Barriers to access to opioid medicines: results of a review of national legislation and regulations of 11 Central and Eastern European countries

Marjolein J. M. Vranken[1], John Lisman[2], Aukje K. Mantel-Teeuwisse[1], Saskia Jünger[3], Willem Scholten[4], Lukas Radbruch[5a,5b] , Sheila Payne[6] , Marie-Hélène D. B. Schutjens[1,7]

Affiliations

1. Utrecht Institute for Pharmaceutical Sciences, Division of Pharmacoepidemiology & Clinical Pharmacology, Utrecht University, Utrecht, the Netherlands

2. Lisman Legal Life sciences, Nieuwerbrug, The Netherlands

3. Institute of General Practice, Hannover Medical School, Hannover, Germany

4. Willem Scholten, Willem Scholten Consultancy, Lopik, The Netherlands

5a. Department of Palliative Medicine, University Hospital Bonn, Germany

5b. Centre for Palliative Care, Malteser Hospital Bonn, Bonn, Germany

6. International Observatory on End of Life Care, Division of Health Research, Lancaster University, Lancaster, United Kingdom

7. Schutjens de Bruin, Tilburg, The Netherlands

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Corresponding author: Aukje K. Mantel-Teeuwisse

Utrecht Institute for Pharmaceutical Sciences, Division Pharmacoepidemiology & Clinical Pharmacology,

PO Box 80 082, 3508 TB Utrecht, The Netherlands

Tel: +31 30 253 7324 / Email: A.K.Mantel@uu.nl

Summary

Control measures designed to prevent abuse of opioid medicines often unintentionally restrict legitimate medical use, leaving millions of patients with cancer in pain. This study aimed to develop and validate an assessment instrument based on the WHO Policy Guidelines, and subsequently to systematically identify legal and regulatory barriers to access to opioids in 11 European countries using this instrument. Relevant legislation and regulations were independently reviewed by three reviewers. Potential barriers were found in all countries, varying from 22 to 132 per country and varying from 1 to 49 per single category. Individual differences in the level of impediment were shown (for example: prescription validity ranging between 5 days and 13 weeks). The results of this review should give rise to a critical national review and revision of provisions that may impede access to opioids in a way that is disproportional to their benefit for the prevention of abuse.

Introduction

Opioid analgesics are indispensable for the treatment of moderate to severe cancer pain.[1] The World Health Organization (WHO) has recognised this medical need by adding morphine to the 'WHO Model List of Essential Medicines':[2] medically necessary medicines that should be available in sufficient quantity at an affordable price. Despite this internationally acknowledged medical need, at least 79% of the world population has no or very low to low access to opioid medicines for pain relief.[3] The WHO estimates that on a global level 5.5 million terminal cancer patients suffer moderate to severe pain due to inadequate access to controlled medicines.[4] A variety of factors is considered to contribute to inadequate access including economic aspects, legislation and policy, lack of knowledge and societal attitudes.[4–6] The latter three factors are strongly interrelated: lack of knowledge and misconceptions about opioids in itself contribute to fear of using opioid medicines in medical practice and hence may restrict access to these medicines.

Additionally, this misguided fear may cause governments and policy makers to implement restrictive policies and legislation. These restrictive policies and legislation in turn foster fear of using opioid medicines, in particular if severe sanctions are involved for unintended violations of these legislation and policies. As a result of this complex interaction of factors influencing access, patients worldwide suffer pain and other concomitant clinical consequences that impair the quality of life, such as physical, psychosocial and psychological malfunctioning.[7]

While other factors as described above are also relevant, legal and regulatory control measures are considered to play an important role in the global problem of inadequate access.[8,9,6,5,10,11,12] Opioid medicines are controlled under the international agreement 'the Single Convention on Narcotic Drugs'.[13] Parties to this Single Convention on Narcotic Drugs are obliged to take measures to prevent abuse and diversion by limiting the use of these controlled medicines to medical and scientific purposes. Despite (inter)national control measures, satisfactory levels of prevention of abuse and diversion are not always achieved which may result in further control actions.[14] In New York City for example, in response to a progressive increase in overdose and deaths from opioid medicines, clinical guidelines were established limiting the prescribing of opioid analgesics in emergency departments to a 3-day treatment period[15] and excluding the prescribing of some long-acting opioid analgesics.[14] These control measures may sometimes be necessary to reduce risks associated with abuse and diversion, although there is little high quality evidence to support this. In the United States for example, strategies focussing on patient and prescriber information showed to be useful to (moderately) decrease opioid over-prescribing and diversion.[16] However, the problems and also the solutions in the United Stated are very specific and are not comparable to the situation in many other countries across the world.[17] These measures may not reduce abuse and diversion in countries where there is no over-prescribing and where there is a different mechanism behind abuse and diversion.

Although implementation of more strict control measures may result in prevention of abuse and diversion, the downside is that legitimate medical use may also

be restricted. As a result, access to opioid medicines is inadequate for millions of patients that rely on their use including patients with moderate to severe cancer pain. Numerous studies have reported on legal and regulatory barriers to access to opioid analgesics, mostly in low and middle income countries. Strict control measures were considered burdensome and complex and were deemed to interfere with medical practice.[10] Frequently reported legal and regulatory restrictions to access include the requirement for permission to prescribe or receive opioids, limitations on the amount to be prescribed, restrictions regarding dispensing privileges and the absence of emergency provisions.[9,18–21]

Where on an international level the prevention of abuse and diversion has prevailed for decades, more recently this focus has shifted towards ensuring access to essential medicines. In this context, governments were urged by the International Narcotics Control Board and other international organisations and agencies to critically examine their national policies and legislations and remove impediments to the adequate availability of opioid medicines for medical and scientific purposes.[10,22,23] Governments that now implement control measures are facing a dilemma in their efforts to achieve maximum public health outcome: how to prevent opioid abuse while not negatively impacting access to opioid medicines for patients in medical need?

An instrument was developed to support government representatives and policy makers in evaluating their national policies and legislation: the WHO Policy Guidelines 'Ensuring balance in national policies on controlled substances: Guidance for availability and accessibility of controlled medicines' (hereinafter: WHO Policy Guidelines).[4] These guidelines were updated at the start of the Access to Opioid Medication in Europe (ATOME) project; a project that aimed to improve access to medication in twelve Central and Eastern European countries with statistical evidence of very low morphine consumption per capita and no major ongoing initiatives to improve access to opioid medicines (Bulgaria, Cyprus, Estonia, Greece, Hungary, Latvia, Lithuania, Poland, Serbia, Slovakia, Slovenia and Turkey). Although the WHO Policy Guidelines give direction and include an assessment checklist, there is no practical assessment instrument available

with detailed information on potential barriers to evaluate legislation and regulations. The aim of this study was therefore twofold: (1) to develop and validate an assessment instrument for the systematic analysis of national legislation and regulations; and (2) to conduct a review using the instrument with the objective to identify potential legal and regulatory barriers to access to opioid medicines in eleven of the twelve countries participating in the ATOME project (all countries except Poland).

