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HUMAN RIGHTS WATCH

HRW.org

WHO Expert Committee on Drug Dependence
WHO Headquarters
Geneva, Switzerland

To whom it may concern:

I am pleased to make this submission to the WHO Expert Committee on Drug Dependence on behalf of Human Rights Watch to provide our perspective on the critical review of the opioid analgesic tramadol which will take place at the committee's 41st meeting on November 12-16, 2018.

Human Rights Watch is an international nongovernmental organization which advocates on behalf of victims of human rights abuses worldwide. Our Health and Human Rights division has worked extensively on international drug policy issues, including the availability of controlled substances for medical and scientific use. We have documented how regulatory barriers and fears around prescribing of controlled substances impede access to controlled medicines for patients with legitimate medical needs in a dozen countries and have advocated, both internationally and at the national level, for balanced reforms to regulations, policies and practices around controlled medicines.

Our research has made us acutely aware of the importance of tramadol in palliative care in many regions of the world. While we have generally focused on identifying barriers to morphine availability and accessibility, we have seen in country after country that patients often have no choice but to rely on tramadol for pain relief because morphine is not available. Because tramadol is not a controlled substance many more doctors are authorized to prescribe it and many more hospitals and pharmacies stock it. Indeed, for many patients, tramadol is the only opioid pain medicine available. Without it, they would often be left with acetaminophens or non-steroidal anti-inflammatory medicines, which are appropriate only for mild pain, to control severe pain from cancer or other conditions.

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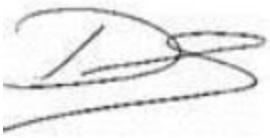
We believe that in weighing the public health risks posed by non-medical use of tramadol versus the clinical importance of the medicine the Committee should take into consideration international human rights principles that provide guidance on when measures that interfere with the enjoyment of the right to health, such as scheduling a

substance with important medical uses, are acceptable. As we outline below, we believe that a decision to schedule tramadol as an internationally controlled substance would be a restriction that is inconsistent with the right to health because of the availability of other, less far reaching, measures that are potentially effective, serious questions about the effectiveness of international scheduling, and the disproportionate impact international scheduling would likely have on patients with legitimate medical needs for opioid analgesics.

We therefore urge the Committee to recommend against international scheduling of tramadol.

Yours sincerely,



Diederik Lohman
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International Scheduling of Tramadol and the Right to Health

Human Rights Watch has prepared this memo in advance of the WHO Expert Committee on Drug Dependence's critical review of tramadol at its 41st meeting on November 12-16 in Geneva. This memo is based on ten years of research and advocacy on the availability of morphine and other opioid analgesics for palliative care and an extensive review of the available literature on non-medical use of tramadol, including WHO's 2014 and 2017 reports on tramadol, INCB's Annual Report for 2012 to 2017, UNODC's World Drug Report for that same period, publications in scientific journals, and reports in the news media covering several years.

International Scheduling of Substances and the Right to Health

Article 12 of the International Covenant on Economic Social and Cultural Rights (ICESCR), ratified by 169 countries, guarantees a right to the "enjoyment of the highest attainable standard of physical and mental health."[1] The Committee on Economic, Social and Cultural Rights (CESCR), the UN body charged with monitoring compliance with ICESCR, has further stipulated that this right requires states to "refrain from interfering directly or indirectly with the enjoyment of the right to health," which includes interfering with existing health services.[2]

This obligation, however, is not absolute. There are many situations where states will be justified to—or may be required to—take steps that interfere with the provision of health services. They may, for example, impose regulations to safeguard or improve the quality of health services or protect patients; ban medications that are shown to pose significant threats to public health; or strip a healthcare provider of its license if it provides inappropriate, substandard or unsafe care. Any interference with existing health services, however, must meet

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1 International Covenant on Economic, Social and Cultural Rights (ICESCR), adopted December 16, 1966, G.A. Res. 2200A (XXI), 21 U.N. GAOR Supp. (No. 16) at 49, U.N. Doc. A/6316 (1966), 993 U.N.T.S. 3, entered into force January 3, 1976, art. 11; also in the Convention on the Rights of the Child (CRC), G.A. res. 44/25, annex, 44 U.N. GAOR Supp. (No. 49) at 167, U.N. Doc. A/44/49 (1989), entered into force September 2, 1990, art. 12.

