, indolizine, pyrrole, pyrazole and quinolone

A cannabimimetic agent or a synthetic cannabinoid of the compounds derived from indole, indolizine, pyrrole, pyrazole or chinolone is any chemical compound that corresponds to the modular structure described below using a structural example with a core structure. The compound is linked to a bridge residue at a defined position over a bridge and carries a side chain at a defined position of the core structure.

The figure shows the modular design for 1-fluoro-JWH-018:



1-fluoro-JWH-018 has a core structure of indole-1,3-diyl, a carbonyl bridge at position 3, a 1-naphthyl bridge residue and a 1-fluorpentyl side chain in position 1.

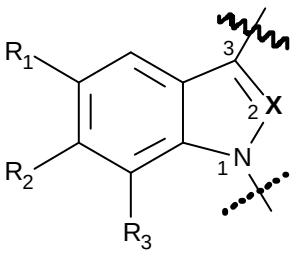
Core structure, bridge, bridge residue and side chain are defined as follows:

2.1.1 Core structure

The core structure includes the ring systems described below in (a) to (l). The ring systems of letters a to j may be substituted in the positions shown in the following figures with any combination of the atoms hydrogen, fluorine, chlorine, bromine, iodine and phenyl-, methyl-, trifluoromethyl-, trimethylsilyl-, methoxy-, trifluoromethoxy- and nitro groups as atom groups (residues R_1 to R_3).

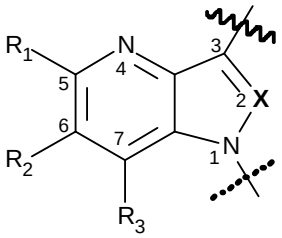
The wavy line indicates the binding site for the bridge. The broken line indicates the binding site for the side chain:

a) Indole-1,3-diyl (X = CH, C-CH_3, C-F, C-Cl, C-Br and C-I) and indazole-1,3-diyl (X = N) (binding site for the bridge at position 3, binding site for the side chain at position 1)

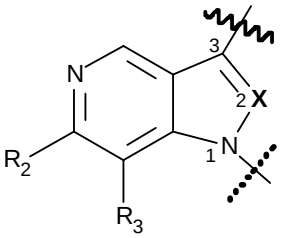


X = CH, C-CH_3, C-F, C-Cl, C-Br, C-I or N

b) 4-, 5-, 6- or 7-azaindole-1,3-diyl (X = CH, C-CH_3, C-F, C-Cl, C-Br and C-I) and 4-, 5-, 6- or 7-azaindazole-1,3-diyl (X = N)
(binding site for the bridge at position 3, binding site for the side chain at position 1)



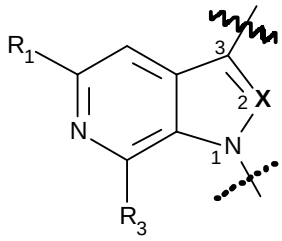
4-Aza-Derivate



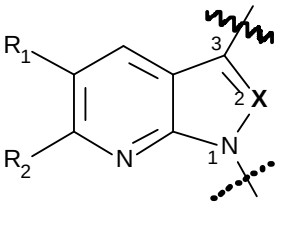
5-Aza-Derivate

respectively:

X = CH, C-CH_3, C-F, C-Cl, C-Br, C-I or N

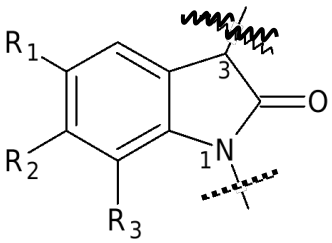


6-Aza-Derivate

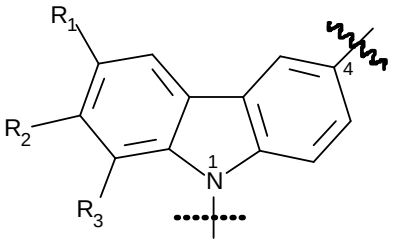


7-Aza-Derivate

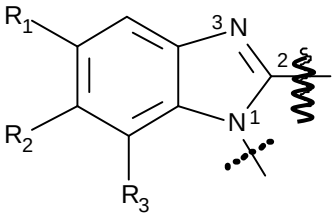
c) 1*H*-indole-2-on-1,3-diyl
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



d) Carbazole-1,4-diyl
(binding site for the bridge at position 4),
binding site for the side chain at position 1)

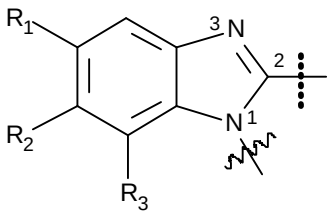


e) Benzimidazole-1,2-diyl isomer I
(binding site for the bridge at position 2,
binding site for the side chain at position 1)

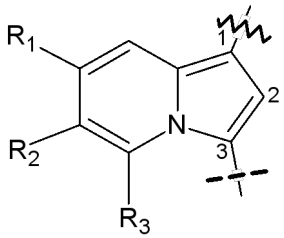


and

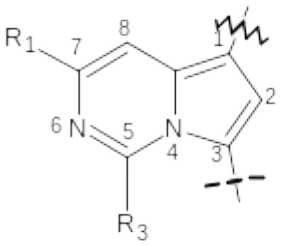
Benzimidazole-1,2-diyl isomer II
(binding site for the bridge at position 1,
binding site for the side chain at position 2)

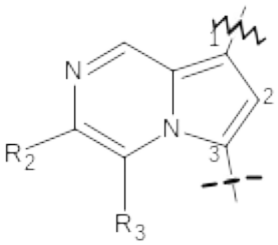


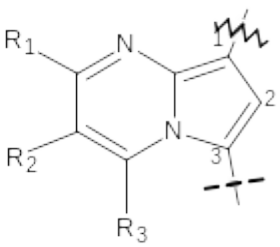
f) Indoolizine-1,3-diyl
(binding site for the bridge at position 1,
binding site for the side chain at position 3)



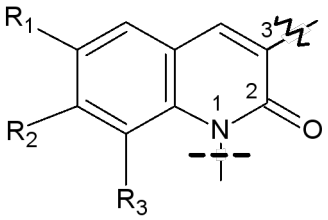
g) 6-, 7-, 8-azaindolizine-1,3-diyl
(binding site for the bridge at position 1,
binding site for the side chain at position 3)



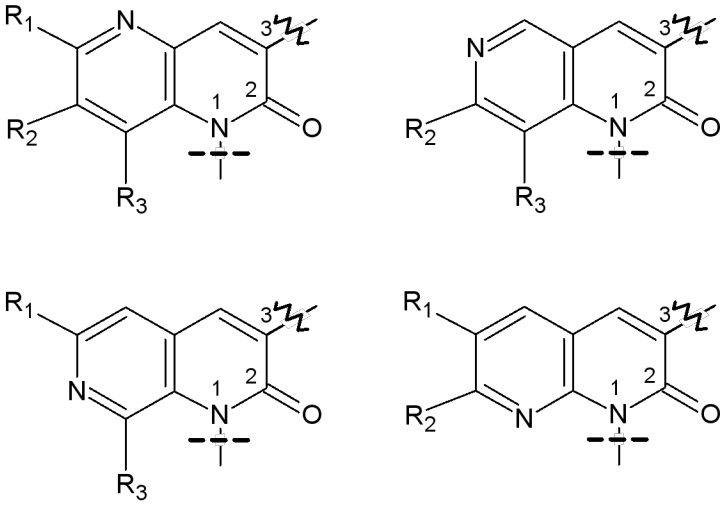




h) 2-chinolone-1,3-diyl
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



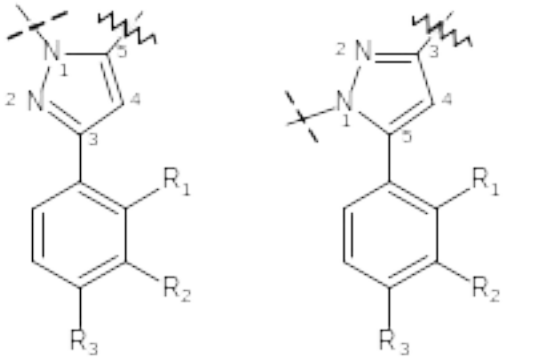
i) 5-,6-,7-,8-aza-2-chinolone-1,3-diyl
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



j) 3-phenylpyrazole-1,5-diyl
(binding site for the bridge at position 5,
binding site for the side chain at position 1)

and

5-phenylpyrazole-1,3-diyl
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



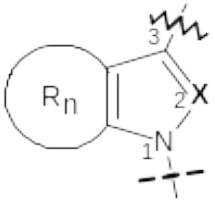
3-Phenylpyrazol-1,5-diyl
3-phenylpyrazole-1,5-diyl

5-Phenylpyrazol-1,3-diyl
5-phenylpyrazole-1,3-diyl

k) In addition to the core structures mentioned under a) and b), the following core structures derived from pyrrole and pyrazole are also covered:

Pyrrole-1,3-diyl (X = CH, C-CH_3, C-F, C-Cl, C-Br and C-I) and pyrazole-1,3-diyl (X = N) with non-aromatic ring alignment in 4- and 5-position

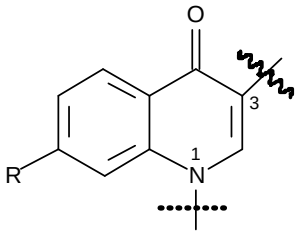
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



X = CH, C-CH_3, C-F, C-Cl, C-Br, C-I or N

The anellated residue R_n may consist of saturated or unsaturated, but not aromatic, mono- and polycycles in this subgroup. Monocycles can have three to eight ring atoms (including the two anellated C atoms in the core structure). In polycycles, each ring may have three to seven ring atoms (including the two anellated C atoms on the core structure). The ring atoms of mono- and polycycles may consist of the atoms carbon, oxygen and sulphur. The anellated ring system R_n may be substituted in arbitrary positions with any combination of the following atoms and atom groups: Hydrogen, fluorine, chlorine, bromine, iodine and phenyl-, methyl-, trifluoromethyl-, trimethylsilyl, methoxy-, trifluoromethoxy and nitro groups.

l) 4-chinolone-1,3-diyl
(binding site for the bridge at position 3,
binding site for the side chain at position 1)



Residue R may consist of one of the following atoms or one of the following atom groups: Hydrogen, fluorine, chlorine, bromine, iodine and phenylthiogroup (binding via sulphur to the core structure).

