European Monitoring Centre
for Drugs and Drug Addiction

GUIDANCE NOTE 2

EMCDDA technical report

EMCDDA operating guidelines for the risk assessment of new psychoactive substances

Document ID: EU-RA-OG-GN-2
Authors: Michael Evans-Brown
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1. Purpose

The purpose of this document is to provide the structure for and general guidance on the information to be included in the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) technical report on a new psychoactive substance. The technical report provides an analyses of the available information on the new psychoactive substance to support the risk assessment conducted by the Scientific Committee of the EMCDDA. This is to help ensure that a systematic, reproducible and transparent approach is used throughout the risk assessment procedure.

2. Scope

This document applies to the EMCDDA.

3. Changes since last revision

Not applicable, as this is an initial guidance note.

4. Responsibilities

It is the responsibility of the EMCDDA to ensure that the guidance provided in this document is adhered to.

5. Documents needed for this guidance note

- EMCDDA Operating Guidelines for the Risk Assessment of New Psychoactive Substances.
- EMCDDA Operating Guidelines for the European Union Early Warning System on New Psychoactive Substances.

6. Technical report

6.1. Introduction

The technical report should contain all relevant information and an analysis of the information needed for the risk assessment. The information collated in the initial report should be supplemented with new information that becomes available after completion of the initial report and by expert review of this information and the literature.

To facilitate the risk assessment, the information should be presented in a way that shows both the likelihood of harm occurring and the severity of that harm. Wherever possible, risk-modifying factors should be identified and their impact on the risks should be described.

The information in the technical report should be reviewed with respect to the reliability and relevance of the data. This qualification of data is needed for the uncertainty analysis, being part of the risk assessment. A full list of references should be included. The methodology for rating the quality of evidence will be further detailed by the EMCDDA.

The technical report is organised into the following headings:

- Chemical and physical properties, methods of and precursors for manufacture or extraction, and analytical methods
- Legitimate use
- Pharmacological and toxicological properties
- Extent and patterns of use, availability and potential for distribution
- Abuse liability and dependence-producing potential
- Harmful health effects
- Harmful social effects
- Other relevant information.

6.2. Chemical and physical properties, methods of and precursors for manufacture or extraction, and analytical methods

In this section, a detailed description of the new psychoactive substance is provided, focusing on the chemical and physical properties. In addition, information on the methods of manufacture or extraction should be included, as well as information on analytical methods. Furthermore, pharmaceutical information, including dosage, purity, pharmaceutical form and route of administration, should be provided. Suggested subheadings are given below.

6.2.1. Name and chemical structure

A new psychoactive substance can be referred to by its common name, which is often a code name or an acronym, which is usually based on a non-standardised nomenclature. It is acceptable to use this common name throughout the report. However, if an international nonproprietary name (INN) has been assigned by the World Health Organization (WHO), this name should be used. In this section, all known names and other identifiers should be provided, including systematic International Union of Pure and Applied Chemistry (IUPAC) names, chemical synonyms, Chemical Abstract Service Registry Numbers (CAS RNs), INN, IUPAC International Chemical Identifier Key (InCHI Key),

simplified molecular-input line-entry system (SMILES) name, proprietary names, street names, and other names and identifiers where available.

The chemical structure should be provided in a two-dimensional diagram, indicating chiral centre(s) if present. If the compound contains chiral centre(s), it should be clarified whether the new psychoactive substance concerns a racemic mixture or consists of one or several stereoisomers. If the new psychoactive substance is chemically closely related to other known new psychoactive substances or drugs, the structure of these compounds can be depicted for comparison.

6.2.2. Physical properties

Information on the physical properties should be provided to the extent available, including appearance, melting point, boiling point, pK_a, LogP_{ow} and solubility in water and other solvents. Where available, information on both the free base and salt forms should be included.

6.2.3. Methods of manufacture or extraction

Information on the manufacture can be derived from the open literature or the patent literature. In addition, internet sources may contain relevant information, although the reliability of this information would be limited. To the extent available, information to be listed should include starting materials (precursors), reagents, routes of synthesis, yield and impurities.