2 UN Committee on Economic, Social and Cultural Rights, "Substantive Issues Arising in the Implementation of the International Covenant on Economic, Social and Cultural Rights," General Comment No. 14, The Right to the Highest Attainable Standard of Health, E/C.12/2000/4 (2000), http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/40d009901358b0e2c1256915005090be?Opendocument (accessed May 11, 2006), para. 43.

certain criteria to be consistent with international human rights law: it must pursue a *legitimate goal*, and *be potentially effective*, *based in law*, and be *proportionate* to the legitimate goal.[3]

Listing a substance that is used in medical products in a schedule of the international drug conventions (or of a national drug law) per definition constitutes an interference with existing health services. Scheduling imposes restrictions on the production, import and export, storage, prescribing and dispensing of any medicines containing that substance.[4] These restrictions affect the availability, accessibility, acceptability and affordability of these medicines. A large body of research suggests that national and international scheduling leads to reduced availability and accessibility, may negatively affect the medicine's acceptability, and may drive up their cost.[5]

Legitimate goal requirement: Reducing the harms associated with non-medical use of a substance is a legitimate state objective. Indeed, states have an obligation under international human rights law to take effective steps to protect the people in their jurisdiction from threats to public health and human rights.

Legality requirement: Scheduling a substance sets a new normative standard that creates the legal basis for subsequent changes to the regulations governing the production, sale, transportation, prescribing and use of the substance and any

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3 Ibid., para. 33.

4 See Article 2 of the 1961 Single Convention on Narcotic Drugs.

5 N. I. Cherny, J. Cleary, W. Scholten, L. Radbruch, J. Torode; The Global Opioid Policy Initiative (GOPI) project to evaluate the availability and accessibility of opioids for the management of cancer pain in Africa, Asia, Latin America and the Caribbean, and the Middle East: introduction and methodology, Annals of Oncology, Volume 24, Issue suppl_11, 1 December 2013, Pages xi7–xi13, https://doi.org/10.1093/annonc/mdt498; WHO, "Ensuring balance in national policies on controlled substances: guidance for availability and accessibility of controlled medicines (2011); De Lima L, Opioid Medications in Expensive Formulations Are Sold at a Lower Price than Immediate-Release Morphine in Countries throughout the World: Third Phase of Opioid Price Watch Cross-Sectional Study, Journal of Palliative Medicine, October 2018; Human Rights Watch, Guatemala, Punishing the Patient https://www.hrw.org/report/2017/05/17/punishing-patient/ensuring-access-pain-treatment-guatemala; Human Rights Watch, Ukraine, Uncontrolled Pain, https://www.hrw.org/report/2011/05/12/uncontrolled-pain/ukraines-obligation-ensure-evidence-based-palliative-care; Human Rights Watch, Mexico, Care When There Is No Cure, https://www.hrw.org/report/2014/10/28/care-when-there-no-cure/ensuring-right-palliative-care-mexico; Human Rights Watch, India, Unbearable Pain, https://www.hrw.org/report/2009/10/28/unbearable-pain/indias-obligation-ensure-palliative-care; Human Rights Watch, Senegal, Abandoned in Agony, https://www.hrw.org/report/2013/10/24/abandoned-agony/cancer-and-struggle-pain-treatment-senegal

products containing it.[6] If proper procedure is followed to schedule the substance, this requirement will be met.

Effectiveness requirement: A state must be able to make a compelling argument that scheduling is a potentially effective measure to achieve the legitimate goal for this requirement to be met.

Proportionality requirement: The principle of proportionality holds that when a state puts in place measures that interfere with the enjoyment of the right to health, it must use the least burdensome or invasive measure to achieve the goal. Further, it must ensure an appropriate balance between the different interests at stake: Reducing public health harms due to non-medical use of the substance and ensuring that patients with a legitimate need for medicines containing that substance have adequate access to them.

