Implications of international law for the treatment of cancer: The Single Convention on Narcotic Drugs and the TRIPS Agreement

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S U M M A R Y
The development, manufacture, trade and distribution of medicines all take place within a web of international legal obligations that states have accepted under a range of multilateral, plurilateral and bilateral agreements. International law can operate either to facilitate or hinder access, depending on how it is developed and implemented. This article examines two areas of international law that are relevant to cancer treatment: the international drug control system, which regulates opioid analgesics; and the World Trade Organization’s Trade-Related Aspects of Intellectual Property Agreement. This article outlines recent developments in relation to both, including in the activities of the Vienna-based agencies that collectively oversee the implementation of the Single Convention on Narcotic Drugs, and in the negotiation of the recent United Nations General Assembly Political Declaration on Non-communicable Diseases. While underlining the importance of law, this article notes that battles over law should not distract from the importance of other essential efforts to enhance access to medicines within the context of the strengthening of health systems.

Access to medicines and international law
Equitable access to essential medicines of assured quality, safety, efficacy and cost-effectiveness is a core component of well-functioning health systems. While ultimately it is a national-level activity that provides or fails to provide medicines to those who need them, the development, manufacture, trade and distribution of medicines all take place within a web of international legal obligations that states have accepted under a range of multilateral, plurilateral and bilateral agreements.

In a globalized world, international agreements are essential to ensuring access to safe and effective medicines. However, international law can operate to facilitate or hinder access, depending on how it is developed and implemented. Relevant factors include the priorities, practices and resources of the public institutions established to facilitate and oversee its implementation both internationally and domestically; and the behavior of corporations, civil society organizations and individual citizens pursuing their often competing interests within (and sometimes outside of) the international legal framework.

If progress is to be made globally in the treatment of cancer, the ways in which international law impacts, both in legal terms and empirically, on access to medicines will need to be appreciated. This article, part of a symposium on legal issues relating to cancer prevention and treatment, focuses on two relevant areas of international law: the international
drug control system, and patent protection under the World Trade Organization’s Trade-Related Aspects of Intellectual Property (TRIPS) Agreement. This article addresses legal rather than empirical issues, and seeks to underline the importance of international law, while not overstating what international law alone can do to enhance the availability of medicines.

**International drug control law and access to opioid analgesics**

*The regulation of opioid analgesics as narcotic drugs*

Approximately 5 billion people live in countries with low or no access to opioid analgesics, which are indispensable for the effective treatment of pain. Each year, tens of millions of people suffer pain without adequate treatment, including 5.5 million patients with terminal cancer and 1 million patients with end-stage human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). The global inequalities in access to opioid analgesics are stark. In 2009, more than 90% of the global consumption of the opioid analgesics morphine, fentanyl and oxycodone occurred in Australia, Canada, New Zealand, the USA and several European countries. Over 80% of the world’s population will have insufficient analgesia, or no analgesia at all, if they suffer moderate to severe pain.

Opioid analgesics are regulated internationally under the United Nations (UN) Single Convention on Narcotic Drugs 1961, as amended by its 1972 Protocol. While the Single Convention recognizes that ‘the medical use of narcotic drugs continues to be indispensable for the relief of pain and suffering and that adequate provision must be made to ensure the availability of narcotic drugs for such purposes’, it is concerned not only with ensuring their availability, but also with preventing their diversion and abuse.

The Convention thus seeks to strike a balance between ensuring availability and preventing diversion and abuse in pursuit of its ultimate concern, ‘the health and welfare of mankind’. In the words of the International Narcotics Control Board (INCB), the ‘independent and quasi-judicial monitoring body for the implementation of the United Nations international drug control conventions’, the ‘primary objective’ of the Single Convention (and the 1971 Convention on Psychotropic Substances) is ‘to ensure the availability of controlled drugs for medical and scientific purposes and to prevent the non-medical use of those drugs’.

The Single Convention establishes a regulatory system for narcotic drugs. Under this system, government authorization is required for participation in the trade and distribution of narcotics: each state must provide to the INCB each year an estimate of its need for narcotic drugs for medical and scientific purposes, and statistical returns covering production, manufacture and consumption, and quarterly statistical returns covering import and export; export and import licences are required for each international transaction; those who trade or distribute narcotic drugs must hold licences and keep detailed records; and medical prescriptions are required for dispensation of narcotic drugs to patients.