Moreover, the presence of adulterants, excipients and other pharmacologically active substances, including other new psychoactive substances or drugs in samples containing the new psychoactive substance under examination, should be mentioned here.

6.2.4. Methods of analysis

The chemical analytical methods used to establish the presence of the new psychoactive substance and quantify the amount or concentration in drug samples, body fluids or other forensic samples should be described briefly. The main characteristics of the methods, such as sensitivity, specificity, detection and quantitation limits, should be summarised, preferably in a table format. Information on the availability of internal standards and reference material can also be included. This information is mainly of importance for determining the reliability of the results obtained with the methods used. There is no need to include details such as spectra.

6.2.5. Pharmaceutical and posological information

All available pharmaceutical information should be provided in this section. Foremost, the pharmaceutical forms that have been observed, such as tablets, powder, fluids, solutions, their presentations, for example flasks used for nasal administration of a spray, and the purity of the

samples that have been analysed should be described. It is important to indicate the degree of variability in concentration, quantity and purity of the new psychoactive substance as observed in samples, as this may affect the potential risks and introduce uncertainty about the actual doses taken when reported by users.

Moreover, information on the posology and route of administration should be provided under this heading. Regarding doses, information may be limited to that provided in user reports. Even if reported doses are correct, there may still be wide variability. It is therefore better to provide information on reported doses as ranges.

6.2.6. Risk-modifying factors

The chemical, physical and pharmaceutical variables mentioned in Section 6 that may modify the risks should be identified and summarised here. These could include variability in the qualitative and quantitative compositions of new psychoactive substance samples, with a high potency of the new psychoactive substance necessitating precise dosing.

6.2.7. Uncertainty analysis

Uncertainty about the actual content — both qualitative and quantitative — of new psychoactive substances taken by users is a main source of uncertainty in the evaluation of risks associated with the use of new psychoactive substances. This may arise from an absence of information on the actual content of new psychoactive substances when reported by users or limited information on the content, for instance only qualitative and not quantitative information being available, from an absence of information on stereoisomers, or from high-potency substances staying under the radar when present below the lower detection limit of the analytical method used.

6.3. Legitimate use

This section should collate all forms of legitimate use of the new psychoactive substance. Where possible, the extent of this use should be indicated.

6.3.1. Medical use

Although the use of the new psychoactive substance as the active substance of an authorised medicinal product for human or veterinary use or a medicinal product for which the marketing authorisation has been suspended, or of an investigational medicinal product would exclude it from a risk assessment in accordance with Article 5d(3) of Regulation (EC) No 1920/2006, the new psychoactive substance may still be used medicinally when used in accordance with Article 5 of Directive 2001/83/EC or when prepared extemporaneously in accordance with point (c) of

Article 10(1) of Directive 2001/82/EC. When applicable, this authorised use of an unauthorised medicinal product containing the new psychoactive substance should be described.

6.3.2. Industrial and commercial use

The available information on the use of the new psychoactive substance in industry as a starting material, reagent, solvent or otherwise or use in a commercial product should be provided here.

6.3.3. Scientific use

The use of the new psychoactive substance for scientific research and development should be mentioned here, for instance its use as a ligand in pharmacological research or its use as a standard or as reference material in analytical methods.

6.3.4. Risk-modifying factors

The presence of the substance on the market as a legitimate product may influence the risks in various ways. A greater availability may increase the risk of diffusion within the EU. On the other hand, production in legitimate manufacturing facilities may mean that the new psychoactive substance is of relatively high quality, including lower variability in content. Moreover, the legitimate use may be accompanied with more detailed information on the new psychoactive substance, which could be used to inform new psychoactive substance users.

6.3.5. Uncertainty analysis

Information on legitimate use will originate generally from trustworthy sources such as the European Medicines Agency (EMA), the European Chemicals Agency (ECHA) or the European Food Safety Authority (EFSA). As such, the degree of uncertainty will not be high. However, as information needs to be gathered in a short time frame, under-reporting may lead to omissions in the information requested.

