Science & Justice 59 (2019) 459–466

Contents lists available at ScienceDirect

Science & Justice

journal homepage: www.elsevier.com/locate/scijus

Review

Scheduling of new psychoactive substance the Swiss way: A review and critical analysis

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ARTICLE INFO

Keywords:
New psychoactive substances
Scheduling
Narcotics law
BetmVV-EDI
SR 812.121.11

ABSTRACT

Since the introduction of the European Early Warning System in 2005, > 700 new psychoactive substances (NPS) have been listed. This review article presents for the first time the Swiss narcotic law in perspective of scheduling of NPS, and compares it to the regulations of the German speaking neighbours Austria and Germany.

The Swiss way is a fast and effective way for scheduling NPS, with the purpose to restrict drug trafficking and for controlling the NPS drug market: the legal basis for scheduling substances of abuse is the "Law about narcotics and psychotropic substances" (BetmG, SR 812.121), which includes the "narcotic law directory (BetmVV-EDI, SR 812.121.11) suitable for listing all controlled substances. The BetmVV-EDI, SR 812.121.11 contains seven indices, with index e specifically designed for the fast scheduling of NPS. Newly appearing NPS can either be controlled under a structure analogues definition or by listing single substances. The list of single substances is updated at least once per year, and structure analogues definitions can be implemented, in order to keep track with new developments on the NPS market. The latest version from November 30th 2018 contains ten different structure analogue definitions and 207 single substances. Requirements to list NPS are their appearance on the NPS market, suspected psychotropic effects and their suggestions by Forensic professionals. As soon as substances are newly placed, on Schedule I of the 1961 Convention or Schedule II of the 1971 Convention by the Commission on Narcotic Drugs of the World Health Organization they can easily be transferred from index e to index a-d of the BetmVV-EDI, SR 812.121.11. The Austrian law uses a structure analogue and single substances approach (introduced in 2012, one update in 2016), whereas the German NPS law (established in 2016, no update yet) only lists two structure-analogue-definitions. All three legislations have defined which core structures, kinds and sites of substitutions are regulated.

1. Introduction

According to the United Nations Office on Drugs and Crime (UNODC) New psychoactive substances (NPS) are "becoming a matter of great concern and a threat to public health" [1]. The UNODC defines NPS as "a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the 1961 United Nations Single Convention on Narcotic Drugs or the 1971 United Nations Convention on Psychotropic Substances, but which may pose a public health threat comparable to that presented by substances listed in these conventions" [1]. Further, they can be defined as chemical compounds that have been modified and developed to mimic the effects of drugs which are already prohibited [2]. The Swiss "Federal Act on Narcotics and Psychotropic Substances" (BetmG, SR 812.121) defines narcotics as "substances and preparations that cause dependence that have the effects associated with morphine, cocaine or cannabis and substances and preparations produced on their basis of or that have a similar effect to the same". Currently the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) has listed over 700 NPS. According to their chemical structure, they are classified into several different classes such as phenethylamines, cathinone derivatives, piperazines, tryptamines and synthetic cannabinoids. Synthetic cannabinoids make the largest class of NPS with 179 reported entities. Since the establishment of the early warning system, there has been a constant rise of newly reported NPS up until 2015. In 2016 a drastic decrease has been observed, and in 2017 only half the amount of NPS compared to 2015 were reported [3]. Furthermore, a decrease in prevalence of NPS has been observed [4].

NPS are sold under different names such as legal highs, herbal drugs, bath salts or research chemicals [5]. Newly emerging synthetic drugs pose new challenges due to the fluctuating market, very little

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https://doi.org/10.1016/j.scijus.2019.03.005
Received 31 May 2018; Received in revised form 27 February 2019; Accepted 3 March 2019

known pharmacological data, and their accessibility on the online drug market before the new emerged drug becomes a controlled substance. Producers are mostly situated in China [3]. They produce and market NPS with the explicit aim of circumventing legislative restrictions [5]. When a substance becomes legally controlled and hence removed from the NPS online drug market, it may be replaced almost immediately by a new legal analogue [5,6]. The EMCDDA concludes that drug suppliers use national and international scheduling of NPS for updating an exclusion list for their range of offered products [7].

NPS scheduling is a national task, and most countries have different approaches. So far, a review [8] and a policy analysis [9] on the Swiss narcotics law have been published with respect to the heroin problem in the 1980s in Switzerland and the introduction of the heroin maintenance treatment. Due to the open drug scene of the late 1980s and early 1990s in Zurich, the Swiss legislative authorities had to establish a new legal approach to overcome this situation, such as the four pillar policy, which will be discussed later. Our article discusses the Swiss narcotics law in the context of regulating and scheduling of NPS, in comparison to legislations in German speaking neighbouring countries (Austria and Germany). This is of special importance as these countries have overlapping drug markets due to the same language.

1.1. International scheduling

Drugs of abuse or substances with supposed psychotropic effects that cause certain behaviour on the side of the user, are internationally scheduled under either the 1961 United Nations Single Convention on Narcotic Drugs, the 1971 United Nations Convention on Psychotropic Substances or the 1988 United Nations Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances.

