

MEMORANDUM

To: Developing Countries' Health Ministries **From:** Andrew Hennessy-Strahs

Re: Legal, Regulatory, and Medical Considerations for Improving Cancer Treatment Access and Outcomes in Low and Middle Income Countries

I. Question Presented

What are the legal, regulatory, public policy, and medical considerations for low and middle income countries wishing to improve cancer treatment access and outcomes?

II. Short Answer

This is a normative analysis, evaluating what types of policies and interventions low and middle income countries should take to improve capacity to better alleviate the public health problems associated with cancer. Faced with limited resources, low and middle income countries must prioritize resources in a different way than developed countries.

III. Factual Statement

Low and middle income countries face a disproportionate burden of new cancer cases and cancer deaths.¹ Additionally, the pathology of cancer in the developing world is different from that of the developed world. The most common type of cancer in Africa, for example, is Kaposi's sarcoma, which is a cancer of the cells of the lymph or blood vessels; it is precipitated by the HIV virus and is considered an "AIDS defining illness," meaning the development of this cancer signifies that someone has officially developed AIDS (as opposed to merely carrying the HIV virus).² The developing world also has a disproportionate incidence of liver and cervical cancers, with 80% of new cervical cancers originating in developing countries and greater than 80% of new liver cancers originating in the developing world.³ Much like Kaposi's sarcoma, these cancers also arise from viral infections, with cervical cancer originating from the human

papilloma virus (HPV), and liver cancer arising from hepatitis B (HBV) and hepatitis C (HCV).⁴ Fully 60% of new stomach cancer cases arise in the developing world and come from an infectious bacterium, helicobacter pylori (H. pylori).⁵

Additionally, the geography of tobacco use is shifting from the developed to the developing world which necessarily means the burden of tobacco related cancers (including lung cancer) will also shift to the developing world.⁶

There are unique challenges around basic infrastructure capacity, lack of financial support for treatment, and intellectual property obstacles to procure novel, life-saving treatment, such as targeted immunotherapy. As Bollyky and Andridge warn: “[u]nless urgent action is taken, the cancer crisis emerging in developing countries will worsen and become harder to address with each passing year.”⁷

IV. Discussion

A. Capacity Building for Cancer Prevention

The first component to any country’s cancer management approach (regardless of economic status) must begin with prevention.

Kaposi’s sarcoma can mostly be prevented with highly active antiretroviral therapy (HAART).⁸ The WHO has published new guidelines making anyone currently living on the planet with HIV eligible for anti-retroviral therapy.⁹ The WHO also recommended that anyone at substantial risk for HIV be offered pre-exposure prophylaxis (PrEP) in order to prevent contracting HIV in the first place.¹⁰ All developing countries must avail themselves of all available resources, including the Bill and Melinda Gates Foundation, the Clinton Foundation, the Global Fund to Fight AIDS, Tuberculosis and Malaria, USAID, UNAIDS, the UN Development Group, UNICEF, PEPFAR. Provided the global community can accelerate the

pace of progress against HIV, the WHO projects the world can end the AIDS epidemic by 2030.¹¹ Progress against HIV would necessarily mean progress against Kaposi's sarcoma.

As Bollyky and Andridge argue, the same global health approaches used to manage HIV can also be leveraged to prevent cancer of other infectious agents.¹² For example, Zambia successfully partnered with PEPFAR to screen and treat HIV-positive women for cervical cancer with a cost effective, low technology approach. The Global Alliance for Vaccines and Immunization (GAVI) already offers support for HPV and HBV vaccines and views these vaccines as an effective cancer prevention strategy for developing countries.¹³ This support is not unconditional, however. Countries must fall below the gross national income thresholds to be eligible for 100% support from GAVI and will transition to fully self-financing as national income increases through a period of co-financing preparatory transition and accelerated transition periods.¹⁴

H. pylori infection may be managed with cost-effective policies in developing countries. The infection is typically transmitted between family members, especially young children as a result of poorly sanitized water.¹⁵ Developing countries can mandate newlywed couples be screened for infection through C-labeled urea breath tests (C-UBT) so that they can prevent transmission to their future children by beginning an antibiotic regimen to eradicate the infection.¹⁶ Other cost-effective measures countries can adopt are education campaigns around familial clustering of the infection, sanitary recommendations around teeth-brushing, hand-washing, dishwashing, and recommendations advising people to boil water before drinking.¹⁷ Countries with greater resources can implement water sanitation testing and facilities.¹⁸