6.4. Pharmacological and toxicological properties

In this section, the available literature describing the pharmacological and toxicological properties should be compiled. Although human data would be of greatest interest, *in vitro* and animal data need to be included as well. Pharmacology entails both *in vitro* and *in vivo* pharmacodynamics, safety pharmacology, clinical pharmacology and pharmacokinetics. Behavioural psychological data not entailing abuse or dependence potential can be included in this section as well. Where appropriate, data on pharmacodynamic or pharmacokinetic interactions should be included.

Toxicological data, if available at all, will usually be limited to data from non-human species. Data on poisonings in humans should be included in Section 6.7, on harmful health effects.

6.4.1. Pharmacodynamics

Under this heading, information on both the primary pharmacodynamics, i.e. related to the primary target known or expected to mediate the desired response, and secondary pharmacology, i.e. describing effects mediated through other receptors/targets not related to the primary effect, should be included.

In vitro *data*

This part concerns data on receptor binding and functional effects. Often limited *in vitro* data are the only data available. These data are relevant for establishing the pharmacological profile of the new psychoactive substance. Sometimes comparative data with other substances (new psychoactive substances or other drugs) are available, which may support a discussion of the similarity with these other substances.

In vivo *data*

In vivo data may consist of potency data reflecting the activity of the new psychoactive substance at the target receptor *in vivo*. Sporadically, *in vivo* data describing secondary effects may be available. When human (i.e. clinical pharmacological) data are available, these can be included under this heading as well.

6.4.2. Psychological and behavioural data

Rarely studies on the psychological effects of the new psychoactive substance in humans or behavioural studies in animals are available. These can be included under this heading, for instance a description of subjective effects in humans or sleep studies. When the data concern abuse or dependence potential, these should be incorporated into Section 6.6. Studies describing the effects of the consumption of the new psychoactive substance on driving can be included here. However, data concerning accidents when driving under the influence should be reported under Section 6.7.1, on acute health effects.

6.4.3. Safety pharmacology

Safety pharmacology concerns functional effects on vital organs (heart, lungs, central nervous system (CNS) and possibly the gastrointestinal tract and kidney). This may concern *in vivo* data in animals or humans or *in vitro* data obtained in cell, tissue or organ culture. These types of data are only rarely

available for new psychoactive substances. CNS effects related to the primary or secondary targets should be mentioned under 6.4.1 and behavioural data related to abuse and dependence potential should be included in Section 6.6. Examples of CNS safety pharmacological data would be functional behavioural test batteries, an Irwin test or a study on epileptogenic potential.

6.4.4. Pharmacokinetics

Pharmacokinetics data describe the fate of the new psychoactive substance in the organism and include data on absorption, distribution, metabolism and excretion. Again, these types of data are often very limited. Pharmacokinetics may concern both human and animal data. In addition, *in vitro* data may be available, for instance related to metabolism, which may be of relevance with respect to pharmacokinetic interactions.

6.4.5. Toxicology

These data concern the effects of new psychoactive substances at doses in excess of the anticipated pharmacologically active dose. Such studies are routinely performed in animals for medicines and other substances, but are usually not available for new psychoactive substances. If they are, they should be included here. In addition to animal data for some end points (e.g. genotoxicity), established *in vitro* models are can be used. Data on new psychoactive substance poisonings in humans should not be included in this section, but incorporated into Section 6.7

When available, toxicological data on excipients, adulterants and impurities known to be present in a substantial portion of the new psychoactive substance samples should be summarised briefly.

6.4.6 Risk-modifying factors

The pharmacological and toxicological properties of the new psychoactive substance are intrinsic. It is these properties that ultimately lead to the harmful effects. However, the likelihood that harmful effects will occur may be affected by many factors. Inter-individual differences in sensitivity related to genetic differences or as a consequence of development of tolerance may affect the outcome of the use of a new psychoactive substance. Genotypic differences as well as potential pharmacodynamic or pharmacokinetic interactions with other substances could modify the risks associated with the use of the new psychoactive substance. Both dose-effect and dose-time relationships affect the likelihood of harmful effects occurring.

