



GUIDELINES FOR **SOcially RESPONSIBLE** MANAGEMENT OF INNOVATION

Making research findings accessible and usable for as many people as possible



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Making research findings accessible and usable for as many people as possible

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CONTENTS

1	EXECUTIVE SUMMARY	5
2	WHY THIS BROCHURE?	9
3	HOW CAN A UNIVERSITY CONTRIBUTE?	12
4	KEY TERMS	14
5	ACTION: INCORPORATE SOCIALLY RESPONSIBLE PRINCIPLES INTO UNIVERSITY GUIDELINES	15
6	ACTION: INCLUDE SOCIAL RESPONSIBILITY IN A CONTRACT (EQUITABLE LICENSING)	17
7	ACTION: EMPLOY NON-EXCLUSIVE LICENCES, SUCH AS THROUGH PATENT POOLING	20
8	ACTION: MAKE USE OF SOCIALLY RESPONSIBLE CONTRACTUAL CONDITIONS FOR RESEARCH COOPERATION	22
9	ACTION: PARTICIPATE IN NOT-FOR-PROFIT PRODUCT DEVELOPMENT PARTNERSHIPS	25
10	ACTION: ISSUE MULTIPLE LICENCES FOR DIFFERENT INDICATIONS	27
11	ACTION: USE ROYALTY-FREE LICENCES FOR DEVELOPING COUNTRIES, OR ENGAGE IN DUAL COMMERCIALISATION	28
12	ACTION: 'DO-IT-YOURSELF' PRODUCT DEVELOPMENT VERSUS THE CREATION OF A START-UP	30
13	ACTION: PUBLISH FINDINGS IN OPEN ACCESS PUBLICATIONS, AND CONTRIBUTE TO OPEN RESEARCH COLLABORATIONS	33
14	ACTION: SEEK FINANCIAL SUPPORT FOR FURTHER RESEARCH AND DEVELOPMENT	35
15	SOCIALLY RESPONSIBLE LICENSING: A DYNAMIC DEVELOPMENT	36
16	KEY QUESTIONS: WHAT CAN I DO AS A PUBLICLY-FINANCED RESEARCHER?	39

EXECUTIVE SUMMARY

Public money plays a pivotal role in the development of new health technologies. The European research framework programme Horizon 2020, for example, dedicated €7.5 billion between 2014 and 2020 to publicly-funded health research in Europe, of which €1.6 billion alone flowed into the Innovative Medicines Initiative. A recent study of the 210 new drugs approved by the US Food and Drug Administration between 2000 and 2016 found that the publicly-financed National Institutes of Health had contributed to published research supporting every single one, largely by funding basic research with more than US\$100 billion in grants.

But public funding neither guarantees that medical products brought to market meet priority health needs nor are priced affordably if they do. Patents—which confer temporary market exclusivity to an inventor of a new medical product—are often seen as the only way to incentivise research. But market exclusivities keep prices high, which can hinder access and place undue pressure on public health services. And they incentivise primarily research that serves high-income markets, neglecting diseases that disproportionately impact low- and middle-income countries as well as critical issue areas such as the need for new antimicrobial medicines.

Public money can and must be used more strategically. “Medicines should be priced such that the public does not pay twice for innovation: first through government funded scientific research and then through high medicine prices,” noted the Lancet Commission on Essential Medicines for Universal Health Coverage in 2017.¹ Universities and research institutions “that receive public funding must prioritise public health objectives over financial returns in their patenting and licensing practices,” agreed a United Nations High Level Panel on Access to Medicines in 2016.

Socially responsible management of innovation can be used to address several gaps that currently limit the contribution of publicly-financed research to the public good. An outline of several actions institutions can take to fill these gaps is below.

ACTIONS TO ADDRESS THE ACCESS GAP

Technology developed with public funding should be made affordable and available to those that need it. High prices should not limit access. To help address this gap, universities and other research institutions can:

- *Incorporate socially responsible principles into university guidelines*, including commitments to facilitate technology transfer; to ensure innovations can be used for follow-on research; and to ensure that when patents are sought over health-related inventions, they are licensed to facilitate broad access.
- *Include social responsibility in a contract* (equitable licensing) to promote the availability of biomedical innovations. Equitable licences may include provisions that: make them non-exclusive (facilitating competition that can bring down prices), stipulate milestones for the development of a medical product, require affordable pricing for end-stage products, and/or have accountability structures to ensure these requirements are implemented.
- *Employ non-exclusive licensing*, a type of equitable licensing, for example through patent pools or other intermediaries. Patent pools create a ‘one-stop shop’ for companies seeking to share intellectual property related to a particular technology and can be particularly helpful in facilitating lower cost versions of complex technologies involving multiple patents held by different actors.

¹ Wirtz, V.J., Hogerzeil, H.V., Gray, A.L., Bigdeli, M., Joncheere, C.P., Ewen, M.A., et al. (2016). ‘Essential medicines for universal health coverage’, *The Lancet*, 389(10067), p403-476. Available at: [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)31599-9.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31599-9.pdf) (Accessed: 20 June 2019).

- *Use socially responsible contractual conditions* for research cooperation: When participating in cooperative schemes to commercialise research, ensure that any contracts between publicly-financed research institutions and commercial enterprises safeguard the right of the research institution to have a say in any resulting products, and that they also include provisions for accessibility.

ACTIONS TO ADDRESS TRANSLATION GAPS

Promising early stage research sometimes stalls before it is translated into useable biomedical products, especially if there are minimal commercial incentives for the development of those products. There are several steps that can help translate early research into useable products for those that need them. They include:

- *Participate in non-profit product development partnerships (PDPs)*, cooperative structures that aggregate resources (both financial and technical) to meet clearly defined public-health research objectives.
- *Issue multiple licences for different indications*. Sometimes the same molecule can be used in different settings to treat different issues. Medicines libraries can be opened to allow screening for potential additional uses of existing innovations, especially to meet public health needs. This can pave the way for translation of those innovations for different fields of use.
- *Use royalty-free licences for low- and middle-income countries (LMICs)*, or engage in dual commercialisation for cases where a product could address needs in both high and low-income markets. A split licensing strategy could allow for two (or more) translation pathways: one driven by a royalty-bearing licence to develop the product for lucrative markets, recouping cost of investment; and one driven by a royalty-free licence to develop the product at lower cost for use in poorer markets, ensuring access.

- *Consider do-it-yourself product development* through the creation of non-profit foundations or through the launch of start-ups, in cases where there is insufficient commercial interest in taking a biomedical innovation forward.

ACTIONS TO ADDRESS RESEARCH GAPS

All of the above steps to improve access and translation also indirectly incentivise research by providing pathways for promising results of that research to be commercialised and reach their target market. Public health successes can drive interest in research targeted to meet public health needs, and can open doors to further collaborations and new, novel models for medical product development. But, even prior to that, public research institutions can take actions to address gaps, including:

- *Publish findings in open access publications*, and contribute to open research collaborations. Open sharing of research results, including data and methodologies, encourages collaboration and can spur development of solutions to identified challenges.
- *Seek financial support for research and development*, including from non-traditional sources. Donor financing is often available to support research targeted at the needs of LMICs. Such financing can also be used to close translation gaps for projects at later stages of maturity.

Case studies, model language, and other resources contained in this brochure show what researchers can do and the opportunities available to university administrations or institutes for socially responsible management of their innovations. Most of the examples stem from the sector of medicines research, but the principles apply to all inventions from public institutions.

WHY THIS BROCHURE?

WHY THIS BROCHURE?

This brochure contains actions that universities and other publicly-financed institutions can take to ensure that their research findings benefit as many people as possible, especially when related to matters of public health.

Public money plays a pivotal role in the development of new health technologies. The European research framework programme Horizon 2020, for example, dedicated €7.5 billion between 2014 and 2020² to publicly-funded health research in Europe, of which €1.6 billion alone flowed into the Innovative Medicines Initiative.³ A recent study of the 210 new drugs approved by the US Food and Drug Administration between 2000 and 2016 found that the publicly-financed National Institutes of Health (NIH) had contributed to published research supporting every single one, largely by funding basic research with more than US\$100 billion in grants.⁴ In general, the NIH contributes US\$32 billion a year to biomedical research. Universities are frequent public grant recipients and play a significant role in research. Nearly every new medicine, vaccine or diagnostic tool that enters the market has benefited at some point from a considerable amount of public financial support (either through funding, tax breaks and/or subsidies).

But public funding neither guarantees that medical products brought to market meet priority health needs nor are priced affordably if they do. Health Action International (HAI), the German Memento coalition and many others aim to ensure that vital research happens even without profit incentive and that its resulting medical commodities are affordable for all people that need them. Encouraging developments have taken place in recent years, and show that change is possible through small steps.

This brochure intends to provide tools so others can continue making strides.