Tobacco control to avoid lung cancer and other tobacco related cancers requires developing countries to summon the political will to apply existing international law as well as

provide public health resources to implement smoking cessation and nicotine replacement therapies. The Framework Convention on Tobacco Control [FCTC] is a treaty adopted in 2003 by the 56th World Health Assembly and the first treaty adopted under article 19 of the WHO Constitution.¹⁹ If countries successfully implement the FCTC treaty provisions they will necessarily reduce tobacco use rates and future cancers resulting from tobacco. Among others, these provisions obligate signatories to restrict tobacco lobbying of lawmakers to prevent undue influence in the legislative process, implement taxes to reduce demand, educate their citizens about the health risks of smoking, label packages to reduce consumer deception, restrict sales to minors who are at higher risk of becoming addicted, prohibit all tobacco advertising, and regulate the actual contents in the tobacco products.²⁰

These preventive measures are the greatest area of opportunity with the highest cost-benefit calculus for developing countries to effectively manage cancer before it even manifests in the first place.

B. Capacity Building for Cancer Treatment

a. Surgery

Paul Farmer and Jim Kim argue that “In Africa, surgery may be thought of as the neglected stepchild of global public health.”²¹ Africa has the fewest physicians per capita of any continent, with surgeons being “rarer still,” despite the fact that surgical disease ranks among the top fifteen causes of disability and up to 15% of disability adjusted life years lost globally.²² Arguably, the two greatest reasons for the neglect of surgery in public health are the complexity of it and the focus of public health resources on communicable diseases.²³ Surgery requires many steps, including anesthesia, preparation of a surgical room and instruments, postoperative care, and blood-banking.²⁴ Because surgical disease is typically not transmissible from person to

person, it is hard to mobilize public health resources.²⁵ On the bright side, there is a minimal level of capacity throughout the developing world, though it is weighted quite heavily towards the affluent. There is also a growing movement among surgeons in the developed world to provide services to the developing world and to expand surgical capacity from within.²⁶

In the context of low and middle income countries, surgery must be a fundamental component of the cancer treatment infrastructure landscape. Given the deficiencies in the existing infrastructure, many patients initially present with late stage locally advanced or metastatic cancer.²⁷ Surgery to remove masses may be the primary or only treatment available for both curative and palliative treatment.²⁸ As Russell White reports in the *Lancet*, “for most patients with cancer in Africa, surgery alone is the only realistic option.”²⁹ The greatest legal and public policy concern is establishing the public financing mechanisms to pay for surgery.³⁰ While many developing countries have a national public health service in place, patients are often asked to pay high out-of-pocket expenses for surgery.³¹ Developing countries must reconsider these out-of-pocket expenses, especially given that many cancer patients are “often young, productive people who support families.”³² Increasing the amount of government subsidization for surgery would necessarily decrease government welfare subsidization in other areas and would offset economic losses due to many of these patients leaving the workforce.

One of the greatest regulatory complications is training surgeons. The regulations for licensure and certification of surgeons vary markedly across the developing world.³³ Surgery itself is also regulated quite differently throughout the developing world. In South Africa, for example, surgery is regulated by the Health Professions Council, through authority from the National Health Act and Health Professions Act.³⁴ The Medical Council of India governs the federal education system for surgeons, while each individual state oversees the actual medical

code and standards of good conduct, in a complex governance structure of shared federal and state responsibility.³⁵