6.4.7. Uncertainty analysis

Often there is a paucity of pharmacological and toxicological data, limiting the possibility to draw conclusions on these properties. When laboratory studies have been published in peer-reviewed

journals, the reliability of these data would generally be sufficient. Reports from internet forums on subjective effects on the other hand would usually be considered of insufficient reliability. When *in vitro* pharmacodynamic data are available, these can be highly relevant for establishing the pharmacological profile. However, the number of receptors studied is usually very limited and in the absence of *in vivo* distribution data the relevance can be uncertain. In such cases, this knowledge gap would have to be bridged by combining the sparse pharmacological data with observations in users who have taken the new psychoactive substance and knowledge on the pharmacology of substances from the same class.

6.5. Extent and patterns of use, availability and potential for distribution

For a new psychoactive substance, there will usually be a lack of epidemiological information, including patterns of use, which includes information such as the extent and frequency of use of a new psychoactive substance (including prevalence, doses, dose regimens) as well as routes of administration, and physical, psychological and behavioural effects. At the time of the production of the initial report, the reporting will generally be based on case reports and anecdotal reports on the use of the new psychoactive substance, including those related to law enforcement seizures and serious adverse events. At that stage, the spread and distribution of the substance, as well as its prevalence, will usually be relatively low, and the triangulation of ethno-epidemiological methods will therefore be needed to assess the patterns of use among specific limited user groups.

In most cases, an expert assessment will be needed of the likelihood that use of a new psychoactive substance will spread. This assessment will primarily be based on a comparison of the characteristics and accessibility of the new psychoactive substance and the setting in which it is used with the characteristics, accessibility and setting of use of other well-known substances.

6.6. Abuse liability and dependence-producing potential

Following the WHO Expert Committee on Drug Dependence (ECDD) definition of drug dependence and the WHO *Lexicon of Alcohol and Drug Terms* definition of abuse liability, dependence-producing potential is taken as ‘The propensity of a drug to produce a cluster of physiological, behavioural and cognitive phenomena of variable intensity, in which the use of a psychoactive drug (or drugs) takes on a high priority. The necessary descriptive characteristics are preoccupation with a desire to obtain and take the drug and persistent drug-seeking behaviour. Determinants and the problematic consequences of drug dependence may be biological, psychological or social, and usually interact.’ Abuse liability is taken as ‘The propensity of a particular psychoactive substance to be susceptible to abuse, defined in terms of the relative probability that use of the substance will result in social, psychological, or physical problems for an individual or for society.’ Both definitions have in common that they are characterised by problematic behavioural patterns causing psychological, social or

physical problems. For a drug to lead to this problematic pattern of use, the substance does not necessarily have to have dependence-producing potential.

Evidence for dependence-producing potential may come from non-clinical, i.e. *in vitro* and animal, data and from observations in humans. Evidence for abuse liability is based either on evidence for dependence-producing potential or on observations in humans.

6.6.1. *In vitro* data

With reference to Section 6.4, binding affinity to and activity at receptors associated with mechanisms leading to dependence potential should be mentioned here. Although this type of data in itself is not proof of dependence potential, such data may be considered a signal of dependence potential.

6.6.2. Animal data

Behavioural observations in animals may also provide signals of dependence potential. In studies not specifically designed for studying these phenomena, these observations may include increased motor activity or sedation. Stronger evidence may come from animal studies specifically designed for investigating dependence potential. These may encompass studies investigating withdrawal phenomena, studies on self-administration, drug-discrimination studies, conditioned place preference studies and others.

6.6.3. Human data

Observations suggesting dependence potential or abuse liability of a new psychoactive substance in humans are usually limited to field observations by social or healthcare workers. On internet forums, self-reporting of dependence potential may be found. Specifically designed studies in humans providing evidence for dependence potential or abuse liability would be available only rarely.