2.1.2 Bridge on the core structure

The bridge on the core structure includes the following structural elements, which are bound to the site on the core structure given in Point 2.1.1:

a) Carbonyl-, methylene carbonyl- (CH_2 group linked to core structure) and azacarbonyl group,

b) Carboxamido group (carbonyl group linked to the core structure) including substituents containing carbon and hydrogen on the amide nitrogen which together with position 2 of the indole core structure (Point 2.1.1(a): X = CH) form a six-membered ring, and methylene carboxamido group (CH_2 group linked to core structure),

c) Carboxyl (carbonyl group tied to core structure) and methylene carboxyl group (CH_2 group linked to core structure),

d) nitrogen heterocycles directly attached to the core structure, which may also contain other nitrogen, oxygen or sulphur atoms, with a ring size of up to five atoms and a double bond to the nitrogen atom at the binding point,

e) hydrazone group with double bonding from nitrogen to position 3 of the core structure as referred to in Point 2.1.1(c).

f) oxaspirocycloalkyl groups with an oxygen atom adjacent to the spirocentre. The ring size of the oxaspiroring may be up to six atoms in total (x = 1 – 4).

2.1.3 Bridge residue

a) The bridge residue may contain combinations of the atoms carbon, hydrogen, nitrogen, oxygen, silicon, sulphur, fluorine, chlorine, bromine or iodine, which may have a maximum molecular mass of 400 u and may include the following structural elements:

aa) arbitrarily substituted saturated, unsaturated or aromatic ring structures, including polycycles and heterocycles, with connection to the bridge also via a substituent;

bb) arbitrarily substituted chain structures with at least one carbon atom which, including the heteroatoms, have a continuous chain length of no more than twelve atoms (not counting hydrogen atoms).

b) Bridges with the possibility of binding multiple bridge residues, e.g. bridges to 2.1.2(b), (d) or (e) may also bear several bridge residues as defined in Point 2.1.3(a)(aa) and 2.1.3(a)(bb). The molecular mass restriction of a total of 400 u applies to the sum of the bridge residues.

2.1.4 Side chain

The side chain may contain any combination of the atoms carbon, hydrogen, nitrogen, oxygen, sulphur, silicon, fluorine, chlorine, bromine and iodine unless they are restricted in (a) and (b). The side chain may have a maximum molecular mass of 300 u and must be connected to the point of the core structure specified in Point 2.1.1. The side chain may contain the following structural elements:

a) arbitrarily substituted chain structures with at least one carbon atom, which may only contain oxygen-, sulphur and silicon atoms within the chain apart from other carbon atoms and have a continuous chain length of three to a maximum of ten atoms (not counting hydrogen atoms) taking into account the heteroatoms,

b) saturated, unsaturated or aromatic ring structures with a total of one to four carbon atoms that are directly attached or coupled via a hydrocarbon bridge (saturated or monounsaturated, branched or unbranched, optionally oxo-substituted in position 2) and have three to seven ring atoms, including polycycles and heterocycles. In polycycles, each ring may have three to seven ring atoms. In addition to carbon, heterocycles may have oxygen, nitrogen and sulphur in the ring. A possible free valence of a nitrogen atom in the ring can carry a hydrogen atom or a methyl or ethyl residue.

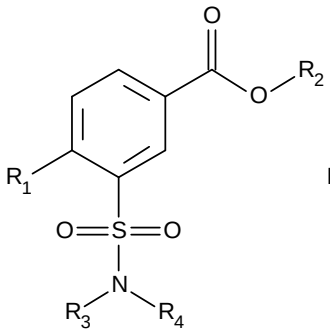
2.2 Compounds derived from 3-sulfonylamidobenzoic acid

This separate group of cannabimimetics/synthetic cannabinoids not having the modular composition described in Point 2.1 includes the substances that have one of the core structures described in Point 2.2.1, that may contain the substituents described in Point 2.2.2, and that have a maximum molecular mass of 500 u.

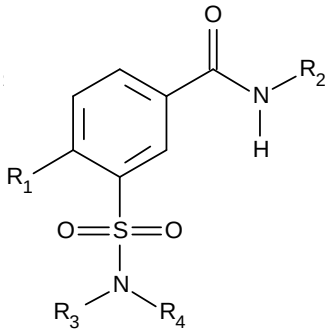
2.2.1 Core structure

The core structure includes the molecules described below in (a) and (b). These may be substituted in the positions shown in the following figures with the atoms or atom groups as specified in Point 2.2.2 (residues R_1 to R_4):

a) 3-Sulfonylamido benzoates



b) 3-Sulfonylamido benzamides



2.2.2 Residues R_1, R_2, R_3 und R_4

a) Residue R_1 may consist of one of the following atoms or one of the following atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl and methoxy groups.

b) Residue R_2 may consist of one of the following ring systems: Phenyl, pyridyl, cumyl, 8-chinolinyl, 3-isochinolinyl, 1-naphthyl, or adamantyl residue. These ring systems may furthermore be substituted with arbitrary combinations of the following atoms or atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, methoxy, amino, hydroxy, cyano, methyl and phenoxy groups.

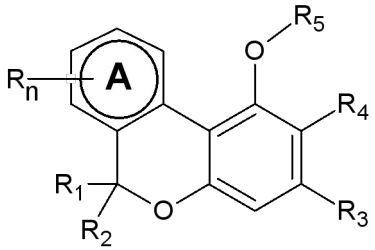
c) Residues R_3 and R_4 may consist of hydrogen atoms, methyl, ethyl, propyl, and isopropyl groups in any combination. Residues R_3 and R_4 may also form a saturated ring system with a size of up to seven atoms including the nitrogen atom. This ring system can contain the other elements nitrogen, oxygen and sulphur and carry any combination of hydrogen, fluorine, chlorine, bromine and iodine. Substitution of the nitrogen atom in such a ring is governed by the substitution options indicated for residues R_3 and R_4 in sentence 1 of (c).

2.3 Compounds derived from 6*H*-benzo(c)chromene-1-ol (6*H*-dibenzo(b,d)pyran-1-ol)

This separate group of cannabimimetic agents/synthetic cannabinoids, which are not composed according to the modular structure described under Points 2.1 and 2.2, include the substances having a core structure described in Point 2.3.1, may be occupied with the substituents described in Point 2.3.2 and have a maximum molecular mass of 600 u.

2.3.1 Core structure

The core structure includes the following compounds derived from 6*H*-benzo(c)chromene-1-ol (6*H*-dibenzo(b,d)pyran-1-ol), regardless of the degree of hydrogenation of the aromatic ring A and the position of the remaining double bonds, where appropriate. The compounds can be substituted at the indicated positions with the atoms and atom groups referred to in Point 2.3.2 (residues R_1 to R_5 and R_n):



2.3.2 Residues R_1, R_2, R_3, R_4, R_5 and R_n

a) The ring A may be substituted in any position with arbitrary combinations of the following atoms and atom groups (R_n): Hydrogen, bromine, chlorine, fluorine, iodine, hydroxy-, alkyl carbonyl- (alkyl residue up to C_5), alkoxyalkyl- (alkyl residue up to C_5), alkoxy- (alkyl residue up to C_5), hydroxymethyl-, methyl- and trialkyl silyl group (maximum twelve C-atoms in the total trichain) and carbon chain (saturated or unsaturated, branched or not branched, up to C_{10}). The above-mentioned nuclear groups, with the exception of the trialkylsilyl groups, may be substituted with the following atoms and groups: Hydrogen, fluorine, chlorine, bromine, iodine and trialkylsilyl groups (maximum 12 C atoms in total trialkylates).

b) The residues R_1 and R_2 may consist of hydrogen or of the following atom groups: Alkyl (up to C_5) and trialkylsilyl group (maximum 12 C atoms in the total trialkylates). The above-mentioned nuclear groups other than the Trialkylsilyl group may be substituted with the following atoms and groups: Hydrogen, fluorine, chlorine, bromine, iodine and trialkylsilyl groups (maximum 12 C atoms in total trialkylates).

c) The residue R_3 may consist of hydrogen or one of the following atom groups: methyl group and carbon chain (saturated or unsaturated, branched or not branched, up to C_{12}) and trialkylsilyl group (maximum twelve C atoms in the total trichain). The above-mentioned nuclear groups other than the trialkylsilyl groups may be substituted with the following atoms and groups: Hydrogen, fluorine, chlorine, bromine, iodine and trialkylsilyl groups (maximum 12 C atoms in total trialkylates).

d) The residue R_4 may consist of hydrogen or one of the following atom groups: alkyl- (up to C_5), alkenyl- (up to C_5), carboxyl or alkyloxycarbonyl groups (alkyl residue up to C_5).

e) The residue R_5 may consist of hydrogen or one of the following atom groups: Alkyl (up to C_7), trialkylsilyl (maximum 12 C atoms in the total trialkyl residues)-, alkyloxycarbonyl (alkyl residue up to C_7), alkylcarbonyl (alkyl residue up to C_7), cycloalkylcarbonyl and cycloalkylmethylcarbonyl- each with three to seven ring atoms including polycycles, arylcarbonyl with three to six ring atoms including polycycles and hetero-cycles, and arylmethylcarbonyl group with three to six ring atoms including polycycles and hetererocycles. For the polycycles, each ring may have three to seven ring atoms. The above-mentioned nuclear groups other than the trialkylsilyl groups may be substituted with the following atoms and groups: Hydrogen, fluorine, chlorine, bromine, iodine and trialkylsilyl groups (maximum 12 C atoms in total trialkylates). In addition to carbon, heterocycles may have oxygen, nitrogen and sulphur in the ring. A possible free valence of a nitrogen atom in the ring can carry a hydrogen atom or a methyl or ethyl residue.