The standardization of surgical care can ensure minimum levels of quality and safety, while reducing avoidable death and morbidity in developing countries.³⁶ In 2009, the World Health Organization (WHO) published guidelines for safe surgery, recognizing a growing need for regulatory standardization in surgery, with the potential to strengthen capacity and save lives.³⁷ The ten essential surgery objectives should be formally codified by all regulatory agencies that oversee surgery. They include: (1) operating on the correct patient at the correct site; (2) using methods to prevent harm from the use of anesthetics while protecting the patient from pain; (3) recognizing and preparing for life-threatening airway or respiratory obstructions; (4) recognizing and preparing for the risk of high blood loss; (5) avoiding inducing allergic or adverse drug reactions for which the patient is known to be at significant risk; (6) consistently using methods known to minimize the risk for surgical site infection; (7) preventing inadvertent retention of instruments and sponges in surgical wounds; (8) securing and identifying all surgical specimens; (9) effectively communicating and exchanging critical information for the safe conduct of operations; and (10) establishing routine surveillance of surgical capacity, volume, and results.³⁸ Responding to the WHO's recommendations, the WHO African Regional Office convened a workshop in Harare, Zimbabwe "to support countries in their efforts to increase adherence to safety standards in surgical care in order to reduce morbidity and mortality caused by unsafe surgery."³⁹ They investigated common surgical errors, adapting the recommendations to the unique situations on the local level, as well as implementing the recommendations on a country-wide basis.⁴⁰ The recommendations included strengthening liaisons with professional

societies, networks and civil society.⁴¹ To date, the WHO reports that Africa has already registered 198 facilities as WHO Surgical Safety Checklist implementing hospitals.⁴²

b. **Radiotherapy**

Radiation therapy is recognized as an essential component of a national cancer treatment program, regardless of that countries' economic status.⁴³ Radiotherapy is one of the most cost effective treatments for cancer, despite the high capital investments necessary to procure the equipment and build the facilities.⁴⁴ Conservative estimates suggest that approximately 50% of all cancer patients can benefit from radiotherapy in either a curative or palliative capacity.⁴⁵ Moreover, radiotherapy is frequently used as an adjuvant therapy with surgery or chemotherapy, creating a synthesized treatment that is greater than the sum of its parts.⁴⁶ However, because of the high initial investment, developing countries have not made the necessary investments, leaving large segments of the population of these countries without access to treatment.⁴⁷ In fact, of the 52 African nations, only 23 offer radiotherapy, with 60% of the infrastructure located in South Africa and Egypt.⁴⁸

The legal and regulatory challenges developing countries face primarily concerns the relative unfamiliarity with this technology. The largest barrier is probably creating enough financial and political support to make the initial investment. International collaboration to overcome this problem is still in its nascent stages. For example, the International Atomic Energy Agency (IAEA) has provided technical assistance, training and education and even financing for countries to pursue radiotherapy.⁴⁹ The Agency has also established its Programme of Action for Cancer Therapy in 2004 to assess the readiness of a country and its existing cancer infrastructure to develop radiation therapy facilities.⁵⁰ Public-private partnerships are another approach. The United States and Kenya have created a public-private partnership, which

includes (among others) the Moi University School of Medicine in Kenya and Indiana University's medical school, called the Academic Model Providing Access to Healthcare Program (AMPATH), to implement radiotherapy as soon as possible in a cancer center under construction in Eldoret, Kenya.⁵¹ Multilateral international cooperation is another strategy. Latin America and the Caribbean have seen 18 countries in the region create the Network of National Cancer Institutes to improve the quality of radiotherapy.⁵² The Network aspires to harmonize “best practices; exchange information and knowledge; identify needs, opportunities, and common interests; foster coordination among member countries; and promote the commitment of every country's corresponding levels of government, with emphasis on the availability of the financial, human, and legislative resources necessary for the development of (radiotherapeutic) cancer control.”⁵³ India and Turkey have also made limited progress in expanding access to radiotherapy.⁵⁴

Other regulatory concerns focus on the implementation of the technology. Specifically, the regulatory challenges involve the facilities, the personnel, the process of treatment, including all stages from diagnosis to administration to follow-up, and the safe and effective operation of the equipment.⁵⁵ The IAEA published extensive guidance on how to commission a radiotherapy program, which addresses the regulatory considerations a country would need to address, including, for example, procurement and disposal of radioactive material, radiation beam room safety, clinical follow up, protections for pregnant workers, calibration of the equipment, procedures for accidental patient exposures, staff training, and hospital budgeting recommendations.⁵⁶ While the decision to install radiotherapeutic facilities is the most cost-intensive aspect of this therapy, the actual use may well provide the most cost effective form of

cancer treatment currently available, in addition to creating highly technical job opportunities if the country is able to successfully *train* and *retain* those workers.⁵⁷