6.6.4. Risk-modifying factors

There are many factors affecting the risk of a new psychoactive substance leading to dependence or abuse liability, with the pharmacology foremost affecting the likelihood. Substances directly interacting with brain systems associated with dependence will have a greater likelihood than substances that do not directly interact with these systems. For instance, dopaminergic substances may trigger brain reward systems and μ-opioid agonists may lead to withdrawal and tolerance after repeated administration.

Pharmacokinetics is also a modifying factor. The level and speed of distribution to the brain would positively correlate with the likelihood of dependence potential. Long brain retention times and slow

metabolism causing extended periods of central activity could be a positive reinforcer for some users, whereas for others this could be a negative reinforcer.

Unpleasant side effects in general during or after the use of the new psychoactive substance could deter users and thus reduce the likelihood of dependence and abuse liability.

Some individuals may be more susceptible to dependence than others, which may be related to their genetic make-up. Yet social conditions, for example poor living circumstances or unemployment, may also increase the likelihood of abuse liability for a substance.

Furthermore, other factors such as availability of the new psychoactive substance, social acceptability, social control (e.g. by peers), availability of objective information on the new psychoactive substance and legal status may affect the likelihood of abuse liability for the new psychoactive substance.

6.6.5. Uncertainty analysis

Usually only limited data are available on the dependence-producing potential or abuse liability of a new psychoactive substance, often only limited data on receptor binding and activity and anecdotal information in humans. In view of the paucity of data, this aspect of the risk assessment will not rarely lead to the conclusion that there are insufficient data to reach a conclusion on the dependence-producing potential or abuse liability of the substance.

Even when available, behavioural animal data need to be taken with caution. Although the predictive value is generally considered good, results that have not been reproduced, especially when negative, should be judged in the context of what is known of the pharmacological class. For μ-opioid agonists, dependence-producing properties are well known. So even in the absence of specific behavioural data for the new psychoactive substance under scrutiny, such a compound should be suspected of dependence potential. On the other hand, for new classes of new psychoactive substances, or for classes for which dependence potential is less well established, the lack of data is problematic in the context of a risk assessment.

6.7. Harmful health effects

In this section, the data on the human health risks should be presented (in addition to those for abuse liability and dependence potential, which are discussed under Section 6.6). Animal and *in vitro* toxicity data are presented in Section 6. In addition, a preliminary risk analysis is included, which should facilitate the risk assessment by the Scientific Committee.

6.7.1. Acute health effects

Acute health effects are those that occur immediately or shortly after the consumption of a new psychoactive substance. These can be subdivided into acute poisonings and medico-legal death investigations. Both cases reported by Member States and those reported in the literature or by other sources are relevant for the risk assessment, although those reported by the Member States are of greater importance for estimating the extent of the risks within the EU. In addition, data describing the harmful consequences of driving under the influence should be reported.

Acute poisonings

In this section, the information is compiled describing the harmful health consequences of the use of a new psychoactive substance with the exception of those cases that lead to death. Rarely, information from clinical studies will be available. Usually, information is retrieved from case descriptions reported by the Member States or in the literature. The cases may be reported by first aid workers, consist of reports on hospitalisation or consist of information retrieved from other sources.

The information should not be limited to the number of cases reported. The symptoms that have been observed or reported by the user should be provided. Wherever possible, information on the circumstances under which the new psychoactive substance was used, the identification of the new psychoactive substance (e.g. laboratory analysis of samples or body fluids, reports on the presence of a new psychoactive substance at the premises or merely self-reported by the user), quantification of the new psychoactive substance in biological samples, dosages and routes of administration, as well as concomitant use of other new psychoactive substances, medicines, illicit drugs or alcohol should be provided. It should be made clear whether cases are EU or non-EU cases and the source of the information should be mentioned.

Preferably, a tabular format is used. To aid the risk analysis, the cases should be categorised with respect to severity of the poisoning and likelihood of occurrence. In addition, the level of uncertainty of the information should be indicated.