THE CHALLENGE

Global health faces multiple challenges. But specifically for innovation on and access to new medicines, vaccines and diagnostics, three problem areas exist:

1. **The research gap:** Many health challenges are not sufficiently addressed by existing research – even though they affect billions of people in the worlds' poorest regions. Diagnostics, medicines and vaccines for 'neglected tropical diseases' (NTDs) such as sleeping sickness, Chagas disease, leprosy or tuberculosis are lacking, obsolete, or unsuitable for use in areas with limited infrastructure. Incentives to invest in developing them by for-profit enterprises is absent due to low purchasing power in target markets. This profit-based incentive structure has also failed to encourage pharmaceutical companies to develop new antibiotics, which are needed to fight the growing global crisis of anti-microbial resistance but which must be kept on reserve once developed, limiting market size.
2. **The translation gap:** Many health problems that are tackled in basic research are not taken forward and developed into actionable products. It is a central challenge to bridge this 'valley of death' between basic and applied research.
3. **The access gap:** High medicine prices, which are the result of the current model of innovation, often block access to vital health products even when they are available. This has been especially true for people living in low- and middle-income countries, and has become an increasing issue in high-income countries.

² European Commission, Horizon 2020 structure and budget. Available at: http://ec.europa.eu/research/participants/docs/h2020-funding-guide/grants/applying-for-funding/find-a-call/h2020-structure-and-budget_en.htm#IndLs (Accessed 20 June 2019).

³ Innovative Medicines Initiative (IMI), IMI funding model. Available at: www.imi.europa.eu/about-imi/imi-funding-model (Accessed 20 June 2019).

⁴ Proceedings of the National Academy of Sciences in the United States of America (PNAS), Contribution of NIH funding to new drug approvals 2010–2016. Available at: <https://www.pnas.org/content/115/10/2329> (Accessed 20 June 2019).

A key driver for these challenges is the current model of biomedical innovation: commercialisation of new health technologies is largely incentivised by the intellectual property system.

In particular, patents grant a period of market exclusivity—usually 20 years—during which time the patent holder can charge any price the market will bear. This means it is less interesting for for-profit companies to develop products to serve lower-income or smaller markets.



BOX 1

Equitable access is a global issue

“Universities and research institutions that receive public funding must prioritise public health objectives over financial returns in their patenting and licensing practices... Universities should adopt policies that ... generate knowledge for the benefit of the public.”

UN High Level Panel on Access to Medicines (2016)⁵

“Medicines should be priced such that the public does not pay twice for innovation: first through government funded scientific research and then through high medicine prices.”

LANCET Commission Essential medicines for universal health coverage (2017)⁶

“Countries should seek through patenting and licensing policies to maximize the availability of innovations ... for the development of products of relevance to public health, particularly to conditions prevalent in developing countries.”

WHO Commission on Intellectual Property Rights, Innovation and Public Health (2006)⁷

UNIVERSITIES AND OTHER PUBLIC INSTITUTIONS' 'THIRD MISSION': AN OPPORTUNITY

Universities and other public institutions have a third mission besides research and education—they should contribute to addressing societal needs. They can do this by ensuring their research is:

Needs-based: Based on priority health needs of people around the world, including populations in LMICs.

Accessible: Research benefits the public most when the results can be used by many. Therefore, research findings should be freely accessibly and published as open access. From this knowledge, usable products such as medicines or vaccines can be developed.

Results in affordable products: High prices for medical products strain health care systems and preclude many people from accessing them. Pricing for products that were initially publicly subsidised should not exclude anyone from their use. **Box 2** contains examples of products supported by public financing and later sold at high prices.

⁵ The United Nations Secretary-General's High-Level Panel on Access to Medicines (2016). The United Nations Secretary-General's High-Level Panel on Access to Medicines Report: Promoting innovation and access to health technologies. www.unsgaccessmeds.org/final-report/

⁶ Wirtz, V.J., Hogerzeil, H.V., Gray, A.L., Bigdeli, M., Joncheere, C.P., Ewen, M.A., et al. (2016). 'Essential medicines for universal health coverage', *The Lancet*, 389(10067), p403-476. Available at: [https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)31599-9.pdf](https://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)31599-9.pdf) (Accessed 20 June 2019).

⁷ World Health Organization, Public health, innovation and intellectual property rights: Report of the Commission on Intellectual Property Rights, Innovation and Public Health (2006), p52. Available at: <https://apps.who.int/iris/handle/10665/21102> (Accessed 20 June 2019).



BOX 2

High prices, in spite of the role of public research spending in blockbuster drugs

Sofosbuvir: Sofosbuvir was a breakthrough medicine for the treatment of Hepatitis C. The original research was the result of work at Emory University in the US. But the branded version of sofosbuvir was brought to the market for the price of US\$ 84,000 for the 12-weekly treatment from Gilead.⁸

Zika vaccine: In the US, public debates arose in 2017/2018 that questioned whether exclusive licences for a vaccine against Zika virus were justified or even legal,⁹ as the potential vaccine being researched by Sanofi was financed by the US-army. Up until the research was halted, at least US\$43 million of tax-payer money had been allocated to it. Plans for exclusive licences for other vaccine candidates have faced criticism as well, because they unnecessarily increase the price of a vaccine.¹⁰

Nusinersen: The first medicine for the treatment of Spinal Muscular Atrophy (SMA), a rare muscular disease, nusinersen was the result of research at the University of Massachusetts Medical School. In the Netherlands, a parliamentary debate emerged in 2017 about the high price of Spinraza (nusinersen's brand name), which would cost €300 million annually to the healthcare system.^{11,12} In Norway, the implementation of a compulsory licence was considered,¹³ which led to a price cut by the patent holder Biogen.¹⁴

⁸ Henry, B. (2018). 'Drug Pricing & Challenges to Hepatitis C Treatment Access', *Journal of Health and Biomedical Law*, 14, p265-283. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6152913/#R27> (Accessed 10 July 2019).

⁹ Knowledge Ecology International, KEI and MSF release comments on the proposed licence of Zika vaccine candidates to PaxVax (2017). Available at: www.keionline.org/23515 (Accessed 20 June 2019).

¹⁰ Ibid.

¹¹ Annual therapy costs in Germany, for example, are approximately 621,000 EUR per patient for the first year of treatment, and approximately 311,000 EUR in subsequent years. Gemeinsamer Bundesausschuss, Decision of the Federal Joint Committee on an Amendment to the Drug Directive [in German] (2017). Available at: www.g-ba.de/downloads/39-261-3169/2017-12-21_AM-RL-XII_Nusinersen_D-294_BAnz.pdf (Accessed 20 June 2019).

¹² BUKO Pharma-Kampagne (2017), 'Bezahlbare Medikamente: Niederlande diskutieren neue Strategien.' *Pharma-Brief* Nr.10/2017. Available [in German] at: https://www.bukopharma.de/images/pharmabrief/2017/Phbf2017_10_inet.pdf (Accessed 21 June 2019).

¹³ Huuse, C. (2018). 'SV vil løse Spinraza-konflikten ved å produsere medisinen i Norge – Har ventet lenge nok', *VG*, 10 February 2018. Available at: www.vg.no/nyheter/innenriks/i/9mKQzr/sv-vil-loese-spinraza-konflikten-ved-aa-produsere-medisinen-i-norge-har-ventet-lenge-nok (Accessed 20 June 2019).

¹⁴ Fouche, G and Solsvik T. (2018). 'Norway to buy Biogen's Spinraza medicine: broadcaster NRK', *Reuters*, 12 February 2018. Available at: <https://www.reuters.com/article/us-norway-biogen/norway-to-buy-biogens-spinraza-medicine-broadcaster-nrk-idUSKBN1FW0TR> (Accessed 20 June 2019).



BOX 3

Donors demand socially responsible access

CEPI: The Coalition for Epidemic Preparedness Innovations (CEPI) supports the development of vaccines against newly emerging diseases. It is mainly funded by the Norwegian government. The charters state: “To ensure public benefit is achieved ..., CEPI and the awardee will need to agree up-front obligations on the awardee ... vaccines will be available in sufficient quantities in affected countries ... vaccines sales prices will be as low as possible to maximize access.”¹⁵

CARB-X: Stimulates the development of new antibiotics. Mainly start-ups are funded,¹⁶ and the resources largely originate from the US-government agency Biomedical Advanced Research and Development (BARDA). The funding contract states: “The purpose of CARB-X is to protect human health from threats related to antibiotic resistant bacteria. ... Over the long term, new products must be sustainably managed... including ... reasonable plans for appropriate access ... especially in low- and middle-income countries ... As the last deliverable at the end of each stage, the sub-recipient shall create a plan reasonably describing how it intends to meet the ... access obligations for the Product.”¹⁷

GHIT: The Japanese government supports the development of technologies for poorer countries with the Global Health Innovative Technology Fund (GHIT). The funding conditions state: “In LDCs, LICs [low-income countries] and middle income countries, product development partners and/or participants will set prices for products on the basis of a no gains/no loss policy that can improve access to the product for patients and citizens.”¹⁸

Wellcome Trust: The Wellcome Trust is one of the most important funders for medical research globally. The patenting policy explains: “The mission of the Wellcome Trust is to foster and promote research with the aim of improving human and animal health. ... To achieve its aims, ... intellectual property issues must be approached carefully in light of individual circumstances ... Some techniques that the Trust uses ... including in grant conditions and funding agreements clauses to ensure that Trust-funded research is exploited for healthcare benefit, including clauses that relate specifically to the delivery of products to benefit developing country markets.”¹⁹

¹⁵ CEPI: New vaccines for a safer world (2017), CEPI Policy Documentation: Equitable access policy; Shared risks/shared benefits policy; management of intellectual property. Available online: https://msfaccess.org/sites/default/files/2018-09/CEPIoriginalPolicy_2017.pdf (Accessed 21 June 2019).