Application of these Criteria to the Scheduling of Tramadol

Tramadol is an opioid medication that is commonly used to treat moderate to severe pain.[7] It is not currently listed in any schedules of the international drug conventions although some countries have placed it under national control. In most jurisdictions, tramadol is available on a doctor's prescription and available in most pharmacies. Although physicians largely consider tramadol inferior to morphine, the very limited availability of that medication, which is an internationally controlled substance, in many countries frequently means tramadol is the only opioid analgesic for moderate pain accessible to patients who need opioid analgesics for their care.[8] The medication thus plays a significant role in healthcare.

There are, however, also numerous reports from various countries, particularly in the Middle East and West Africa, about non-medical use of tramadol.[9] Egypt reports large numbers of patient

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6 See Article 3 of the 1961 Single Convention on Narcotic Drugs.

7 WHO, Tramadol. Pre-Review Report, 2017.

8 Tramadol is not included in the WHO Model List of Essential Medicines, whereas morphine is.

9 WHO, Tramadol – Pre-review report, 2017; WHO, Update review report, 2014; Nazarzadeh M, The association between tramadol hydrochloride misuse and other substances use in an adolescent population, Addictive Behavior (2013); Mohamed N, An epidemiological study of tramadol HCI dependence in an outpatient addiction clinic at Heliopolis Psychiatric Hospital, Menoufia Medical Journal (2014); Alblooshi H, The pattern of substance use disorder in the United Arab Emirates in 2015: results of a national rehabilitation centre cohort study, Substance Abuse Treatment, Prevention and Policy (2016); Conference room paper submitted by the Arab Republic of Egypt on

admissions due to tramadol dependence.[10] A Lancet article quotes various Togolese men saying they use tramadol to gain strength.[11] Numerous articles have appeared in the Ghanaian press discussing non-medical use of tramadol which is considered a public health threat.[12]

The reason the government of Egypt and others propose international scheduling of tramadol is to counteract the non-medical use of tramadol and the associated public health risks—clearly a legitimate objective. The legality requirement is similarly unlikely to pose problems as the process for international scheduling set out in the 1961 Single Convention on Narcotic Drugs is currently being followed—the critical review of the substance by the WHO Expert Committee on Drug Dependence is an integral part of that process.

There are, however, significant questions as to whether international (or national) scheduling of tramadol meets the effectiveness requirement. UN publications, scientific literature and news media include primarily two scenarios in which non-medical use of tramadol occurs:

- **Tramadol is sold over-the-counter in pharmacies to any customer able to pay.** It appears that in some countries tramadol is categorized under national pharmaceutical regulation as a prescription medication[13]—and should thus only be sold to individuals with a legitimate medical prescription—but that pharmacy staff routinely

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strengthening international cooperation in addressing the non-medical use and abuse, the illicit manufacture and the illicit domestic and international distribution of tramadol (2017); Salm-Reifferschiedt, Tramadol: Africa's opioid crisis, Lancet (2018); Progler Y, Drug addiction in Gaza and the illicit trafficking of tramadol, Journal of Research in Medical Sciences (2010); Fawzi, Some medicolegal aspects concerning tramadol abuse: The new Middle East youth plague 2010. An Egyptian overview, ScienceDirect (2011); International Narcotics Board, Annual Reports 2012 – 2017, https://www.incb.org/incb/en/publications/annual-reports/annual-report.html

10 WHO, Tramadol – Pre-review report, 2017

11 Salm-Reifferschiedt, Tramadol: Africa's opioid crisis, Lancet (2018)

12 Investigations into the extent of use and abuse of Tramadol in the Ashanti Region, Food and Drug Administration, Ghana (2003), available via: https://fdaghana.gov.gh/index.php/investigations-into-the-extent-of-use-and-abuse-of-tramadol-in-the-ashanti-region/; War on Tramadol Abuse Takes New Turn Altogether, Modern Ghana (2014), available via: https://www.modernghana.com/news/875663/war-on-tramadol-abuse-takes-new-turn-altogether.html; Accra Prostitutes Reveal Why They Take Tramadol, Ghana Web (2018), available via: https://www.ghanaweb.com/GhanaHomePage/regional/Accra-prostitutes-reveal-why-they-take-Tramadol-655708; Ghana Alarmed by Tramadol Abuse by Young People, Africa Feeds (2018), available via: https://africafeeds.com/2018/05/03/ghana-alarmed-by-tramadol-abuse-by-young-people/; Ghana: High Dose Tramadol Floods Market, All Africa (2017), available via: https://allafrica.com/stories/201709250546.html

13 WHO, Tramadol. Pre-Review Report, 2017.

ignore that requirement and that national authorities fail to enforce that requirement adequately.[14] It is possible that some countries do not categorize tramadol as a prescription medicine, but we found no examples of that in the literature.