f)

3. Benzodiazepines

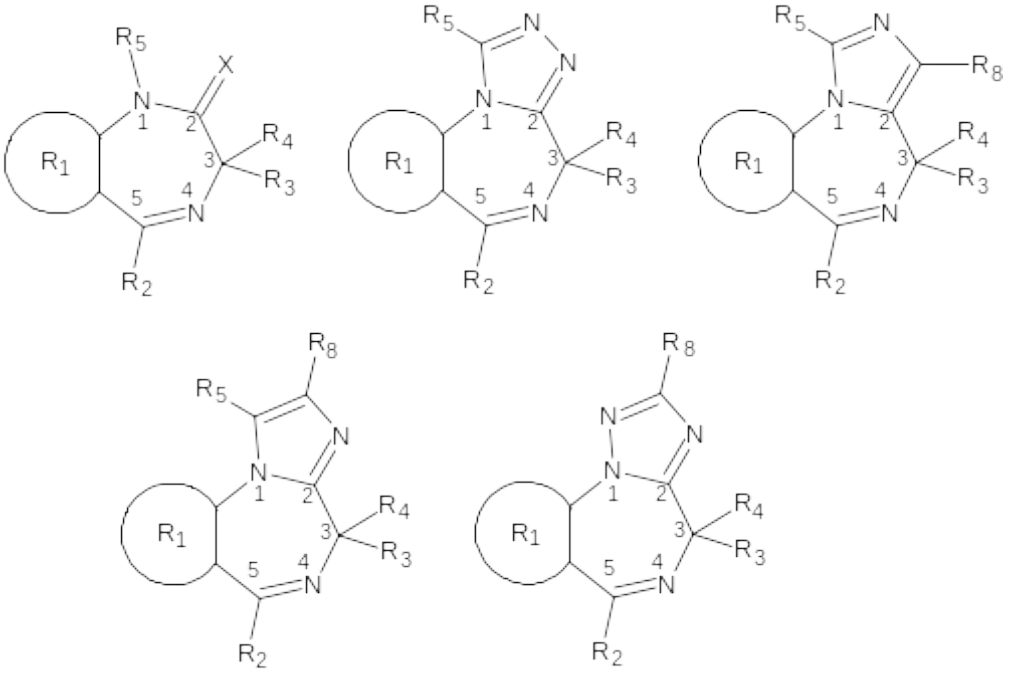
The group of benzodiazepines comprises 1,4- and 1,5-benzodiazepines and their triazole and imidazole derivatives (Point 3.1.1(a) and (b)) as well as some specially substituted subgroups of these benzodiazepines (Point 3.1.1(c) to (g)) as well as some open-chain benzodiazepine prodrugs (Point 3.2.1). The maximum molecular mass is 600 u in each case.

3.1 Cyclical representatives

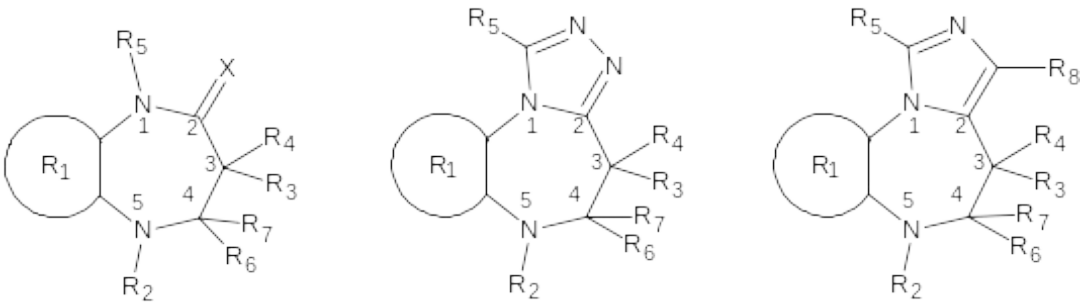
3.1.1 Core structure

The core structure includes the ring systems described below in Letters (a) to (g). These ring systems may be substituted in the positions shown in the following figures with the atoms or atom groups as specified in Point 3.1.2 (residues R_1 to R_8 and X):

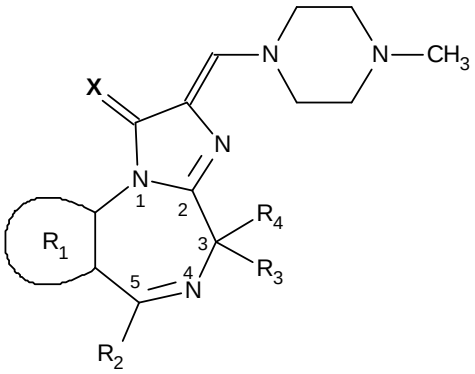
a) 1,4-benzodiazepines



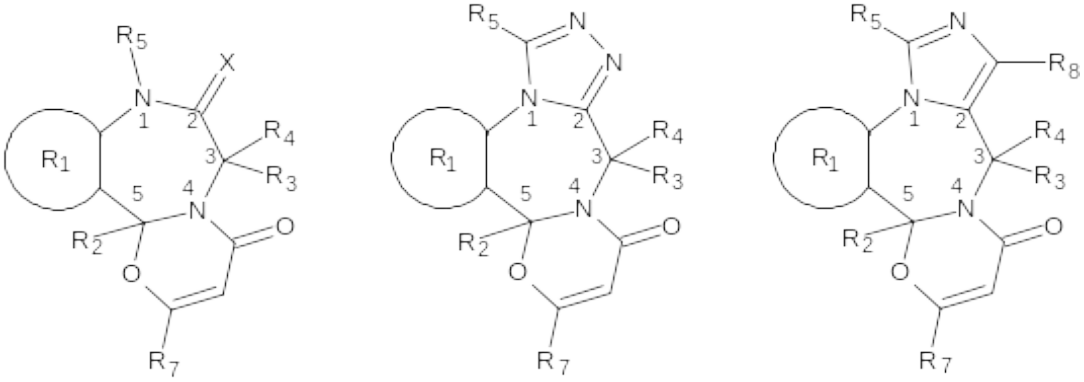
b) 1,5-benzodiazepines



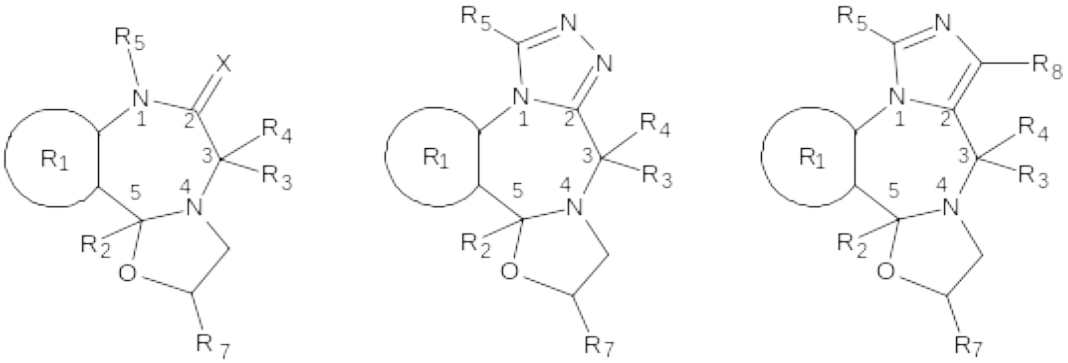
c) Loprazolam derivatives



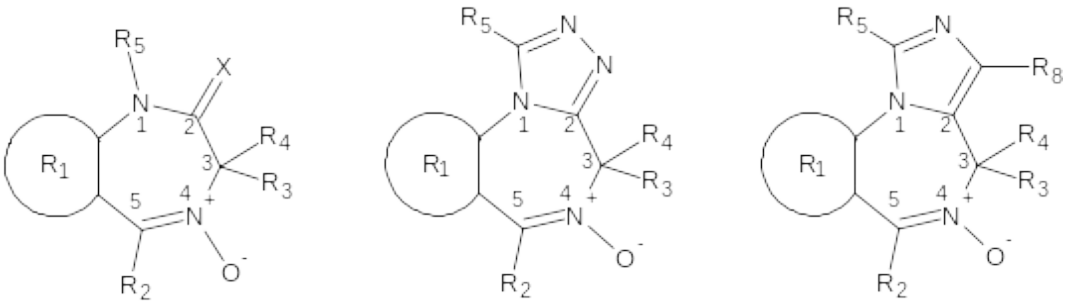
d) Ketazolam derivatives



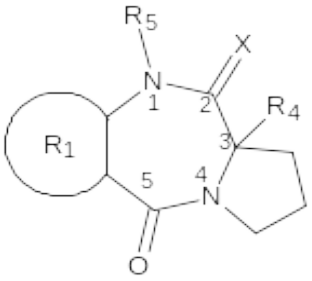
e) Oxazolam derivatives

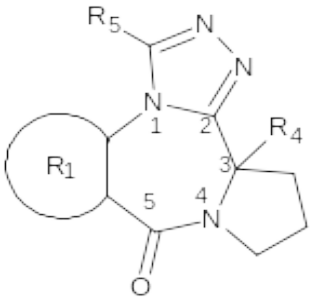


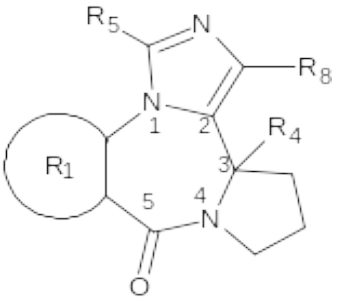
f) Chlorodiazepoxide derivatives



g) Bretazenil derivatives







3.1.2 Residues R_1 to R_8 and X

a) Residue R_1 includes one of the following ring systems, anellated to the seven-membered rings of the core structures:

Phenyl, thienyl, 4,5,6,7-tetrahydrobenzo[b]thienyl, furanyl and pyridyl ring; the heteroatoms in the thienyl, furanyl and pyridyl ring can be located at any position outside the seven ring of the core structure.