¹⁶ Combating Antibiotic Resistant Bacteria (CARB-X). Available at: www.carb-x.org/ (Accessed 21 June 2019).

¹⁷ CARB-X, Cost Reimbursement Research Subaward Agreement, 'Attachment 6: Research Subaward Agreement.' CARB-X Special Terms & Conditions (5/2017). Example available at: https://carb-x.org/wp-content/uploads/2019/02/CARB-X_Research-Subaward-Agreement-for-profit_31-Jan-2019-SAMPLE-1.pdf (Accessed 21 June 2019).

¹⁸ Global Health Innovation Technology (GHIT) Fund. Access policy. Available at: www.ghitfund.org/afag/policies (Accessed 21 June 2019).

¹⁹ Wellcome, Policy on intellectual property. Available at: <https://wellcome.ac.uk/funding/managing-grant/approach-wellcome-trust-managing-intellectual-property-maximise-public-health-benefit> (Accessed 21 June 2019).

HOW CAN A UNIVERSITY CONTRIBUTE?

HOW CAN A UNIVERSITY CONTRIBUTE?

This brochure introduces different measures universities and other research institutions can take to facilitate the development of new, marketable medicines that meet public health needs while simultaneously ensuring their availability and affordability and safeguarding follow-on research.

Case studies show what researchers can do and opportunities for university administrations or tech-transfer institutions. Most of the examples originate in biomedical research, yet the principles are applicable to all inventions. None of the proposed actions are exactly alike, nor will their implementation be identical. Usually, a framework for development will be agreed and details are negotiated at pre-determined milestones. What this brochure offers is suggestions and resources that can help publicly-financed institutions develop frameworks that support their mission of meeting societal needs.

The brochure offers many suggested actions. They are organised loosely on the gap they address, though it should be noted that most of these actions address either indirectly or directly all three.

For addressing access gaps, actions include:

- Incorporating socially responsible principles into university guidelines. (page 15)
- Including social responsibility in a contract (equitable licensing). (page 17)
- Employing non-exclusive licences, such as through patent pools. (page 20)
- Using socially responsible contractual conditions for research cooperation. (page 22)

For addressing translation gaps, actions include:

- Participating in non-profit product development partnerships. (page 25)
- Issuing multiple licences for innovations with different indications. (page 27)
- Using dual commercialisation pathways when a product has relevance in different types of markets. (page 28)
- Considering do-it-yourself product development through creation of foundations or start-ups. (page 30)

For addressing research gaps, actions include:

- Publishing in open access publications and contributing to open research collaborations. (page 33)
- Seeking financial support from non-traditional sources to support research. (page 35)

KEY TERMS

Active Pharmaceutical Ingredient (API): This refers to the part of a medicine that has an impact on the patient's system (as opposed to, for example, the medicines casing or the substance in which the API is suspended).

Equitable Licensing: Licensing that incorporates socially responsible provisions, including non-exclusivity of licences (to allow competition and flexibility in how the invention is used), technology transfer agreements, and provisions to ensure affordability and availability of any final product.

Exclusive Licensing: The practice of licensing a patent to only one licensee. There are situations in which this makes economic sense (e.g., small markets that cannot support competition), but it can also have the effect of transferring the patent monopoly to the licensee.

Licence: A licence can allow third parties to use a patented invention even during the monopoly period. Licences can either be voluntary (granted with the consent of the patent holder) or compulsory (granted without the consent of a patent holder, but with remuneration). Compulsory licences are granted by government authorities. A licence does not transfer ownership of the patent—it merely grants the licensee permission to use the technology within the patent, under the terms and conditions detailed in the licence.

Patent: Patents are a type of intellectual property rights intended to reward inventors through the granting a temporary monopoly (usually 20 years), during which time the patent holder can prevent others from making, using, or selling their invention. The intention is to incentivise innovation (through the potential for financial reward) in exchange for disclosure of new knowledge can be used by others once the monopoly period has ended.

Open Access: Open access publishers are those that provide their content online and free of charge to readers. There are many different models for these types of publications, but the overarching principle is to ensure that access to publications is not limited to those who can afford to pay high prices for them.

Technology Transfer: The transfer of technology from an organisation or person with to secondary organisation or person. It is frequently used to describe the transmission of knowledge from developed to less developed economies, and can include transfer of the right to use technology via a licensing agreement, skills transfer and trainings, and other means of sharing know-how.

ACTION

INCORPORATE SOCIALLY RESPONSIBLE PRINCIPLES INTO UNIVERSITY GUIDELINES



ACTION SUMMARY

A central mission of universities must be to support the development and spread of knowledge. This is especially the case when their research concerns public health. Enshrining socially responsible principles into research policies and other knowledge-related policies, including a progressive approach to licensing of any medical patents arising from research, supports and facilitates the implementation of that vision.

This action:

- Emphasises the societal importance of university research.
- Expands justification and motivation for technology transfer.
- Creates room for action if principles not met in practice.

In 2007, representatives from US universities gathered to discuss how their research findings could better benefit the public good. The result was a document that laid out “Nine Points to Consider when Licensing University Technology,”²⁰ including, among others: designing licences that reserve the right to use patented inventions for further research or educational purposes, that facilitate technology transfer, that seek to limit patenting of ‘follow-on’ innovations, and that ideally include provisions to address unmet needs of neglected patient populations, such as those in developing countries.

Nearly 70 US research institutes have since endorsed these principles. The Association of University Technology Managers (AUTM), a non-profit focusing on technology transfer, subsequently developed a “Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies” to further concretise the principles (see Box 4).

²⁰ Association of University Technology Managers (AUTM). In the Public Interest: Nine Points to Consider in Licensing University Technology. Available at: www.autm.net/AUTMMain/media/Advocacy/Documents/Points_to_Consider.pdf (Accessed 21 June 2019).

Resources

Numerous universities globally have incorporated the principle of social responsibility into their research dissemination strategies; their examples both demonstrate successful implementation and can be a model to other universities seeking to do

the same. These examples include: University of British Columbia (UBC),²¹ University of California, Berkeley,²² Emory University,²³ University of Oxford,²⁴ University of Bristol,²⁵ University College London (UCL),²⁶ Maastricht University,²⁷ and many others.



BOX 4

Excerpts from “The Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies”²⁸:

- In our negotiations with potential licensees, we will make vigorous efforts to develop creative and effective licensing strategies that help to promote global access to health-related technologies.
- Our intellectual property should not become a barrier to essential health-related technologies needed by patients in developing countries.
- In those cases where we pursue patent rights, we will negotiate licence agreements to promote broad access to health-related technologies in developing countries.
- It is not always possible at the time of licence negotiation to anticipate all of the ways a health-related technology may be used in developing countries. Accordingly, we will strive to preserve our institutions’ future rights to negotiate effective global access terms.
- Without regard to the economic value to our respective institutions, we will further support the development of new health-related technologies aimed at diseases that disproportionately burden individuals in the developing world, such as tuberculosis, AIDS, water-borne disease, tropical- and other region-specific ailments and parasitic infections.

Signing parties: Association of University Technology Managers (AUTM), National Institutes of Health as well as 20 US universities, among them Boston University, Brown University, Harvard University, Oregon Health & Science University, University of Pennsylvania, and Yale University.

²¹ The University of British Columbia. UBC Global Access Principles. Available at: <https://uilo.ubc.ca/technology-transfer/ubc-global-access-principles> (Accessed 21 June 2019).

²² Berkeley Intellectual Property & Industry Research Alliances (IPIRA). Socially Responsible Licensing. Available at: <https://ipira.berkeley.edu/socially-responsible-licensing> (Accessed 21 June 2019).

²³ Emory University, Office of Technology Transfer. Technology Transfer for Global Access: Guiding Principles. Available at: http://ott.emory.edu/documents/policies/emory_global_access_principles.pdf (Accessed 21 June 2019).

²⁴ University of Oxford: University policies. Access to essential medicines in the developing world. Available at: <https://researchsupport.admin.ox.ac.uk/policy/oxford/medicines> (Accessed 21 June 2019).

²⁵ University of Bristol (2012). University of Bristol humanitarian medical IP commercialisation policy. Available at: www.bristol.ac.uk/media-library/sites/red/migrated/documents/ems.pdf (Accessed 21 June 2019).

²⁶ At UCL, the Researchers using Established Workflows to Archive Research Data (REWARD) project highlights the institutional support to “archiving, dissemination and reuse of research data from government, funding bodies, institutions and researchers.” More detail is available from the Reward project, Available at: <https://www.ucl.ac.uk/reward/about> (Accessed 28 June 2019).

²⁷ Maastricht University: Faculty of Health Medicine and Life Sciences. Research. Available at: www.maastrichtuniversity.nl/about-um/faculties/health-medicine-and-life-sciences/research (Accessed 21 June 2019); Maastricht University and Universities Allied for Essential Medicines. Maastricht University Socially Responsible Research and Licensing Policy in the field of Health, Medicine and Life Sciences. Available at: www.maastrichtuniversity.nl/sites/default/files/srrl_policy.pdf (Accessed 21 June 2019).