Severe poisonings are those that were likely to have led to death in the absence of an intervention. Moderate poisonings are those for which the user seeks medical assistance, but were not likely to be life threatening, even in the absence of medical help. Mild poisonings are those that may cause temporary discomfort, but for which medical help is not needed.

The likelihood of occurrence of severe, moderate of mild poisonings can only be approximated, as precise figures are not available for new psychoactive substances. Important factors used to estimate the likelihood of occurrence are the number of incidences reported, an appraisal of the level of under-reporting and an assessment of the extent of use (see Section 6.5). For expressing likelihood, a standardised terminology should be used.

The level of uncertainty is mainly determined by the source of the information and the quality of the additional information, foremost the identification of the new psychoactive substance in the cases described. As the information is usually very limited, a quantitative method to derive a level of uncertainty is normally not possible. Instead, uncertainty may be expressed by giving a range (boundaries) for the severity and the likelihood discussed in the previous two paragraphs.

Medico-legal death investigations

In this section, the information should describe cases where the use of the new psychoactive substance has possibly, been likely to or has certainly led to the death of the user. Similarly to the section on acute poisonings, all available information qualifying the cases should be presented, again preferably in tabular format. The information compiled should be reviewed by forensic experts to assess the likelihood that the new psychoactive substance was the cause of death or contributed to death. By nature, a death is graded as severe.

Driving and operating machinery under the influence

Under this heading, the data describing the adverse health effects when driving or operating machinery while intoxicated by the new psychoactive substance should be reported. These can be both fatal and non-fatal, and may concern the driver/operator or other persons. Studies investigating the effect on driving in controlled settings should be reported in Section 6.4.2, on psychological and behavioural data.

All available information qualifying the cases should be presented, preferably in tabular format. The cases can be graded by severity. Fatal accidents are by nature severe. However, non-fatal accidents may also be graded as severe, since the consequences of an accident can be expected to be coincidental. Finding that a user has been driving under the influence in the absence of an accident should not be considered a harmful consequence. An appraisal of the likelihood of occurrence can be difficult. The number of accidents may be estimated based on the available reports. However, figures on the number of people driving under influence of a new psychoactive substance will usually not be available. Thus, usually it will not be known what proportion of people driving under the influence will cause an accident. If available, studies investigating the effect on driving in controlled setting as reported under Section 6.4.2 can be of help. Important for the estimation of uncertainty is information on means to establish the involvement of the new psychoactive substance in the accidents reported. The actual determination of the new psychoactive substance in blood samples in a laboratory would provide a high level of certainty, whereas the presence of the new psychoactive substance in the vehicle, or reports from witnesses or self-reporting of users, would be associated with a lower level of certainty.

6.7.2. Chronic health effects

Chronic health effects are those that emerge after long-term use of the new psychoactive substance. Permanent or long-term health effects following short-term use would be reported under acute health effects. For example, a permanent physical injury resulting from an accident as a consequence of an intoxicated state of mind is an acute health effect, whereas accumulating deterioration of dopaminergic neurons in the substantia nigra causing Parkinson's disease or fibrosis of the liver causing liver dysfunction following chronic use of a new psychoactive substance are chronic health effects.

Chronic health effects should be graded as severe when they lead to premature death, severe disease or severe physical or mental impairment (e.g. Parkinson's disease, schizophrenia, liver dysfunction). When they lead to a physical or mental condition necessitating medical help, but are not considered severe, they could be graded as moderate (e.g. sleep disorders, heart arrhythmia or considerable loss of body weight). Mild health effects are those that do not require medical help, or can be resolved by a restricted medical intervention (e.g. poor dental health or flashbacks that do not significantly affect social or psychological functioning). As new psychoactive substances have usually appeared on the market quite recently, data on chronic effects will often not be available or are very limited. Based on the incidence of the reported effects and an estimate of the extent of use, an attempt can be made to appraise the likelihood of occurrence, but this will not usually be possible. Since users will often consume other new psychoactive substances, drugs, alcohol or medicines, it will be difficult assess with any certainty the causal relationship between the new psychoactive substance and the reported effect. Consequently, the level of uncertainty for the estimates of risk for the chronic health effects will be high.