Residue R_1 may continue to be substituted with one or more of the following atoms or atom groups, in arbitrary combinations and in arbitrary positions outside the seven-membered ring: Hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl, nitro and amino groups.

b) The residue R_2 shall include one of the following ring systems:

Phenyl, pyridyl (with nitrogen atom at arbitrary position in the pyridyl ring) and cyclohexenyl ring (with double bond at arbitrary position in the cyclohexenyl ring).

Phenyl and pyridyl ring may bear one or more of the following substituents in an arbitrary combination and at arbitrary position: Hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl, nitro and amino groups.

c) The residue R_3 may consist of hydrogen or one of the following atom groups:

Hydroxy, carboxyl, ethoxycarbonyl, (N,N-dimethyl)carbamoyl-, succinyloxy-, alkoxycarbonyl alkyl- (alkoxy to C_4, alkyl group to C_4) and methyl group.

d) The residue R_4 may consist of hydrogen or one of the following atom groups:

Methyl and ethyl group.

e) Residues R_3 and R_4 may also form a carbonyl group (C=O) together.

f) The residue R_5 may consist of hydrogen or one of the following atom groups:

Methyl, ethyl, (N,N-dimethylamino)methyl, (N,N-diethylamino)methyl, (N,N-dimethylamino)ethyl-, (N,N-diethylamino)ethyl-, (cyclopropyl)methyl-, (trifluoromethyl)methyl-, hydrazidomethyl- and prop-2-in-1-yl group.

g) The residue R_6 may consist of hydrogen or one of the following atom groups:

Hydroxy, and methyl group.

h) The residue R_7 may consist of hydrogen or one of the following atom groups:

Methyl and ethyl group.

i) Residues R_6 and R_7 may also form a carbonyl group (C=O) for the 1,5-benzodiazepines.

j) The 1,5-benzodiazepines may also have a R_6-substituted (instead of R_2 and R_7) double bond to the 5-nitrogen atom.

k) The residue R_8 may consist of hydrogen or an alkyloxycarbonyl (alkyl residue up to C_6) or a N,N-dimethylcarbamolyl group.

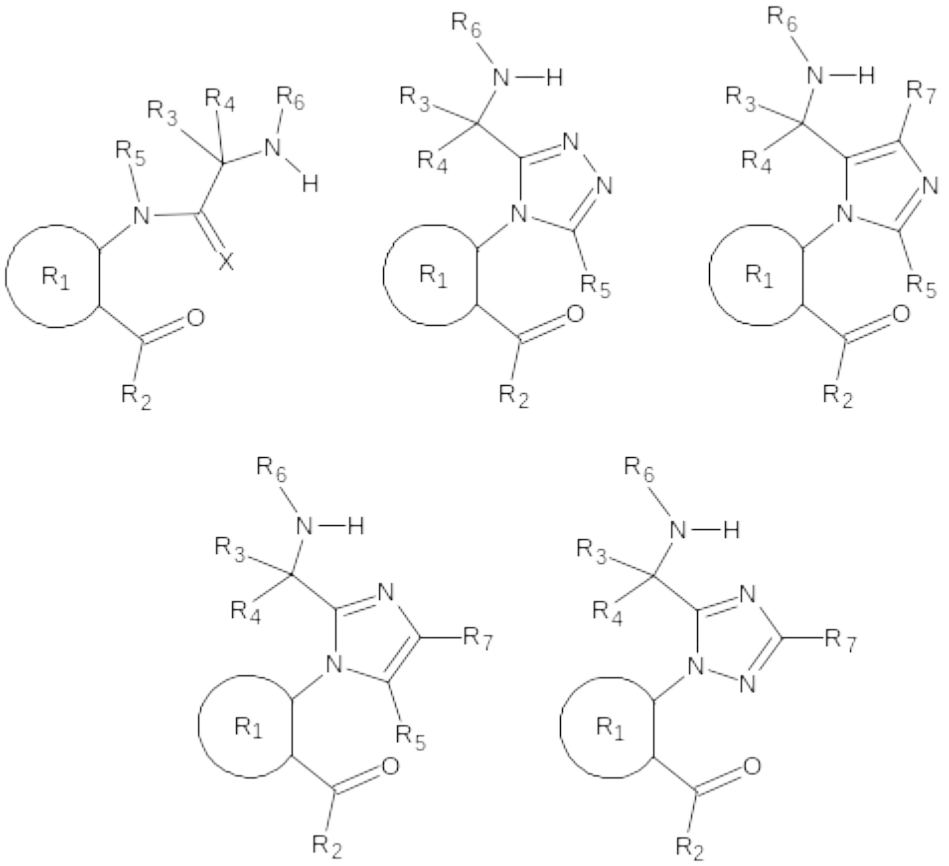
l) the residue X includes one of the following atoms or one of the following atom groups:

Oxygen, sulphur, imino and N-methylimino group. If R_3, R_4 or R_5 consist of hydrogen, the corresponding enols, thioenols or enamines can also be present as tautomeric forms.

3.2 Open chain benzodiazepine prodrugs

This separate group of benzodiazepine analogues, which are not composed according to the modular structure described in Points 3.1.1, include the substances which have a core structure as described in Point 3.2.1 and which may be occupied by the substituents described in Point 3.2.2.

3.2.1 Core structure



3.2.2 Residues R_1 to R_7 and X

a) The residue R_1 shall include one of the following ring systems:

Phenyl, thienyl, 4,5,6,7-tetrahydrobenzo[b]thienyl, furanyl and pyridyl ring; the heteroatoms in the thienyl, furanyl and pyridyl ring may be located at any position outside the R_1 residue. The connections from R_1 shall be at adjacent positions of the above-mentioned ring systems.

Residue R_1 may continue to be substituted with one or more of the following atoms or atom groups, in arbitrary combinations and in arbitrary positions: Hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl, nitro and amino groups.

b) The residue R_2 shall include one of the following ring systems:

Phenyl, pyridyl (with nitrogen atom at arbitrary position in the pyridyl ring) and cyclohexenyl ring (with double bond at arbitrary position in the cyclohexenyl ring).

Phenyl and pyridyl ring may bear one or more of the following substituents in an arbitrary combination and at arbitrary position: Hydrogen, fluorine, chlorine, bromine, iodine, methyl, ethyl, nitro and amino groups.

c) The residue R_3 may consist of hydrogen or one of the following atom groups:

Hydroxy, carboxyl, ethoxycarbonyl, (N,N-dimethyl)carbamoyl-, succinyloxy-, alkoxycarbonyl alkyl- (alkoxy to C_4, alkyl group to C_4) and methyl group.

d) The residue R_4 may consist of hydrogen or one of the following atom groups:

Methyl and ethyl group.

e) Residues R_3 and R_4 may also form a carbonyl group (C=O) together.

f) The residue R_5 may consist of hydrogen or one of the following atom groups:

Methyl, ethyl, (N,N-dimethylamino)methyl, (N,N-diethylamino)methyl, (N,N-dimethylamino)ethyl-, (N,N-diethylamino)ethyl-, (cyclopropyl)methyl-, (trifluoromethyl)methyl-, hydrazidomethyl- and prop-2-in-1-yl group.

g) The residue R_6 may consist of hydrogen or an alkyl carbamoyl group (alkyl residue up to C_6). In addition, R_6 may consist of the following amino acid particles (binding over the C-terminus): glycine, alanine and lysine.

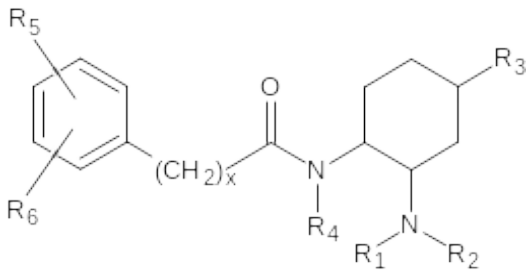
h) The residue R_7 may consist of hydrogen or an alkyloxycarbonyl (alkyrest to C_6) or N,N-dimethylcarbamolyl group.

i) the residue X includes one of the following atoms or one of the following atom groups:

Oxygen, sulphur, imino and N-methylimino group. If R_3, R_4 or R_5 consist of hydrogen, the corresponding enols, thioenols or enamines can also be present as tautomeric forms.

4. N-(2-aminocyclohexyl)amide -derived compounds

A compound derived from N- (2-aminocyclohexyl) amide is any chemical compound which can be derived from the basic structure shown below, has a maximum molecular mass of 500 u and can be occupied by the substituents described below.



The number x of methylene groups $(CH_2)_x$ between the phenyl ring and the carbonyl group in the core structure can be zero or one.

The base structure N-(2-aminocyclohexyl)amide may be substituted at the positions shown in the figure with an arbitrary combination of the following atoms, branched or unbranched atom groups, or ring systems (residues R_1 to R_6):

a) R_1 and R_2:

Hydrogen and alkyl group (up to C_7).

It also includes substances in which the nitrogen atom is part of a cyclic system (e.g. pyrrolidinyl).

Residue R_1 or R_2 can also connect to the binding site of the NR_1R_2 group at the six-membered ring (by forming a so-called spiro compound). These nitrogen-containing rings may have a ring size of 3 to 7 atoms (one nitrogen atom and 2 to 6 carbon atoms).

b) R_3:

Hydrogen and oxaspiro group (ring size of three to eight atoms including the oxygen atom).

c) R_4:

Hydrogen and alkyl group (up to C_5).

d) R_5 and R_6:

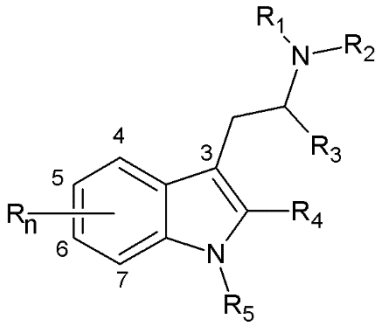
The phenyl ring may contain arbitrary combinations of the following substituents at positions 2, 3, 4, 5 and 6: Hydrogen, bromine, chlorine, fluorine, iodine and trifluoromethyl group.