²⁸ Association of University Technology Managers (AUTM). Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies. Available at: https://otd.harvard.edu/upload/files/Global_Access_Statement_of_Principles.pdf (Accessed 21 June 2019).

ACTION **INCLUDE SOCIAL RESPONSIBILITY IN A CONTRACT** **(EQUITABLE LICENSING)**

“‘Equitable Licensing’ ... aims to ensure access to essential medicines resulting from publicly funded research that are protected by patents. This model can help ensure that the social goals of publicly funded research are met under the conditions of modern, patent-based technology transfer.”²⁹



ACTION SUMMARY

Equitable licensing—sometimes called socially responsible licensing or global access licensing—is the practice of incorporating socially responsible principles into patent licences. Patent licences are a type of contract allowing third parties to make use of innovations under patent, under certain terms and conditions. In equitable licensing, contractual obligations thus become tools to promote access to needed technologies, for example by promoting market competition that can bring prices down.

This action:

- Avoids ‘exclusive licensing,’ where only one licensee is picked by the patent holder.
- Can help guide the product development plan, ensuring it respects access principles.
- Contract templates can be found at www.med4all.org.

Universities often engage in early stage research, and often hand it over to an external enterprise for further development and/or commercialisation. When this happens, it is preferable that equitable licensing practices are used over any patented innovation. It is important to note that licensing does not transfer ownership of the patent; that, the university would keep. There are several steps that universities can take to ensure their licence agreements are equitable:

Ideally, ensure non-exclusivity. Non-exclusive licences mean that more than one third party can make use of an invention; this can contribute to market competition and lead to cheaper prices of any resulting products. Exclusive licences (where there is only one licensee, who often has greater control as a result) should be used only in exceptional circumstances.

²⁹ Godt, C, Wagner-Ahlf, C, and Tinnemann, P. (2013). ‘Equitable Licensing – Ensuring Access to Innovation’ in Bollier, D. and Helfrich, S. The Wealth of the Commons: A World Beyond Market & State. Levellers Press <http://wealthofthecommons.org/essay/equitable-licensing-%E2%80%93-ensuring-access-innovation> (Accessed 21 June 2019)

A combination of exclusive and non-exclusive licences is also possible, for example an exclusive licence for Europe and several non-exclusive licences for LMICs outside of Europe (page 20). One particularly useful model for non-exclusive licensing—patent pools—is detailed in the next section.

Plan for development and commercialisation: Contracting parties agree on a development plan with milestones where they stipulate further actions concerning production, price, and availability. (For examples of this type of arrangement, see the section on **Product Development Partnerships**).

Ensure affordability and availability: Price stipulations and manufacturing stipulations (including sub-licensing, for example, to lower-cost producers) can be a part of the contract to ensure that access goals are met.

Have set controls: The contract should regulate how milestones are to be achieved, how the development plan will be managed, and set an accountability structure for agreed arrangements.

The table below describes different combinations of contractual arrangements that achieve the goal of equitable licensing.

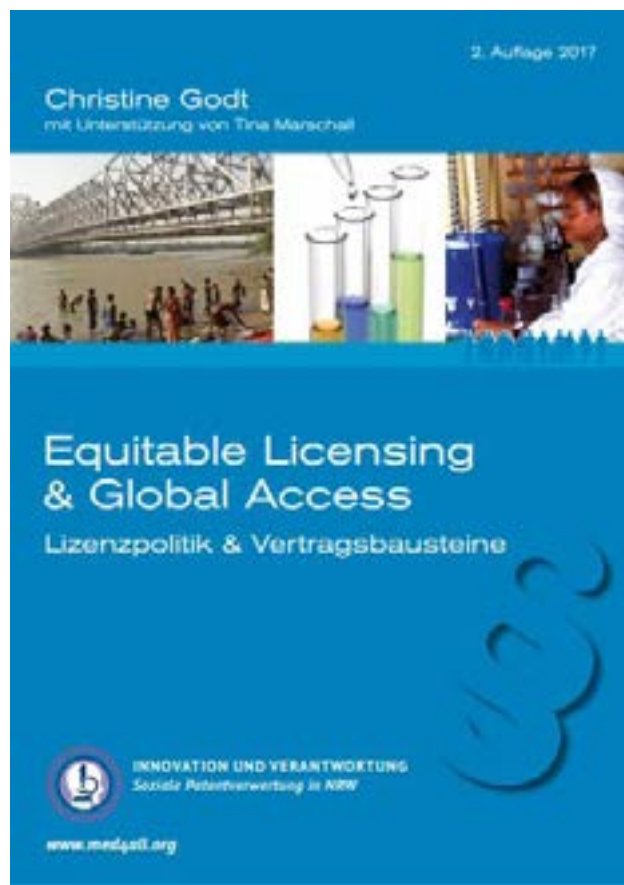
Table 1: Different combinations of contractual arrangements that achieve the goal of equitable licensing

	Type of licence	Objective	Exploitation	Controls	Grant Back
Optimal	University retains management of the invention with the goal to maximise societal benefit (instead of maximising financial return) Non-exclusive licence	Best possible provisions: on the price of eventual products, on technology transfer, and on training of health personnel	Concept: publicly accessible Concrete project milestones linked to responsible parties	Monitoring and penalties regulated; controlled by an independent party	Licensee grants unrestricted, royalty-free use rights on all dependent technologies to the original patent holder (aka, the university)
Acceptable	Exclusive licence	Differential pricing	Simple licence to producers in developing countries	Cheaper (less resources) and simpler (easier procedure)	Grant back is ensured, but requires royalty payment
Not ideal	Exclusive licence		Non-assert agreement by the licensee		No grant back provision

Since the concept of equitable licensing first emerged in 2005,³⁰ experiences on implementation have been gathered. These have been analysed within the scope of the project med4all³¹, who developed pre-formulated contract clauses.

Resources

The leaflet 'Equitable Licensing & Global Access: licensing policies and pre-formulated contract clauses' provides pre-formulated contract clauses that can be used as a model for research partnerships, single innovation transfers, spin-off products and the engagement of product development partners similarly. Additional options for non-exclusive licensing are detailed in the next section.



The leaflet 'Equitable Licensing & Global Access: licensing policies and pre-formulated contract clauses' (Christine Godt, 2017) provides pre-formulated contract clauses.³¹ The introduction of the leaflet is in German, but the contract clauses are also in English. (Download at http://www.med4all.org/images/downloads/lizenzbroschuere_2017_final.pdf)

³⁰ Kapczynski Amy et al. (2005) 'Addressing Global Health Inequities: An Open Licensing Approach for University Innovations', Berkley Technology Law Journal 20(2), p.1031-1114. Available online: https://www.jstor.org/stable/24116640?item_view=read_online&refreqid=excelsior%3A9dc6de323c1d4619c36670bf169e3d8f (Accessed 21 June 2019).

³¹ Godt, C. (2011) 'Equitable Licences in University-Industry Technology Transfer', GRUR Int 2011, p. 377-385. Available at: http://www.med4all.org/images/downloads/Godt_Equit_Lic_GRUR_Int_2011_377_385.pdf (Accessed 21 June 2019).

ACTION **EMPLOY NON-EXCLUSIVE LICENCES, SUCH AS THROUGH PATENT POOLING**



ACTION SUMMARY

Non-exclusive licences allow utilisation by multiple users. They thus avoid a monopoly, create competition and thereby reduce the price of the final product. In this way they serve the actual goal of technology transfer: they ensure the broadest possible use of research and they improve care. One common way to achieve this is through patent pooling, which essentially creates a ‘one-stop shop’ for companies seeking to share intellectual property related to a particular technology.

This action:

- Allows multiple third parties access to and right to use the technology.
- Avoids monopolies, which can keep prices high.
- Creates competition that brings down prices.

Exclusive rights are generally problematic in platform technologies that are crucial for further downstream research. The US National Institutes of Health recommended in 1999 to ensure the broadest possible application of publicly-financed research tools through non-exclusive licences. Patent pools are one non-exclusive licensing model. They facilitate access to legal rights needed to develop technologies by cutting down on lengthy, uncertain, and often expensive individual licence negotiations. They are particularly useful in cases where an innovation requires use of multiple patented elements, which are often owned by different patent holders. Recently, patent pools have been used as well to forward public health goals. Two case studies are below.

Case Studies

Case Example—Medicines Patent Pool

The Medicines Patent Pool (MPP) was established in 2010 to promote the greater access to affordable HIV drugs for the needs of people in

poorer countries. The MPP negotiates voluntary licence agreements with patent holders, in most cases pharmaceutical companies, and then makes them easily available to generic company sub-licensees to facilitate lower-cost production of key medical technologies. The ‘pool’ of licences enables the production and marketing of affordable HIV drugs, in particular for combination preparations with active ingredients coming from different patent holders as well as medicines for children, by easing access to the legal rights needed for that production. All licence agreements are published in full and online (www.medicinespatentpool.org).

MPP’s mandate was extended to tuberculosis and hepatitis C in 2015. Licence agreements have been signed covering 15 products for the three diseases (primarily HIV); 24 generics manufacturers have taken sub-licences and more than 100 products are in development. As of 2018, the expansion of MPP’s mandate to include patented medicines on the World Health Organization’s (WHO) Model List of Essential Medicines is being considered.