- **An unauthorized product labeled as tramadol is sold on the street.** This appears to be by far the most common scenario. INCB, UNODC and the World Customs Organization all report regular seizures of large amounts of a product that is labeled as tramadol but is not, in fact, a licensed pharmaceutical product.[15] In Ghana, for example, the product sold on street markets as tramadol has a strength that is not actually registered as a medical product in the country.

Many publications fail to clearly differentiate between these scenarios and leave it unclear whether the substance being misused is the pharmaceutical product tramadol or the falsified medical product labeled as tramadol. This sometimes makes it difficult to determine whether specific incidents involve diversion of the medical product tramadol from licit supply channels or smuggling and sale of an unauthorized product that is presented as a medicine. It is surprising—indeed disturbing—that UN agencies such as INCB and UNODC seem to make little or no effort to differentiate between these scenarios, even though their policy implications are vastly different.

In the first scenario, international or national scheduling is potentially effective at preventing non-medical use of the pharmaceutical product because it would impose stringent additional requirements for dispensing the medication and make pharmacists liable to often harsh criminal penalties for inappropriately dispensing the medication. However, as discussed in more detail below, governments have alternative measures at their disposal that can be effective and have much less far-reaching consequences for patients who need the medication.

In the second scenario, these unauthorized products presented as tramadol meet the WHO definition of a falsified medical product:

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[14] Human Rights Watch research found this to be the case in Russia and Ukraine before these countries scheduled tramadol as a controlled substance.

[15] See INCB Annual Reports for 2012-2017; UNODC, World Drug Report 2018: opioid crisis, prescription drug abuse expands; cocaine and opium hit record highs, https://www.unodc.org/doc/wdr2018/WDR_2018_Press_ReleaseENG.PDF; World Customs Organization, Illicit Trade 2015, https://illicittrade.com/reports/downloads/OMD_ITR_Complete_LR_2016_12_04.pdf

> Unregistered/unlicensed: Medical products that have not undergone evaluation and/or approval by the National or Regional Regulatory Authority (NRRA) for the market in which they are marketed/distributed or used, subject to permitted conditions under national or regional regulation and legislation.
>
> Falsified: Medical products that deliberately/fraudulently misrepresent their identity, composition or source.[16]

These falsified medicines appear to originate from India and China and are smuggled into destination countries.[17] Little is known about the production process.

Production and sale of falsified medical products is prohibited—or should be—in every country in the world, as these substances pose a significant threat to public health.[18] The 2006 Declaration of Rome, adopted at the WHO International Conference on Combating Counterfeit Medicines, calls counterfeiting medicines a "vile and serious criminal offense that puts human lives at risk and undermines credibility of health systems" and calls for countries to combat and punish the practice accordingly.[19] Interpol considers pharmaceutical crime a "major issue."[20] Under the right to health, state parties have an obligation to ensure that health goods and services are of "good quality," which includes "scientifically approved drugs."[21]

Thus, individual countries as well as the international community more broadly have—or should have—have adequate legal tools available to respond to the manufacture, trafficking and distribution of falsified tramadol. National customs officers already have the authority to stop these products from entering the country; law enforcement officers in consumer countries

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16 WHO Member State Mechanism on Substandard/Spurious/Falsely Labelled/Falsified/Counterfeit (SSFFC) Medical Products Working Definitions, World Health Organization, (2017). Available via: http://www.who.int/medicines/regulation/ssffc/A70_23-en1.pdf?ua=1

17 WHO, Tramadol: Pre-Review Report, 2017, p. 27

18 International Medical Products Anti-Counterfeiting Taskforce Handbook (2006 – 2010). Available via: http://apps.who.int/medicinedocs/documents/s20967en/s20967en.pdf

19 Declaration of Rome, "Conclusions and Recommendations of the WHO International Conference on Combating Counterfeit Medicines," 18 February 2006, http://www.who.int/medicines/services/counterfeit/RomeDeclaration.pdf?ua=1