Included are also substances where R_5 and R_6 together form a ring system (up to C_6) on neighbouring C atoms while including heteroatoms (oxygen, sulphur, nitrogen). If there is a nitrogen in this ring system, it may bear the substituents hydrogen and methyl group.

5. Tryptamine-derived compounds

5.1 Indole-3-alkylamine

An indole-3-alkylamine-derived compound is any chemical compound that can be derived from the base structure shown below, has a maximum molecular mass of 500 u, and may bear the substituents as described below. Except for tryptamin, the naturally occurring neurotransmitters serotonin and melatonin as well as their active metabolites (example: 6-hydroxymelatonin).



The base structure indole-3-alkylamine may be substituted at the positions shown in the figure with the following atoms, branched or unbranched atom groups, or ring systems (residues R_1 to R_5 and R_n):

a) R_1 and R_2:

Hydrogen, alkyl (up to C_6), cycloalkyl (ring size up to C_6), cycloalkyl methyl (ring size up to C_6), allyl, alkyloxycarbonyl- (alkyl residue up to C_6), alkylthiocarbonyl- (alkyl residue up to C_6) and alkylcarbamoyl group (alkyl residue up to C_6).

Furthermore, substances are included in which the nitrogen atom is part of a pyrrolidinyl, piperidinyl or morpholinyl ring system.

b) R_3:

Hydrogen and alkyl group (up to C_3).

c) R_4:

Hydrogen and alkyl group (up to C_2).

d) R_5:

Hydrogen, alkyl (up to C_3), alkylcarbonyl (up to C_{10}), cycloalkylcarbonyl (ring size C_3 to C_6), cycloalkylmethylcarbonyl (ring size C_3 to C_6), cycloalkylethylcarbonyl (ring size C_3 to C_6), cycloalkylpropylcarbonyl (ring size C_3 to C_6), alkyloxycarbonyl (alkyl residue up to C_6), alkylthiocarbonyl (alkyl residue up to C_6), alkylcarbamoyl (alkyl residue up to C_6), benzylcarbonyl and (trialkylsilyl) alkylcarbonyl group (alkyl residues up to C_6, maximum 12 C atoms in the total trialkylates).

e) R_n:

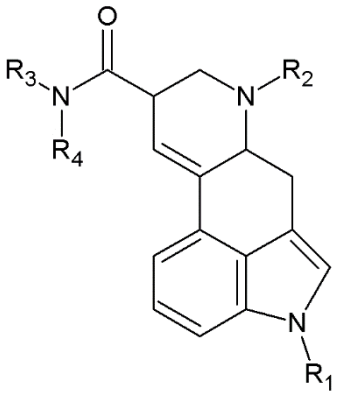
The indole ring system may be substituted at positions 4, 5, 6 and 7 with the following atoms or groups of atoms: Hydrogen, fluorine, chlorine, bromine, iodine, alkyl (up to C_4), alkyloxy (up to C_{10}), benzyloxy, carboxamido, methoxy, trialkylsilyl (up to 12 carbon atoms in total in the trialkyl residues), trifluoromethyl, trifluoromethoxy,

acetoxy, hydroxy und methylthio groups, at position 4 in addition with dihydrogen phosphate.

Substances where R_n bridges two neighbouring carbon atoms in positions 4, 5, 6 and 7 with a methylenedioxy group are also included.

5.2 $\Delta^{9,10}$-Ergolenes

A compound derived from $\Delta^{9,10}$-ergolene is any chemical compound that can be derived from the basic structure shown below, has a maximum molecular mass of 600 u and may bear the substituents described below.



The base structure $\Delta^{9,10}$-ergolene may be substituted at the positions shown in the figure with the following atoms, branched or unbranched atom groups, or ring systems (residues R_1 to R_4):

a) R_1:

The residue R_1 may consist of any combination of the atoms carbon, hydrogen, nitrogen, silicon, oxygen, sulphur, fluorine, chlorine, bromine and iodine, unless they are restricted in accordance with (aa) and (bb). Residue R_1 may have a maximum molecular mass of 300 u and the following structural elements:

aa) Hydrogen or arbitrarily substituted chain structures with at least one carbon atom, which can only contain silicon, oxygen and sulphur atoms within the chain in addition to other carbon atoms.

bb) directly attached or coupled via a hydrocarbon bridge (saturated or monounsaturated, branched or not branched with a total of one to five carbon atoms) or a carbonyl group or an alkyl carbonyl group (alkyl residue up to C_4, binding of the carbonyl group to the nitrogen of the ergolene) or an alkyloxycarbonyl group (alkyl residue up to C_4, binding of the carbonyl group to the nitrogen of the ergolene) or a sulfonyl group, arbitrarily substituted, saturated, unsaturated or aromatic ring structures with three to seven ring atoms, including polycycles and heterocycles. In polycycles, each ring may have three to seven ring atoms. In addition to carbon, heterocycles may have oxygen, nitrogen and sulphur in the ring. A possible free valence of a nitrogen atom in the ring can carry a hydrogen atom or a methyl or ethyl residue.

b) R_2:

Hydrogen, alkyl (up to C_4), allyl and prop-2-in-1-yl groups.

c) R_3 and R_4:

Hydrogen, alkyl (up to C_5), cyclopropyl, 1-hydroxyalkyl (up to C_2) and allyl groups. Furthermore, substances are included in which the amide nitrogen atom is part of a morpholino, pyrrolidino or dimethylazetidid ring system.

6. Compounds derived from arylcyclohexyl(methyl)amine

A compound derived from arylcyclohexyl(methyl)amine is any chemical compound which can be derived from the basic structure shown below, has a maximum molecular mass of 500 u and can be occupied by the substituents described below.

The basic structures may be substituted at the positions shown in the figure with the following atoms, branched or non-branched atom groups or ring systems (residues R_1 to R_4 and R_n):

a) R_1/R_2:

Hydrogen, alkyl (up to C_6), cycloalkyl (ring size up to C_6)), alkenyl (up to C_6), alkinyl groups (up to C_6).

The atom groups listed may continue to be substituted with any chemically possible combinations of the elements carbon, hydrogen, nitrogen and oxygen. The resulting substituents R_1/R_2 may have a continuous chain length of a maximum of nine atoms (not counting hydrogen atoms). Atoms of ring structures are not included in the count.

In addition, these include substances in which the nitrogen atom is part of a cyclic system (e.g. pyrrolyl, pyrrolidinyl, piperidinyl, morpholino residues). These ring systems may contain the elements carbon, oxygen, sulphur and nitrogen in the ring and have a ring size of up to seven atoms. The ring systems may be substituted at any position with the following atoms or atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, hydroxy, alkyl (up to C_6) and phenyl groups.

b) R_3:

alkyl (up to C_6), alkynyl group (up to C_6) or one of the following ring systems: Phenyl, pyrrolyl, pyridyl, thienyl, furanyl, methylene dioxyphenyl, ethylene dioxyphenyl, dihydrobenzofuranyl and benzothiophenyl ring systems.

The ring systems may be connected to the core structure at any chemical position as R_3 and may be substituted at any position with the following atoms or atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, hydroxy, thiol, alkyl (up to C_6), alkoxy (up to C_6), alkylsulfanyl (up to C_6) and amino groups, including chemical compounds in which substitutions or direct connection lead to a ring closure with the cyclohexyl ring. These ring systems may have a ring size of four to six atoms.

c) R_4:

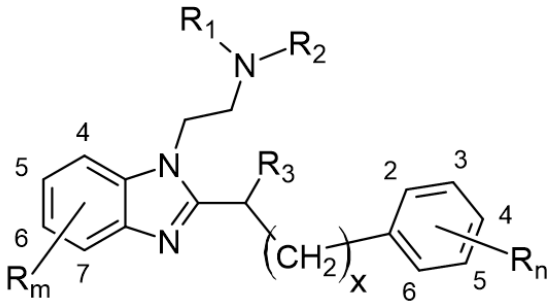
Hydrogen, methyl, ethyl, alkyl carbonyl (up to C_4), alkoxycarbonyl (alkyl residue up to C_4) and trialkyl silyl group (maximum of twelve C atoms in the total trichain length).

d) R_n:

The cyclohexyl ring system may be substituted at positions 2 to 6 with the following atoms or atom groups: Hydrogen, alkyl (up to C_6), alkoxy (up to C_6), hydroxy, phenylalkyl groups (in the alkyl chain C_1 to C_4) and oxo groups (=O, doubly-bonded oxygen atom on the ring).

7. Compounds derived from benzimidazole

A compound derived from benzimidazole is any chemical compound that can be derived from the basic structure shown below, has a maximum molecular mass of 600 u and may bear the substituents described below:



The number x of methylene groups $(CH_2)_x$ may be zero or one.

The basic structure may be substituted at the positions shown in the figure with the following atoms, branched or non-branched atom groups or ring systems (residues R_1 to R_3, R_m and R_n):

a) R_1 and R_2:

Hydrogen, alkyl (up to C_6), trialkylsilyl (maximum 12 C atoms in the total trialkyl residues), alkyloxycarbonyl (alkyl residue up to C_6), alkylthiocarbonyl (alkyl residue up to C_6), alkylcarbamoyl (alkyl residue up to C_6) and benzyl groups.