Methods

Selection of national legislation and regulations

The ATOME review of national legislation and regulations consisted of a two-step method: a quick scan of legislation[24] provided a basis for a more thorough review. At the start of the ATOME project, country teams were composed based on their expertise and role in their country to ensure relevance to the project activities. These country teams included representatives from the national controlled substances authorities and national Ministries of Health, experts representing regulatory and law enforcement authorities and leading healthcare professionals and patient representatives. Within these country teams a legal expert was appointed to collaborate on the ATOME legislation review. Eleven of the twelve countries participated in the ATOME legislation review; the Poland ATOME country team decided not to participate and was therefore not included in this legislation review.

Key experts in each country selected legislation concerning controlled substances and opioid medicines for the quick scan in the period the period March – November 2011. This quick scan consisted of the identification of obvious impediments in selected legal documents using eight of the 21 WHO Guidelines. In the framework of the more thorough review, the key experts in the selected countries were requested to update information about the legislation and provide information on forthcoming changes in the originally selected legislation. Initially collected and additional relevant legislation and regulations (collected until February 2013) were translated into English

by a translation agency (NOVA Language Services, Barcelona, Spain) if it was only available in the national language (see supplementary annex 1 for a full overview of selected and translated legislation and regulations).

Analysis of national legislation and regulations

In order to review legislation and regulations, a method was developed using an assessment instrument with potential barriers to access to opioid medicines focusing on nine different categories: prescribing; dispensing; manufacturing; usage; trade and distribution; affordability; penalties; language; and other (to include potential barriers that did not fit into one of the other categories). The assessment instrument was developed by authors JL, MHS and MV based on the WHO Policy Guidelines and additional literature regarding barriers to access.[4,8,25–27] A selection of sub-categories (referred to as items) of potential barriers in the category prescribing and language is provided in Table 1.

All relevant national legislation and regulations were analysed by one reviewer (author MV) and legal or regulatory provisions related to controlled substances and opioid medicines were selected for further review. These selected provisions were subsequently independently reviewed by three reviewers (authors JL, MHS and MV) using the assessment instrument and potential barriers to access to opioid medicines were identified. Differences of views between the reviewers regarding the identification of potential barriers were discussed until consensus was reached. Newly identified barriers were added to the assessment instrument and the reviewed legislation and regulations were checked retrospectively to complete the process.

Validation of methods and results

The reliability of the selection of provisions for further review by one reviewer (author MV) was validated by assessing the inter-rater reliability of the selection of provisions between two reviewers (authors MHS and MV) for a selected number of countries. The controlled substances law of three randomly selected countries (Hungary,

Serbia and Slovakia) was reviewed by the two reviewers and provisions were independently selected for further review. The selection by the two reviewers was compared using Cohen's kappa statistics and was rated to be very good (kappa= 0.87). Following validation of the selection of provisions, the assessment instrument was piloted by all three reviewers to align the review process: selected provisions of one country (Greece) were analysed based on the assessment instrument and the three reviewers met to discuss differences of views which concerned general interpretation of the assessment instrument.

Individual country reports containing the provisional results of the analysis of national legislation and regulations were disseminated to the ATOME country teams and discussed during the ATOME legislation review workshop in Utrecht, the Netherlands.[28] In total 14 representatives from nine of the eleven countries participating in the ATOME project (all countries except Bulgaria and Turkey) attended the meeting. Additionally, the country teams were invited to provide feedback in writing, using a feedback form that addressed several questions, including the correctness of the translation and the results (see supplementary annex 2). Feedback in writing was received from six of the eleven countries. Small changes were made to the results based on feedback received regarding small errors in translation, recent amendments in legislation or differences in interpretation of definitions and/or terminology. The changes did not lead to modification of the assessment instrument.

Data analysis

The total number of initially selected provisions was calculated per country and in total. Additionally, the total number of provisions that was considered to contain at least one potential barrier to access to opioid medicines was assessed in relation to the total number of provisions selected for review (per country and in total). Potential barriers were identified according to category and according to item within the categories (all categories except 'language'). The presence of potential barriers in the category language was recorded qualitatively according to item to correct for language

repetitions. Individual differences between the countries were highlighted for the following items: limited prescription validity, special prescription forms required, multiple copies required, amount of controlled medicine to be prescribed is limited and daily dosage is limited.

Results

Potential barriers identified

In total, 925 provisions were initially selected for further review (author MV) varying from 35 provisions (Cyprus) to 144 provisions (Lithuania). A total of 86% of the initially selected provisions were considered to contain at least one potential barrier (including category 'language'), ranging from 72% (Serbia) to 98% (Slovenia). Potential barriers to access were found in all eleven countries with the number of categories where items were found varying between six (Slovenia) to all (Bulgaria & Latvia) of the nine categories (Figure 1). In total, 778 potential barriers (excluding the category language) were identified in eleven countries, with the smallest number in Cyprus (n=22) and the largest number in Lithuania (n=128). Each country showed potential barriers in the categories 'prescribing', 'dispensing' and 'usage', while the total number of barriers in each category varied from 1 (several countries, several categories) to 49 (Greece, prescribing) (Figure 1). Most barriers were identified for the prescribing and dispensing of opioid medicines, ranging from 5 (Cyprus) to 14 (Latvia) of the 20 items (see Table 2).

Individual differences in barriers to access (categories prescribing and dispensing)

Prescribing and dispensing restrictions and administrative requirements were the most common barriers identified in the categories 'prescribing' and 'dispensing', with individual differences in the level of impediment (Table 3). For example, the prescription validity varied from 5 days to 13 weeks, and special prescription forms were used in duplicate and triplicate. Restrictions regarding the total amount to be prescribed on a single prescription were identified in the legislation of several countries with

quantifications in the number of treatment days or by weight. Additional restrictions regarding the daily dosage were identified in the legislation of three countries.