c. **Medication**

Chemotherapy is difficult to administer, typically requiring multiple visits each month for patients to receive the medication, as well as the supporting blood chemistry analysis necessary to modify the dosing depending on how the patient responds.⁵⁸ Tamoxifen, which is a selective estrogen receptor modulator, should be used in all countries, provided a single laboratory test is available to confirm the hormone receptor pathology of breast cancer patients, due to its high efficacy in multiple pathologies, low cost, oral administration (pill or liquid), well toleration in patients, and typically manageable side effects.⁵⁹ Orally administered morphine and other oral pain control medicines must be available across all economic settings, provided the country has effective laws and regulations to prevent abuse and diversion.⁶⁰

1. *WHO Essential Medicines List*

The WHO maintains a list of essential medicines of which thirty-eight are cytotoxic and adjuvant chemical medications for cancer, and eight are hormonal based treatments for cancer, including tamoxifen; two are opioid analgesics, and fifteen are other medications for palliative care.⁶¹ This list represents the 2015 WHO revision of its essential medicine list, in which it added 16 new anticancer medicines (for a total of 46 anticancer drugs) to its list for low and middle income countries.⁶² There is considerable variability in procurement among nations, however.⁶³ Developing countries should aspire to procure as many drugs as possible on this list.

2. *Compulsory Licenses, Intellectual Property, and Corporate Assistance*

Another area of opportunity for developing countries to obtain anticancer medications lies in the compulsory license. The World Trade Organization's (WTO) Trade-Related Aspects

of Intellectual Property Rights (TRIPS) Agreement authorized the use of compulsory licenses for pharmaceuticals.⁶⁴ A compulsory allows a government to produce a patented product without the patent owner's approval.⁶⁵ While the compulsory license has typically been used for communicable diseases, Thailand, India, Ecuador and Colombia have successfully used or threatened compulsory licenses to obtain dramatic price savings beginning in 2006 with India's rejection of Novartis' patent on Gleevec, a leukemia medicine and Thailand's threat to issue a compulsory license on the same drug in 2007.⁶⁶

The threat of the compulsory license as well as the looming loss of patent expiration prompted GlaxoSmithKline to announce, on March 31, 2016, that it would voluntarily waive patent protection in low-income countries and issue voluntary licenses in low-income and middle-income countries to produce generic oncology medications.⁶⁷ Novartis subsequently debuted its own program to offer 15 drugs, including oncology drugs, for \$1 per treatment per month in developing countries.⁶⁸ GlaxoSmithKline further offered to commit its oncology portfolio to patent pooling, possibly via the United Nations' Medicines Patent Pool, which helps expand access in developing countries to the WHO's essential medicine portfolio.⁶⁹ These steps by Novartis and GlaxoSmithKline may help pave the way for developing countries to expand access to highly-efficacious, next-generation biologics and immunotherapies.⁷⁰

V. Conclusion

Notably, this memorandum does not cover two critical generalized issues of health infrastructure which substantially impact cancer treatment and outcomes: (1) the global health workforce shortage and corresponding diaspora of workers *away from* low- and middle-income nations *toward* high income nations; and (2) the financial support system for medical care, including issues of insurance coverage and global health justice for poor people, (i.e., the right to

health). The issues are worth mentioning here as these two issues are salient for any developing nation wishing to improve cancer treatment and outcomes. The second issue is quite palpable in many privileged nations as well, including the U.S. Nevertheless, there is a growing realization that the global health burden is shifting from infectious disease to noncommunicable disease. Policymakers in developing nations can make significant inroads by applying the legal, medical, and political infrastructure that was developed over many years in the battle against infectious disease to the emerging scourge of cancer. For example, the pathology of cancer in developing nations reflects the infectious disease burden that has already afflicted these nations. Prevention of cancer arising from infectious disease can leverage this infrastructure, including antiretroviral therapy and vaccination. Cancers arising from lifestyle choices, such as tobacco use, can be overcome by applying the FCTC treaty developed by the World Health Assembly. For already existing cancers, developing nations can expand surgical, radiological, and medicinal capacities through international guidance, cooperation, and assistance. Already, in many African nations, we see a commitment to WHO safe surgical guidelines. We also see the UN's IAEA assisting nations in creating one of the most cost effective cancer treatment modalities. On the medicinal front, the WHO has expanded its list of essential anticancer medications. International intellectual property policy decisions by some nations are dramatically expanding access to these medications as pharmaceutical companies recognize cooperation is a more viable approach than litigation. Developing nations must recognize the progress they have made and continue implementing these improvements. They must continue advocating for their populations as well. As the battle against infectious disease continues succeeding and the as the global health resources are finally freed for other purposes, the global health infrastructure must shift toward one of the most evil plagues of all, that of cancer, the dreaded emperor of all maladies.

¹ See, e.g., Michael B. Barton, Role of Radiotherapy in Cancer Control in Low-Income and Middle-Income Countries 7 *The Lancet* 584, 584 (Jul. 2006).

“More than half the cases of cancer in the world arise in people in low-income and middle-income countries. This proportion will rise to 70% by 2020.”

² American Cancer Society, “What is Kaposi Sarcoma,” (2017) <https://www.cancer.org/cancer/kaposi-sarcoma/about/what-is-kaposi-sarcoma.html>; Lawrence N Shulman, *Cancer Care in Developing Countries: An Underdeveloped Public Health Priority*, HARVARD SCHOOL OF PUBLIC HEALTH (Nov. 2, 2009), http://archive.sph.harvard.edu/breastandhealth/files/shulman_pih_dfci_program_nov_2_09.pdf

³ Michael J. Thun et al., The Global Burden of Cancer: Priorities for Prevention 31 *Carcinogenesis* 100, 104,106.

⁴ *Id.*

⁵ *Id.* at 107.

⁶ *Id.* at 101

“With the decline of tobacco use in many industrialized countries, the geography of smoking has shifted from the developed to the developing world, especially for men. About 50% of men and 9% of women are current smokers in developing countries, compared with 35% of men and 22% of women in high-resource countries.”

⁷ Thomas J. Bollyky & Caroline Andridge, Cancer Prevention and Treatment in Developing Countries: Recommendation for Action, *Cancer Control* 31-32 (July 2015), http://www.cancercontrol.info/wp-content/uploads/2015/07/31-38-Bollyky_cc2015.pdf.

⁸ American Cancer Society, “What is Kaposi Sarcoma,” (2017) <https://www.cancer.org/cancer/kaposi-sarcoma/about/what-is-kaposi-sarcoma.html>

⁹ WHO, “New WHO Guidelines Make All Persons Living with HIV Eligible for Antiretroviral Treatment,” (Apr. 29, 2016), <http://www.afro.who.int/en/media-centre/pressreleases/item/8584-new-who-guidelines-make-all-persons-living-with-hiv-eligible-for-antiretroviral-treatment.html>.

¹⁰ *Id.*

¹¹ WHO, “New Recommendations Show How to Treat All People Living with HIV and Decrease New Infections,” (Nov. 27, 2015), <http://www.afro.who.int/en/media-centre/pressreleases/item/8189-new-recommendations-how-to-treat-all-people-living-with-hiv.html>.

While progress has been made, it is not perfect, and there are still issues of gender disparities:

“‘In the last 15 years, new HIV infections have reduced by 41% in the African Region, more than in any region in the world,’ said Dr Matshidiso Moeti, WHO Regional Director for Africa. ‘But the number of people acquiring HIV infection is still too high and young women and adolescent girls continue to be disproportionately at risk.’”

¹² Bollyky & Andridge, *supra* note 7 at 34

¹³ GAVI, Cancer Leaders Call to Fund Gavi, the Vaccine Alliance (Dec. 2014).

“Vaccinating against the primary causes of liver and cervical cancers is critical to poorer countries in preventing the rising tide of cancer. Hepatitis B vaccine is highly effective in preventing a primary cause of liver cancer, and the elimination of its transmission is an achievable public health goal. Human papillomavirus (HPV) causes virtually all cervical cancer, and current HPV vaccines protect against 70% of cervical cancer cases.”

¹⁴ GAVI, “Eligibility and Transition Policy,” (2017) <http://www.gavi.org/about/governance/programme-policies/eligibility-and-transition/>.

¹⁵ Barik A. Salih, Helicobacter pylori Infection in Developing Countries: The Burden for How Long? 15 *Saudi J. Gastroenterol.* 2009, *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2841423/>.