It also includes substances in which the amine nitrogen atom is part of a morpholino, pyrrolidino or piperidinyl ring system.

b) R_3

Hydrogen, alkyl (up to C_4), hydroxy, methoxy, alkylcarbamoyl- (alkyl residue up to C_6) and carbamoyl group.

c) R_m :

Benzimidazoles can bear any combinations of the following substituents at positions 4, 5, 6 and 7: Hydrogen, fluorine, chlorine, bromine, iodine, alkyl (up to C_6), trialkylsilyl (maximum 12 C atoms in total trialkyl residues), nitro-, trifluoromethyl, methoxy, trifluoromethoxy, cyano- and acetyl groups.

Substances where R_m bridges two neighbouring carbon atoms in positions 4, 5, 6 and 7 with a vinylenoxy- (1-oxyethene-2-yl), methylenedioxy, ethyleneoxy of ethylenedioxy group are also included.

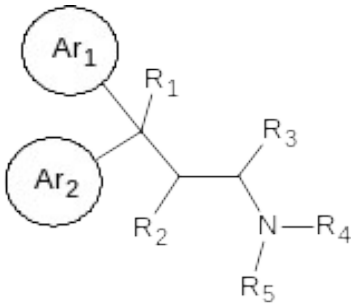
d) R_n:

The phenyl ring may be substituted at positions 2 to 6 with the following atoms or atom groups in any combination: Hydrogen, fluorine, chlorine, bromine, iodine, alkyl (up to C_6), alkoxy (up to C_5), acetoxy, alkylsulfanyl (up to C_5), hydroxy and cyanogroups. The atom groups above may be substituted with the following atoms and atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, alkyloxy- (alkyl residue up to C_4) and trialkylsilyl groups (maximum 12 C atoms in total trialkyl residues).

It also includes substances in which, by Rn, two adjacent carbon atoms of positions 2, 3, 4, 5 and 6 are bridged with a vinylenoxy- (1-oxyen-2-yl), methylenedioxy, ethyleneoxy or ethylenedioxy group.

8. Compounds derived from 3,3-diphenylpropan-1-amine

A compound derived from diphenylpropylamine is any chemical compound that can be derived from the basic structure shown below, has a maximum molecular mass of 500 u and may bear the substituents or aromatic ring systems described below:



The basic structure may be substituted at the positions shown in the figure with the following atoms, atom groups or aromatic ring systems (residues R_1 to R_5, Ar_1 and Ar_2):

a) R_1:

Alkylcarbonyl (alkyl residue up to C_6), alkylsulfonyl (alkyl residue up to C_6), piperidyl 1-carbonyl, pyrrolidinyl-1-carbonyl and morpholinyl-4-carbonyl group.

b) R_2 and R_3:

Hydrogen, methyl and ethyl groups.

c) R_4 and R_5:

Hydrogen and alkyl groups (up to C_4).

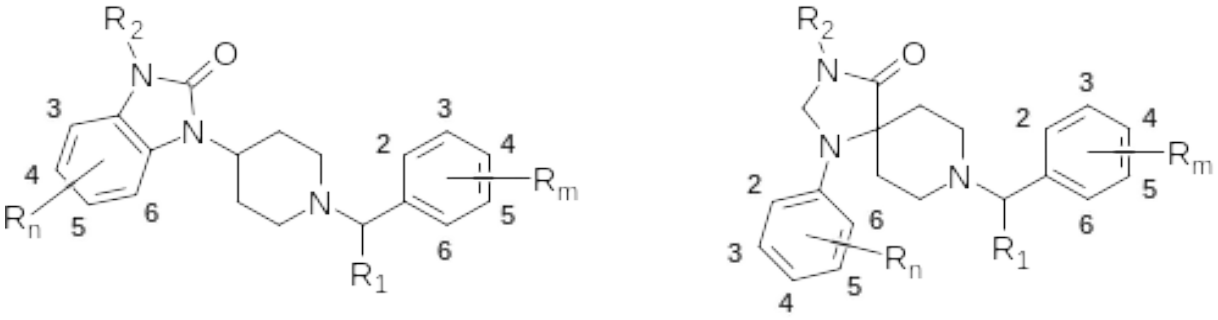
It also includes substances in which the amine nitrogen atom is part of a morpholino, pyrrolidino or piperidinyl ring system.

d) Ar_1 and Ar_2:

Phenyl, pyrrolyl, pyridyl, thienyl and furanyl rings. The heteroatoms in the heterocycles can be at any point of the ring.

9. Compounds derived from 4-amino-1-benzylpiperidine

A compound derived from 4-aminobenzylpiperidine is any chemical compound that can be derived from the base structure shown below, has a maximum molecular mass of 500 u and may bear the substituents described below.



The basic structure may be substituted at the positions shown in the figure with the following atoms, atom groups or ring systems (residues R_1, R_2, R_n and R_m):

a) R_1:

Hydrogen, methyl and ethyl groups.

b) R_2:

Hydrogen, methyl, ethyl, cyanoalkyl (alkyl residue up to C_4) and phenyl group.

c) R_n and R_m:

The phenylrings may be substituted in the positions two to six (in the benzimidazalonring, heading 2 does not apply) with the following atoms or atom groups in any combination: Hydrogen, fluorine, chlorine, bromine, iodine, alkyl (up to C_6), alkoxy (up to C_5), acetoxy, alkylsulfanyl (up to C_5), hydroxy and cyanogroups. The atom groups above may be substituted with the following atoms and atom groups: Hydrogen, fluorine, chlorine, bromine, iodine, alkyloxy- (alkyl residue up to C_4) and trialkylsilyl groups (maximum 12 C atoms in total trialkylates).

Also included are substances where two adjacent carbon atoms of positions 2, 3, 4, 5 and 6 are bridged in R_n with a vinyl oxy- (1-oxyethen-2-yl-), methylenedioxy, ethyloxy- or ethylenedioxy group.

Justification

A. General part

I. Objective of and need for the provisions

For the new drug zuranolone, current scientific findings indicate that a potential for dependence and abuse cannot be ruled out. Therefore, a anaesthetic legal monitoring is required for zuranolone by inclusion in Annex III to the BtMG. The Expert Committee pursuant to § 1(2) BtMG was consulted and has endorsed the inclusion in Annex III to the BtMG.

Article 2 of this Ordinance has the purpose of counteracting the emergence and spread of ever new chemical variants of new psychoactive substances (NPS) on the drugs market, which directly or indirectly poses a threat to the health of individuals and the population.

The New Psychoactive Substances Act (NpSG), supplements the single-substance approach of the Narcotics Act (BtMG) with a substance group-based approach to enable more effective action against the emergence of these substances and to limit their distribution and availability.

Since the entry into force of the NpSG on 26 November 2016, the substance groups have been further developed and adapted in line with the findings of the continued monitoring of market developments. Most recently, the Fifth Ordinance amending the Annex to the New Psychoactive Substances Act of 21 June 2024 (Federal Law Gazette 2024 I No. 210) updates the substance groups to record further NPS (including the substance group of synthetic cannabinoids and the substance group of compounds derived from tryptamine).

With the present Ordinance, further clarifications and additions to the existing substance groups are made, as well the addition of two new substance groups, since the boundaries of the substance group definitions have again been crossed by actors on the drug market through targeted changes.

The experts to be involved under § 7 NpSG were consulted. Taking into account their positive votes, the Annex to the NpSG will be revised by Article 2 of this Ordinance on the basis of the competence in § 7 NpSG and taking into account the scope of the amendments.

In recent years, the European Early Warning System on NPS has increasingly recorded and transmitted information about psychoactive substances that have not yet appeared in Europe and are therefore new. The information system operated by EMCDDA and Europol is based on national data. In Germany, information about newly appearing substances is gathered in particular by criminal authorities.

Scientific findings are available on the NPS. These findings include pharmacological-clinical data on the mode of action and toxicity and also data on the extent of misuse and the associated direct or indirect risk to human health. Due to the mode of action, the extent of abuse and the associated health risks of other NPS, it is necessary to add these NPS to the existing seven substance groups in the Annex to the NpSG and to expand it with another two substance groups.

The dissemination of new substances is favoured by a rapid exchange of information and corresponding offers by those active in the drug market via the Internet and social media.

The protection of public health therefore requires a rapid response from the authority responsible for issuing relevant ordinances to the changing market conditions.

II. Main content of the draft

Article 1 amends Annex III to the BtMG on the basis of the empowerment in § 1(2)(1)(3) of the BtMG. Zuranolone is included in Annex III to the BtMG, together with an exemption. This is a new drug belonging to the category of neurosteroids, which is included with a derogation.

Article 2 recasts the Annex to the NpSG on the basis of the legislative competence in § 7 NpSG. The existing seven substance groups will be updated and two additional substance groups will be added to the Annex to effectively limit the risk of abuse of emerging psychoactive substances.

III. Alternatives

None.

IV. Regulatory competence

With regard to Article 1, the regulatory power of the Federal Government follows from § 1(2)(1)(3) BtMG.

With regard to Article 2, the legislative competence of the Federal Ministry of Health for the recast of the Annex to the NpSG arises from § 7 NpSG.

V. Compatibility with European Union law and international treaties

This Ordinance is compatible with European Union law and with international treaties concluded by the Federal Republic of Germany. The changes in Articles 1 were notified in accordance with Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services (OJ L 241 of 17.9.2015, p. 1). Article 1 is not a provision subject to notification.

VI. Impact of the Ordinance

The expansion to Annex III to the BtMG by Article 1 means that the medicinal product containing the active substance zuranolone is also marketable under narcotics law and can be prescribed. Zuranolone is exempt from the narcotics regulations provided that up to 50 mg of zuranolone is placed on the market without a further substance listed in Annexes I to III, in each divided form. These exempted preparations may be prescribed without a narcotic prescription.

The updates made by Article 2 to the substance groups previously included in the Annex to the NpSG means that the administrative ban on the handling of NPS as provided for in § 3(1) NpSG is expanded to all substances that fall under the updated substance groups in the Annex. The same applies to the criminal offences set out in § 4 NpSG of the prohibition of handling NPS, placing them on the market, prescribing them, manufacturing them and importing them into the territory to which the Act applies for the purpose of placing them on the market. This will allow customs and police authorities to intervene

against illicit handling, in particular against trade, in the NPS covered by the Annex to the NpSG in future.