Substances are grouped into categories with different regulatory and control requirements [9]. Recommendations for scheduling of these drugs are provided by the World Health Organization (WHO) Expert Committee on Drug Dependence. This committee gives a scheduling recommendation after reviewing potential harms and the degree of medical application [10], in three steps: routine collection of information by the Secretariat, pre-review, and finally critical review conducted by the Expert Committee. A critical review is conducted in cases where, one of the following criteria is met. Firstly, when there has been notification from a Party to the 1961 or 1971 Convention concerning the scheduling of a substance; or there has been the request for review of a substance by the Commission on Narcotic Drugs; or the pre-review of a substance leads to the recommendation for a critical review; or the WHO has been notified of a substance being clandestinely manufactured posing serious risk to the public health and no recognized therapeutic use. Information included in a critical review are: substance name including the Chemical Abstracts Service (CAS) registry number, chemistry, general pharmacology, toxicology, pharmacokinetics, dependence potential, abuse potential, nature and magnitude of public health problems, national control, therapeutic and industrial use, production, consumption and international trade, illicit manufacture and illicit trafficking and current international controls. Especially when it comes to NPS it is difficult to obtain all data needed for a critical review such as pharmacological or toxicological data in animals or humans. In order to conduct studies to obtain in vivo data, ethical approval form the corresponding ethics committee of the country needs to be obtained. Because NPS have no medical benefits, ethics committees are very reluctant to allow such studies. According to WHO guidelines it is possible for the Expert Committee to base its assessment on limited data, nevertheless it would need to provide full justification for reaching conclusions on incomplete data and hence to schedule a substance [10].

The United Nations then schedule a substance based on the recommendations of the WHO and Member States are obliged to regulate the scheduled substance with at least as much stringency [9].

In this sense, following WHO recommendations ten NPS (Single Convention on Narcotic Drugs of 1961: AH-7921; Convention on Psychotropic Substances of 1971: 25B-NBOMe, 25C-NBOMe, 25I-NBOMe, N-benzylpiperazine, JWH-018, AM-2201, mephedrone, MDPV and methylone) were scheduled under international control in March 2015 [11], seven (Single Convention on Narcotic Drugs of 1961: acetylfentanyl, MT-45; Convention on Psychotropic Substances of 1971: PMMA, α-PVP, 4,4′-DMAR, MXE, phenazepam) in March 2016 [12,13], nine substances (Single Convention on Narcotic Drugs 1961 Schedule I: U-47700, butyrfentanyl; Single Convention on Narcotic Drugs 1971 Schedule II: 4-MEC, ethylone, pentedrone, ethylphenidate, MPA, MDMB-CHMICA, 5F-APINACA, XLR-11) in March 2017 [14], and eleven (Single Convention on Narcotic Drugs 1961 Schedule I: carfentanil, ocfentanil, furanylfentanyl, acryloylfentanyl, 5-fluoroisobutyrfentanyl, tetrahydrofuranylfentanyl; Single Convention on Narcotic Drugs 1971 Schedule II: AB-CHMINACA, 5F-ADB, AB-PINACA, UR-144, 4-FA) in March 2018 [15].

1.2. Basis of scheduling NPS in the European Union

In 2013, the European Union (EU) proposed a new approach to tackle the NPS problem. The earlier approach implemented in 2005, was deemed by the European Commission itself as inadequate [16]. The European Commission argued that the approach was too lengthy and hence unable to tackle the large number of NPS arising; the approach was rather reactive than proactive and lacking options for regulatory and control measures [17]. The new EU proposal established in 2013 has the ability to implement a twelve month immediate ban on a substance based on both groups of prevalence rates and patterns of use and on fatalities and severe health consequences [2,18]. However, in these twelve months, risk assessment of the substance needs to be performed, which is difficult due to the lack of scientific evidence about the effects and potential harms of substances [16]. The EMCDDA has published an operating guideline for the risk assessment of NPS [19]. This process is time consuming and depends on forensic institutes and the police to report incidence relating to NPS and researchers to perform studies investigating the analytical, pharmacological and toxicological properties of an NPS. The twelve-month immediate ban makes it possible to react fast to newly occurring substances and hence reducing their availability. It does not have a negative impact on the current system of scheduling, and furthermore considers other applications of the NPS in the chemical and pharmaceutical industry.

Member states of the EU also have the possibility to establish a national narcotics law, in order to cover a broader range of substances. Three different approaches have been observed: existing laws on consumer and health protection or on medication are used, existing drug laws are modified or new laws are developed [7]. In 2014 the Court of Justice of the EU ruled that substances are not medicinal products if they do not have beneficial effects on human health. Hence, it became unfeasible to use medicinal product laws as the legal basis for sanctioning the possession, production or trade of NPS and furthermore, new laws had to be established to schedule NPS.