Case Example—CRISPR-CAS9 Pool

The CRISPR genome editing technology has become an important tool for health research. Several dozen patent owners, including many public research institutes, such as University of California Berkeley and the Broad Institute of MIT and Harvard, claim patents for the technology; the establishment of a patent pool is currently being discussed to enable uncomplicated and various use through non-exclusive licences.^{32,33}

This would resolve the current legal uncertainty of the usage rights. Huge public interest exists in an open, non-discriminatory licensing of CRISPR patents on reasonable terms.³⁴

³² Broad Institute: Press Releases (2017). Broad Institute of MIT and Harvard joins discussions to create worldwide CRISPR-Cas9 licensing pool. Available at: www.broadinstitute.org/news/broad-institute-mit-and-harvard-joins-discussions-create-worldwide-crispr-cas9-licensing-pool (Accessed 21 July 2019).

³³ MPEG LA: CRISPR. The Initiative: MPEG LA calls on CRISPR-Cas9 Patent Holders to Solve the CRISPR IP Conundrum. Available at: www.mpegla.com/main/pid/CRISPR/Initiative.aspx (Accessed 21 July 2019).

³⁴ KEI (2017). Letter from KEI to Thomas Price, Secretary of the Department of Health and Human Services, urging the adoption of a policy on licensing CRISPR patents. Available at: www.keionline.org/wp-content/uploads/CRISPR-SecPrice-6Jan2017.pdf (Accessed 21 July 2019).

ACTION

MAKE USE OF SOCIALLY RESPONSIBLE CONTRACTUAL CONDITIONS FOR RESEARCH COOPERATION



ACTION SUMMARY

Universities frequently collaborate with companies to commercialise their research; there are several key conditions universities could put in research contracts to uphold socially responsible principles, including requiring any resulting products be accessible and retaining a say in their use.

Suggested contractual conditions for research cooperation include:

- Universities remain co-owner of findings
- Universities retain the right to have a say in the use of findings
- Obligations to make eventual products accessible

Cooperations are an everyday part of contemporary biomedical research—not only between academic partners, but also between commercial companies. Contracting parties may have different interests: a scientific institution wants to advance knowledge, while a company by definition wants to make a profit. To maximise the benefits of a research cooperation between different parties for the public good, two cornerstone agreements are necessary:

Researchers must remain co-owners of findings and retain the right to have a say in their use:

Scientists should not lose their rights to research findings. This applies not only to the freedom to use the findings for further research, but also to the right to have a say in their application.

The university needs to retain its influence in the longer term. Therefore, exploitation rights should not automatically be assigned to the commercial partner.

Accessibility should be a contractual obligation:

Research contracts should stipulate that LMICs be able to access any fruits of the cooperation. At a minimum, commercial partners should undertake to make products (drugs, vaccine, diagnostics) available at fair prices and guarantee their availability for relevant countries or population groups. What this means in practice depends on the diseases being researched, including its regional importance and other parameters. Since these details often cannot be fully clarified in the early stages of development, it makes sense

to contractually agree on the further steps, e.g., define milestones for further decisions, name the actors involved in the decisions and develop a control mechanism for the implementation of the decisions.

Case Studies

Case Example—International AIDS Vaccine Initiative (IAVI)

This research consortium aims to develop vaccinations against HIV/AIDS and to make them available. A large number of public research institutions are involved, as are various companies. Founded in 1996, IAVI systematically compares vaccine concepts and candidates in both basic research and clinical trials. It also works to build research capacity in affected regions of Africa and Asia. Clinical trials are conducted in Europe, Africa and Asia. The partners contractually commit themselves to ensuring global access to any future HIV vaccines.

Any vaccine developed by IAVI will be registered, produced and delivered to LMICs.³⁵

Case Example—European Vaccine Initiative (EVI)

This product development partnership based in Heidelberg, Germany cooperates with partners in over 100 countries to promote the development of vaccines against poverty-associated diseases (such as malaria, zika, dengue, and leishmaniasis) and influenza. The most advanced are malaria vaccines, which are currently in Phase II clinical trials. EVI's access policies are detailed in Box 5.

Resources

Suitable contract modules are provided by Godt (2017) *Equitable Licensing Global Access: licence policy and contract modules* (see page 19). The introduction of the leaflet is in German, but the contract clauses are also in English. It is available at: http://www.med4all.org/images/downloads/lizenzbroschuere_2017_final.pdf

³⁵ International AIDS Vaccine Initiative (IAVI). Global Community Engagement. Available at: <https://www.iavi.org/our-work/global-community-engagement> (Accessed 21 July 2019).



BOX 5

Three Questions for Stefan Jungbluth of EVI



© Jungbluth

Dr Stefan Jungbluth,
Head of Business Development at EVI
(University Hospital Heidelberg)

Question 1: Are there contractual obligations to ensure supply to developing countries?

Dr Jungbluth: The contracts with our partners have clauses that the products must be made available at affordable prices. In doing so, we are guided by the European Commission's regulation for graduated prices for poorer and industrialised countries. There are two ways to set the retail price in poorer countries: it is either a maximum of 25% of the average price for OECD countries, or manufacturing costs plus a 15% surcharge.³⁶

Question 2: How does EVI ensure compliance?

Dr Jungbluth: If a contractual partner does not comply with this regulation, we can reclaim the financing. If the partner does not want to develop the project further, we can claim the IP rights for further development for use in developing countries.

Question 3: Has EVI already taken vaccines to market?

Dr Jungbluth: No, so far our projects have reached clinical phase II. For phase III, we need large companies as partners. Of course, the market is not that profitable for applications exclusively in developing countries, but we are also working on vaccines for a dual market. An influenza vaccine is also interesting for Germany - this is an extra incentive for companies to participate.

³⁶ EUR-Lex: Access to European Union law (2016). Regulation (EU) 2016/793 of the European Parliament and of the Council of 11 May 2016 to avoid trade diversion into the European Union of certain key medicines. Available at: <http://eur-lex.europa.eu/legal-content/EN/TXT/?qid=1513784643963&uri=CELEX:32016R0793> (Accessed 21 July 2019).

ACTION

PARTICIPATE IN NOT-FOR-PROFIT PRODUCT DEVELOPMENT PARTNERSHIPS



ACTION SUMMARY

Not-for-profit product development partnerships are cooperative structures designed to aggregate resources (including both know-how and financing) from multiple actors towards the development of needed biomedical products.

This action:

- Offers financing opportunities for development of needed medical products.
- Takes global health needs into account.
- Considers affordable supply of eventual products in its model.

For diseases that particularly affect people in LMICs, a special form of research cooperation has developed over the last two decades: not-for-profit product development partnerships (PDPs). Generally, many different actors are involved, including public institutions and companies, as well as civil society organisations. Professional portfolio management ensures that financial resources are used effectively. Characteristically in this form of cooperation, medicines, vaccines and diagnostics are developed in a global network. The focus lies on neglected and poverty-associated diseases—above all tropical infectious diseases, but also tuberculosis, malaria and HIV. Consequently, research is being expanded in LMICs. Research objectives are based on global needs and include an affordability provision. Typically, PDPs are financed through a multiple sources, mainly state donors (Germany, US, UK, European Union) and foundations (Gates Foundation, Wellcome Trust).

For public research institutions and their scientists, PDPs offer the opportunity to bring promising results of basic research to product development.

Many European universities are already involved in PDPs and are thus opening up new sources of funding.

Case Studies

Case Example—Drugs for Neglected Diseases Initiative (DNDi)

The DNDi was founded in 2003 by Medecins Sans Frontieres (MSF) and several public research institutes. Since then, seven new medicines have been developed, including two patent-free malaria medicines,³⁷ and 30 more medicines are in the pipeline. In 2016, more than €37 million was invested in research and development; in 2017, this grew to €43.5 million.³⁸ The work is distributed among 160 partners on all continents. The principle: Laboratories are paid for preclinical studies, manufacturers are paid for the production of the trial medication, and DNDi coordinates the development of the necessary infrastructure for clinical trials in target countries. Two principles form the basis of the cooperation between the numerous actors³⁹: Firstly, that medicines should be affordable and available for all patients who need them; and

³⁷ Fischer, C. and Wagner-Ahlf, C. (2011) 'Medicines in the Public Domain: How the patent-free malaria drug ASAQ has changed research.' In: Studies: Medicine as Public Domain. Germany: Rosa Luxemburg Foundation (2013). Available at: www.rosalux.de/fileadmin/rls_uploads/pdfs/Studien/Studien_Arznei-als-Gemeingut.pdf (Accessed 21 July 2019).

³⁸ Drugs for Neglected Diseases initiative (DNDi). (2017) Annual Report 2017: Responding to Neglected Patients' Needs Through Innovation, p. 71. Available at: https://www.dndi.org/wp-content/uploads/2018/08/DNDI_AR_2017.pdf (Accessed 21 June 2019).

³⁹ Drugs for Neglected Diseases initiative (DNDi). DNDi's Policies. Available at: www.dndi.org/wp-content/uploads/2009/03/ip%20policy.pdf (Accessed 21 June 2019).

secondly, that whenever possible medicines are developed as public goods. Licence and research agreements are therefore negotiated accordingly.