1. Legal and administrative simplification

For the newly included drug zuranolone in Annex III to the BtMG, Article 1 also introduces a derogation which results in the substance not being subject to narcotic drugs legislation up to 50 mg in each separate form and can therefore be prescribed without a prescription. Article 2 does not provide for a repeal of any provisions or a simplification of any administrative procedures.

2. Sustainability aspects

The draft Ordinance takes into account the objectives and principles of the German Sustainability Strategy (DNS). In particular, it serves the sustainability objective 3 ‘Ensure healthy life for all people of all ages and promote their well-being’ by limiting the spread and abuse of the synthetic substances hazardous to health by updating the substance groups contained in the Annex to the NpSG. The proposed provisions, both in Annex III to the BtMG and in the Annex to the NpSG, thus serve to protect the health of individuals and the general public as a whole, and thus also comply with guiding principle 3b of the DNS, ‘Avoiding dangers and unacceptable risks to human health’.

3. Budgetary expenditure without compliance costs

The federal, state and local authorities are not charged with additional costs.

4. Compliance costs

Article 1:

There are no added compliance costs for citizens.

For businesses, minor added compliance costs for manufacturers of zuranolone may arise in individual areas, whose amount are hard to quantify.

For the Federal Administration, the amendment of Annexes II and III to the BtMG results in a minor additional enforcement cost to customs authorities, the Federal Criminal Police Office and the Federal Institute for Drugs and Medical Devices, as the monitoring of narcotics traffic is expanded due to the inclusion of additional substances in the Annexes to the BtMG.

For state monitoring and police authorities, this may entail increased, but currently not quantifiable, enforcement costs since the monitoring of the circulation of narcotic drugs will increase due to the inclusion of an additional substance in the Annex to the BtMG.

Article 2:

There are no added compliance costs for citizens.

There are no added compliance costs for businesses.

For the Federal Administration, the expansion of the monitoring by the newly added NPS as a result of the continuation of the substance group definitions contained in the annex to the NpSG only creates slight additional enforcement effort for prosecution by the customs authorities and the Federal Criminal Police Office. The number of checks is the same.

For the monitoring and police authorities at Land level, the above-mentioned expansion to NPS monitoring may result in increased but currently non-quantifiable enforcement costs. Here too, the additional burden is assumed to be very low in individual cases.

5. Other costs

None.

6. Other consequences of the ordinance

This Ordinance has no impact on demographic or equal opportunities policies.

VII. Time limit; evaluation

The Ordinance is not intended to have a time limit. The annexes to the BtMG and NpSG are subject to ongoing reviews based on the experience gained with their enforcement as well as on the basis of new scientific findings.

B. Specific part

Re Article 1

The substance zuranolone is a new drug in the chemical substance group of benzodiazepines. An application under medicinal products law for a central European marketing authorisation for an orally administered medicinal product (hard capsules 20 mg, 25 mg, 30 mg) with the active substance zuranolone is pending with the European Medicines Agency (EMA). A decision by the Committee for Human Medicinal Products (CHMP) at EMA on the treatment of postpartal depression (PPD) in adults for short-term treatment over 14 days is expected by Q3 2025. In the event of a positive recommendation from the CHMP, authorisation could be granted by the European Commission, which means that a new medicinal product containing this active substance can be expected to be placed on the market. Under the name Zurzuvae (manufacturer Sage Therapeutics), a medicinal product containing the active substance zuranolone in strengths 20 mg, 25 mg, 30 mg was approved in the USA in August 2023 for the treatment of PPD.

In the USA, zuranolone has been classified in list IV as part of the authorisation. Typical of inclusion in List IV are drugs, substances or chemicals with a low potential for abuse compared to the drugs or other substances in List III. The substance has a currently recognised medical use in treatment in the United States and misuse of the substance may lead to limited physical or psychological dependence compared to other substances in List III.

Zuranolone acts as a positive allosteric modulator at the $GABA_A$ receptor, the precise mechanism of action is not yet fully clarified. Against the background that zuranolone has been on the market only since mid-2023 and only in the USA, there is only limited practical data on a possible dependence and abuse potential. For zuranolone, the potential for abuse and dependence is assessed as likely to be lower or at most similar to benzodiazepines on the basis of available chemical, non-clinical and clinical data.

On the basis of scientific knowledge concerning the mode of action of the substance, especially with regard to the possible causation of dependence and misuse, it is therefore necessary but also sufficient to include the substance zuranolone in Annex III to § 1(1) BtMG.

The creation of an ‘exempted preparation’ in Annex III (cf. § 2(1)(3) BtMG) creates an exceptional legal regime with regard to the pharmaceutical form and potency so that authorised medicinal products can legally be made available without delay for the care of patients without the need for a prescription on a narcotic prescription form. However, this exception is strictly limited. Only preparations of the substance zuranolone that contain up to 50 mg of the active substance zuranolone are excluded from the prescription requirements under narcotics law.

As a result of the exemption, the domestic availability of the pharmaceutical preparation in the form of an authorised finished medicinal product for the purpose of patient care is not hindered by the provisions of narcotics law.

Re Article 2

Due to the scope and complexity of the updating of the substance groups previously contained in the annex to the NpSG caused by this ordinance, it is necessary to rewrite the annex. No change is being made by modification commands relating to individual points or sub-items of the Annex. With a view to the experience gained from enforcement practice after the entry into force of the NpSG, the update of the previous substance groups serves both to clarify the interpretation of the respective substance group definition and to expand the substance groups to include other market-relevant, health-endangering psychoactive substances.

The preliminary remarks

In order to improve comprehensibility, the preliminary remark is editorially recast. At the same time, the number of scheduled substance groups is expanded from seven to now nine to take account of newly identified structural groups. In addition, a clarification is made to the effect that hydrogen atoms already contained in the previous substance group definitions as possible substituents in the individual structural elements are now expressly named. This measure addresses any interpretation uncertainties that have arisen in practice and simplifies the application of the law.

Re Point 1 ‘Compounds derived from 2-phenethylamine’

Re Point 1.1

The first paragraph adds to the list of structural element A of the benzocyclobutene ring. In addition, the ring systems are structurally adapted in line with the substance group of cannabimimetic agents. The restructuring and new introduction of the bicyclic and tricyclic ring systems will cover the ring systems Naphthyl-, Tetrachlorophenyl-, Methylenedioxyphenyl-, Ethylenedioxyphenyl-, Benzofuranyl-, Dihydrobenzofuranyl-, Indanyl-, Indenyl-, Tetrahydrobenzodifuranyl, benzodifuranyl and tetrahydrobenzodigranpyranyl which were previously listed individually. The unchanged monocyclic core structures are simply regrouped.

In order to standardise the spelling, in the last paragraph, the term ‘cyclisch’ [cyclic] is replaced by the term ‘zyklisch’ [cyclic].

In addition, the content of the provisions corresponds to the current provisions.

Re Point 1.2

In Point 1.2(a), in Paragraphs 1 and 2, in order to standardise the spelling, the term ‘cyclisch’ [cyclic] is replaced by the term ‘zyklisch’ [cyclic].

In Point 1.2(c), the term ‘b/k derivatives’ is replaced by the term ‘beta-keto derivatives/cathinones’. The purpose of the adaptation is to clarify the previous provision.

In addition, the content of the provisions corresponds to the current provisions.

Point 2 ‘Cannabimimetic agents / synthetic cannabinoids’

Re Point 2.1

In Point 2.1, the title and Sentence 1 is adapted by adding the words ‘Indolizine, Pyrrole’. As a result of these adjustments, the newly included additional core structures and an additional spiro bridge are included in Point 2.1.1.

In Point 2.1.1, in Paragraph 1, the words ‘a to h’ and the words ‘a to g’ are replaced by the words ‘a to l’ and the words ‘a to j’. In addition, the terms ‘trifluoromethyl-, trimethylsilyl-, trifluoromethoxy-’ are added to the list of core structures. The new core structures (anellated pyrazole, 2-quinolones and indolizines) and new bridge structures are included, as the compounds to be produced have been explicitly and exclusively developed for the circumvention of the NpSG in Germany and similar laws in other European Member States. Some of the effects are uncertain and there is a high risk potential for consumers. Paragraph (2) is moved to Letter (m) due to the expansion of the core structures to which it refers. This serves to improve readability.

In Point 2.1.1(c), the words ‘(binding site for the bridge at position 3, binding site for the side chain at position 1)’ are added to standardise the system structure.

In Point 2.1.1(e), the benzimidazole isomers I and II are structurally grouped under one letter. For this purpose, the term ‘and benzimidazole-1,2-diyl-isomer II (binding site for the bridge at position 1, binding site for the side chain at position 2)’ is supplemented. The summary is based on the pyrazolisomers (Letter (j)).

In Point 2.1.1(f), the indolizine scaffold is newly inserted with the words ‘indolizin-1,3-diyl (binding site for the bridge at position 1, binding site for the side chain at position 3)’ and in Point 2.1.1(g) with the words ‘6-, 7-, 8-azaindolizin-1,3-diyl (binding site for the bridge at position 1, binding site for the side chain at position 3)’. The previous specification in Letter (f) is moved to Letter (e). The current Letter (g) becomes Letter (j).

In Point 2.1.1(h), the 2-chinorene basic scaffolding is newly inserted with the words ‘2-chinolone-1,3-diyl (binding site for the bridge at position 3, binding site for the side chain at position 1)’ and in Point 2.1.1(i) with the words ‘5-,6-,7-,8-aza-2-chinolone-1,3-diyl (binding site for the bridge at position 3, binding site for the side chain at position 1)’. The current Letter (h) becomes Letter (l).

In Point 2.1.1, Letters (i), (j), (k) and (l) are added. Letter (j) corresponds to the previous Letter (g) and Letter (l) to the previous Letter (h).