2. The peculiarity of the Swiss narcotics legislation

The Swiss “Federal Act on Narcotics and Psychotropic Substances” (BetmG, SR 812.121) was passed on October 3rd 1951 and took effect on June 1st 1952. It is available in three official languages of Switzerland, German, French and Italian, and a translation into English with no legal force (https://www.admin.ch/opc/en/classified-compilation/19981989/index.html) [20]. Accordingly, consumption, production and trading of controlled substances without a special permission are penalised. Special permissions can be given under defined circumstances by the Swiss Agency for Therapeutic Products (Swissmedic), which is the Swiss authority responsible for the authorisation and supervision of therapeutic products. Such special permissions include company licenses to handle listed substances and permits for

import and export. In 2011 the BetmG, SR 812.121 was completely revised, and one of the three new regulations is the "narcotic law directory" (BetmVV-EDI, SR 812.121.11) suitable for listing all controlled substances.

The BetmVV-EDI has seven indices, for the different types of controlled substances. The indices a to c regulate pharmaceuticals; index d regulates substances with pharmaceutical marginal importance including substances listed by the UNODC. As an innovation, in 2011 a new index e was added, as a reaction to NPS occurring on the international and the Swiss drug market. The purpose of this index e is to rapidly schedule newly emerging substances with potential psychoactive properties such as NPS. Furthermore, index f and index g were added for controlling precursor and auxiliary chemicals. Index e is aimed to restrict drug trafficking and not to prevent the use of listed chemicals for research or industrial purposes. One advantages of the BetmVV-EDI is that structure analogues definitions and single substances can be listed. The latest version from November 30th 2018 contains ten different structure analogue definitions, namely: cathinones, naphthylpyrovalerones, naphthoylindoles and naphthylmethylindoles, naphthoylpyrroles, napthylmethylindenes, phenylacetylindoles, cyclohexylphenoles, phenethylamines and fentanyls (Fig. 1). Categories and names of compounds are mainly trivial names, which can easily be found by internet research without profound chemical knowledge, making it possible that even individuals with little or no training in chemistry can easily identify regulated substances.

Structure analogue means any compound that is deduced from a similar compound by chemical reactions. For structure analogues to become legally controlled substances, the legislator has to define, which chemical substitutes they intend to control. The BetmVV-EDI index e No. 1 lists cathinone as a class of structure analogue. It includes every substance in which the structure is derived from 2-amino-1-phenyl-1-propanon (Fig. 2). The Swiss legislator defined controlled modifications of the core compound as follows: it differentiates between three different sites of substitution: on the phenyl ring, on the third position or on the amine-nitrogen. Furthermore, different kinds of substitutions are defined at the phenyl ring: alkyl, alkoxy, alkylendioxy, halogenalkyl or halogen.

In the current version from November 30th 2018, 207 single substances are listed in the order of their registration. Fig. 3 depicts the number of listed substances, newly added and removed substances per update. In the update from October 2018, 23 single substances listed in index e were moved to index a or d, due to international scheduling. This happened for the first time since the establishment of the narcotic law directory. Also, the latest update from November 2018 moved ten substances from index e to index d.

An advantage is that the BetmVV-EDI is updated regularly on a yearly basis since 2012; in acute situations it is possible to expansion it in three months. Updates are executed with minimal bureaucratic effort: in the first instance, forensic chemists at the Forensic Institute Zurich, pharmacists at the Swiss Agency for Therapeutic Products (Swissmedic), chemists at the Federal Customs Administration, and forensic chemists and toxicologists at the Swiss Association of Forensic Medicine (SGRM/SSML: Schweizerische Gesellschaft für Rechtsmedizin/ Societe de Suisse de Médicine Légale), are invited to place NPS, on the so-called suggestion list, which in their opinion should be legally controlled. In the next step these suggestions list is presented to the Conference of the Cantonal Police Commandants, the Conference of Federal Prosecutors, the Swiss Association of Addiction