Examples of provisions identified

Other potential barriers in the category of prescribing included requirements for a permit or license, restrictions regarding the authorisation to prescribe, administrative requirements and requirements for the storage of controlled medicines or prescription forms (see Table 2). Potential barriers in the category of dispensing included limitations regarding the pharmacies that are authorised to dispense, limitations on the dispensing on (designated) controlled medicines, administrative requirements, storage requirements and delivery restrictions. Besides the frequently reported prescribing and dispensing restrictions, potential barriers also include strict requirements for accessing education on controlled medicines, disproportional punitive sanctions for healthcare professionals, geographical restrictions to accessing opioid medicines, the violation of the privacy of patients and strict requirements for the storage of controlled medicines during international transportation (see Table 2).

Language in legislation and regulations

The legislation in all eleven countries referred to (patients with) dependence in a disrespectful manner (Table 4). Ten countries (all except Hungary) used incorrect definitions and/or unclear language in their legislation. These ten countries also had provisions in their legislation that do not make a clear distinction between medical use and illicit use or abuse. See Table 1 for examples of potential barriers in the category of language including an explanation.

Discussion

This study shows that the reviewed national legislation and regulations contain many potential barriers to access to opioid medicines that are indispensable for the management of cancer pain. Additionally, the study shows that all countries assessed

were considered to have language in their legislation that contributes to the stigmatisation of the use of opioid medicines. Most potential barriers concerned the prescribing and dispensing of opioid medicines, with individual differences in the level of impediment of several important items, such as limitations concerning the prescription validity, treatment duration and daily dosage. While legal and regulatory barriers to access to opioids have previously been identified by others, this is the first study showing detailed insight in the qualitative aspects of potential barriers by a systematic external review of legislation taken into account all elements in the pharmaceutical supply chain (from manufacturing to usage) and by using a newly developed assessment instrument based on the WHO Policy Guidelines[4] that can be used in an universal manner by others.

Other studies describing legal, regulatory or policy barriers to access to opioid medicines either conducted a survey[18–21,25,29,30,22] or evaluated legislation and policies building on similar content as the WHO Policy Guidelines.[31,27,26] Regulatory barriers to the accessibility of opioids for cancer pain in Central and Eastern Europe were previously reported by Cherny et al. based on surveys distributed among senior clinicians in the period 2007-2009.[25] Results that were similar to the results of the current study were found concerning reported limitations on the treatment period and the requirement to use special forms or prescribe in multiple copies. Small differences between findings may be associated with the high level of detail in the present review and the availability of information on recent amendments. Different results were seen regarding the use of stigmatising language in legislation, which may be the result of underreporting by the survey's respondents. A worldwide follow up of the European survey by Cherny et al. revealed that regulatory barriers and restricted formularies also play an important role in inadequate access to opioid medicines for the treatment of cancer pain in Africa, Asia, Latin America, the Caribbean and the Middle East, affecting hundreds of millions of patients.[18–21,29,30] While the focus of both abovementioned surveys – and most other studies – was restricted to a predefined subset of potential barriers, the scope of our study allowed for identification of every potential barrier encountered by systematically

reviewing all selected legislation. Due to this broad and systematic approach potential hurdles to accessing opioids were also located in less obvious areas. Additional research is needed to refine the assessment instrument and to assess the intention of the respective legal provisions and their impact on access in clinical practice.

Several limitations of the present external review of legislation should be mentioned. First of all, legal and regulatory data were analysed based on the selection made by key experts in the specific countries and in many cases after translation into English. Both incorrect translation and incomplete selection of documents may have caused incomplete or incorrect reporting of potential barriers. By training and guidance of carefully selected key experts and by following a two-step method with an additional update of legal and regulatory text, the omission of data was minimised. Inconsistencies in translation were reduced as much as possible by working with a professional translation agency, specialised in the area of law and health and by dissemination of the results to the ATOME country teams with the explicit request to provide feedback on errors in translation. Secondly, as the methods of this study comprised an analysis of legal text, inevitably variation of interpretation may occur. By involving three reviewers and by determining the general interpretation of the assessment instrument the chance of divergent interpretations has been minimised.

This external review of national legislation was not only shown to be useful for the identification of potential barriers, but the detailed level of information on these potential barriers has led to specific recommendations for improvement as a part of the ATOME project. Several participating countries have already implemented some of these recommendations. For example in Lithuania, the total number of special prescription forms physicians are allowed to receive has been doubled from 10 to 20 forms. In Estonia, the requirement for pharmacies to obtain a special permit which makes them authorised to dispense controlled medicines was removed. Due to this requirement, pharmacies were reluctant to apply for a license with the result that patients had difficulties identifying a pharmacy that could dispense their opioid medicines.[32] Although all these examples are considered to contribute to better access

to opioids for patients, the impact of these revisions on clinical practice has not been assessed and therefore remains unknown. Additional research is recommended to assess the impact of lifting potential barriers in these countries. Additional research is also needed to assess the level of impact of different types of barriers as it can be assumed that some types of barriers are more likely to influence access than others. Finally, scientific data are also needed in a broader context to gain insight in how a restrictive control system exerts impact on access to opioid analgesics in comparison to a very liberal system. So far only anecdotal evidence exists showing a direct correlation between strict prescribing or dispensing requirements and patients being denied adequate pain treatment.[33,34] Society would benefit from solid data showing how we can achieve less drug related risks and better clinical outcomes for patients with moderate to severe cancer pain by optimising legislation and regulations.

In conclusion, the potential barriers identified by this external review of national legislation give rise to a critical national review and revision of provisions that impede access to opioid medicines for patients with cancer pain in a way that is disproportional to their (intended) benefit for the prevention of abuse and diversion. To provide a legal framework that focuses on access to opioid medication with maximum health outcome, these revisions should take place in consultation with healthcare professionals and patient organisations. Several countries participating in the ATOME project are already in the process of revising legislation and implementing recommendations for improvement, bringing patients in medical need one step closer towards adequate access to opioid medicines.

Search strategy and selection criteria

A literature search was done in PubMed and Google Scholar to identify relevant publications published in English language. We used the following keywords in titles or abstracts: “barriers” OR “impediment’s” combined with the search terms “legislation” OR “legal” OR “regulation(s)” combined with the search terms “opioids” OR “opioid medicines” OR “opioid analgesic(s)” OR “narcotic drug(s)”. The search was not limited to

year of publication. The relevance of the publications was determined by a preliminary review of the abstracts. In addition to the electronic search using keywords, the reference list of relevant documents were also searched to identify additional relevant publications.

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Contributors

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Project management: Lukas Radbruch (project coordinator); Saskia Jünger (project executive officer); Willem Scholten (scientific coordinator); Sheila Payne.