International law thus requires the implementation of a set of control measures by states. However, in their domestic laws and policies, many states have adopted measures that exceed those required by the Convention. A survey conducted by the INCB revealed that unduly restrictive laws and burdensome regulations were commonly perceived as playing a significant role in limiting the availability of opioids. Other identified impediments to availability included addiction-related concerns among healthcare professionals and patients, reluctance to prescribe or stock opioids, insufficient training for healthcare professionals, difficulties involving distribution and supply, and cost.

Examples of laws and policies that exceed the Convention’s minimum requirements include: the limiting of prescription authority to medical professionals who qualify for specific licences; special prescription procedures for opioids (e.g. the use of specific prescription forms and/or a requirement that multiple copies of the prescription be maintained); a requirement that prescriptions be approved by a healthcare worker’s colleagues or superiors, and/or that dispensing be witnessed by multiple healthcare workers; a requirement that patients receive special permission or registration to render them eligible to receive opioid prescriptions; unreasonable limitations on the number of days’ supply that may be provided in a single prescription; unreasonable limitations on maximal daily doses that may be prescribed; arbitrary restrictions on the number of pharmacies permitted to dispense opioid medications; unreasonable requirements relating to the storage of opioid medications; and overly burdensome bureaucratic procedures that dissuade healthcare institutions from using opioids.

In addition, a range of factors can combine to create fear among healthcare workers that prescribing opioids may make them liable to legal sanction, including: ambiguity in regulations; poor communication by drug regulators to healthcare workers about the rules for handling opioids; the availability of harsh sanctions; and, in some countries, prosecutions of healthcare workers for unintentional mishandling of opioids.

While the Convention recognizes the indispensability of opioid analgesics, it has been argued that the primary organs of the international legal regime that give effect to the Convention – the UN Commission on Narcotic Drugs (CND), the INCB and the UN Office on Drugs and Crime (UNODC) – have historically focused more on preventing misuse than on ensuring availability. These agencies exercise significant influence over domestic policy making and enforcement activities in many ways, including development and reinforcement of normative understandings of international obligations, and the way in which they set priorities across technical assistance activities and budgetary allocations generally.

**Recent progress at international level to enhance the availability of opioids**

In March 2010, the CND – the UN’s drug-policy making organ which oversees the UNODC’s drug-related work – adopted an important resolution re-affirming the need for a balanced approach in the international drug control system and its national implementation. The Commission noted its
concern that access to opioid-based medications is ‘non-existent or almost non-existent in many countries and regions’. It made a number of requests of INCB, UNODC and states, including the following:

• it requested the UNODC ‘to continue its efforts to ensure the adequate availability of internationally controlled drugs for medical and scientific purposes, cooperating, as appropriate, through the Access to Controlled Medications Programme of the World Health Organization, while continuing its activities to prevent diversion and abuse’;
• it invited Member States to ensure that the INCB and UNODC are funded adequately to support their activities to ensure adequate availability of narcotic drugs and psychotropic substances for medical and scientific purposes; and
• it invited Member States to consider ways to leverage existing health and development programmes in countries without adequate availability of narcotic drugs and psychotropic substances for medical and scientific purposes, including by building the capacity of those countries through training.

The resolution was important not only in the requests it made, but also in the language it used.15 The request to UNODC ‘to continue its efforts to ensure the adequate availability … while continuing its activities to prevent diversion and abuse’ differed, in a significant way, from the wording in the first draft of the resolution: ‘Requests UNODC to continue its activities to prevent abuse and diversion while also seeking to ensure access to medications covered under the conventions … ’. A similar difference can be observed in the CND’s encouragement of Member States ‘to consider working with’ INCB and UNODC ‘to update policies and legislative frameworks, as appropriate, to ensure adequate availability of internationally controlled substances and to prevent the diversion and abuse of those substances’. The draft encouraged Member States ‘to update policies and legislative frameworks to prevent diversion and abuse while ensuring availability of internationally controlled licit drugs, in line with the treaties’.