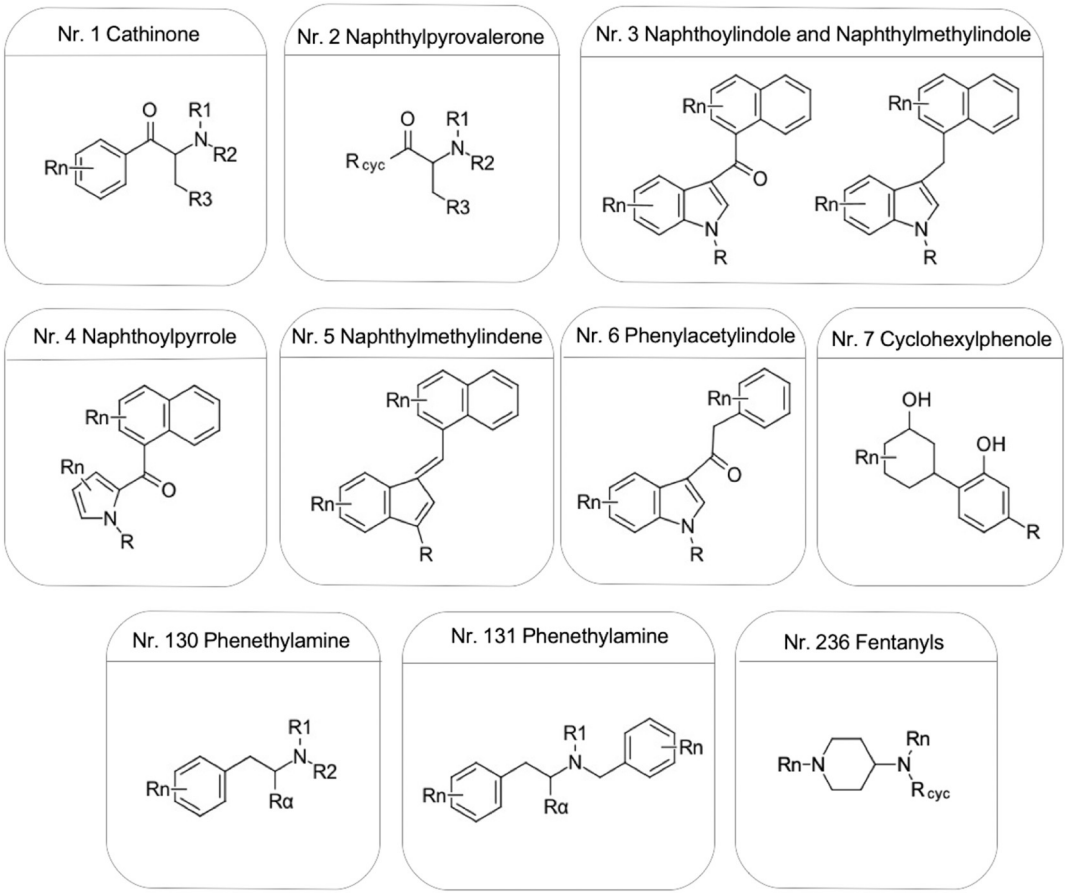

Fig. 1. The nine listed classes of structure analogue regulations with their core structures and regulated sites of substitution listed in the BetmVV-EDI index e. Rn indicates one or more substituents. Rcyc in analogue No 2. can be any ring substitute except for phenyl or alkylendioxyphenyl (which is covered by analogues No 1), and R1-N-R2 can be a cyclic structure, such as pyrolidinyl in the compound naphthyolpyrolvalerone, where Ncyc is the naphthyl-ring system.

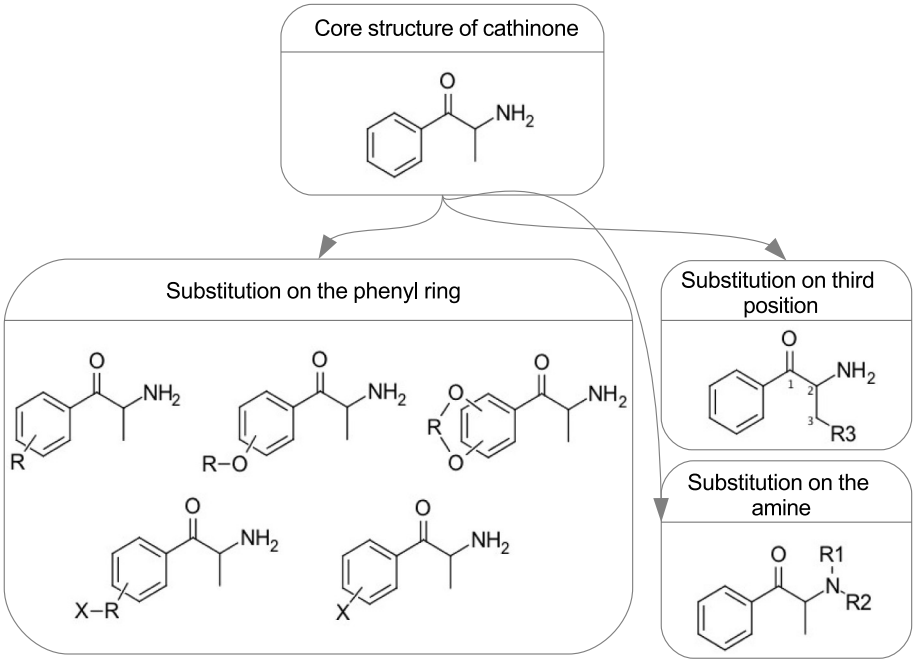

Fig. 2. The structure analogue regulation of BetmVV-EDI index e No 1 cathinones with three possible sites of substitution.