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40. Article 32, Order of the Minister of Health of the Republic of Lithuania No. 112 of 8 March 2002 “On Medical Prescriptions and Disbursement (Sale) of Medi-cines” (Published: Official Gazette Valstybės Žinios, 16/03/2002, No. 28, Publication No. 1013).

41. Article 38 (2), Rules on classifying, prescribing and dispensing medicinal products for human use.

42. Article 4.9.4, Republic of Lithuania Government Resolution No. 591 of 30 May 2005 “On the Approval of the Description of the Procedure for Monitoring the Use of Narcotic and Psy-chotropic Substances, Consequences thereof, the Circulation of the Precursors of Narcotic and Psychotropic Sub-stances".

43. Article 4.10, Republic of Lithuania Government Resolution No. 591 of 30 May 2005 “On the Approval of the Description of the Procedure for Monitoring the Use of Narcotic and Psy-chotropic Substances, Consequences thereof, the Circulation of the Precursors of Narcotic and Psychotropic Sub-stances”.

44. Article 1(1), Act No. 3459/2006 on Legal Codes for Drugs.

45. Article 14, Rulebook on the prescription and dispensing of medicines (FRY Official Gazette No. 16/94, 22/97, 52/02.

46. Article 68 (2) (amend. and suppl. – SG 22/10), LAW FOR CONTROL OVER THE NARCOTIC SUBSTANCES AND PRECURSORS (1999).

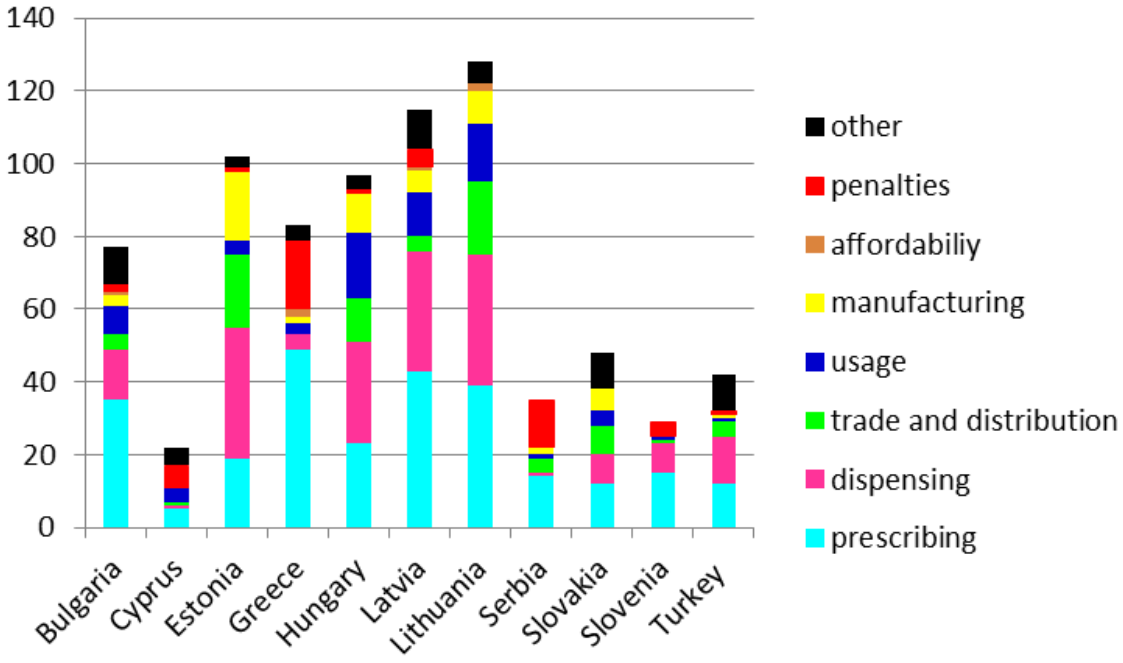

Figure 1: total number of potential barriers identified per country according to category (except category language)

Table 1: assessment instrument examples of potential barriers in the category prescribing and language

ITEM	POTENTIAL BARRIER FOR EXAMPLE IF…	RELATES TO WHO POLICY GUIDELINE	EXAMPLES: POTENTIAL BARRIERS IDENTIFIED IN LEGISLATION
authorisation to prescribe is restricted	…. the competence to prescribe controlled medicines is restricted to a limited number of medical specialists (such as oncologists only) and other appropriately trained and qualified physicians are not authorised to prescribe controlled medicines.	GUIDELINE 11	"If it appears that a patient will need to use a controlled substance for longer than 30 days or will need it repeatedly, the family practitioner only shall be authorized to prescribe it (…)."[35]
special permit/ license required for prescribing	…only designated institutions are allowed to prescribe controlled medicines or if a special permit or license is required for prescribing controlled medicines, in particular if the application procedure is complex and if high fees apply to applicants.	GUIDELINE 11	"(…) In cases of cancer patients, and only after a relevant permit by the health department of the local prefectural administration, the physician can dispense a special narcotics prescription for an amount that exceeds the maximum daily dose for a five-day (5) treatment. The local prefectural administration's permit is valid for one (1) month."[36]
special prescription forms required / prescribing in multiple copies required	…if special forms or multiple copies are required, in particular if these special prescription forms are not readily available and/or are not free of charge and/or entail many administrative requirements for healthcare professionals, in particular if unintended violation of these administrative requirements may result in severe sanctions.	GUIDELINE 9	"The persons involved in activities related to narcotic substances shall purchase the special forms from the regional healthcares centres."[37] "The size of the original copy of a prescription for narcotic drugs is 127×158 mm, three sheets. The pharmacy shall have the original prescription and one copy thereof and the health care provider shall have one copy."[38]
limited prescription validity	…patients in need of controlled medicines - especially patients with chronic conditions – have to visit the physician and pharmacy frequently, in particular if additional rules aggravating the impact apply, such as rules that limit the total amount of controlled medicine to be prescribed.	GUIDELINE 9	"Prescriptions issued by physicians are valid for the following periods of time: (…) Narcotic drugs - 5 days, including the day the prescription was issued; (...)"[39]
amount of controlled	...patients who require medical treatment with	GUIDELINE 9	"If there is no other way to suppress the pain, it shall be allowed to exceed 3 times the norms, indicated in the table of