Case Example—Global Antibiotic Research and Development Partnership (GARD-P)

This worldwide network for the development of new antibiotics was established by WHO. GARD-P follows a not-for-profit model to find new treatment options for antibiotic-resistant pathogens. The first projects target neonatal sepsis and sexually transmitted diseases (e.g., gonorrhoea). The new antibiotics are expected to be affordable, and the costs for research and development are fully covered by donors.⁴⁰ In parallel with the R&D, programmes that will ensure appropriate and restricted use (stewardship) will slow the onset of resistance.⁴¹

Case Example—Foundation for Innovative New Diagnostics (FIND)⁴²

FIND coordinates the development of diagnostics for infectious diseases with global significance: hepatitis, HIV, and malaria, as well as Ebola and other infections with epidemic potential. In cooperation with over 200 partners worldwide, 21 diagnostic tools have been developed to-date. Diagnostic tools have to meet the needs of LMICs and also be applicable in weak health systems. All products need to be registered in LMICs and brought to the market where they are needed. The prices have to be adapted to the needs of target countries.⁴³

Resources

PDPs develop products for the needs of people in LMICs and enjoy professional portfolio management. When a public research institution participates, new opportunities for cooperation and funding arise. The table below depicts a non-exhaustive selection of PDPs.

Table 2: Non-exhaustive selection of PDPs.

Project	Diseases	More info
International Aids Vaccine Initiative (IAVI)	HIV/AIDS vaccine	www.iavi.org
Drugs for Neglected Diseases Initiative (DNDi)	Medicines for sleeping sickness, Chagas, malaria, HIV, worm diseases, mycetoma (Madura foot), hepatitis C	www.dndi.org
Medicines for Malaria Venture (MMV)	Anti-malarials	www.mmv.org
Foundation for Innovative New Diagnostics (FIND)	Diagnostics for hepatitis, HIV, tuberculosis, trypanosomes, and others.	www.finddx.org
Infectious Disease Research Institute (IDRI)	Diagnostics, vaccines, medicines for leishmaniasis, tuberculosis, leprosy, Chagas	www.idri.org
TB Alliance	Tuberculosis	www.tballiance.org

⁴⁰ German Federal Ministry of Education and Research (BMBF) (2017) 'Important step in the fight against antibiotic resistance.' Press release, 4 September 2017. Available [in German] at: <https://www.bmbf.de/de/wichtiger-schritt-im-kampf-gegen-antibiotika-resistenzen-4733.html> (Accessed 21 June 2019).

⁴¹ Global Antibiotic Research & Development Partnership (GARDP): R&D Strategy. Sustainable Access. Available at: www.gardp.org/rd-strategy/sustainable-access/ (Accessed 21 June 2019).

⁴² FIND: Because diagnosis matters. Available at: www.finddx.org/ (Accessed 21 June 2019).

⁴³ FIND (2018). Global Access Policy. Available at: www.finddx.org/wp-content/uploads/2018/02/FIND-Global-Access-Policy_26FEB18.pdf (Accessed 21 June 2019).

ACTION **ISSUE MULTIPLE LICENCES FOR DIFFERENT INDICATIONS**



ACTION SUMMARY

Some medical technologies have multiple uses. In such cases, multiple licences may be offered on the same material, each for a different field of use.

This action:

- Be alert for when an active ingredient can be used or developed for different indications.
- Awards several licences for different indications.
- Thus expands the range of uses of the invention.

If an invention could lead to the development of several products that have nothing to do with each other, an exclusive licence is likely not the best solution. Instead, licences can be given to different developers, with different and non-conflicting specialities.

Commercial biomedical development is primarily oriented towards lucrative markets, such as cardiovascular diseases, oncology or neurodegenerative diseases. But medicinal candidates developed for these purposes could also be suitable for tropical infectious diseases, among other uses.

For this reason, many pharmaceutical companies have now opened their medicine libraries for product development partnerships (see page 25) to allow screening for potential additional indications.

When a public research organisation is looking for licensees, it should always be considered whether there are applications of the technology relevant for global use that do not seem to be related to the original field of research.

Case Studies

Case Example—Miltefosine

The development of miltefosine as a drug to treat leishmaniasis, an infectious disease that overwhelmingly affects people in LMICs, began in 1984 at the pharmaceutical company Burroughs Wellcome (now GlaxoSmithKline). Its effectiveness against leishmaniasis became apparent, but the tropical medicine department was dissolved. Meanwhile, the chemist Hansjörg Eibl registered a patent for miltefosine as an oncology treatment at the Max-Planck-Institute for Biophysical Chemistry (MPI Göttingen) in 1986. The pharmaceutical company ASTA Medica secured an exclusive licence and received approval for Miltefosin in 1992, which used miltefosine for the treatment of skin metastases in breast cancer. Finally, WHO, ASTA and MPI Göttingen agreed on a cooperation for the development of a leishmaniasis drug. Miltefosin was approved in India in 2002 for the treatment of leishmaniasis in adults.⁴⁴ The branded medicine, Impavido, is now provided for developing countries at reduced prices and is now an important part of the treatment of leishmaniasis.

⁴⁴ Wagner-Ahlf, C., and Wolf, J. (2010) 'Miltefosin - A case study on how public inventions can be made available to poor countries', *Chemotherapie Journal* 19(3), p.63-69. Available at: https://www.researchgate.net/publication/286298016_Miltefosine_-_A_case_study_how_a_public_invention_can_be_made_available_for_developing_countries (Accessed 21 June 2019).

ACTION

USE ROYALTY-FREE LICENCES FOR DEVELOPING COUNTRIES, OR ENGAGE IN DUAL COMMERCIALISATION



ACTION SUMMARY

Royalty-free licences can facilitate access in LMICs. 'Dual commercialisation' can be useful when a biomedical product has both the potential for profit and also the potential to be impactful on public health, particularly in low- and middle-income markets. The product can thus take two or more commercialisation pathways, one employing royalty-free licences and the other requiring royalty payments.

This action:

- Increases the use of the innovation, especially in lower-income markets.
- Allows different commercialisation pathways for products used differently in different markets.
- Could stimulate new, novel sources of financing.

Royalty-free licensing in dual commercialisation, a commercial for-profit licence covers the needs of wealthier markets and requires royalties; a second, non-profit licence would be royalty-free, facilitating its use in markets with lower purchasing power. In this way, even the development of regionally different products can be stimulated; for example, medicines for the needs of tropical countries.

This royalty structure fulfils a dual function: royalty-free licences facilitate access in poorer markets; while royalty-bearing licences in wealthier markets generate resources for further research.

Case Studies

Case Example—Royalty-free Licensing UC Berkeley/Tuberculosis Vaccine

An agreement was concluded with a commercial vaccine supplier for research on a tuberculosis vaccine. In case this research at UC Berkeley results in a vaccine, its use "outside Europe, North America, Japan, South Korea and Taiwan" would be free of charge.⁴⁵

Case Example—Royalty-free Licensing Sustainable Science Institute

The Sustainable Science Institute is a not-for-profit organisation from San Francisco (USA), with project partners in Nicaragua and Egypt.⁴⁶ Besides education and training for healthcare workers, inexpensive diagnostics to meet the health needs of partner countries are being developed.^{47,48} One project is a simple and portable diagnostic test for dengue fever. US universities have contributed important inventions and refrained from requiring royalties for its use in LMICs. This commitment, in turn, stimulated sponsorship from other donors, including the Acumen Fund for Social Investment and the Doris Duke Charitable Foundation.⁴⁹

Case Example—Dual Commercialisation University of California, Berkeley (UCB)/ Amyris

The objective of the project is a biotechnological method for the production of terpenes, organic compounds usually found in plants. The technology was developed by Professor Jay Keasling at UCB and is widely applicable. It was commercialised through a spin-off company, Amyris.

In 2004, a contract was negotiated that allowed different parties to pursue a for-profit and a non-profit direction simultaneously.⁵⁰ On the one hand, Amyris was to take the classic path and use venture capital to develop synthesis processes to market maturity—which it succeeded in doing.

Today, Amyris produces medicines, cosmetic fragrances and biofuels. For this purpose, royalties are due to UCB.

At the same time, a non-profit project was enabled: in cooperation with the Institute for

One World Health (iOWH), the production of artemisinin was facilitated. This important raw material for many malaria medicines is derived from plants, and biotechnological synthesis was expected to reduce the price. The Gates Foundation sponsored the project with US\$ 8 million for the UCB, US\$ 22.6 million for iOWH and US\$ 12 million for Amyris.⁵¹ This development branch was exempted from licence fees. In return, Amyris was obliged to make the technology usable/available with sub-licences for artemisinin production for “economically disadvantaged countries.”⁵²



⁴⁵ Mimura, C. (2006). 'Technology Licensing for the Benefit of the Developing World: UC Berkeley's Socially Responsible Licensing Program', *Journal of the Association of University Technology Managers*. Fall 2006, p.15-28. Available at: www.autm.net/AUTMMain/media/Advocacy/Documents/MimuraAUTMJournalFall06.pdf (Accessed 21 June 2019).

⁴⁶ Sustainable Sciences Institute. FIRST (Fighting Infections through Research, Science, and Technology). Available at: <http://sustainablesocieties.org/f-i-r-s-t-projects/> (Accessed 21 June 2019).

⁴⁷ Murphy, P. (2014). 'UCSF Global Health Sciences Receives \$6 Million for Three Neglected Diseases', *University of California San Francisco*. Available at: www.ucsf.edu/news/2014/05/114586/ucsf-global-health-sciences-receives-6-million-three-neglected-diseases (Accessed 21 June 2019).

⁴⁸ Sustainable Sciences Institute. ICTs for Health. Available at: <http://sustainablesocieties.org/ict-for-health/> (Accessed 21 June 2019).

⁴⁹ Mimura C (2010) Nuanced Management of IP rights. In: *Working within the boundaries of intellectual property*. Dreyfuss R, First H, Zimmerman D (ed.), Oxford University Press, 2010.

⁵⁰ Ibid.

⁵¹ Mimura, C. (2006). 'Technology Licensing for the Benefit of the Developing World: UC Berkeley's Socially Responsible Licensing Program', *Journal of the Association of University Technology Managers*. Fall 2006, p.15-28. Available at: www.autm.net/AUTMMain/media/Advocacy/Documents/MimuraAUTMJournalFall06.pdf (Accessed 21 June 2019).

⁵² Mimura, C., Cheng, J., and Penhoet, B. (2011). 'Perspective: Socially Responsible Licensing, Euclidean Innovation, and the Valley of Death', *Stanford Journal of Law, Science and Policy*, 2011 UC Berkeley Public Law Research Paper No. 192883

ACTION

CONSIDER ‘DO-IT-YOURSELF’ PRODUCT DEVELOPMENT VERSUS THE CREATION OF A START-UP



ACTION SUMMARY

In some cases, a commercial partner is not easy to find. Universities could in these cases consider setting up a foundation or launching a start-up company to bring the medical product to market. In either case, the original research institution should retain a degree of control over the end-product (see “make use of socially responsible contractual conditions” for guidance). The choice between a do-it-yourself approach and a start-up can have consequences for the degree of control retained.

This action:

- Details options for avoiding the “valley of death” between research and product development, if no industrial partner can be found.

Many scientists know the situation: you have promising research results and believe in the future of the project, but there is no company willing to develop the innovation further. How can this “valley of death” between research and product development be resolved?

Some universities decide to set up a foundation, which can be an innovative way to bring in collaborators and even new sources of funding (e.g., from development cooperation bodies). Some universities decide to set up their own business, which can add entrepreneurial challenges on top of scientific challenges. Can the search for investors be combined with a project orientation towards principles of social equity? Can the business model afford the university adequate control of how the innovation is

eventually made available and accessible? There is no simple, general answer to these issues. The search for investors or cooperation partners is a challenge for all founders, and it is certainly not easy to maintain social standards in the process. The example below shows the benefits of addressing this barrier.

The university or public research institution should, as a matter of principle, remain connected to the project. This is the only way it can retain its right to influence any follow-up towards a socially appropriate usage. If the research institution does not remain a direct co-owner via an associated company, it should, for example, remain in dialogue with the responsible actors via an advisory board.



BOX 6

Case Example—Innovative Medicines for Tuberculosis Foundation (iM4TB)



© Clerc

Gabriel Clerc
Head of the EPFL Technology
Transfer Office

The iM4TB Foundation was created in 2014 by the École Polytechnique Fédérale de Lausanne (EPFL), a Swiss university, to advance the development of a new antibiotic (PBTZ169) against multi-resistant tuberculosis. Interview with Gabriel Clerc, Head of the EPFL Technology Transfer Office.

Question: Why did EPFL decide to take on further development of the tuberculosis drug?

Clerc: We already had a cooperation with a German company in this area and both partners were willing to sign a licence agreement for PBTZ169.

Unfortunately and surprisingly, the company has completely stopped its TB research and development—although the preclinical data were very good. So, we were faced with the question: How do we continue? Larger pharmaceutical companies were interested, but didn't want to get involved at such an early stage. Therefore we had to overcome the “valley of death” and do the clinical trials ourselves.

Question: You then set up a foundation. Why not a start-up?

Clerc: We discussed intensively what the best way would be. A start-up requires venture capital, and investors want to see an ‘exit’ after five or six years. TB research focuses on public health, so we cannot promise high profits. This is why EPFL, together with the two inventors, Dr. Cole and Dr. Makarov, created a foundation in 2013. As a charitable foundation, we are able to collect donations and acquire further not-for-profit funds, too. The Gates Foundation in particular has made a lot possible with two funding rounds. Conversations with the tax authorities have pointed out the fiscal benefits for intellectual property to remain entirely with EPFL. This is advantageous for later licensees, too, since companies find it more attractive and clearer if the IP is in one hand.

The foundation's first major financial resources came from a licensing agreement with a medium-sized Russian pharmaceutical company that develops the medicine for Russia and neighbouring countries. Since TB is a serious problem in Russia, the company receives public support there.

Normally, the income would go in equal shares to the inventors, the institute and the EPFL. In agreement with everyone involved, however, we invested the money in the foundation in order to pay for preclinical research. We also pay for the maintenance of the IP rights from these initial licence revenues. The foundation was thus able to hire a pharmacologist with experience in the industry to lead the project. Of course, we are



BOX 6 (continued)

not able to carry out all the necessary preclinical developments and studies at EPFL and had to outsource most of the tasks. We have agreed on an information exchange with the Russian company, but since the regulatory conditions in Europe are different, we carry out all essential studies ourselves.

Question: If a company picks up the active ingredient, how do you ensure that the product will be available in the end?

Clerc: We will complete clinical phase I this year in collaboration with the University Hospital in Lausanne. Since 2014, more than 5 million Swiss francs have been used for this purpose. At this moment, we are negotiating a second licence with a pharmaceutical company outside of Russia and of neighbouring countries to continue the development. It is not even necessary to discuss global availability—it is contractually determined. Gates Foundation funding includes a Global Access clause, therefore, each licence must include such a Global Access commitment. This is no surprise for companies operating in this field.

(Interview conducted in 2017)

ACTION

PUBLISH FINDINGS AS OPEN ACCESS AND CONTRIBUTE TO OPEN RESEARCH COLLABORATIONS

“What society wants, is for all this information to be out there, free of charge, no patents, no restrictions. And that’s what we do.”⁵³

Dr Aled Edwards, CEO of the Structural Genomics Consortium



ACTION SUMMARY

Open access publishers are those that provide their content online and free of charge to readers. There are many different models for these types of publications, but the overarching principle is to ensure that access to publications is not limited to those who can afford to pay high prices for them. Open research aims to take the same principle and apply it to data and methodologies: Researchers share knowledge related to facilitate wide collaboration to solve identified challenges.

This action:

- Ensures research findings are available to and usable by everyone.
- Avoids unnecessary duplication of research.
- Combines the expertise of many researchers.
- Accelerates the discovery of solutions to shared problems.

Open access publications are increasingly common. They have many advantages: being freely accessible, they do not exclude anyone from accessing or reading research outputs and is the ideal case for oversight of research financed by public money. The German Ministry of Education and Research (BMBF) is implementing this with its Open Access strategy. Since 2016, funding announcements and BMBF project funding communications contain an open access clause.

The idea of open research goes a step further. The concept is based on the open source model for software development. The idea is that issues are posted online and ideas about solutions and improvements are shared on specific platforms. Ideally, neither restrictions on use nor property rights would exist in that space, though in

practice there are many models that facilitate open research with varying degrees of restriction. In pharmaceutical research, there have been projects for several years called 'open source', where the knowledge is shared openly and collaboration from third parties is invited.⁵⁴ Generally, such initiatives apply to neglected diseases.

Case Studies

Case Example—Open Synthesis Network⁵⁵

Since 2016, students from Switzerland, India, the United Kingdom and the US have been researching active ingredients for the treatment of visceral leishmaniasis. The findings are published without intellectual property rights in the public domain. The DNDi continues the development of this model.

⁵³ Structural Genomics Consortium. 'Why release your research into the public domain?' Frequently asked questions. Available at: https://www.thesgc.org/about/mini_faq#faq_8 (Accessed 21 June 2019).

⁵⁴ German Federal Ministry of Education and Research (BMBF) (2016), Open Access in Germany: The Strategy of the Federal Ministry of Education and Research. Available [in German] at: https://www.bmbf.de/upload_filestore/pub/Open_Access_in_Deutschland.pdf (Accessed 21 June 2019).

⁵⁵ Drugs for Neglected Diseases initiative (DNDi). Open Synthesis Network. Available at: www.dndi.org/2017/open-innovation/openinnovation-all-kinetoplastids/open-synthesis-network/ (Accessed 21 July 2019).

Case Example—Structural Genomics Consortium (SGC)

The SGC decrypts the structures of potential active ingredients candidates. Aled Edwards (Director) explains: “What society wants is for all this information to be out there, free of charge, no patents, no restrictions. And that's what we do.”⁵⁶ Public institutions and companies are included in the venture, and a 2014 evaluation of the SGC⁵⁷ concluded that both groups of stakeholders benefit from the open access collaboration.

Case Example—Open Source Drug Discovery (OSDD)⁵⁸

The Indian government has funded the OSDD since 2008. It currently has 7,900 research projects in 130 countries on tuberculosis and malaria.