The CND resolution has led to a range of noteworthy activities within both the INCB and UNODC. In response to the CND’s invitation to include, in its 2010 Annual Report, information on the consumption of narcotic drugs (and psychotropic substances) worldwide, including an analysis of impediments to availability and actions to be taken to overcome these impediments, the INCB published a special supplement.4

Employing strong language, the INCB observed that ‘[i]t appears that a number of countries have not yet recognized that adequate availability of medicines, including narcotic drugs and psychotropic substances, is an essential part of their responsibility toward their populations’. Some countries showed ‘negligence’ to their populations by not even estimating requirements, and appearing to have no knowledge of the quantities of drugs needed by their populations for medical treatment. In other countries, other obstacles continued to prevail, including outdated restrictive regulations, uninformed interpretations of regulations, and misguided fears and ingrained prejudices about the use of opioids for medical purposes. The INCB made detailed recommendations to governments relating to availability, appropriate use, national control systems, and prevention of diversion and abuse.

The UNODC held an informal technical consultation on access to controlled medications for the treatment of pain in January 2011, and produced a report for the March 2011 session of CND.11 The report acknowledged that UNODC has long worked pro-actively to assist states to implement the diversion and abuse aspects of their obligations under the Conventions. While this would remain an essential element of its work, UNODC would ‘focus equally on all elements necessary to guarantee availability and accessibility with particular attention to avoiding any control measures unintentionallyimpeding high quality medical treatment’. The report included recommendations for actions that can be taken to enhance access to opioid analgesics and prevent diversion and abuse, and a commitment from UNODC to review its model laws to ensure that they fully reflect the Convention obligations concerning ensuring availability and preventing diversion and abuse, and make any necessary revisions.

This momentum continued with a follow-up resolution of the CND in March 2011, which underlined the importance of continuing efforts to improve availability in general, and the particular need for appropriate laws and regulations.16 The CND requested UNODC, in consultation with INCB and the World Health Organization (WHO), to review and, where necessary, update its model laws to ensure that they reflect an appropriate balance between ensuring adequate access to internationally controlled drugs and preventing their diversion and abuse. WHO remains active in this domain, recently releasing updated guidelines entitled ‘Ensuring balance in national policies on controlled substances’.10

For all of this activity to mean anything tangible, it must lead to changes on the ground – the improvement of laws and regulations and, ultimately, to more people receiving treatment for cancer pain (and for pain related to other conditions). Over the last 2 years, the international drug control system – as represented by the Vienna-based agencies that exercise key roles within that system – has become increasingly engaged in efforts to make this happen.

The TRIPS Agreement and access to medicines

The TRIPS Agreement, the Doha Declaration, and the different politics and economics of infectious and non-communicable diseases

The majority of critical cancer medicines are off-patent and can be manufactured and sold at relatively low prices.17,18 Expanding access to inexpensive but effective off-patent cancer medicines is one of the keys to improving outcomes for cancer patients, particularly in low-resource countries.17–19 However, at the same time, newer, more expensive cancer therapies are being developed and brought to market. Some offer only incremental improvements in survival, but some can have dramatic life-saving or life-extending results. For example, in the case of HER2-positive breast cancer, access to on-patent medicines as part of treatment provided after
surgery has been shown to dramatically reduce the risk of disease recurrence and death by nearly 50%.20,21 The current breast cancer treatment guidelines developed by the Breast Health Global Initiative include recommendations for use of both off-patent drugs and newer targeted therapies as part of multidisciplinary approaches to treatment that are appropriate for varying levels of resources.20 Thus, although most effective cancer drugs are off-patent, the implications of international patent law on cancer treatment remain important, and may become increasingly so in the coming years.

The rationale for providing patent protection is that information is a public good, meaning that it is impossible to exclude anyone from consuming it once it is produced. The consequence of this ‘non-excludability’ is that the market offers a suboptimal incentive for the production of information. Patents, and other intellectual property rights, ‘grant legal excludability to information’ to remove the disincentive to produce it.22 Incentivizing the production of information is particularly important in the case of pharmaceutical products, with successful drug discovery and development often being a complex, lengthy and costly activity,23 and the costs of unsuccessful research and development also needing to be considered.24,25 Patent protection incentivizes drug development by guaranteeing monopoly rents for a certain period of time. These rents are reflected in the price of the final product, acting as a barrier to affordability.22

Providing sufficient research and development incentives through intellectual property protection in order to ensure that new and improved medicines are developed and brought to market, while not overprotecting intellectual property rights in a way that leads to their unjustifiable unaffordability, is a difficult exercise. The optimal balance varies with the individual product (what its function is, how it compares with other available products, the size of its market), across countries (size of the population, disease burden, wealth) and over time. International patent law provides a framework — legal, institutional and normative — in which laws and policies are implemented domestically, but cannot prescribe optimal outcomes for particular products in particular countries at particular points in time.