medicine to be prescribed is limited	controlled medicines for a longer period have to visit the physician and pharmacy frequently, in particular if in addition to this potential barrier the validity of a medical prescription for controlled medicines is limited.		paragraph 31, indicating in the prescription "Special assignment" and confirming it additionally by affixing the physician's signature and personal stamp."[40]
daily dosage is limited	…the maximum dosage is lower than evidence based medical treatment guidelines advice and/or individual patient needs may require higher dosages.	GUIDELINE 11	"Per day of treatment, a general practitioner may only prescribe one tenth of the quantities specified in the previous paragraph per individual patient, while the total quantity of a medicinal product prescribed may not exceed the quantity specified in the previous paragraph."[41]
no clear distinction between medical use and illicit use/abuse	…the language used in legislation does not provide a clear distinction between medical use and illicit use/abuse and as a result causes confusion and/or fear for the use of opioid medicines in medical practice, in particular when severe sanctions are involved for unintended violations.	GUIDELINE 10	"Preventive measures (…) in order to reduce the supply of narcotic and psychotropic substances (…)."[42] "(…) when the use of narcotic and psychotropic substances was the main reason causing death."[43]
incorrect definitions are used	…the language used contains biased definitions or presuppositions regarding the nature, effect, or rational use of opioids that may encourage distorted knowledge or assumptions and/or may cause fear for the use of opioid medicines in medical practice, in particular when severe sanctions are involved for unintended violations.	GUIDELINE 10	"According to their legal definition, narcotic drugs are artificial or natural substances that act on the central nervous system and cause the individual in question to develop an addiction to them."[44]
unclear language is used	…the language used contains wording and/or terminology that leave space for interpretation (for example, the use of vague adjectives) and cause confusion and/or cause fear for the use of opioid medicines in medical practice, in particular when severe sanctions are involved for unintended violations.	GUIDELINE 10	"Medicines containing narcotic drugs can be prescribed only if their use is necessary and if they are marketed under the Law on production and marketing of medicines."[45]
controlled medicines are referred to as dangerous, toxic or addictive drugs	…the language used contributes to the stigmatisation of opioid medicines and/or causes fear for the use of opioid medicines in medical practice.	GUIDELINE 10	"For medical products, containing intoxicating substances, the packing must be marked diagonally by two red strips (…)."[46]

Table 2: assessment instrument showing potential barriers identified in eight categories (all except language) according to item (subcategory) per country

Category	IITEM	BULGARIA	CYPRUS	ESTONIA	GREECE	HUNGARY	LATVIA	LITHUANIA	SERBIA	SLOVAKIA	SLOVENIA	TURKEY
PRESCRIBING	authorisation to prescribe is restricted											
	permit/license required for prescribing											
	special prescription forms required											
	multiple copies required											
	limited prescription validity											
	amount of controlled medicine to be prescribed is limited											
	daily dosage is limited											

	prescribing of (designated) controlled medicines is limited											
	administrative requirements for prescribing[1]											
	amount of controlled medicine to be prescribe is limited to complete package units											
	patient supervision requirements for prescriber											
DISPENSING	limitations on dispensing privileges: special license required											
	limitations on dispensing privileges: special license pharmacy / designated pharmacies											
	limitations on the dispensing of (designated) controlled medicines											
	administrative requirements for dispensing											

[1] Requirements that increase the administrative burden and may cause medical practitioners to be unable or reluctant to treat patients with controlled medicines and do not solely concern any of the other categories. For example, the requirement that physicians are allowed to receive a limited number of prescription forms which need to be stored in a designated safe.

	requirements for storage (dispensing)											
	delivery restrictions of controlled medicines											
	limited prescriptions validity (dispensing)											
	amount of controlled medicine to be dispensed is limited											
	dispensing in emergency situations /correction of small errors restricted											
USAGE	possession of controlled medicines by patients restricted											
	geographical restrictions											
	continuation of treatment restricted											
	access to pain treatment for HIV patients or patients with (a history of) dependence											

	strict requirements for accessing dependence treatment											
	administrative requirements for receiving controlled medicines											
	limitations for certain patient groups											
	possession of utensils											
TRADE AND DISTRIBUTION	requirements for storage (trade and distribution)[2]											
	administrative requirements for trade and distribution[3]											
	requirements for transportation[4]											

[2] Requirements that may cause legal entities to be unable or reluctant to store controlled medicines due to the high costs of the security measures. For example, requirements regarding the safes, security systems or requirements that dictate the thickness of the bars in the windows.

3 Requirements that increase the administrative burden and may cause legal entities to be unable or reluctant to trade in controlled medicines. For example, very strict timelines for completing the application for an import or export license, in particular if the information requested cannot be easily retrieved.

4 Requirements that may cause legal entities to be unable or reluctant to transport controlled medicines due to the high costs of these security measures. For example, the requirement that controlled medicines can only be transported in a vehicle that is equipped with metal containers with special security locks.

	trade and distribution limited to designated parties											
MANUFACTURING	requirements for storage (manufacturing)[5]											
	administrative requirements for manufacturing[6]											
AFFORDABILITY	costs of controlled medicines[7]											
PENALTIES	punitive sanctions for healthcare professionals											
	punitive sanctions (other)											
	punitive sanctions for patients											

[5] Requirements that may cause legal entities involved in manufacturing to be unable or reluctant to store controlled medicines due to the high costs of the security measures. For example, requirements regarding the safes, security systems or requirements that dictate the thickness of the bars in the windows.

6 Requirements that increase the administrative burden and may cause legal entities to be unable or reluctant to manufacture controlled medicines. For example, very strict timelines for completing the application to receive a permit for manufacturing opioid medicines, in particular if the information requested cannot be easily retrieved.

7 For example, costs are not reimbursed by statutory funding schemes; high prices/taxes due to state monopoly; high monthly fee for patients to be able to receive dependence treatment.

	punitive sanctions for persons involved in manufacturing / trade and distribution											
OTHER	medical activities restricted[8]											
	violation of privacy											
	requirements for the destruction of controlled medicines[9]											
	storage requirements (other)[10]											
	administrative requirements (other)											
	limited access to education											

8 Restrictions that have an impact on medical activities and do not solely concern any of the other categories. For example, specific requirements for healthcare institutions providing treatment with controlled medicines.

9 Requirements for the destruction of controlled medicines that may deter legal entities or healthcare professionals from working with controlled medicines. For example, complex reporting requirements for the disposal of controlled medicines or the requirement that unusable controlled medicines can only be destroyed in the presence of a representative from the government.

10 Storage requirements that do not fit any of the other categories. For example, storage of opioid medicines during international transportation.