In Point 2.1.1(j), the words ‘Pyrazole-1,5-diyl (binding site for the bridge at position 5, binding site for the side chain in position 1) and pyrazole-1,3-diyl (binding site for the bridge at position 3, binding site for the side chain in position 1)’ are replaced by the words ‘3-phenylpyrazole-1,5-diyl (binding site for the bridge at position 5, binding site for the side chain in position 1) and 5-phenylpyrazole-1,3-diyl (binding site for the bridge at position 3, binding site for the side chain in position 1)’. Due to the introduction of the new core structures under letter k, a renaming of the group is necessary for differentiation.

In Point 2.1.1(k), the core structures derived from pyrrole and pyrazole are added as new.

Letter (l) in Point 2.1.1 corresponds to the previous Letter (h). It will be indicated by the words ‘the residue R may consist of one of the following atoms or the following atom group: Hydrogen, fluorine, chlorine, bromine, iodine and phenylthiogroup (binding via sulphur to the core structure).

In Point 2.1.2, Letter (f) is added. This expands the bridge definitions.

In Point 2.1.3, in Letter (a), the word ‘silicon’ is added. The addition covers already occurring derivatives with silicon atoms in the side chain.

Re Point 2.3

In Point 2.3.1, the words ‘residues R_1 to R_5’ are supplemented by the words ‘and R_n’. The aim of the addition is to expand the existing definition to include halogenated derivatives and thus ensure the full coverage of relevant derivatives.

In Point 2.3.2, the expansion to include halogenated derivatives on the ring A, hydroxylated derivatives (on the ring A), their (carbonic acid) esters and silyl groups due to seizures is included. For this purpose, the heading is adjusted by the words ‘and R_n’. Letters (a), (b) and (c) are also recast by the expansion.

The former Letter (d) in Point 2.3.2 becomes Letter (e) and is adapted to the expansion.

Point 2.3.2(d) includes the expansion of the residue R_4. The expansion covers alkyl and alkenyl substituted derivatives as well as THCA-A and their esters as prodrugs of THC.

Otherwise the content of the provisions in Point 2 corresponds to the current provisions.

Re Point 3 'Benzodiazepines'

In Sentence 1, due to the insertion of a new subgroup with the new Point 3.2.1 from the specification ‘Point 3.1’ the specification ‘3.1.1’, from the specification ‘(c) to (f)’ the specification ‘(c) to (g)’ and Sentence 1 is expanded to the phrase ‘as well as some open chain benzodiazepine prodrugs (Point 3.2.1)’.

Point 3.1 is newly inserted with the subheading ‘cyclic representatives’. This makes a distinction from the newly inserted Point 3.2.

Point 3.1 is renamed to Point 3.1.1.

In Sentence 1 of Point 3.1.1 the words ‘a to f’ are replaced by the words ‘a to g’. In Sentence 2, the reference ‘Point 3.2’ is replaced by the reference ‘Point 3.1.2’. Likewise, the term ‘Residues R_1 to R_7 and X’ is replaced by the term ‘Residues R_1 to R_8 and X’. The insertion of the new residue serves to include the bretazenil and rilmazolam substitution to the imidazole, 1,2,4 triazole structure on the basis of the occurrence of rilmazolam and the inclusion of the 1.4 imidazole structure on the basis of the occurrence of remimazolam. The new NPS in the substance group ‘benzodiazepines’ are problematic benzodiazepine derivatives with considerable potential for abuse and dependence.

In accordance with Letter (f), the list is expanded to include the Letter ‘(g)’ to include the basic fracture structure.

Point 3.2 is renamed to Point 3.1.2 with an adjusted heading with the words ‘residues R_1 to R_8 and X’.

In Point 3.1.2(c), the substance remimazolam and its derivatives are covered with the statement ‘alkoxycarbonyl alkyl (alkoxy to C_4, alkyl group to C_4)’.

In Point 3.12., Letter (k) is inserted after Letter (j). The insertion of the new letter (k) serves to record rilmazolam and bretazenil and the next homologues.

The former Letter (k) of Point 3.1.2 is renumbered as (l).

New Point 3.2, entitled ‘Open chain benzodiazepine prodrugs’ is added. This substance group is inserted because the prodrugs, also referred to as precursors, are immediately converted into strong benzodiazepines by heat development, acid pH values or absorption in the body. The new Point 3.2 is divided into Point 3.2.1 core structures and Point 3.2.2 residues R_1 to R_7 and X.

The residues in Point 3.2.2 are defined in analogy to Point 3.1.2, as they lead to the benzodiazepines referred to therein.

Otherwise the content of the provisions in Point 3 corresponds to the current provisions.

Re Point 4 ‘Compounds derived from N-(2-aminocyclohexyl)amide’

Under Point 4, the structural formula is amended editorially. The specification ‘n’ in the structural formula is replaced by the specification ‘x’. The alignment of the placeholder n to x is used for editorial adjustment. For easier comprehensibility, the associated descriptive sentence, which is listed as Sentence 4 in Point 4(d), is moved directly below the structural formula figure. The specification ‘n’ is also replaced by the specification ‘x’.

In Sentence 2 of Point 4(a), the term ‘cyclisch’ [cyclic] is replaced by the term ‘zyklisch’ [cyclic].

Otherwise the content of the provisions in Point 4 corresponds to the current provisions.

Re Point 5 ‘Compounds derived from tryptamine’

Point 5.1(a) and (d) is reworded as a result of newly occurring compounds with carbonated ester groups. Carboxylic acid ester protection groups are included.

In Point 5.1(e), the words ‘trialkylsilyl- (maximum 12 C atoms in the total trialkylates), trifluoromethyl, trifluoromethoxy-’ are added as a result of new transformations of methyl and methoxy atom groups. In addition, the silyl group is absorbed.

In Point 5.2(a), the words ‘silicon’ are added in Sentence 1 and in Point (aa) by the increased presence of 1S-lyseric acid diethylamide (1-S-LSD). 1-S-LSD is a structural isomer of lyseric acid diethylamide. The inclusion of LSD isomers in the NpSG is for security, abuse prevention and practical law enforcement purposes. This consistently implements the purpose of the law – protecting the population against new psychoactive substances.

Otherwise the content of the provisions in Point 5 corresponds to the current provisions.

Re Point 6 ‘Compounds derived from arylcyclohexyl(methyl)amine’

The substance O-desmethyl-tramadol (O-DSMT) is added to substance group number 6. For this purpose, the heading, Sentence 1 and Sentence 2 and the structural formula of the substance group are updated. In addition, we insert a new Letter (c). O-DSMT, the pharmacologically active main metabolite of tramadol, is classified as a addictive substance due to its μ-opioid receptor affinity. There is a proven potential for psychological and physical dependence, especially in the case of repeated or high-dose consumption.

In Paragraph 3 of Point 6(a), the term ‘cyclisch’ [cyclic] is replaced by the term ‘zyklisch’ [cyclic], in order to standardise spelling.

In Point 6(b), the term ‘residues’ in Paragraph 1 is replaced by the term ‘ring systems’ in order to standardise the spelling.

The current Letter (c) becomes Letter (d).

Otherwise the content of the provisions in Point 6 corresponds to the current provisions.

Re Point 7 ‘Compounds derived from benzimidazole’

The substance group definition in Point 7 is expanded by changing the indication of the maximum molecule size. The maximum molecular mass shall be increased to 600 u to cover newly encountered derivative structures in this Ordinance. In order to adapt the substance group definition, the structural formula is updated and it is indicated that the number x of the methyl groups $(CH_2)_x$ can be zero or one. This means that known ethylene homologues are included in the previous basic structure.

In Point 7(a), benzyl and carboxylic acid ester protection groups are inserted by the rewording of the first paragraph.

In Point 7, the previous Letter (b) is divided and describes the residue R_3. Residue R_3 is newly inserted due to newly encountered derivatives.

In Point 7, the former Point (b) becomes Point (c) and is also expanded. The expansion includes possible substitution points that are grouped together under the new residue R_m. The expansion covers alkyl-substituted benzimidazole opioids, such as etomethazene and other obvious modifications. These opioid derivatives represent a highly toxicologically relevant, acutely life-threatening substance class, the hazard potential of which is to be classified as significant, in particular in connection with uncontrolled use, black market spread and lack of analytical detectability.

The newly introduced Letter (d) in Point 7 contains the newly occurring halogen and alkyl-alkoxy-substituted derivatives (fluoroetonitazene, fluoroetonitazepyne, etoetonitazene) and silicon and ethyleneoxy- and methylenedioxynitazene. These halogen substituted nitazene derivatives are a toxicologically highly hazardous substance class. Their extreme μ-receptor activity, their extremely low therapeutic width, the high risk of toxicity even at minimal doses and their limited detectability justify a clear classification as NPS with significant risk to public health.

Otherwise, the content of the provisions in Point 7 corresponds to the current provisions.

After Point 7, a new substance group with the number 8 is included. This substance group is given the heading ‘Compounds derived from 3,3-diphenylpropane-1-amine’.

The new substance group number 8 includes derivatives of methadone, some of which are already subject to the BtMG (methadone, dipipanone, dextromoramide, phenadoxone). They are highly effective synthetic opioid derivatives with significant toxic and addictive potential. The risks arise in particular from the strong and long-lasting effect, the low therapeutic width, the high level of lethality in the event of abuse, the cardiotoxic properties (especially methiodone) and the high dependence potential.

Point 8 is followed by the addition of a new substance group with the number 9. This substance group is given the heading ‘4-amino-1-benzylpiperidine-derived compounds’.

The new substance group number 9 includes derivatives of high-potential synthetic opioids borphine and spirochlorphine. Brorphine is already listed in Annex II to the BtMG. These highly dangerous synthetic opioids present a marked risk of respiratory depression and are highly suitable for abuse. In addition they pose a threat to public health. Intoxication resulting in death has been reported in connection with spirochlorphin.

Re: Article 3:

Article 3 provides for the entry into force of the Ordinance on the day following its promulgation.