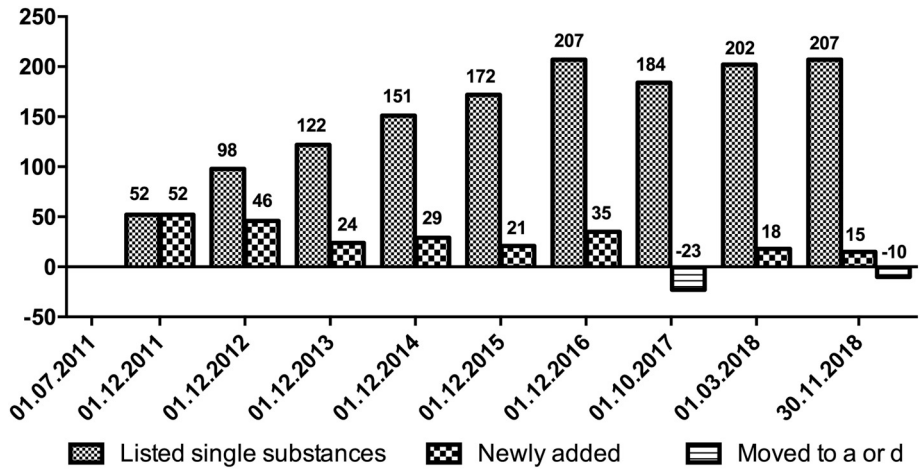

Fig. 3. Listing of single substances in index e: the total amount of single substances listed in each version, newly added substances and substances which were moved from index e to index a or d.

Science, the Conference of the Cantonal Health Directors (including cantonal pharmacies), Interpharma, Science Industries and the Association of Pharmaceutical Companies Switzerland (VIPS) for examination. Finally, the new BetmVV-EDI index e is presented to the minister of interior of Switzerland, which decides to put it into effect. Requirements to list NPS in the index e are their novelty and suspected psychotropic effects, which are inferred from reports from forensic toxicology and chemistry institutions, customs and the police. No additional pharmacological information or scientific data on possible health risks are needed to list an NPS in the index e. Newly placed substances on Schedule I of the 1961 Convention or Schedule II of the 1971 Convention, by the Commission on Narcotic Drugs of the World Health Organization, can easily be transferred from index e into index d of the Swiss BetmVV-EDI. Once a substance is scheduled by the United Nations it is assumed that it has potential harmful effects and danger to the health.

2.1. Four-pillar policy and its usage in monitoring of the Swiss NPS market

The revised federal act introduced a “four-pillar” policy consisting of “prevention” (pillar 1), “therapy/ reintegration” (pillar 2), “harm reduction/ survival support” (pillar 3) and “control/ law enforcement” (pillar 4). The goal was to protect the public health and minors [8,21].

Measures concerning the four-pillar policy are programs such as drug checks which belongs to both pillars of “prevention” and “harm reduction/survival report”. Since 1998 the Office of the Cantonal Pharmacist (Health & Social Welfare Department, State of Berne, Switzerland) in cooperation with ContactNetz (Foundation Drug Addiction) is offering mobile drug checks [22]. In 2001, the first stationary drug checking service was opened in Zurich, followed by one in 2014 in Bern. Drug checking is the analysis of the chemical composition of a supposed narcotic drug [22]. It is performed following a questionnaire and a counselling session with a street worker at parties and in nightclubs (pillar 1- “prevention”). Samples are documented in detail, prepared and tested using a high performance liquid chromatography coupled to a diode array detector (HPLC-DAD) [23]. The

mobility drug checking service analyses about 600 samples per year in Switzerland. The stationary drug checking laboratories analyse about 600 and 1500 samples per year in Bern and Zurich, respectively. NPS make about 5 to 10% of all cases per year, most of them being analysed in the stationary drug checking facilities (personal communications Daniel Allemann Cantonal Pharmacy Bern). Benefits of drug checking are to get in direct contact with users and be able to provide individual and personalized information about the substances and the risks involved (pillar 3- "harm reduction/survival report"), to have an insight about the current drug market and hence be able to set up an alert system when pills or powders are potentially dangerous [22]. In this context a drug is defined as dangerous, when it contains an unexpected composition, a wrongly declared composition or a highly active component content (e.g. MDMA content higher than 120 mg per tablet).

Programs regarding the second pillar therapy and reintegration were already started in the late 1980s and early 1990s when Switzerland took counter measurements facing a fast-growing drug related HIV epidemic [8,21]. Programs such as needle-exchange programs, low-threshold methadone programs and heroin-assisted therapy were implemented. New HIV infections related to drug injections could be reduced from 68% to 15% (in 1997) and further down to 5% (in 2009) [21]. When the revised narcotics law took effect in 2011 these programs became statutory regulated by law and are included in the narcotic addiction directory (Betäubungsmittelsuchtverordnung, BetmSV, 812.121.6).

Switzerland is not part of the EU and hence not part of the customs union, therefore all international mail has to go through the Federal Customs Administration. Thus, the Federal Customs Administration is able to check a high throughput of packages crossing the national border and has therefore a high detection rate regarding drug shipments into Switzerland. Last year alone Swiss customs seized 32.8 kg of listed NPS in 263 drug shipments (total number of drug shipments in 2016: 1702), send to enter the Swiss drug market. 324 g listed NPS were confiscated in street surveillance. Further 59.9 kg of unlisted NPS were confiscated in post shipments and 940 g in street surveillance by the Federal Customs administration (unpublished data by Swiss Federal Customs, Thomas Heeb). This also has the advantage that customs and therefore, the executive are detecting changing trends in the drug market at an early stage. The concept of drug control thus belongs to the fourth pillar law enforcement.