6.7.3. Preliminary analysis of health risks

In the preliminary risk analysis, the information on harmful health effects is integrated by making use of risk matrices, where likelihood of occurrence and severity together lead to a certain risk level. The level of uncertainty for each outcome measure should be reflected together with this information. An example table is presented below.

Risk category	Description of risk(s)	Likelihood of occurrence	Severity of harm	Risk level	Uncertainty
Non-fatal intoxications					
Fatal intoxications					
Driving and operating machinery					
Chronic toxicity					

The risk level is determined by both the likelihood of occurrence and the severity of harm. An example table for deriving risk level is provide below.

		Severity of harm		
		Mild	Moderate	Severe
Likelihood of occurrence	Likely	5	9	12
	Likely as not	3	7	11
	Unlikely	2	6	10
	Exceptionally unlikely	1	4	8

In this example, the red boxes represent a severe risk level, the yellow boxes represent a moderate risk level and the green boxes represent a low risk level. Using risk levels in a semi-quantitative way using numbers, as indicated in the table, could also be considered.

Because this section is the primary basis for the chapter on health risk analysis in the risk assessment report, it is appropriate to provide arguments and reasons explaining why a certain risk level has been assigned to a certain risk, discussing the uncertainties regarding likelihood and severity and providing the relevant arguments, while also giving room for counter arguments.

6.8. Harmful social effects

This section should include information related to harmful social effects. Elements to consider for assessing social risks include:

- individual social risks (e.g. impact on education or career, problems with personal relationships);
- possible effects on direct social environment (e.g. neglect of family, violence);
- possible effects on society as a whole (public order and safety, acquisitive crime);
- economic costs (demands on healthcare);
- possible effects related to cultural context (e.g. marginalisation);
- possible appeal of the new psychoactive substance to specific population groups within the general population.

6.9. Criminal activities

This section should include information related to the involvement of criminal groups and criminal activities, including organised crime, associated with the new psychoactive substance and whether they are systematic. Information should also be provided on the illicit profits and the economic costs related to the involvement of criminal groups, for example:

- evidence that criminal groups are involved in production, trafficking and distribution for financial gain;
- evidence on the impact on the production, trafficking and distribution of other substances, including existing as well as new psychoactive substances;
- evidence that the same groups or people are involved in different kinds of crime;
- evidence on the impact of violence from criminal groups on society as a whole or on social groups or local communities (public order and safety);
- evidence of money-laundering practices, or impact of organised crime on other socioeconomic factors in society;
- evidence of economic costs and consequences (evasion of taxes or duties, costs to the judicial system);
- evidence of the use of violence between or within criminal groups;
- evidence of strategies to prevent prosecution (e.g. through corruption or intimidation).

6.10. Other relevant information

Any other relevant information for the risk assessment should be included in this section.

7. Additional information

None.

8. Changes since last version

Not applicable.

9. References

Directive (EU) 2017/2103 of the European Parliament and of the Council of 15 November 2017 amending Council Framework Decision 2004/757/JHA in order to include new psychoactive substances in the definition of 'drug' and repealing Council Decision 2005/387/JHA, OJ L 305, 21.11.2016, pp. 12-18. (https://eur-lex.europa.eu/legal-content/en/TXT/?uri=CELEX:32017L2103).

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Regulation (EU) 2017/2101 of the European Parliament and of the Council of 15 November 2017 amending Regulation (EC) No 1920/2006 as regards information exchange on, and an early warning system and risk assessment procedure for, new psychoactive substances, OJ L 305, 21.11.2016, pp. 1-6 (https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R2101).

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WHO (World Health Organisation) (1994), *WHO Lexicon of alcohol and drug terms*, World Health Organisation, Geneva (https://www.who.int/substance_abuse/terminology/who_ladt/en).