NO POTENTIAL BARRIERS IDENTIFIED	1-5 POTENTIAL BARRIERS IDENTIFIED	6-10 POTENTIAL BARRIERS IDENTIFIED	11-15 POTENTIAL BARRIERS IDENTIFIED	16-20 POTENTIAL BARRIERS IDENTIFIED	≥ 21 POTENTIAL BARRIERS IDENTIFIED

Table 3: Individual differences in the level of impediment of potential barriers (category prescribing)

country	limited prescription validity	multiple copies or special forms required	total amount or treatment period limited	maximum daily dosage
Bulgaria	7 days from the date of issuance	three copies: original and two copies in different colours (yellow and green) printed on carbon paper	30 days	not identified
Cyprus	13 weeks	not identified	13 weeks	not identified
Estonia	30 days (non-controlled medicines 60 days)	three copies, 127 x 158 mm sheets printed in green on red self-copying paper with 80 mm binding holes on the left, a security print on the margins and a 7-digit number in black in the upper left-hand corner	30 days	not identified
Greece	not identified	two copies, serial numbered containing a double red line on the top right side and the text 'special narcotic drug prescription'	the amount to be dispensed on a single prescription varies: 1 day (substances listed in Tables B & C); 5 days (dextropropoxyphene, methyphenidate, pentazocine); 15 days (fentanyl transdermal patches); 30 days (treatment of patients with cancer, provide that a permit is granted: permit valid 1 month).	maximum daily dosages in legislation, e.g. morphine 50 mg; maximum daily dosages can be exceeded for the treatment of patients with cancer, during maximum 5 days, provided that a permit is granted
Hungary	5 days	not identified	15 days / 30 days (prescribed by general practitioner) / 90 days (prescribed by general practitioner for patients travelling); repeat prescription allowed by general practitioner for max 30 days	not identified

Latvia	30 days (non-controlled medicines 90 days)	margins and part to be completed by the pharmacy is coloured in light red	maximum amounts to be prescribed in Annex 5 of Regulation No175; treatment period limited to 14 days (buprenorphine) / 30 days / 90 days (only narcotic analgesic products prescribed by a psychiatrist, narcologist, neurologist or family doctor)	daily dosage of buprenorphine legally restricted.
Lithuania	5 days, including the day of issuance.	blank form 2 for 'narcotic medicines' and blank form 3 for compensated 'narcotic medicines'	maximum amounts to be prescribed for a patient on a single occasion, e.g. morphine 2 g. total amount limited to a 7 day treatment course; transdermal: 30 days	not identified
Serbia	7 days from the date of issuance	two copies, serial numbered, with the second copy marked 'copy'.	maximum amounts to be prescribed for a patient on a single occasion, e.g. 0.2g morphine; amount limited to treatment period of 30 days; for the treatment of malignant diseases: duration of treatment limited to 14 days	not identified
Slovakia	5 days	three copies, forms marked with blue diagonal stripe	30 days; no repeat prescriptions allowed.	not identified
Slovenia	5 days, excluding the day of issuance	two copies, serial numbered, with the second copy marked 'copy'.	30 days; no repeat prescriptions allowed; maximum amounts to be prescribed specified in legislation	daily dosage may not exceed 1/10 of maximum amounts specified
Turkey	not identified	three copies, serial numbered, carbon paper in green (psychotropic substances) or red (narcotic substances)	maximum amounts to be prescribed on a single prescription specified in legislation, e.g. morphine (oral) 2700 mg	not identified

Table 4: Potential barriers identified in the category ‘language’ in legislation

IITEM/COUNTRY	BULGARIA	CYPRUS	ESTONIA	GREECE	HUNGARY	LATVIA	LITHUANIA	SERBIA	SLOVAKIA	SLOVENIA	TURKEY
reference to (persons with) dependence in a disrespectful manner in legislation (e.g. addicts or addiction)											
incorrect definitions and/or unclear language in legislation											
absence of a clear distinction between medical use and illicit use or abuse in legislation											
reference to controlled medicines as dangerous, toxic or addictive drugs in legislation											

IDENTIFIED IN LEGISLATION	NOT IDENTIFIED

Annex 1: legal and regulatory documents (partly) translated (printed in bold) and (partly) analysed per country

Documents (partly) analysed	controlled substances legislation (general)	medicinal products legislation	legislation concerning healthcare	controlled substances legislation (dependence)	other
BULGARIA	Law for Control over the Narcotic Substances and Precursors (1999)	Law on the Medicinal Products in Human Medicine (2007)	Ordinance No. 34/2005 on the procedure for state budget funding of the treatment of Bulgarian citizens with regard to diseases beyond the scope of compulsory health insurance	Ordinance No. 24/2000 on the rules and procedures for the implementation of substitution and maintenance programs for the reduction of health damage for persons addicted to narcotic drugs	
	Ordinance No. 21/2000 on the requirements for documentation and reporting during activities involving narcotic substances and their preparations	Ordinance No 4/2009 on the rules and procedures for the prescription and supply of medicinal products			
CYPRUS	The Narcotic Drugs and Psychotropic Substances Law 1977, incorporating amendments up to 1992.				
	The Narcotic Drugs and Psychotropic Substances Regulations 1979, incorporating amendments up to 1987.				
	The Narcotic Drugs and Psychotropic Substances (Amendment) Regulations of				

	1995 (P.I.79/95)				
	The Narcotic Drugs and Psychotropic Substances (Amendment) Law 91(I) of 2003				
	The Narcotic Drugs and Psychotropic Substances (Amendment) Decree of 1996 (P.I. 4/96)				
	The Narcotic Drugs and Psychotropic Substances (Amendment) Law 24(I) of 2010				
ESTONIA	Act on Narcotic Drugs and Psychotropic Substances and Precursors thereof (passed 11 June 1997, RT I 1997, 52, 834, entered into force 1 November 1997)	Medicinal Products Act (Passed 16 December 2004 (RT I 2005, 2, 4)Entry into force 1 March 2005)	Health Insurance Act		The Conditions and Procedure for the Import and Export, Carrying for Personal Use and Sending by Post of Goods Requiring Special Authorisation of the State Agency of Medicines, the Forms of Special Authorisations and the List of Goods Requiring Special Authorisation of the State Agency of Medicines (Passed with Regulation No. 31 on 18.02.2005, RTL 2005, 23, 316, Entered into force 01.03.2005)