20 Pharmaceutical Crime and Organized Criminal Groups: An analysis of the involvement of organized criminal groups in pharmaceutical crime since 2008, INTERPOL (2014). Available via: https://www.interpol.int/Crime-areas/Pharmaceutical-crime/Pharmaceutical-crime

21 UN Committee on Economic, Social and Cultural Rights, "Substantive Issues Arising in the Implementation of the International Covenant on Economic, Social and Cultural Rights," General Comment No. 14, The Right to the Highest Attainable Standard of Health

already have the authority to counter their distribution and sale to customers; and law enforcement officers in producer can shut down manufacturing of these products. Interpol is already coordinating operations in the field to disrupt transnational criminal networks involved in trafficking of falsified medical products and offer trainings to build "the skills and knowledge of all those agencies involved in the fight against pharmaceutical crime",[22] although some authors argue that the lack of a stronger international legal framework on this issue seriously hampers the ability of the international community to act against producers and traffickers of falsified medicines.[23]

As the production, trafficking, distribution and sale of falsified tramadol is already banned by law, the primary problem appears to be inadequate enforcement of existing laws and regulations on falsified medicines, rather than the absence of legal tools to act. Thus, it is very doubtful that international scheduling, which creates additional legal tools, has the potential to be effective at preventing the smuggle and distribution into countries of a product that already is illegal.

It is conceivable that international scheduling would allow governments to impose more stringent penalties on traffickers than those stipulated penalties for falsified medical products or allows for better international legal cooperation. However, changing criminal penalties for manufacturing, trafficking or sale of falsified medical products does not require international scheduling; these issues can be resolved through national legislative processes.

The situation in countries that have already placed tramadol on national schedules suggests that this measure has limited effect on non-medical use. In Egypt, for example, national scheduling does not appear to have significantly reduced the availability of falsified tramadol on the streets, even as doctors report that the legally produced and registered medication tramadol has become increasingly difficult to obtain, even upon presentation of a medical prescription, and the medication has become stigmatized.[24]

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22 Pharmaceutical Crime and Organized Criminal Groups: An analysis of the involvement of organized criminal groups in pharmaceutical crime since 2008, INTERPOL (2014). Available via: https://www.interpol.int/Crime-areas/Pharmaceutical-crime/Pharmaceutical-crime

23 Attaran et al, How to achieve international action on falsified and substandard medicines, British Medical Journal (2012).

24 Alsirafy S.A. The fear of using tramadol for pain control (tramadolophobia) among Egyptian patients with cancer. Journal of Opioid Management 2015.

(In fact, there are significant questions about the effectiveness of both international and national scheduling of a substance as a tool to protect society from the public health risks posed by that substance. Heroin, cocaine and cannabis have all been scheduled substances for decades, yet are more widely available and cheaper in many countries today than ever, despite investments of hundreds of billions of dollars in supply control and drug enforcement budgets.)

It is also hard to see how international scheduling meets the proportionality requirement. As noted above, a large body of literature exists that describes the impact of international scheduling on the availability, accessibility and affordability of medicines. Indeed, one of the reasons why tramadol is such an important medicine is that the availability of morphine is very limited in many countries as a result of its status as a scheduled medicine. Scheduling tramadol internationally is highly likely to result in significant harmful effects for patients with moderate to severe pain who need opioid analgesics for pain relief.

In the case of the over-the-counter sales of the legitimate pharmaceutical product tramadol, countries have other, far less invasive options to prevent non-medical use of the medication. If tramadol is not categorized under national pharmaceutical law as a prescription-only medicine, countries can easily change that. If tramadol is considered a prescription-only medicine but is de facto sold over-the-counter, countries could make greater effort to enforce existing regulations.

In the case of falsified tramadol, countries and the international community should enforce existing law on falsified medical products or strengthen them. Enforcement of these laws would not have the same negative impacts as scheduling on patient access to licitly prescribed tramadol and would, in fact, protect people from the risks of using unauthorized products of unknown quality.

In conclusion, we believe that international scheduling of tramadol would be inconsistent with the right to the highest attainable standard of physical and mental health.