The relationship between patent protection and access to medicines has long been the subject of fierce global contestation, focused, until more recently, most prominently on the relationship between the TRIPS Agreement2 and access to medicines for the treatment of infectious diseases, primarily HIV/AIDS. The TRIPS Agreement, concluded in 1994 as part of the package of World Trade Organization (WTO) Agreements, introduced global minimum standards for intellectual property protection. These standards have been raised over the last decade through the conclusion of bilateral and plurilateral agreements that include so-called ‘TRIPS-plus’ provisions,22,25 meaning that the TRIPS Agreement is now only one piece of the puzzle of international patent law. However, as the one truly multilateral instrument and the locus of significant recent international controversy, it is the focus of this section.

In November 2001, the WTO Ministerial Conference adopted the Doha Declaration on the TRIPS Agreement and Public Health (Doha Declaration).26 The Doha Declaration was negotiated and adopted in the context of enormous concern about the likely impact of the TRIPS Agreement on the supply of generic pharmaceutical products, particularly those manufactured in India, and the potentially disastrous consequences for developing and least developed countries already reeling from the burden of catastrophic health problems, of which HIV/AIDS was the most prominent.27 It commenced with a recognition of the ‘gravity of the public health problems afflicting many developing and least developed countries, especially those resulting from HIV/AIDS, tuberculosis, malaria and other epidemics’.26 It stressed the need for the TRIPS Agreement ‘to be part of the wider national and international action to address these problems’, and recognized that ‘intellectual property protection is important for the development of new medicines’ and the existence of ‘concerns about its effects on prices’.

The Doha Declaration affirmed that the TRIPS Agreement ‘can and should be interpreted and implemented in a manner supportive of WTO Members’ right to protect public health and, in particular, to promote access to medicines at all’, and emphasized the ‘flexibilities’ included in the Agreement, including with respect to the granting of compulsory licences. It affirmed that each WTO member has the right to grant compulsory licences, and has the freedom to determine the grounds upon which such licences are granted and to ‘determine what constitutes a national emergency or other circumstances of extreme urgency, it being understood that public health crises, including those relating to HIV/AIDS, tuberculosis, malaria and other epidemics, can represent a national emergency or other circumstances of extreme urgency’. The significance of the expression ‘national emergency or other circumstances of extreme urgency’ under the TRIPS Agreement and the Doha Declaration has sometimes been misunderstood.28 National emergency or circumstances of extreme urgency are not a prerequisite to the granting of a compulsory licence. If such circumstances exist, however, a state need not seek to ‘obtain authorization from the right holder on reasonable commercial terms and conditions’ over ‘a reasonable period of time’ before granting a compulsory licence.

While the Doha Declaration was negotiated in the context of concern about access to medicines for infectious diseases, reflected in its specific references to HIV/AIDS, tuberculosis and malaria, its implications are not confined to these diseases. First, it clearly applies to access to medicines generally; attempts led by the USA to confine its application to specified diseases were not successful.29 Second, even in the two places in which HIV/AIDS, tuberculosis and malaria are mentioned specifically, so too are ‘other epidemics’.

Nevertheless, like all treaties, the TRIPS Agreement is understood and implemented domestically in a highly political context. The global attention that the HIV/AIDS epidemic has garnered, and the sense of emergency that it has generated, have set the context in which the TRIPS Agreement and its flexibilities have been applied to medicines for HIV/AIDS treatment, affecting, for example, the willingness of states to use their powers to grant compulsory licences or to use the threat of compulsory licences to pressure pharmaceutical companies into lowering product prices. Until recently, non-communicable diseases (NCDs) have not generally been viewed as a global emergency or crisis. Actions by states to grant compulsory licences over NCDs have been met by strong
resistance from Western developed countries and originator pharmaceutical companies.24,29,30

In addition to the politics and perceptions relating to expectations of treatment for those with cancer and other NCDs, economic considerations also impact on states’ actions relating to intellectual property rights. For example, under the TRIPS Agreement, where a state grants a compulsory licence, it must ensure that ‘adequate remuneration’ is paid to the patent holder ‘taking into account the economic value of the authorization’. The term ‘adequate remuneration’ is not defined and is to be understood ‘in the circumstances of each case taking into account the economic value of the authorization’. It has often been pointed out that, for many pharmaceutical products, such as those to treat chronic diseases, manufacturers recoup their investments and reasonable profits from high-income countries, in which high prices can be paid either by private individuals, or a mix of private and public health insurance arrangements.24,31 This underlines that the importance of developing and least developed country markets to the commercial decision-making of originator pharmaceutical companies varies by product, by country and over time.23,27,31 The ‘adequacy’ of remuneration should vary with such circumstances.