	Conditions and Procedure for Handling of Narcotic Drugs and Psychotropic Substances for Medical and Research Purposes, and Conditions and Procedure for Maintaining Records and Reporting in that Area and Schedules of Narcotic Drugs and Psychotropic Substances (Regulation No. 73 of the Minister of Social Affairs of 18 May 2005 (RTL 2005, 57, 807),entered into force 5 July 2005)	The Conditions and Procedure for the Issue of Prescriptions for Medicinal Products and for the Dispensing of Medicinal Products by Pharmacies and the Format of Prescriptions (Approved by Regulation No. 30 of the Minister of Social Affairs of 18 February 2005 (RTL 2005, 23, 315), entered into force 01.03.2005)			
		Conditions and Procedure for Wholesale Distribution of Medicinal Products (Approved by Regulation No. 27 of the Minister of Social Affairs of 17 February 2005 (RTL2 2005, 22, 308), entered into force 01.03.2005)			
GREECE	**Act No. 3459/2006 on Legal Codes for Drugs**				
	Presidential Decree 148/2007 on the codification of the provisions stipulated in the regulatory decrees and ministerial orders regarding national legislation on				

	drugs				
	Ministerial Order No. A6b/6543/15-07-1988 on the definition of terms and conditions of the availability of substances provided for in article 4 of Act No. 1729/1987				
HUNGARY	Government Decree 162/2003. (X. 16.) On cultivation, distribution and use of plants suitable for the production of narcotic drugs	**Act XCV of 2005 on Medicinal Products for Human Use and on the Amendment of Other Laws Regulating the Pharmaceutical Market**	Act CLIV of 1997 on Health	**Joint Decree 42/2008 (XI. 14.) EüM-SZMM of the Minister of Health and the Minister for Social Affairs and Labour on the rules of treatment for narcotic drug dependence of other services attending to drug use and of prevention and counselling service**	
	Government Decree No. 66/2012 (2nd of April) on the activities that may be conducted with narcotic drugs, psychotropic substances and new psychoactive substances, and on the inclusion of such substances in schedules, and on the amendment of such schedules	**ESzCsM (Ministry of Health, Social and Family Affairs) Decree 44/2004 (IV. 28) on prescribing and dispensing medicinal products for human use.**			
	EüM (Ministry of Health) Decree 43/2005 (X.15.) on the system for physician's prescriptions, trading in pharmacies,				

	consumption, recording and storage at healthcare providers of medicinal products classified as controlled drugs				
LATVIA	National Law On Procedures for the Legal Trade of Narcotic and Psychotropic Substances and Medicinal Products (Including separate amendments 28/10/2010, 10/07/2008, 27/09/2007, 03/05/2007, 11/05/2006)	Cabinet of Ministers 23/03/2010 Regulations No 288 "Regulations Regarding Operating of Pharmacies"	Policy document Oncologic diseases control program for years 2009-2015	Programme for Limiting the Spread of Human Immunodeficiency Virus (HIV) for 2009–2013, approved by Decree of Cabinet of Ministers No 437 of 30/06/2009	
	Cabinet of Ministers 8/11/2005 Regulations No 847 "Regulations regarding Narcotic Substances, Psychotropic Substances and Precursors to be controlled in Latvia" (including separate amendments 12/05/2009 and 3/11/2009)	Cabinet of Ministers 26/06/2007 Regulations No 416 "Procedures regarding the Distribution and Quality Control of Medicinal Products" (including separate amendment on 27/07/2010).	Cabinet of Ministers 31/10/2006 Regulations No 899 "Procedures for the Reimbursement of Expenditures for the Acquisition of Medicinal Products and Medicinal Devices Intended for Out-patient Medical Treatment"	Cabinet of Ministers 24/09/2002 Regulations No 429 "Procedures for the Treatment of Patients Addicted to Alcohol, Narcotics, Psychotropic and Toxic Substances"	
	Cabinet of Ministers 17/06/2008 Regulations No 441 "Procedures for the Purchase, Receipt, Storage, Distribution, Dispensation, Accounting and Destruction of Narcotic and Psychotropic Substances and Medicinal Products in Manufacturing of Medicinal Products and Veterinary Medicinal Products, at Drug and Veterinary Drug Wholesalers and	Medical Treatment Law	**Cabinet of Ministers 19/12/2006 Regulations No 1046 "Procedures for organization and financing of health care"**		

	Pharmacies”				
	Cabinet of Ministers 13/08/1996 Regulations No 327 “Regulations on the Transit of Narcotic and Psychotropic Substances and Drugs” (including separate amendments 24/07/2007 and 04/08/1998)	Cabinet of Ministers 08/03/2005 Regulations No 175 ”Regulations for Manufacture and Storage of Prescription Forms, as well as Writing out and Storage Prescriptions” (Including separate amendment on 12/04/2011 of Regulations No 175)			
	Cabinet of Ministers 21/04/2008 Regulations No 293 “Procedures by which a Permit for the Utilisation of Plants, Substances and Medicinal Products Included in Schedules I, II or III of Narcotic Substances, Psychotropic Substances and Precursors Controlled in Latvia for Medical and Veterinary Medical Scientific Research, Specification of Physical and Chemical Properties or for Educational Purposes is Issued, Suspended and Revoked”	Cabinet of Ministers 27/03/2007 Regulations No 220 “Procedures for Acquisition, Storage, Use, Registration and Disposal of Medicinal Products in Medical Treatment Institutions and Social Care Institutions” (Including separate amendments on Regulations 220 on 08/04/2008, 10/03/2009, 31/08/2010 and 25/01/2011)			
LITHUANIA	**Republic of Lithuania Law on the Control of Narcotic and Psychotropic Substances**	**Order of the Minister of Health of the Republic of Lithuania No. 112 of 8 March 2002 “On Medical Prescriptions and Disbursement (Sale) of Medicines” (Published: Official Gazette *Valstybės Žinios*, 16/03/2002, No. 28, Publication No. 1013).**		**Order No. 204 of the Minister of Health of 3 May 2002 “On the Approval of Standards for Treatment and Rehabilitation of Dependency Diseases” (Official Gazette *Žin.*, 2002, No. 47–1824).**	

	Republic of Lithuania Law on the Control of Precursors of Narcotic Drugs and Psychotropic Substances			**Order No. V-653 of the Minister of Health of the Republic of Lithuania of 6 August 2007 "On the Approval of Procedure Descriptions for Assigning Substitution Treatment and its Application to Treat Opiate Dependency, and Prescription, Disbursement, Storage and Accounting of Substitution Opiate Medicinal Preparations in Personal Health Care Institutions"**	
	Government of the Republic of Lithuanian Resolution regarding the approval of regulations of issuing licenses to produce, import and export narcotic and psychotropic substances, and to engage in their wholesale and retail trade (*Last amended on 2011 July 22: No. 887, 13.07.2011, Zin. (Official Gazette), 2011, No. 93-4403 (21.07.2011))*				
	Republic of Lithuania Government Resolution No. 591 of 30 May 2005 "On the Approval of the Description of the Procedure for Monitoring the Use of Narcotic and Psychotropic Substances, Consequences thereof, the Circulation of the Precursors of Narcotic and Psychotropic				