3. Scheduling of NPS in the German speaking countries Austria and Germany

The Narcotic Law (Suchtmittelgesetz SGM) regulates narcotics in Austria, psychotropic substances and drug precursors and controls in detail possession, trade and consumption of scheduled substances [24]. Substances which are legally controlled under the SGM have to be listed either in the narcotic drug directory (Suchtmittelverordnung) or the psychotropic substances directory (Psychotropenverordnung) [25,26]. These directories also cover and list substances internationally controlled by the UNO. In order to tackle the NPS situation, which started in 2008 in Austria, the Austrian Medicinal Products Act (Arzneimittelgesetz) was first used, listing single substances. Already in 2009 it became clear that this way of controlling NPS was not feasible due to the fast changing market [27]. Therefore, the "New-psychoactive-substance-law" (NPSG) was established and took effect on February 1st 2012. According to the Austrian NPSG, NPS are defined as a substance or preparation which hasthe capability to cause a psychoactive effect in the human body. In contrast to the Swiss narcotics law solely the production, distribution or trading are criminalized with the goal to prosecute vendors and dealers but not consumers. Appendix I lists nine different single substances. Appendix II lists ten different structure analogue definitions consisting of the chemical classes of cannabimetics, phenethylamines, amino-phenyl-ethanones, alpha-keto-benzylamines, 2-aminoindanes and 2-aminotetralines, tryptamines, piperazines, arylcyclohexyl-amines, arylcyclohexyl-pyrrolidines and arylcyclohexyl-piperidines, benzyl-piperidines and benzyl-pyrrolidines and 2-amino-phenyl-oxazoles and 2-amino-phenyl-oxazolones [28]. This law from 2012, revised in 2016,is irregularly updated by the Federal Ministry of Health and Women's Affairs.

The German Act on the Trade in Narcotic Drugs-Narcotic Drugs Act (Betäubungsmittelgesetz BtMG), which took effect on January 1st 1930, is used for scheduling narcotic substances. It has three appendices. Appendix I lists non-negotiable narcotics (trade and disposal forbidden), appendix II lists negotiable but not prescription able substances (trade allowed, disposal forbidden), and lastly appendix III lists negotiable and prescription substances (regulated disposal allowed) (https://www.gesetze-im-internet.de/btmg_1981/, accessed 01.11.2017) [29]. Although it is conceptualized for classical drugs also a few NPS such as fentanyl analogues are listed in appendix I and synthetic cannabinoids such as JWH-018 are listed in appendix II (https://www.gesetze-im-internet.de/btmg_1981/anlage_i.html, https://www.gesetze-im-internet.de/btmg_1981/anlage_ii.html, accessed 01.11.2017). On November 26th 2016, the "Act to control the distribution of new psychoactive substances" (NpSG) took effect in Germany. Similar to the Austrian NPSG this new act was not integrated into the already established German narcotic law. The NpSG uses a structure analogue approach and bans structure analogues of 2-phenethylamines and cannabimimetics/ synthetic cannabinoids [7,30]. It is defined that a substance derived from 2-phenethylamine with a maximal molecular weight of 500 amu and consists of the two structure modules A and B, is legally controlled. Structure modules A are ring structures such as phenyl, naphthyl, tetralinyl or pyrrolyl. Structure modules B are substitutions such as alkyl, cycloalkyl, alkylcarbonyl or halogens. This law prohibits the production, trade, import, offer and possession, however not the consumption of NPS [7].

4. Discussion

Currently ten different structure analogue definitions cover three chemical classes of NPS, cathinones (Nr. 1), cannabinoids (Nr. 2-7) and phenethylamines (Nr. 130 and 131) in index e. This seems to be insufficient, because classes such as benzodiazepines, tryptamines and benzodiazepines are not regulated by a structure analogue definition. In recent years the presence of fentanyl analogues on the NPS market has grown significantly. From 2012 to 2015, 17 fentanyl analogues were reported to the UNODC Early Warning Agency [31] and the numbers of fatal intoxications due to fentanyl analogues has risen [32,33]. Therefore, a fentanyl analogue regulation (Nr. 236) is implemented in the update of November 30th 2018.

Even though the narcotic law directory is updated on a yearly basis, only in October 2017 substances were moved from index e to index a or d for the first time, due to their international scheduling in Schedule I or II in 2015, 2016 or 2017. This is a rather long time, when considering how fast an update can be conducted. The Commision on Narcotic Drugs is publishing recommendations of NPS international scheduling on a yearly basis in March of every year. Therefore, it would be recommended and feasible to adapt the narcotic law directory to international scheduling faster in December of every year. As mentioned in section 1.1, member states have to regulate the scheduled substance with at least as much stringency as their international regulation. Therefore, Switzerland should have reacted faster to the international scheduling of substances in 2015.

4.1. Comparison of the Swiss BetmVV-EDI index e with the Austrian NPSG and the German NpSG

For the comparison of scheduling of NPS in Switzerland, Austria and Germany the approach of scheduling, the process of scheduling, decision bodies involved, occurrence of updates and penalties are assessed (compare Table 1). Finally, advantages and disadvantages of every act or law are evaluated.

Table 1
Comparison of the Swiss BetmVV-EDI index e, the Austrian NPSG and the German NpSG.

	Switzerland	Germany	Austria
Name	"Federal Act on Narcotics and Psychotropic Substances" (BetmG, SR 812.121) Index e	"Act to control the distribution of new psychoactive substances" (NpSG)	"New-psychoactive-substance-law" (NPSG)
Approach	Structure analogues and single substances	Structure analogues	Structure analogues and single substances
Number of single substances	207	–	9
Number of Structure analogues	9	2	10
Chemical classes	cathinones, naphthylpyrovalerones, naphthyoylindole and naphthylmethylindole, naphthoylpyrrole, napthylmethylindene, phenylacetylindole, cyclohexylphenole, phenethylamines;	2-phenethylamines, cannabimimetics/ synthetic cannabinoids;	Cannabimimetics, phenethylamine, amino-phenyl-ethanone, alpha-keto-benzylamine, 2-aminoindan/ 2-aminotetralin, tryptamine, 1-phenyl/ 1-benzyl piperazin, arylcycloheyl-amine, pyrrolidine, piperidin, benzyl-piperidine, benzyl-pyrrolidine, 2-amino-phenyl-oxazole, 2-amino-pheyl-oxazolon;
Decision body	Swissmedic, SGRM, Federal Customs Administrations, Forensic Institute Zurich;	Ministry of Health	Ministry of Health and Women's Affairs
Penalises	Consumption, production and trade	Production, trade, import, offer, possession	Production, distribution, trade
Established	July 1st 2011	November 26th 2016	February 1st 2012
Updates	2012 2013 2014 2015 2016 2017 2018	–	2016

The market of NPS in Switzerland, Austria and Germany, differs a lot from each other. Due to different legislations, different substances are available on the online market, which will be commented later on. Out of these three countries, Germany has the biggest market. Furthermore, the prevalence for NPS is higher in Germany compared to Switzerland and Austria. This is evident by the numbers in the following paragraphs.

In 2008 Auwärter et al. could show for the first time that herbal blends sold in Germany as "Spice" contained two different synthetic cannabinoids [34]. Since then the market has evolved constantly [6]. About 2.8% of adults (> 25 years) and 2.2% of young adults (18–25 years) in Germany have used any kind of NPS [35]. Opposed to that, the EMCDDA reports for Austria that the lifetime prevalence of NPS use among the general population remains low and mostly young people like to experiment with it [36]. As previously mentioned the Swiss Federal Customs regularly seizes postal shipments containing NPS and about 5–10% of all samples analysed by the Swiss drug checking contain NPS. Nevertheless, NPS are seldom detected in Forensic Medicine Institutes in Switzerland. This could be explained by the efficient and well organised Swiss illegal drug market for traditional drugs (such as cannabis, cocaine or MDMA), having high quality substances. Further, the high Swiss salary makes it possible to purchase the more expensive classic drugs [37].

4.2. Type of scheduling

Both the Swiss BetmVV-EDI index e and the Austrian NPSG use the structure analogue definitions and single substances approach but the NPSG has only nine single substances listed opposed to 198 in index e. The Swiss BetmVV-EDI index e covers the chemical classes of cathinones, cannabinoids, phenethylamines and fentanyls, the Austrian NPSG additionally tryptamines. Opposed to that, the German NpSG only schedules structure analogue definitions of two chemical classes, the cannabinoids and phenethylamines. It has two core structures defined with several different possible substitution sites and substitutions. This means that the German NpSG can be easily circumvented by the addition of not regulated residues. In fact Angerer et al. (2017) showed that already one month after the law was implemented, drug suppliers replaced regulated drugs with the unregulated substance Cumyl-Pegaclone. Both the Swiss index e and the German NpSG do not cover tryptamines in their structure analogue definitions. The BetmVV-EDI overcomes this problem by listing all synthetic tryptamines as single substances hence, they are nevertheless regulated in Switzerland. As a result of the lack of a regulation of synthetic tryptamines in Germany, these substances are available on online vendor homepages delivering to Germany [38]. The example of synthetic tryptamines, points out that the combination of an analogoue regulations and single listings is better suitable to regulate a broader range of NPS.

Furthermore, the NpSG is phrased in such a way, that profound chemical knowledge is needed to understand it, and that experts are needed for explanation to jurisdictions. This means that an organic chemist will be able to understand, which substances are regulated, but it is very doubtful that a person not trained in organic chemistry has this knowledge, such as consumers, police officers or judges.