Controversy over the TRIPS Agreement at the recent United Nations General Assembly high-level meeting on non-communicable diseases

Not surprisingly, controversy over the application of TRIPS flexibilities flared in the negotiation of the Political Declaration adopted at the recent UN high-level meeting on the prevention and control of NCDs.32 Reportedly, the USA and European Union strongly resisted the inclusion of references to the TRIPS Agreement or the Doha Declaration in the Political Declaration, and use of the term ‘epidemic’ for NCDs in the Declaration, which is the term applied by WHO. Brazil, India, Mexico and other G77 countries strongly opposed these efforts.33–35

In the ‘Zero Draft’ of the Declaration — the draft released by the Co-Facilitators on which negotiations commenced — the word ‘epidemic’ appeared four times.36 In the Declaration ultimately adopted by the General Assembly, it only appeared once, and as an adjective rather than a noun.37 A ‘rising epidemic’ had become a ‘challenge of epidemic proportions’. Concern that ‘all people, rich and poor, without distinction as to age, gender and race, are affected by the non-communicable disease epidemic’ had become a concern that ‘the rapidly growing magnitude of NCDs affects people of all ages, gender, race and income levels’. The need for a ‘whole-of-government’ and ‘whole-of-society’ effort to respond to ‘the epidemic’ had become a need for such a response to ‘the challenge’. An acknowledgment that ‘resources devoted to combating the epidemic, both at the national and international levels are not commensurate with the magnitude of the problem’ had become an acknowledgment that ‘resources devoted to combating the challenges posed by NCDs’ are not commensurate with its magnitude.

The ‘trade-off’ for the agreement that NCDs not be named ‘an epidemic’ was that two references to the TRIPS Agreement and its flexibilities were included in the Declaration. The Zero Draft’s ‘[i]mprove access to affordable, good-quality, effective medicines and diagnostics, including through the use of TRIPS flexibilities’ was strengthened to ‘[p]romote access to comprehensive and cost-effective prevention, treatment and care for the integrated management of NCDs, including, inter alia, increased access to affordable, safe, effective and quality medicines and diagnostics and other technologies, including through the full use of TRIPS flexibilities’. International organizations were urged to provide technical assistance and capacity building to developing countries, especially least developed countries, in the areas of NCD prevention and control, and promotion of access to medicines for all, ‘including through the full use of TRIPS flexibilities and provisions’. The Declaration also implicitly acknowledged the role of intellectual property in research and development. States agreed to actively promote national and international investments, and strengthen capacity for quality research and development ‘in a sustainable and cost-effective manner, while noting the importance of continuing to incentivize innovation’.

This recent battle over the implications of intellectual property for global efforts to improve access to medicines for NCDs, and specifically the place of TRIPS flexibilities in these efforts, serves as another reminder of the highly charged contests over the relationships between intellectual property rights and access to medicines. As global attention toward NCDs continues to increase in the years ahead in the follow-up to the UN high-level meeting, battles over the relationship between international intellectual property law and access can be expected to escalate at both international and domestic levels.

Conclusion

This article has outlined two areas of international law that are relevant to cancer treatment. In both areas, balances need to be struck between different concerns and interests: in the case of drug control law, between ensuring availability and preventing the harms of abuse; and in the case of the TRIPS Agreement, between incentivizing research and development, and making products affordable. How these balances are struck internationally and implemented domestically is a critical determinant of whether or not people obtain the medicines they need. It is important, however, to underline that the law, both international and domestic, is only one of many critical variables. Battles over the law should not distract from the importance of other essential efforts to enhance access to medicines within the context of the strengthening of health systems, including: building and training health workforces; developing reliable supply and distribution chains; strengthening medicines regulatory agencies; promoting rational use; and improving equity of access to medical treatment generally.

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32. General Assembly of the United Nations. High-level meeting on non-communicable diseases. United Nations. Available at:


