Tuberculosis innovation approaches in South Africa and strategies to secure public returns

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Executive summary

Background

TB is the leading reported cause of death in South Africa, and the leading cause of death by a single infectious agent globally. While South Africa has experienced significant declines in TB incidence over the past decade largely due to the broad roll-out of antiretroviral therapy, new TB cases and TB mortality remain extremely high. South Africa is one of only five countries globally that experiences over 500 TB cases per 100 000 people. According to the World Health Organisation’s best estimates, South Africa had 322 000 new TB cases in 2017 alone. In that year, 15 986 and 747 patients were diagnosed with multi-drug resistant and extremely drug resistant TB respectively. These patients have fewer treatment options with longer treatment durations, more severe treatment side effects and lower treatment success and survival rates.

South Africa’s public sector provides diagnostic and treatment services for TB with no out-of-pocket costs. However, health facility access barriers including transport costs, health systems challenges and inadequate diagnostics often impede the diagnosis of TB and initiation of treatment. The World Health Organisation estimates that only around 68% of people with TB in South Africa are diagnosed and initiated on treatment. Among these patients, it is estimated that 82% of drug susceptible patients, 55% of multi-drug resistant patients and 48% of extremely drug resistant patients are successfully treated.

While inadequate investment has significantly impeded the development of new diagnostics and treatments for TB, South Africa has spearheaded the use of the few new important health technologies that have entered the market in recent years. South Africa was one of the first countries to implement the GeneXpert TB diagnostic following recommendations by the WHO. GeneXpert significantly reduced the turnaround times for diagnosing both drug-susceptible TB and rifampicin resistant TB. South Africa has also spearheaded the use of bedaquiline, announcing that the drug will be used as part of standard MDR TB treatment regimens in the country and expanding the use of this medicine beyond what is currently recommended by the WHO. Bedaquiline has replaced painful injectables with severe side-effects and low treatment success rates.

In addition to pioneering new health technologies, South Africa has demonstrated significant political will and leadership in pushing for global action and investment to address TB. South Africa’s President Cyril Ramaphosa was the only head of state from a BRICS country to attend the 2018 UN High-Level Meeting on TB during which he called for greater TB R&D investment, affordable drugs and the adoption of intellectual property laws that promote public health. South Africa’s Minister of Health Dr Aaron Motsoaledi chairs the Stop TB Partnership and the country’s Director General for Health Precious Matsoso chairs the Life Prize steering committee. South Africa has also demonstrated political will by significantly increasing domestic investment in TB R&D in recent years (see table 2), becoming the largest funder of TB R&D as a percentage of government expenditure on R&D. In 2016, South Africa committed more to TB R&D as a percentage of GDP than any other country. Despite this, South Africa’s share of global TB research investment remains much lower than its share of the global TB burden and South African funding for TB research pales in comparison to countries with far greater GDPs such as the United States.

Recognising the urgent need for new health technologies to address TB in South Africa and the strong political will to address TB needs in this country, we undertook this analysis to gain greater understanding of the TB innovation landscape in South Africa. We also sought to understand whether adequate safeguards are in place to ensure that public financing for TB R&D serves public interest – for example by ensuring that health technologies developed with public financing are affordable and accessible. We conducted an online survey and various in-depth, in-person interviews with researchers, policy makers and technology transfer officers in South Africa between June and December 2018. Interviewees included officials from the Department of Science and Technology, the Department of Health, the South African Medical Research Council, two university technology transfer offices, and researchers from various South African universities and research organisations. We also consulted various reports and other relevant policy documents and publications. Below is a summary of our findings.
Findings

There was wide agreement among interviewees that TB research is underfunded in South Africa. South African government investment in medical research increased significantly from 2012 to 2014, after which it stagnated and then declined from the 2016/2017 to the 2017/2018 fiscal year. However, funding specifically for TB research increased significantly in 2016 and 2017, suggesting increased prioritisation of TB research in this period. Even though South Africa invests more than most countries in TB research measured as a percentage of GDP or GERD, absolute investment is low compared to wealthy countries such as the United States. Arguably, South African government investment in TB research is insufficient given the country’s severe TB burden.

Government funding for TB research is channelled through several government entities, including the South African Medical Research Council (SAMRC), the Department of Science and Technology (DST), the National Research Foundation (NRF) and the Technology Innovation Agency (TIA). These various entities have differing mandates and differing funding priorities. The Strategic Health Innovation Partnerships (SHIP) within the MRC is the key entity tasked with funding TB innovation in South Africa.

Much TB research in South Africa is funded or co-funded by foreign donors such as the United States National Institutes for Health (NIH) or the Bill and Melinda Gates Foundation (BMGF). Almost half of the MRC’s budget is derived from foreign donors. The high level of dependence on these foreign donors is a key feature of the TB research landscape in South Africa.

A wide variety of TB research is conducted in South Africa. The country has substantial clinical trial capacity and trials of TB drugs or TB vaccines receive significant funding from foreign donors. There is also significant basic TB research being conducted in the country, particularly in relation to identifying better diagnostic and prognostic biomarkers or sets of biomarkers. Work on TB diagnostics has led to three diagnostic products being spun-off into companies – with one diagnostic product used to calibrate Gene Xpert machines already in wide use. There is some drug discovery work being done – both as part of the TB Drug Accelerator (an international project) and independently. There is also substantial investment in operational or implementation TB research in South Africa.

Decision-making regarding what research to fund appears generally to be made in a relatively open and consultative manner. SHIP, the key grant-making entity for TB innovation, has a steering committee with wide representation from different government departments and donors. The work of SHIP is supplemented by the TB Think Tank, a Department of Health initiated, and BMGF funded group, with wide participation from researchers and policy makers. Interviewees report that research priorities are relatively well-aligned with those of foreign donors and that foreign donors tend to consult with local experts when setting research priorities.

There are multiple examples of South African researchers participating in international networks or projects. One such example is RePORT, a project that aims to standardise sample collection and data capturing across clinical trial sites in multiple countries to allow for better pooled analysis and better comparisons between clinical trials. Participation in RePORT is symptomatic of a wider trend toward greater data sharing and data standardisation in South Africa. In line with ambitions set out in the recently published draft White Paper on Science, Technology and Innovation, the South African government is investing in improving domestic data collection and management capacity. In building new TB data repositories government is drawing on expertise and capacity developed on the Square Kilometre Array – a major international astronomy project with a large footprint in South Africa.

A key focus of our research was ownership of intellectual property generated from publicly funded research and access conditions placed on products resulting from publicly funded research. While funders and research entities in South Africa have some flexibility to negotiate terms on a case-by-case basis, these negotiations take place within parameters set by predominantly the Intellectual Property from Publicly Financed Research and Development Act (IPR Act), but also other key documents depending on the specific donor – examples include the SAMRC’s Socially Responsible licensing guidelines and the Grand Challenges Canada Global Access Policy. Between these various laws, policies and guidelines, and considering the nature of the TB market, most interviewees are satisfied that products resulting from publicly funded TB research in South Africa will be affordable and available in the areas where it is most needed – put another way, the perception is that there is
no incentive for companies to develop TB products that are unaffordable. However, while funding agreements typically include provisions on access and affordability, these provisions are not always clear and may turn out to be hard to enforce should the need arise given the ambiguity around key terms and limited capacity for oversight of industry behaviour across low- and middle-income countries (LMICs).

South Africa’s Bayh-Dole-style IPR Act seeks to ensure that IP falling under the Act is identified, protected, utilised and commercialised for ‘the benefit of the people of the Republic’. It does not include any specific guidance on how to deliver or measure public benefit when commercialising technologies, nor on how to ensure that technologies are affordable and accessible. The Act recommends that IP holders use non-exclusive licensing approaches but does not require them. The Act also provides walk-in rights to government to address the state’s health, security and emergency needs. The only research excluded from the IPR Act is research that is funded in full by non-public sources – with full-cost including all direct and indirect costs incurred during the research, including staff and overhead costs at institutions. The Act is currently under review.

None of the interviewees expressed ideological opposition to non-exclusive licensing, however they raised practical challenges to its implementation. Additionally, they raised concerns that requirements for non-exclusive licensing approaches as a condition for receipt of public financing could impede their efforts to deliver new health technologies. Technology transfer officers and policy makers viewed their IP and ability to make exclusive deals as critical leverage tools for raising research funding and generating commercialisation investment from local and international funders and investors.

Interviewees were generally of the view that, in the context of publicly funded TB research in South Africa, exclusive licensing would not lead to excessive pricing or limited access to resulting products. Testing whether this assumption is correct is an important area of future research. Presently it is hard to assess given that very few products have reached the market. Either way, in this regard, the incentive and market dynamics surrounding TB research in South Africa are perceived to be fundamentally different to, for example, the dynamics surrounding cancer research conducted in the United States. In addition, while South African government objectives such as job creation and economic development may at times conflict with public health objectives, most interviewees felt that these various objectives were in fact quite well balanced at present.

Interviewees expressed support for the principles of delinkage as well as for specific examples such as the Life Prize (a delinkage-based TB drug regimen development initiative previously known as the 3P Project). There was however wide scepticism about the likelihood of getting such projects funded. While South Africa’s Director General of Health Precious Matsoso chairs the Life Prize steering committee, no prize funds have yet been funded through the Life Prize mechanism. According to interviewees, the scale of investment required makes it extremely unlikely that the South African government could fund any major delinkage-based projects on its own.

While also supportive in principle, interviewees were generally sceptical about the prospects of international collaboration in funding delinkage-based projects, a R&D convention, or research collaborations such as the BRICS TB Research Network. In negotiations toward such agreements the perception among interviewees is that countries’ short to medium-term national economic interests hold sway over common longer-term interests, including health benefits. In addition, the imperative for economic development in low- or middle-income countries with relatively small budgets, such as South Africa, arguably makes it extremely irrational to enter into such agreements without at least reciprocal commitments from other, hopefully wealthier, countries.

In conclusion, a compelling argument can be made that the South African government must increase its funding for TB and other medical research – something that will have both health and economic benefits. The existing research infrastructure, funding mechanisms, and the legal and regulatory framework in South Africa appear to function well, although benefit may be derived from increased coordination in some areas and further guidance regarding socially responsible licensing and affordability and access, including through the development of an enforceable access policy for publicly funded research. South Africa has, and should continue to play, an important role in promoting delinkage-based drug-development and to support greater international collaboration on TB research. Such international collaboration will be critical to funding and properly testing alternative innovation models. (See section 9 for a full set of recommendations).
Methodology

This analysis was conducted to gain greater insight into the TB innovation landscape in South Africa, the role of public financing in driving and supporting innovation, as well as expectations of public returns (i.e. affordable, user friendly health technologies) from R&D efforts and expenditure, and strategies employed to promote public returns.

We used qualitative research approaches to collect and analyse data. Data included in this study was collected through reviewing relevant academic and grey literature, surveying TB research groups in South Africa, and conducting in-depth interviews. Data was collected and analysed between July and December 2018.

Survey recipients and interviewees were identified through mapping the TB landscape in South Africa through online searches, our existing professional knowledge of the TB landscape in South Africa, and ‘snowball sampling’ approaches which allowed for existing interviewees to recommend additional interviewees. Six of twenty research groups surveyed provided responses. The respondents predominately undertook basic science and pre-clinical research related to drugs and diagnostics, although some conducted later-stage clinical trial research and operational research (see table 1). Nine of fifteen individuals contacted agreed to participate in in-depth interviews. Two individuals who agreed to an in-person interview also responded to the surveys. The nine interviewees included three policy makers, two technology transfer officers and four leading researchers. The four researchers interviewed are conducting a broad range of research including basic research, drug development, diagnostic development and operational research. Our attempts to reach TB vaccine researchers in South Africa were unsuccessful. All the data was analysed using thematic analysis techniques.

Table 1

<table>
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<th>Research Area</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Phase IV</th>
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<td>2</td>
<td>1</td>
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<tr>
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<td>2</td>
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<td>Operational</td>
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<tr>
<td>Other</td>
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1. Funding for TB R&D in South Africa

1.1. TB research funding from domestic sources

According to data gathered by Treatment Action Group (TAG - a New York-based NGO) South Africa invested a total of US$34 million in tuberculosis research in the eight years from 2009 to 2017. There was a notable, if not a steady, upward trend over this period, with new highs of US$6.5 million and US$8.4 million reached in 2016 and 2017 respectively. While South Africa invests more in TB research than most countries when measured as a percentage of GDP or a percentage of GERD (Gross Expenditure on Research and Development), the country’s absolute investment trails far behind wealthy countries. The United States alone invested US$309 million in TB research in 2017. According to TAG’s data, the South African Medical Research Council (SAMRC) is by far the largest South African government funder of TB research having invested just over US$5 million in 2017. Other notable South African government investors include the Department of Science and Technology (DST) with US$1.9 million, the National Research Foundation (NRF) with US$0.8 million, and the Technology Innovation Agency (TIA) with US$0.6 million. The picture is somewhat
complicated by the fact that the SAMRC and its various projects receives funding from the Department of Health (DoH) and the Department of Science and Technology, among others.

Table 2

<table>
<thead>
<tr>
<th>Year</th>
<th>South African government funding for TB R&amp;D per year in US$</th>
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<tbody>
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<tr>
<td>2010</td>
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<td>2017</td>
<td>9000000</td>
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</table>

These various government funders have different priorities and areas of focus. So, for example, the SAMRC has a mandate to “improve the health and quality of life of South Africans”, the Department of Science and Technology has a strong focus on job creation and stimulating local industry, the NRF funds students and research infrastructure, and TIA funding is mostly focused on the commercialisation of health products.

In the 2017/2018 fiscal year the SAMRC received a total of R539 million (around US$38 million) in South African government grants (including TB and other disease areas such as HIV). This was a 6.5% decrease from the previous year. In 2017/2018 the SAMRC generated around R461 million (around US$32 million) through contracts with entities such as the Gates Foundation and the United States National Institutes of Health – thus compensating to some extent for the decrease in South African government funding. These contracts made up just less than half of the SAMRC’s total budget. Just less than R250 million of the SAMRC’s R1 billion budget was directly invested in research.

After substantial increases from 2012 to 2014, the SAMRC’s grant from the South African government has stagnated in the last two years.

It is notable that even though South African government funding for the SAMRC has stagnated in the last two years, government investment in TB research has increased substantially in the same period. This suggests that TB research has benefited from a shift in research priorities rather than an increase in total South African government funding for medical research.

Most interviewees agreed that South African government funding for TB is much lower than would be ideal. Richard Gordon, Executive Director of Grants, Innovation and Product Development at SAMRC explained “you could probably double our government research budget and we’d probably still not have enough”.

1.2. TB research funding from foreign sources

The real or perceived under-funding of TB research has implications for almost all aspects of TB research and agreements relating to TB research in South Africa. Maybe most notably for the purposes of this paper, it means that a key objective of the SAMRC and of various individual research entities is to raise funds from donors outside of South Africa – mostly the United States or Europe. The extent to which this outward focus and the constant struggle to secure funding from institutions such as NIAID has become part of the fabric and day-today functioning of research in South Africa should not be underestimated. Entities such as NIAID and the Gates Foundation are ever-present in
TB research in South Africa, although it increasingly appears to be as equal partners with mostly well aligned priorities.

Investment from foreign donors is a critical pillar of the TB research landscape in South Africa. While we have not attempted to quantify total foreign donor investment in TB research conducted in South Africa, it seems plausible that it could exceed domestic investment. It is also not a free-standing pillar, since donor funding is often entangled with domestic funding through co-funding or match-funding agreements.

SAMRC’s Richard Gordon identifies two reasons for the SAMRC’s success in attracting funding from foreign donors. Firstly, he explains, “most funders have realized that if you want to meaningfully address the HIV and TB burden, you really need to be working with patients and healthcare providers in affected countries”. Secondly, he suggests that donors increasingly see the SAMRC as “good collaborators” with good governance, clean audits and producing high quality reports.

Given the high level of dependence on foreign donors, we asked interviewees about what implications this dependence has for TB research being conducted in South Africa. Our questions focussed on two areas: implications for what research does and does not get funded and implications for intellectual property and access provisions tied to the funding.

Most interviewees were of the view that the values and interests of local researchers or research organisations are relatively well-aligned with those of key foreign donors such as the NIH and the Gates Foundation. There appears to be substantial consultation and shared decision-making regarding what research should be prioritised. That said, there is a perception that, in comparison to domestic funding, foreign funding is skewed toward clinical trials and implementation research rather than pre-clinical research.

Interviewees did not express any serious concerns regarding intellectual property and access provisions tied to foreign funding. This is likely because these provisions are generally considered to be fair and reasonable – as is the case regarding the BMGF/Grand Challenges Canada Global Access Policies. In addition, for any project that receives co-funding from the South African government, various provisions of South Africa’s IPR Act become applicable, thus placing clear limits on what can and cannot be negotiated with regards to IP ownership and access provisions. (The influence of foreign donors on IP and access is discussed in more detail in section 5.)

The relative dependence on donor funding from outside of South Africa creates a complex dynamic that underlies much of what is written in this report. While this dependence may in some cases require compromises, the consensus appears to be that these compromises are relatively minor. In addition, the associated partnerships and knowledge exchanges are often seen as intrinsically valuable. Either way, this underlying dynamic is not often explicitly expressed, but appears to be a critical determining factor in the TB research landscape in South Africa.

Biomedical TB researcher Bavesh Kana explained “South Africa by and large relies on foreign investment to fund a large proportion of the academic work going on in the country, and a large proportion of that foreign funded work is for implementation. Fundamental research for new products is not funded in any meaningful or serious way.”

1.3. Prospects for increased domestic funding for TB research

One intervention that might change this dependence dynamic would be a large increase in South African government funding for TB research. If the South African government is the sole or main donor of a research project, it will be in a position to set its own parameters for how IP is to be used and how final products are to be made available.

While a dramatic increase in South African government funding for TB research seems highly unlikely given the country’s short to medium term economic outlook, it cannot be ruled out. Multiple interviewees in our study credited an investment case promoted by Professor Salim Abdool Karim for a substantial increase in South African government funding for the SAMRC from 2012 to 2014 – the period in which Karim was SAMRC President. In a report Karim prepared in 2012 he wrote that “the size of the MRC’s baseline grant is so grossly inadequate that it threatens South Africa’s standing in
medical research”, and “the growth in the MRC’s budget has simply not kept pace with the needs of medical research in South Africa”. A 2014 Nature Medicine editorial reported that on Karim’s watch the SAMRC grew its base line grant budget from 246 million rand (R) ($22 million) in the 2012–2013 fiscal year to R446 million in the 2014–2015 cycle. At the time Karim left the SAMRC in 2014 the base line grant budget was projected to grow to R648 million by 2016–2017. In his 2012 report Karim estimated that the grant would have to grow to R850 million by 2017. Both the R648 million projection quoted in Nature Medicine and the R850 million estimate in Karim’s report turned out to be overly optimistic, with the actual grant amounting to only R539 million in the 2017-2018 fiscal year. Either way, Abdool Karim’s example suggests that individual agency and leadership can play an important part in securing increased funding.

The need for increased funding for research and development is recognised in the Department of Science and Technology’s Draft White Paper on Science, Technology and Innovation (White Paper) – although not specifically for the health sector. The White Paper commits the government to “increasing the levels of R&D investment in the economy so that gross expenditure on R&D reaches 1.5 percent of GDP in the next decade”. Recent stagnation in the MRC grant has meant that targets and projections have now been missed and that South Africa is no longer on the trajectory mapped out by Abdool Karim in 2012 for medical research. Whether the White Paper is indicative of a coming change in this regard remains to be seen.

There appears to be at least some political will to respond more effectively to the TB crisis in South Africa – as can be seen in government’s support of the Life Prize, in President Cyril Ramaphosa’s attendance at the 2018 United Nations High-Level Meeting on Tuberculosis, in Health Minister Dr Aaron Motsoaledi’s work as chair of the Stop TB Partnership, in the establishment of a parliamentary TB caucus, and in the recent increase in funding for TB research. At the same time, the South African economy is only just out of a technical recession and government is facing severe fiscal constraints. Large increases in state funding for medical research, and specifically for TB research, seems unlikely in this context. The severe economic pressures also go some way to explaining government’s focus on research investment that builds local industry in addition to addressing health needs.

2. Types of TB R&D underway in SA

A variety of types of TB research, both pre-clinical and clinical, is being conducted in South Africa – including basic research, diagnostic, drug, vaccine and operational research. According to data collected by TAG, South Africa invested US$3.7 million in basic TB research in 2017. This outstrips investment in all other TB research areas in South Africa and amounts to 44% of the US$8.4 million total. Roughly US$1.9 million was invested in drug research, US$1.5 million in operational research, US$1.1 million in paediatric research and roughly US$1 million in diagnostics research in the same period – with hardly any South African government investment in TB vaccine research.

However, as some interviewees pointed out, the distinctions between areas of research can be fluid and overlapping. So, for example, basic research aimed at the development of better TB diagnostics might be classified as either basic research or diagnostic research. One interviewee also argued that the TAG figures do not fully capture investment in infrastructure and salaries and that actual investment might be much greater if these are factored in. The figures quoted above might thus not present a fully accurate picture regarding what types of TB research is being funded by the South African government.

The TAG figures also exclude funding from international sources for TB research conducted in South Africa – there is for example large TB vaccine and drug clinical trials being conducted in South Africa that are being funded by international donors and almost half of the SAMRC’s revenue is generated from contracts with foreign donors.

Multiple interviewees suggested that foreign donors tend to fund clinical trials in South Africa rather than basic or pre-clinical research. Biomedical researcher Bavesh Kana explained that “internationally South Africa is viewed as a premier destination to do clinical trials,” adding that “what we do, what the large majority of our academic resource does is we test interventions that other companies and
countries have developed. Bedaquiline we didn’t develop, the GeneXpert we didn’t develop, linezolid we didn’t develop. You know if you look at some of the combinations of TB medications in the stream trial, and now the new combinations to test regimen shortening, we didn’t develop any of them.”

Yogan Pillay, Deputy Director General (DDG) at the Department of Health, highlighted that clinical trials are South Africa’s strength and stressed the health benefit since these trials “tell us what drugs and what combinations and what dosing and what the side effects are”.

There is also substantial work being conducted in South Africa on TB diagnostic research and development. This ranges from early stage work aimed at identifying diagnostic or prognostic biomarkers, or sets of biomarkers, to relatively late-stage product development. So, for example, a promising, mobile TB diagnostic test that distinguishes between live and dead TB bacteria has been developed by Dr Anne Grobler’s team at North-West University. Professors Lesley Scott and Bavesh Kana’s team at Wits University have developed assays used to calibrate Gene Xpert machines. Both these products have been spun-off into start-up companies (see more in section 6.1.).

While TB drug discovery is more difficult and expensive than diagnostic development, here too there is some activity in South Africa. Maybe most notably, South Africa participates in the TB Drug Accelerator – an international collaboration between various universities, pharmaceutical companies, and research institutes and supported by the Gates Foundation. While South Africa’s participation is primarily through the Drug Discovery and Development Centre (H3D – a unit focussing on primarily malaria and TB drug discovery) at the University of Cape Town, other entities such as the University of Stellenbosch also participate, creating what one interviewee describes as a virtual pharmaceutical company. However, one interviewee reported that their unit will likely have to stop its TB basic drug discovery work due to a lack of government support.

The scale of drug discovery work in South Africa pales in comparison to clinical trials being conducted on drugs or drug combinations in the country. Many critically important TB drug trials have been or are being conducted partially or entirely in South Africa. These include NEXT-TB, NIX-TB, ZeNIX, STREAM, END-TB and REMOX-TB. In addition to drugs, key TB vaccine trials have also been conducted in South Africa – including the landmark M72 vaccine trial. ClinicalTrials.gov lists a total of 159 tuberculosis clinical trials with at least one trial site in South Africa – of these, 33 are listed as currently recruiting or yet to start recruiting. There is thus ample evidence to support the assertion by some interviewees that South Africa is a leading destination for TB clinical trials – both because the country has the patients, but also because it has the research infrastructure and expertise.

There are substantial differences in focus area and approach between different research groups in South Africa. For example, while the Centre for Biomedical TB Research, headed by Prof Bavesh Kana at Wits University, does work on basic drug discovery, biomarker identification, translational research and indigenous knowledge systems, the Centre for AIDS Programme of Research in South Africa (CAPRISA) does mostly clinical trials – including the SAPIT trial (also known as CAP003) which compared three treatment strategies in people co-infected with HIV and TB.

Some interviewees expressed a fear that an increased focus on commercialisation could result in a reduction in the amount of funding available for basic or early stage pre-clinical research. Our reading of the White Paper suggests that such fears may well be justified – not only for basic and pre-clinical research – where it might take decades to achieve a return on investment, but also for operational or implementation research where there is no new product. One interviewee explained that even now “fundamental research for new products is not funded in any meaningful or serious way”.

The argument was also made that the pressure to come up with the next “magic bullet” has distorted research coordination in South Africa and resulted in gaps in the “continuum of product development”. One interviewee explained “if you have well-funded research, through the Medical Research Council, Department of Health and perhaps the Department of Science and Technology, that gives you a vibrant research program that hands over hits and potential outcomes to the Technology Innovation Agency (TIA), TIA then incubates those with industry partners, because industry is a very important component of this, they bring a lot of gravitas from the perspective of scalability and commercial aspects and then TIA incubates those promising ideas with researchers at universities as partners, as happened for the work we’ve done, and then a new product emerges. Now that new product then feeds back into the academic enterprise where again these same groups say okay let’s run them as clinical trials, let’s do implementation work to see how does the product work and how we implement
and then you come back again to TIA and then it becomes a product that can be marketed in a way that’s sustainable and affordable in South Africa. I think that works in some cases, but in many cases this system is broken.”

The White Paper envisages a series of decadal implementation plans. It is however not clear whether this would include a plan or framework to ensure a well-functioning product development continuum. It is also not clear how such plans will link to work done through SHIP and the TB Think Tank (both discussed in section 3). Either way, it appears that while there is already significant coordination in TB drug research in South Africa, there may nevertheless still be a need for further planning and coordination in order to more fully exploit existing research capacity and potential.

Finally, the White Paper includes several statements expressing the view that internationally there has been a move toward industry funding a greater share of R&D. While this may be the case in some fields of technology, there is little evidence that it is the case in medical research. Indeed, it seems likely that the commercial success of United States pharmaceutical companies is largely underpinned by that country’s high levels of sustained funding for basic research through the NIH. Most interviewees appeared to take it for granted that government support is critical to medical innovation in South Africa. Indeed, our interviews leave little doubt that government support is essential to medical innovation, and particularly basic and pre-clinical TB research, in South Africa and by implication any economic benefits that will result down the line. Put another way, it appears to be taken as a given that an over-reliance on industry will leave critical research areas, such as basic research, dangerously underfunded – thereby compromising the entire innovation ecosystem in South Africa.

3. Decision making and funding allocation procedures for TB R&D in SA

As described in section 1, the South African government funds TB research in South Africa through a variety of channels – including the SAMRC, the Department of Science and Technology, the National Research Foundation and the Technology and Innovation Agency. These various entities have a variety of funding mechanisms. Some of these entities also co-fund research projects with foreign donors. These underlying funding arrangements impact how funding decisions are made in South Africa.

The largest funder of TB research in South Africa is the SAMRC. The mandate of the MRC is to “improve the health and quality of life of South Africans”. The SAMRC falls under the Department of Health, regularly has to report to parliament, and receives much of its funding from the Department of Science and Technology.

SAMRC’s Richard Gordon explained that “there are a number of different grant making activities at the SAMRC. It is a similar model to the US NIH model where they have intramural and extramural research with external grant funding. The SAMRC has intramural research where we have a number of intramural research units which seek to address the national disease burden – for example the SAMRC has TB and HIV research groups, health systems, gender-based violence, trauma, violence and injury. We also have a number of extramural units”.

MRC SHIP is likely the most important and influential health research coordinating mechanism in South Africa. On the MRC website it is described as “a partnership between the MRC and the Department of Science and Technology that “funds and manages innovation projects focused on the development of new drugs, treatments, vaccines, medical devices and prevention strategies”. Gordon explained that the, MRC SHIP was set up in 2013 with a grant from the Department of Science and Technology, adding it “was really focussing on a product development for Africa by Africa so to speak. So, it’s kind of what you would call a local PDP (product development partnership)”. MRC SHIP currently has around 40 ongoing projects.

MRC SHIP has a steering committee where the Department of Science and Technology, the Department of Health, the Department of Trade and Industry, the MRC, industry, the TIA and the
Gates Foundation are all represented and collectively make funding decisions. One interviewee explained that “we all sit together on the steering committee and see what are the next things that should go out and be funded. So, the call for proposals come out, then it’s peer reviewed and then we make decisions on what should be funded.” Gordon of SAMRC is also positive about the role of the steering committee noting: “I think the one strength around it is that when we send out a call, we don’t just sit in a room and think what’s the cool idea now. We actually have the Department of Health, the Department of Trade and Industry, their input, you know from a health perspective, what are the gaps? Do we need another this or do we need another that?” Gordon also notes a shift over the last five years from using international reviewers (done to avoid conflicts of interest) to include local reviewers “because it’s really important that what we fund is going to be applicable and scalable and fit in the health system”.

Most of the interviewees we interviewed were positive about MRC SHIP’s grant-making and coordination role and appear to see SHIP as both approachable and responsive. Some questions were however raised about how responsibility for supporting product development is divided between MRC SHIP and TIA. While TIA is represented on the MRC SHIP steering committee, at least one interviewee was of the view that there is insufficient coordination and clarity about roles between the two entities.

MRC SHIP’s focus is mainly on product development, or research that would in a relatively direct way contribute to product development. Gordon explained “the DST’s money is health innovation, so there is an expectation that it creates patents, innovations and it creates jobs, which could mean new companies”. As a result, areas such as basic research must be funded through other mechanisms such as the MRC’s self-initiated research grants.

One of the other ways in which basic research has been supported in South Africa is through the Department of Science and Technology and National Research Foundations’ Centres of Excellence. The Centre of Excellence for Biomedical Tuberculosis (TB) Research (co-hosted by the University of Cape Town, University of Stellenbosch and the University of the Witwatersrand) “contributes to local and global research efforts that are aimed at developing new tools for controlling tuberculosis and to use the research as a vehicle for training a new generation of high-quality biomedical research scientists”. The future of the Centre is however in doubt since its funding runs out in April 2020. Our research did not explore how decisions are made regarding whether to fund Centres of Excellence.

Though it is not a grant-making entity, the BMGF funded, and Department of Health-run TB Think Tank also plays an important role in the TB research landscape in South Africa. As one interviewee put it “the TB think tank needs money for their research and the money is sitting in SHIP”. The TB Think Tank, together with the MRC, has developed a draft TB R&D Plan for South Africa that will help inform MRC SHIP’s grant-making decisions. The plan was under review at the time of writing. Yogan Pillay, Deputy Director General of the Department of Health, explained that “in South Africa we have a draft national TB research plan, but the idea of the plan is not to constrain anyone, it’s a high-level plan that kind of gives a sense of the things we need to eliminate TB by 2030, that’s the goal right. But it’s not supposed to constrain. So, what we need is besides that, we need a way to coordinate research, so that we can figure out with the researchers not only what research we need and what kind of products we need, but how they would work in practice”.

Nesri Padayatchi from CAPRISA explained that “the mandate of the TB Think Tank and the SHIP grant is very different. The SHIP grant is focused on the science, the TB Think Tank is more focused on operations. (…) For example, finding the missing millions of patients with TB, that’s the kind of thing that the TB Think Tank would focus on, so the TB Think Tank is very operational. The experiences have been very different, very positive, very collaborative, but what you are not going to see coming out of the TB Think Tank is high impact science – it is not going to happen – because that’s more around strengthening health systems, that kind of thing. And, its huge, its I’d say about 80 people there at least, so you’re not going to get high impact science out of that. In a nutshell, SHIP and TB think tank are two completely different fora – SHIP is about the science, looking at innovative science and the Think Tank is operational and implementation science – how can we make things work better?”

Some interviewees were very positive about the value of the TB Think Tank and the way in which it supplements the work of MRC SHIP. One interviewee noted that “the whole system is about
partnerships and collaborations. We all work together”. While another was of the view that while the TB Think Tank does valuable work, it could be better coordinated with other efforts and entities such as the TIA. Either way, it appears that both through the TB Think Tank and through MRC SHIP, processes are in place to gather a variety of views and to facilitate a variety of perspectives.

Interviewees were also remarkably positive about how entities such as the NIH or the Gates Foundation go about setting research priorities in TB. Biomedical researcher Valerie Mizrahi noted the extent to which such funders have “evolved to thinking about us more as partners with whom they engage”. There was no suggestion in our interviews that donors such as the NIH or the Gates Foundation failed to consult local TB experts in decision-making regarding which projects to fund.

There are significant differences in the extent to which research groups in South Africa initiate their own research as opposed to participating in research collaborations that were initiated elsewhere. So, for example, Padayatchi of CAPRISA stressed that from the get-go 80% of CAPRISA’s research were their own research “where the idea comes from CAPRISA, we write the protocol, we apply for the funding, so by applying to do a specific type of research you get funded to do that research, so the funder is not dictating what you do.” We did however get the impression that much of the other TB research conducted in South Africa is done in response to decisions taken by funders and donors – albeit decisions taken in consultation with local experts.

4. Data management procedures for TB R&D in SA

Most interviewees we spoke to are in principle in favour of open sharing of data generated through South African TB research. That said, it appears that most data sharing until recently has been handled on a non-standardised, case-by-case basis. That seems to be changing with new efforts at building data repositories in South Africa and through the RePORT consortium.

There is a sense among some interviewees that, despite their support for greater data sharing, data is valuable, and it should not simply be given away. One interviewee questioned “why are you going to give all your crown jewels away?”, adding that “we need to have some kind of bargaining tools as well”. The interviewee further stressed that while previously international groups would say “give us access to your people, we will do the research for you, give us access to your people, we will save you - that’s not going down very well at the moment.”

The White Paper proposes a commitment to open access and open data repositories. This commitment is in line with several current developments in South Africa. Ela Romanowska from Wits’ technology transfer office (TTO) commented that: “It is interesting that government on the one hand has the IPR Act to promote registration of IP rights so as to give SA institutions and companies a protected ability to compete internationally, and simultaneously advocates open access. There needs to be clarity on how these principles co-exist”.

Another interviewee explained that at present blood samples and datasets generated through research conducted in South Africa are often not available to South African researchers. In response to this there is now a push, involving the MRC, NICD (National Institutes for Communicable Diseases) and others to build the ability to do the full laboratory analysis in South Africa “so we can control the data, as well as the samples”. But, as the interviewee explained, even when these new data repositories are in place, researchers will have to apply for access and explain why they want to have access to the data.

As an aside that sheds some light on the kind of coordination that government likes to promote, one interviewee pointed out that in building this new data infrastructure, government is building upon the capacity created through the Square Kilometre Array astronomy programme and the Department of Science and Technology are facilitating data management workshops involving both biomedical researchers and astronomers – given certain similarities in data requirements and data analysis between astronomy and certain aspects of TB research – both fields require storing and sharing of large data sets and identifying patterns in the data.
Another related development is the growth of the NIH-funded RePORT (Regional Prospective Observational Research in Tuberculosis) consortium, described by one policy maker as a “collaborating clinical network”. Founded in 2012, (the MRC became involved in 2015) RePORT aims to standardise data collection and certain aspects of clinical trial protocols across multiple clinical trial sites in multiple countries to allow for the more meaningful pooling of data and comparing of findings from different clinical trials – around 20 sites in three countries are currently involved. Such an initiative seems particularly valuable in the TB field, given the relative lack of good predictive biomarkers by which to measure TB disease progression. UCT biomedical researcher Valerie Mizrahi explained: “Funders have realised that the R&D needed to develop new tools for TB control cannot be compared with the HIV/AIDS field because much HIV science was already known and key tools to guide product development, such as the viral load and CD4 count were available. In contrast, in TB, we are doing research and development in parallel. We are learning as we are developing which has created a virtuous cycle between the two.”

“Progress in TB clinical research is hampered by a lack of reliable biomarkers that predict progression from latent to active tuberculosis, and subsequent cure, relapse, or failure. RePORT International represents a consortium of regional cohorts (RePORT India, RePORT Brazil, RePORT South Africa, RePORT Indonesia and RePORT China) that are linked through the implementation of a common protocol for data and specimen collection and are poised to address this critical research need. Each RePORT network is designed to support local, in-country TB-specific data and specimen biorepositories and associated research. Taken together, the expected results include greater global clinical research capacity in high-burden settings and increased local access to quality data and specimens for members of each network and their domestic and international collaborators.”

5. Regulatory and policy frameworks guiding IP protection, access and affordability in SA

5.1. The Intellectual Property from Publicly Financed Research and Development Act

Any research undertaken with public financing in South Africa or utilising publicly funded resources is governed by the Intellectual Property from Publicly Financed Research and Development Act (“the IPR Act”). The Act was signed by the President in 2008 and came into force in 2010 along with related regulations prescribed by the Minister of Science and Technology.xix

The IPR Act was modelled on the United States Bayh-Dole Act (and similar legislation elsewhere) which sought to promote patenting and commercialisation of federally funded research in the U.S. However, the national contexts in which the two Acts were adopted were quite different, which influenced the impact of the Acts. Prior to the introduction of the Bayh-Dole Act IP ownership was retained by the U.S. government. The Bayh-Dole Act provided for institutions to retain IP developed with federal funds and encouraged collaboration with industry to commercialise IP. The Act has been criticized for broadly privatising tax-payer funded innovations in the U.S., which has allowed private holders of IP and exclusive licensees to charge excessive prices that impede access to publicly funded innovations. While similar provisions related to IP ownership and commercialisation were established in South Africa’s IPR Act, the Act is perceived as increasing government’s oversight of, and rights to, IP developed at publicly funded institutions in the country. Ela Romanowska of Wits TTO (WITS Enterprise) explained that “until this legislation was passed, people would pay for the bursary and then just use the IP, whether they legally had the rights to or not”.

The IPR Act seeks to ensure that IP falling under the Act is identified, protected, utilised and commercialised for ‘the benefit of the people of the Republic’. The IPR Act and its regulations includes requirements and provides guidance for licensing IP to third parties to commercialise technologies. The Act recommends that IP holders use non-exclusive licensing approaches but does not require them.

The IPR Act introduced obligations for management of IP resulting from research supported through public financing in South Africa, regardless of the proportion of public financing to overall R&D expenditure. For institutions listed in the Act, the only research excluded from the Act’s obligations in
South Africa, is research that is paid for at least at the deemed full-cost from non-public sources. Full-cost must include all direct and indirect costs incurred during the research, including staff and overhead costs at institutions undertaking research.

In addition to setting out obligations for IP management by institutions that receive public financing for research, the IPR Act requires the establishment of technology transfer offices at designated institutions (higher education institutions and schedule 1 institutions and science councils) to implement the requirements of the Act and established the National Intellectual Property Management Office (NIPM) to oversee compliance with the Act.

The IPR Act provides for ownership of IP developed with public funding by the institution (i.e. university or science council) that receives funding - known at the 'recipient' - and provides for benefit sharing (where benefits can include financial and/or non-financial considerations) between the recipient institution and the individuals within the institution who created the IP. If the recipient chooses not to retain the IP, it must notify NIPMO who may then elect to acquire the IP. Private and philanthropic funders may co-own IP with funding recipients provided that certain conditions have been met, including the contribution of resources towards R&D and the joint creation of the IP.

The Act further provides walk-in rights to government to address the state’s health, security and emergency needs:

Section 11 (1) (e) each intellectual property transaction must provide the State with an irrevocable and royalty-free licence authorising the State to use or have the intellectual property used throughout the world for the health, security and emergency needs of the Republic;

Further, the state retains the right to license IP to any third party under reasonable terms in cases where IP holders fail to commercialise IP for the benefit of society (section 14).

While the Act provides for walk-in rights to intellectual property resulting from publicly funded research, it remains an open question as to whether government will exploit this right to address public needs. Similar walk-in rights exist within the U.S. Bayh-Dole Act, "however, the US government has consistently refused to exercise its march-in rights in order to lower drug prices". South Africa has also never used compulsory licensing to protect public health. Compulsory licensing is an important safeguard allowed in the country’s Patent Act that allows government to grant licenses without the permission of the patent holder to address public needs, including health needs.

While the IPR Act sets out the obligations for management of IP, it is important to note that the Act is currently under review by a ministerial review panel in the context of South Africa’s shifting IP and technology and innovation policy landscapes. According to the 2018 White Paper on Science, Technology and Innovation “the review will focus on support for openness, improved support for SMEs, expanded impact of offices of technology transfer, and the appropriate structure and positioning of the National Intellectual Property Management Office”. It is possible that a Bill to reform the Act will follow the conclusion of this review.

5.2. Provisions incorporated in research contracts and licensing agreements to promote public benefit, affordability and access

While the IPR Act requires that IP is commercialised for the benefit of people living in South Africa, it does not include any specific guidance on how to deliver or measure public benefit when commercialising technologies, nor on how to ensure that technologies are affordable and accessible.

The lack of clear guidance in the Act is seen by some interviewees as providing flexibility to public funders and technology transfer offices in delivering and assessing public benefit. Public funders and technology transfer offices use a range of tactics to deliver public benefit, including through incorporating socially responsible licensing provisions in research contracts, collaboration agreements and commercial licenses. The types of provisions used depend on the stage of research, nature of the technology and its commercial route to the market.
For example, MRC SHIP’s early stage research contracts generally only include broad language on access and affordability (see example below), whereas more detailed provisions are included in commercialisation agreements and licenses when more is known about the target market, efficacy of the health technology and potential commercial partners. According to the MRC SHIP, detailed provisions incorporated into licensing agreements are informed by:
- The Intellectual Property from Publicly Funded Research Act, 2008
- MRC’s Socially Responsible Licensing Guide for Technology Transfer Offices, 2013
- Grand Challenges Canada’s Global Access Policy, 2018

A standard clause found in the MRC’s research contracts for early stage research:

“The Institution undertakes that any agreement concluded for the commercialization of the Foreground Intellectual Property shall provide that any resulting products shall be made available and accessible at an affordable price to people most in need within developing countries, including the Republic of South Africa.”