4.3. Updates

The scheduling of NPS in Switzerland follows a simple scheme as described earlier, making it possible to implement new single substances in updates once or twice per year. Index e has been updated on a yearly basis since its implementation in 2011 but can also be updated within three months in acute situations. It takes effect with the signature of the ministry of interior, which is a simple and fast procedure. Opposed to this, adapting and changing the German NpSG and the BtmG needs to be brought forward and discussed in the German parliament, which is a long and effortful process. However, single substances can be added to the appendix II of the German BtMG in summary proceedings. For example Cumyl-Pegaclone was added on April 26th 2018 (https://www.gesetze-im-internet.de/btmg_1981/anlage_ii.html, accessed 14.11.2018) [39]. The Austrian NPSG has only been updated once in 2016 and the German NpSG has not yet been updated. This is of special concern, as the NPS market is constantly and fast changing, which is evident from the data of the European drug monitoring by the EMCDDA. Therefore, it seems more adequate to have at least yearly updates.

4.4. Legal prosecution

In contrast to the German NpSG and the Austrian NPSG, in Switzerland NPS are scheduled using the already established narcotics law, namely the Swiss "Federal act on narcotics and psychotropic substances" (BetmG, SR 812.121). Hence, consumption of any drug of abuse is legally prosecuted following the same scheme. Distribution or sale of a listed substance is penalised with up to three years of imprisonment. Consumption is prosecuted with a monetary fine. Possession of small amounts of a substance is not liable to prosecution (e.g. 10 g of cannabis will not be fined as it is considered a small amount) [40].

The Austrian NPSG aims to prosecute and punish vendors and dealers but not consumers. The distribution or sale of substances scheduled in the Austrian NPSG may be punished by imprisonment for up to two years for basic offences or one to ten years when the distribution of the substances has led to serious bodily harm or death. The possession for personal use is not punishable [28,36].

The German NpSG regulates penalty as following: The distribution and sale of scheduled substances is penalised with up to three years of imprisonment. In aggravating circumstances imprisonment of one to ten years can apply [30]. The approach to prosecute vendors and dealers but not consumers, has been very successful in Portugal where the use of drugs is decriminalized since 2001 under the Law 30/2000 [41]. It was observed that the number of drug-related injuries, drug usage and the criminal justice burden and costs were reduced [42]. Even though consumption of narcotics is penalised in Switzerland, it is only prosecuted with a monetary fine. The possession of larger amounts of narcotics, which is a characteristic for dealing, is punished with imprisonment. Therefore, one could argue that also prosecution aims towards the vendors and dealers.

4.5. Advantages and disadvantages of the BetmVV-EDI index e

A clear advantage of the Swiss index e is that it is updated at least once a year and therefore reacts fast to changes on the NPS market. In addition, it takes effect by the signature of the ministry of interior. Involving different Forensic and police institutions and the chemical and pharmaceutical industry means, that all expertise on the current NPS situation is considered and also that the industry is not anguished by index e. Drawbacks are that not all chemical classes monitored by the EMCDDA do have structure analogue definitions listed in index e. Another issue is that it took two years to react to the first international scheduling of ten NPS and hence moving them from index e to index a or d. Nevertheless substances moved from index e to index a or d in the update from October 2017 were previously to international scheduling listed and hence legally controlled in Switzerland.

As previously mentioned the German NPS market is bigger compared to Austria and Switzerland. Therefore, a law to regulate the NPS market should be effective, covering all chemical classes of NPS and understandable for every person involved in the jurisdiction process.

5. Conclusion

The Swiss "Federal act on narcotics and psychotropic substances" (BetmG, SR 812.121) schedules not only ten different structure analogues but also 207 single substances with presumed psychotropic effects. Scheduling in index e does not require a toxicological risk assessment of a compound. It is updated at least yearly, in acute cases a supplement can be added within three months. Updates are installed after suggestion and profound inspection by forensic chemists and toxicologists (Swiss Society of Forensic Medicine), pharmacists in chemical and pharmaceutical industry and in authorities such as Swissmedic and the Federal Office of Public Health. New versions are set into effect with little bureaucratic effort by the signature of the Federal Council of Switzerland.

Nevertheless, there are certain drawbacks. In 2015 UNODC scheduled for the first time ten NPS on the Single Convention on Narcotic Drugs of 1961 or the Convention on Psychotropic Substances of 1971. Only in October 23 NPS were moved for the first time from index e to index a or d, even though the narcotic law directory is updated on a yearly basis. The Swiss BetmVV-EDI index e makes it possible to react fast and flexible to developments of the NPS market, to update and implement international regulations and hence to be a valuable instrument in the restriction and control of NPS drug-trafficking.

Acknowledgements

The authors would like to thank Daniel Allemann of the Office of the Cantonal Pharmacist for providing information on the mobile drug-checking Bern, Thomas Heeb of the Federal Customs Administration for providing data on drug seizures in Switzerland, Dr. Florian Messner of the Institute of Criminal Law of the University of Innsbruck for providing explanation on the Austrian NPSG, Irene Scholz of the Clinical Pharmacology, Inselspital Bern for proof reading of the manuscript and Christian Bissig at the Forensic Institute Zurich and Dr. Patrick Juchli from the University of Lausanne for fruitful discussions.

Conflict of interest

The authors declare no conflict of interest.

Funding

This research received financial support by the Swiss Federal Office of Public Health (BAG project No. 15.029013).

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