Only registered OSDD members are granted free access to ongoing research findings.⁵⁹

Even though involved actors retain the right to patent their own innovations, they are obliged to provide the OSDD a free, non-exclusive licence.⁶⁰

Case Example—Open Source Malaria Consortium (OSM)

This research project aims to develop new active ingredients for malaria.⁶¹ It was founded by Australian chemist, Matthew Todd, from the project *The Synaptic Leap*, which is committed to biomedical open source research.⁶² All research steps are documented online. OSM is currently funded by the Australian government and the Medicines for Malaria Venture, a product development partnership based in Geneva (see page 25).



⁵⁶ SGC. Available at: www.thesgc.org/ (Accessed 21 June 2019).

⁵⁷ Morgan Jones, M. et al. (2014). The Structural Genomics Consortium: A knowledge platform for drug discovery. RAND Corporation. Available at: www.rand.org/pubs/research_reports/RR512.html (Accessed 21 June 2019).

⁵⁸ Open Source Drug Discovery. Available at: www.osdd.net/ (Accessed 21 June 2019).

⁵⁹ Open Source Drug Discovery. SysBorg 2.0. Available at: <http://sysborg2.osdd.net/web/guest> (Accessed 21 June 2019).

⁶⁰ Open Source Drug Discovery. Attribution & Authorship Policy. Available at: www.osdd.net/about-us/osdd-policies/attribution-authorship-policy (Accessed 21 June 2019).

⁶¹ Open Source Malaria: Looking for New Medicines. Available at: <http://opensourcemalaria.org/> (Accessed 21 June 2019).

⁶² Todd, M. (2011). 'Open Source Drug Discovery for Malaria', The Synaptic Leap: Open Source Biomedical Research. Available at: www.thesynapticleap.org/node/343 (Accessed 21 June 2019).

ACTION

SEEK FINANCIAL SUPPORT FOR FURTHER RESEARCH AND DEVELOPMENT



ACTION SUMMARY

Non-traditional financing opportunities should be explored. In particular cases, donor financing specialised in supporting innovation geared at low- and middle-income country health needs may be available.

This action:

- Helps support research targeted to meet the needs of low- and middle-income countries by unlocking new sources of financing
- Facilitates collaborations with partners in low- and middle-income countries, who are expert in local research needs

If an invention could be relevant to the needs of people in low-resource settings, it is worth researching specialised donors as well as commercial partners. The European Commission, for example, supports clinical trials for therapies that benefit LMICs through the European Developing Countries Clinical Trials Partnership (EDCTP) programme. When a project is already close to maturity, interim financing through the Global Health Investment Fund can be considered. Foundations such as the Bill and Melinda Gates Foundation and the Wellcome Trust support projects at all stages of development.

Examples

Example European Developing Countries Clinical Trials Partnership (EDCTP)

The EDCTP was founded in 2003 and is mainly financed by the European Commission. The programme aims to promote cooperation between researchers from Europe and developing countries in the execution of clinical trials. Initially, facilitation was limited to HIV, malaria and tuberculosis.

In 2014, the spectrum became considerably more colourful: projects for poverty-related and neglected tropical diseases are now eligible. In 2017, the budget amounted to €262 million, of which €147 million came from the EU.

Example—Global Health Innovative Technology Fund (GHIT)⁶³

The Japanese government launched the GHIT Fund in 2013 to work “with life science companies, universities and research institutions to discover and develop new health technologies, including drugs, vaccines and diagnostics, that are both accessible and affordable for the poorest of the poor. From the very early stages of investing in a potential product, we assess its ‘accessibility.’”⁶⁴

Example—Global Health Investment Fund

This investment fund supports projects relevant to global health, such as malaria, preeclampsia (pregnancy-induced hypertension), cholera, HIV and river blindness. Advanced development stages up to and including market launch are supported. Different options are available in this fund: project financing, loans or convertible bonds. In the case of a successful market launch, a refund including return is due; however, with more favourable conditions than investment from the private capital market. The fund’s financial resources, currently US\$ 108 million, stem, among others, from the German Ministry for Economic Cooperation and Development (BMZ). Examples of sponsored projects include the introduction of the world’s cheapest oral cholera vaccination to date, EuBiologics (Euvichol®), as well as a malarial rapid test for less than US\$ 0.50.⁶⁵

⁶³ Global Health Innovative Technology (GHIT) Fund. Available at: <https://www.ghitfund.org/general/top> (Accessed 21 June 2019).

⁶⁴ GHIT Fund. Access Policy. Available at: <https://www.ghitfund.org/afag/policies> (Accessed 21 June 2019).

⁶⁵ KfW Development Bank (2016). Project Information. Available at: www.kfif.com/download/12536/ (Accessed 21 June 2019).

SOCIALLY RESPONSIBLE LICENSING: A DYNAMIC DEVELOPMENT

SOCIALLY RESPONSIBLE LICENSING: A DYNAMIC DEVELOPMENT

- **2003** UC Berkeley introduces the Social Responsible Licensing Policy and concludes corresponding contracts.
- **2005** Equitable Licensing: first contractual model is published.
- **2006** WHO Commission on Intellectual Property Rights, Innovation and Public Health: "Public research institutions should take actions to support access to [...] research findings and its resulting products for [...] developing countries through corresponding licensing schemes".
- **2007** Association of University Technology Managers AUTM: "Statement of Principles and Strategies for the Equitable Dissemination of Medical Technologies".
- **2007** DNDi launches first malaria medicine without patent on the market.
- **2010** Foundation of Medicines Patent Pool. First agreement with the National Institutes of Health (Darunavir).
- **2012** University of Bristol humanitarian medical IP commercialisation policy.
- **2014** University of Münster (Germany): Patent strategy include equitable licensing.
- **2015** Maastricht University signs the Socially Responsible Research and Licensing Policy (SRRLP)⁶⁶, endorsing biomedical R&D "aimed at preventing and treating diseases that disproportionately burden people in resource-poor settings, both domestically and globally" and a responsible use of patents that do not harm access to medicines, among other principles.
- **2016** UN High Level Panel on Access to Medicines: "Universities and research institutions that receive public funding must prioritise public health objectives over financial returns in their patenting and licensing practices. [...] Universities should adopt policies that [...] generate knowledge for the benefit of the public".
- **2017** The European Parliament issues its report on EU options for improving access to medicines (2016/2057(INI))⁶⁷ stressing the important role played by public investments in R&D and calling on "the Commission and the Member States to establish full transparency on the results of publicly financed R&D so that patenting and licensing conditions guarantee a public health return on public investments and reflect the structure of R&D funding" and urging "Calls on the Member States to support research and development (R&D) that focuses on the unmet medical needs of all citizens, and to guarantee non-exclusive licensing where R&D is publicly funded and that access to medical advances in the European Union is non-discriminatory".
- **2019** Netherlands Federation of University Centres (NFU) launches "Ten principles for Socially Responsible Licensing"⁶⁸, addressing the need for universities to guarantee access conditions to the results of their research (principle 10).

66 Maastricht University signs the Socially Responsible Research and Licensing Policy (SRRLP). Available at: https://www.maastrichtuniversity.nl/sites/default/files/srrl_policy.pdf (Accessed 11 September 2019).

67 European Parliament Report on EU options for improving access to medicines. Available at: http://www.europarl.europa.eu/doceo/document/A-8-2017-0040_EN.html (Accessed 11 September 2019).

68 Ten principles for Socially Responsible Licensing. Available at: https://www.nfu.nl/img/pdf/19.4511_Ten_principles_for_Socially_Responsible_Licensing.pdf (Accessed 11 September 2019).

**WHAT CAN I DO AS
A PUBLICLY FUNDED
RESEARCHER?**

KEY QUESTIONS: WHAT CAN I DO AS A PUBLICLY-FINANCED RESEARCHER?

Ensuring access to publicly-financed research:

- Are socially responsible principles enshrined in my institution's guidelines?
- If my innovation is patented, are non-exclusive licences possible?
- Is there a suitable patent pool I can use to licence my innovation?
- Which contractual conditions would be relevant to facilitate access? Can I put price, production, availability, and other stipulations in the contract?

Ensuring publicly-financed research is translated into useable products:

- Are there cooperation partners, such as product development partnerships, that could help translate my research into products for use in developing countries?
- Is my innovation possibly relevant for a disease in developing countries? (Tip: check possible indications that at first glance are not linked to the primary research area).

- Are there within my university any partner projects with LMICs with which my research could tie-in?
- Are dual commercialisation pathways conceivable in the case that my innovation has relevance in both lucrative and lower-income markets?

Ensuring publicly-financed research is incentivised and widely available:

- Is open source publishing of my research findings possible?
- Can I participate in open research collaborations to share data and methodologies?
- Are there foundations or other non-traditional donors that could support non-profit research and development?

Public research can make a central contribution to solving major challenges of global health impacted by access to medical products. This brochure presents various actions universities and other public research institutes can take to help achieve three important objectives:

- to facilitate development to market maturity,
- guarantee global availability,
- to ensure affordable prices.

Examples from health research reveal the diversity of the opportunities available. This brochure provides actions and suggestions for researchers, university administration staff and Technology Transfer Officers alike.

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