	Substances”				
	Republic of Lithuania Government Resolution No. 221 of 9 March 2006 “On the Approval of the Regulations for the Licensing of Activities Involving the Precursors of Narcotic and Psychotropic Substances, Registration of the Place Thereof, Issuance of Import and Export Authorisations, and Control of such Activities”				
	Order No. 275 of the Minister of Health of the Republic of Lithuania of 24 May 2000 “On the Premises for Keeping Narcotic and Psychotropic Medicines and Medicinal Substances in Hospital Pharmacies“				
	Order of the Minister of Health of the Republic of Lithuania No. V-2 of 23 April 2003 “On Recommendations for Determining Small, Large and Very Large Amount of Narcotic and Psychotropic Substances” (Published: Official Gazette *Valstybės Žinios*, 30/04/200, No. 41, Publication No. 1899).				
	Order No. 342/482 of several institutions (Minister of Health				

	of the Republic of Lithuania and Minister of the Interior of the Republic of Lithuania) of 25 August 1998 "On the Approval of the Description of Special Requirements for Premises where Narcotic and/or Psychotropic Substances of Schedules II and III are Produced and Stored, their Wholesale and Retail Sale Takes Place" (Published: Official Gazette *Valstybės Žinios*, 02/09/1998, No. 77, Publication No. 2195; Official Gazette *Valstybės Žinios*, 16/10/2008, No. 119, Publication No. 4521).				
	Order No. 409 of the Minister of Health of the Republic of Lithuania of 25 July 2001 "On the Ensuring of Control of Import and Export of Narcotic and Psychotropic Medicines and Medicinal Substances" (Published: Official Gazette *Valstybės Žinios*, 01/08/2001, No. 66, Publication No. 2429; Official Gazette *Valstybės Žinios*, 14/07/2005, No. 85, Publication No. 3184).				
	Order No. V-138 of the Minister of Health of the Republic of Lithuania of 2 March 2007 "On the Approval of the Description of Procedure for Issuance of the				

	Certificate for Transportation of Narcotic and/or Psychotropic Substances for Personal Usage for Medical Purposes" (Published: Official Gazette *Valstybės Žinios*, 10/03/2007, No. 30, Publication No. 1109).				
	Order No. 294 of the Minister of Health of the Republic of Lithuania of 4 June 1998 "On the Procedure of Keeping Narcotic and Psychotropic Medicines and Medicinal Substances in Means of International Transportation" (Published: Official Gazette *Valstybės Žinios*, 19/06/1998, No. 56, Publication No. 1568).				
SERBIA	**Law on psychoactive controlled substances**	**Rulebook on the prescription and dispensing of medicines (FRY Official Gazette No. 16/94, 22/97, 52/02)**	**Rulebook on contents and scope of health care from compulsory health insurance and on participation for 2012**		The criminal code
		Rulebook on advertising of medicines and medical devices	Draft National Palliative Care Strategy		Law on criminal procedures

		Law on medicines and medical devices (Official Gazette no 30/10)	Action Plan for Palliative Care in the Republic of Serbia for the Period 2008-2015		
SLOVAKIA	**Act. N. 139/1998 on Narcotic Drugs, Psychotropic Substances and Preparations**	**Act. N. 140/1998 on medicinal products and medical devices, replaced by Act. N. 362/2011 on medicinal products and medical devices**[11]	**Regulation regarding standards for diagnosis and treatment**	**Vocational guidance No. M/0509/2003 on the standards for the diagnosis and treatment of drug dependencies**	
	Decree 158/2010 of 23 March 2010 of the Ministry of Health laying down formal requirements for the book of narcotic substances and keeping records of narcotic substances proving receipt and dispensing of narcotic and psychotropic substances	**Act. N. 147/2001 on Advertising of Medicinal Products**			
SLOVENIA	Order on the Promulgation of the Prevention of the Use of Illicit Drugs and Dealing with consumers of Illicit Drugs Act	**Rules on classifying, prescribing and dispensing medicinal products for human use**	Law on Health Care and Health Insurance		The constitution of the Republic of Slovenia
	Production of and Trade in Illicit Drugs Act		Act(s) Amending the Health Care and Health Insurance Act		

[11] Although Act. N. 140/1998 has been replaced by Act. N. 362/2011, no important changes have been made to the parts that were indicated as relevant by the national counterpart. Therefore, Act. N. 140/1998 has been (partly) reviewed.

	Decree on the Scheduling of Illicit Drugs		**General agreement 2010**		
	Rules Governing the Procedures for the Issue of Licences for Illicit Drugs Marketing		**Resolution on National plan of health care 2008-2013**		
	Rules on Method And Form of Record-keeping and of Reports on Illicit Drugs				
	Rules on Technical And Sanitary Conditions And on the Method of Insurance of Premices for Storage and Dispensing of Illicit Drugs from Groups I and II				
TURKEY	**Law No.2313 (12/06/1933) on Supervision of Narcotic Drug**	Pharmaceuticals Track&Trace System		**Regulation No. 25375 on Substance Abuse Treatment Centres (16/03/2004)**	**Law No.984 (12/03/1927) on stores where toxic and effective chemical substances used in pharmaceutical businesses and in vocational & agriculture businesses are sold**
	Circular No.5725 (26/01/1984) on submitting consumables of controlled substances and pharmaceutical preparations	**Law No.1262 (26/05/1928) on the Pharmaceuticals and Medicinal products**			
	Circular No.5768 (29/05/1985) on the prescription of narcotics, controlled drugs and				

	preparations				
	Circular No.09/2677 (02/01/1986)				

Annex 2: Feedback form ATOME legislation review

Feedback document: ATOME legislation review country report, country X Date
Is the reviewed legislation (paragraph 6.1) still valid? If not, please specify….
Are the translations correct? This is even more important for the translation of provisions that are identified as potential barriers in the category 'language'. Please specify….
Are there any doubts or disagreements regarding the identification of potential barriers? Please specify….
Are there potential legal or regulatory barriers missing? Please specify…
Are there any doubts or disagreements regarding the proposed recommendations? Please specify…
Are there any recommendations missing that should be added? Please specify…
Are there any other questions, comments or concerns we should take into account? Please specify…