Here is an example of an antibiotic regimen for H. pylori. Countries need to carefully monitor these programs to guard against antibiotic treatment plans to avoid antimicrobial resistance:

“A trial of empiric therapy for H pylori infection in 7 Latin American sites found higher eradication rates with 14 days of standard triple therapy (LAC) than with shorter 4-drug therapies. Neither 5 days of concomitant lansoprazole, amoxicillin, clarithromycin, and metronidazole nor 10-day sequential treatment (5 days of LA, then 5 days of LCM) was significantly better than the standard therapy at any site.”

¹⁶ Salih, *supra* note 15; Luigi Santacrose, Helicobacter Pylori Infection Treatment & Management *Medscape* (Mar. 15, 2016, *available at* <http://emedicine.medscape.com/article/176938-treatment>

¹⁷ Salih, *supra* note 15

¹⁸ *Id.*

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- ¹⁹ WHO Framework Convention on Tobacco Control, WHA Res. 56.1, World Health Assembly, 56th Ass., 4th plen. mtg, Agenda Item 13, Annex, WHO Doc. A56.VR/4 (May 21, 2003), <http://www.who.int/tobacco/fctc/text/en/fctc-en.pdf> [hereinafter FCTC].
- ²⁰ FCTC, arts. 3, 5, 6, 7, 9, 10, 12, 13, 14, 16.
- ²¹ Paul E. Farmer & Jim Y. Kim, Surgery and Global Health: A View from Beyond the OR 32(4) World J. of Surgery 533-36 (Apr. 2008).
- ²² *Id.*
- ²³ *Id.*
- ²⁴ *Id.*
- ²⁵ *Id.*
- ²⁶ *Id.*
- ²⁷ Anna J. Dare et al. Cancer, Disease Control Priorities Series, 223 (2015) (3rd Edition) (Ch. 13, Surgical Services for Cancer Care).
- ²⁸ *Id.*
- ²⁹ Russell E. White, Cancer Surgery in Africa: If All You Have is a Hammer... 16 The Lancet 1190; 1190 (Sept. 2015).
- “However, in The Lancet Oncology Commission on global cancer surgery, surgery is shown to be a vital method in the management of cancer, with surgery being a necessary part of care in most patients with cancer. Although in many parts of the world surgeons provide diagnostic and therapeutic services, including endoscopy and radiological procedures, as well as surgery and chemotherapy, for most patients with cancer in Africa, surgery alone is the only realistically available option.”
- ³⁰ *Id.*
- ³¹ *Id.*
- ³² *Id.*
- ³³ Catherine R. deVries and Raymond R. Price, Global Surgery and Public Health: A New Paradigm, 15 (2012).
- ³⁴ National Health Act 61 of 2003 (S. Afr.); Health Professions Act 56 of 1974 (S. Afr.).
- ³⁵ Han de Vries et al. International Comparison of Ten Medical Regulatory Systems, 61 (2009).
- ³⁶ Anna J. Dare et al. Cancer, Disease Control Priorities Series, 226 (2015) (3rd Edition) (Ch. 13, Surgical Services for Cancer Care).
- ³⁷ WHO, WHO Guidelines for Safe Surgery 2009 (2009).
- ³⁸ *Id.*
- ³⁹ WHO, “Safe Surgery in Africa,” (2017), http://www.who.int/patientsafety/news/ssl_articles/en/.
- ⁴⁰ *Id.*
- ⁴¹ *Id.*
- ⁴² *Id.*
- ⁴³ David A. Jaffray and Mary K. Gospodarowicz. Cancer, Disease Control Priorities Series, 239 (2015) (3rd Edition) (Ch. 14, Radiation Therapy for Cancer).
- ⁴⁴ *Id.*
- ⁴⁵ *Id.*
- ⁴⁶ *Id.*
- ⁴⁷ *Id.*
- ⁴⁸ Peter Kingham et al. Treatment of Cancer in Sub-Saharan Africa 14 The Lancet e158, e163 (Apr. 2013).
- ⁴⁹ Jaffray, *supra* note 24 at 245.
- ⁵⁰ *Id.*
- ⁵¹ *Id.*; Purdue University, “AMPATH - The Academic Model Providing Access to Healthcare Program Background,” (2017), <https://ampath.pharmacy.purdue.edu/>.
- ⁵² Jaffray, *supra* note 24 at 245.
- ⁵³ *Id.*
- ⁵⁴ *Id.*
- ⁵⁵ *Id.* at 242.
- ⁵⁶ International Atomic Energy Agency, Setting Up A Radiotherapy Programme: Clinical, Medical Physics, Radiation Protection And Safety Aspects (Feb. 2008).
- Here is an example of regulatory guidance from the IAEA for the first stages of building a radiotherapy facility:

“The radiotherapy installation needs to be licensed by the national regulatory authority. As a radiotherapy installation requires major construction work, it is most likely that regulatory authorities in Member States shall provide authorization before construction begins. Therefore, the application for a licence must be prepared at an early stage. It should contain all relevant elements to assure the regulatory authority that the planned facility will be safe. An example of a detailed outline of the elements of a licence is given in Appendix XII.” (page 15).

⁵⁷ Borton, *supra* note 1.

“Findings of published studies of costs consistently show that radiotherapy is one of the most cost-effective forms of cancer treatment because most people are treated as outpatients, equipment and buildings have a long life, and throughput on equipment is high.

...

Provision of a safe and effective radiation oncology service is complex. It needs not only substantial capital investment in radiotherapy equipment and specially designed buildings but also continuous investment in maintenance and replacement of equipment, in expert teams of doctors, therapists, and physicists, and in good access to engineering support. Even if funds are available, necessary medical, scientific, and technical expertise is in short supply in many countries. This issue is the main constraint in many regions of low or middle income. The scarcity of trained staff can restrict the number of patients who can be treated to the point of underuse of equipment.”

⁵⁸ Susan Horton & Cindy L. Gauvreau. Cancer, Disease Control Priorities Series, 265 (2015) (3rd Edition) (Ch. 16, Cancer in Low- and Middle-Income Countries: An Economic Overview).

⁵⁹ *Id.*; Lawrence N. Shulman, et al., Breast Cancer in Developing Countries: Opportunities for Improved Survival J. Oncol. (Dec. 29, 2010), *available at* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3021855/>; Nicholas J. Robert, Clinical Efficacy of Tamoxifen J. Oncol. (Feb. 1, 1997), *available at* <http://www.cancernetwork.com/review-article/clinical-efficacy-tamoxifen>.

⁶⁰ Horton & Gavreau *supra* note 58

⁶¹ WHO, *Essential Medicines: WHO Model List*, 2015.

⁶² See Roxanne Nelson, WHO Essential Cancer Drug List: Out of Reach for Many Medscape (Oct. 21, 2016), *available at* http://www.medscape.com/viewarticle/870768#vp_1.

⁶³ *Id.*

⁶⁴ WTO, AGREEMENT ON TRADE-RELATED ASPECTS OF INTELLECTUAL PROPERTY RIGHTS [hereinafter TRIPS]; WTO, TRIPS and Health: Frequently Asked Questions, Compulsory Licensing of Pharmaceuticals (2016), https://www.wto.org/english/tratop_e/trips_e/public_health_faq_e.htm

⁶⁵TRIPS

“Article 31

Other Use Without Authorization of the Right Holder:

Where the law of a Member allows for other use of the subject matter of a patent without the authorization of the right holder, including use by the government or third parties authorized by the government, the following provisions shall be respected[...]

⁶⁶ Cinthia Leite Frizzera et al. Compulsory Licenses for Cancer Drugs: Does Circumventing Patent Rights Improve Access to Oncology Medications? 2 J. Oncol. (Oct. 5, 2016); Public Citizen, “Colombia’s CL Campaign Story” (2017), *available at* <http://www.citizen.org/colombia-CL-campaign-story>.

⁶⁷ The Lancet, Improved Drug Access in Low and Middle-Income Countries 17 The Lancet (May 2016), [http://thelancet.com/pdfs/journals/lanonc/PIIS1470-2045\(16\)30068-7.pdf](http://thelancet.com/pdfs/journals/lanonc/PIIS1470-2045(16)30068-7.pdf).

⁶⁸ *Id.*

⁶⁹ *Id.*

⁷⁰ *Id.*