Given that TB research is often co-funded by several funders, other funders may also require access and affordability conditions in research contracts, collaboration agreements and licenses. In our interviews, the Bill & Melinda Gates Foundation (BMGF) and Grand Challenges Canada (GCC) access requirements were highlighted as mechanisms used to promote affordability and accessibility of TB health technologies developed in South Africa. This is unsurprising given that BMGF is one of the largest funders of TB R&D in South Africa. BMGF and GCC collaborate closely and commonly co-fund projects.

Global Access Requirements of the Bill and Melinda Gates Foundation and Grand Challenges Canada (see annexures 3 and 4)

Both BMGF and GCC require commitments to global access in their funding contracts with research institutes. BMGF requires that grantees agree to its global access commitments and develop a global access strategy that is updated annually during each year of the project:

“You will conduct and manage the Project and the Funded Developments in a manner that ensures Global Access... “Global Access” means: (a) the knowledge and information gained from the Project will be promptly and broadly disseminated; and (b) the Funded Developments will be made available and accessible at an affordable price (i) to people most in need within developing countries, or (ii) in support of the U.S. educational system and public libraries, as applicable to the Project”

BMGF further seeks to retain a humanitarian license on technologies developed with Foundation funding in the form of a “non-exclusive, perpetual, irrevocable, worldwide, royalty-free, fully paid up, sublicensable license to make, use, sell, offer to sell, import, distribute, copy, create derivative works, publicly perform, and display Funded Developments and Essential Background Technology”.

Similarly to BMFG, GCC requires that grantees make commitments to global access and “develop action plans to achieve access and affordability in the relevant context and setting.” GCC requires that grantees provide periodic reports on progress in achieving global access, continuing after the funded project has concluded. GCC’s global access policy further clarifies that when applicable GCC will retain the rights to exercise IP in global health emergencies or in contexts where access and affordability is not achieved. This right may be in the form of an assignable non-exclusive license.

5.3. The SAMRC socially responsible licensing guide

In our communication with MRC SHIP, they highlighted that they seek to use socially responsible licensing practices to promote global access in global access markets. The socially responsible
licensing provision sought by the MRC are informed by its 2013 publication Socially Responsible Licensing Guide for Technology Transfer Offices.

Key definitions used by the SAMRC:

- **Global access** means the provision of meaningful access to the Licensed Product(s) for those most in need, specifically the public sector in low- and middle-income countries, where meaningful access means the Licensed Product(s) is made broadly and quickly available at costs that are reasonable in each country context.\(^{xxi}\)

- **Global access** markets means the public sector in the low- and middle-income countries included in the Licensed Territories.\(^{xxii}\)

- **Socially responsible licensing (SRL)** is the licensing of intellectual property (IP) so as to ensure access to health technologies or products for underserved populations at affordable cost, while also seeking to encourage dissemination of know-how in all relevant markets. SRL is a way to leverage IP to accelerate the development of solutions in a manner that leads to optimised access to medicines and other health technologies by populations most in need. Optimised access includes availability, affordability and acceptability of such technologies by the populations in need.\(^{xxiv}\)

The MRC’s SRL guide highlights the importance of SRL practices, as well as new business and funding models, to address market failures of the patent system that inhibits medicine access for poor populations and creates ‘neglected diseases’ which fail to attract adequate innovation investment. While the guide recommends SRL practices to address market failures in developing countries, it does not seek to influence the use of the profit-driven patent model in developed countries. Rather, the guide recommends the use of market segmentation approaches to pursue global access. This allows the licensor to negotiate different licensing terms in different territories. For instance, a market segmentation clause may provide for exclusive rights in developed countries, while providing non-exclusive rights in developing countries to foster competition. Alternatively, a market segmentation clause could require differential pricing models in different territories. For example, a company could be granted exclusive rights to market a health technology in developed countries using a for-profit approach, in exchange for commitments to market the health technologies at-cost, at a ‘cost-plus cap’ or at a subsidised price in developing countries. A typical market segmentation clause related to pricing reads as follows:

> The Licensee shall employ methods of market segmentation within Licensed Territories, including by applying tiered pricing for the Licensed Products between wealthier consumers and the Global Access Markets in Licensed Territories and, where necessary, investigating alternate distribution or implementation channels in Global Access Markets;

In addition to market segmentation approaches, the guide recommends the use of performance clauses to remove exclusive rights or terminate licenses in global access markets that the licensor is unable or unwilling to serve or develop. Performance clauses may include provisions to 1. terminate licenses, 2. convert exclusive licenses to non-exclusive licenses, 3. require mandatory sub-licensing or 4. provide ‘walk-in’ rights to the licensor in unserved markets.

Finally, while the guide recommends the use of SRL practices to license IP, it also highlights that decisions to pursue patent protection in different territories must be informed by whether “patent protection is likely to promote or hinder availability and accessibility of a technology”. In territories where IP may hinder availability or accessibility of health technologies, a decision may be taken not to pursue IP.

5.4. SA government autonomy in setting requirements for IP ownership and access

A key concern when initiating this research was to establish whether South Africa’s high level of reliance on external funds for TB R&D would undermine the country’s ability to set requirements for IP access and ownership.
Several interviewees stressed that when the South African government contributes public financing or in-kind contributions to R&D, the IPR Act applies, thus setting certain concrete parameters for what can and cannot be negotiated in terms of IP and access. We also found that there were broad similarities between SAMRC and Gates conditions for access, allowing them to co-exist without impeding on local autonomy. Further, the IPR Act requires approval by the National Intellectual Property Management Office (NIPMO) for offshore transactions related to publicly financed intellectual property.

One issue that was raised by an interviewee was the potential for conflict between Gates requirements for walk-in rights and walk-in rights held by the South African government in terms of the IPR Act. The tension around walk-in rights arose from the lack of a clear and common definition of ‘access’, which could potentially result in disagreements related to the use of such walk-in rights. There has been no test case for how such potential disagreements may play out.

6. Perceptions and use of exclusive licensing, non-exclusive licensing and delinkage approaches

6.1. Licensing approaches employed to commercialise TB health technologies

In our interviews we explored the types of licensing approaches being used for TB health technologies developed in South Africa undergoing commercialisation. While the IPR Act recommends the use of non-exclusive licensing for IP developed with public financing, it does not require it. A recent review of licensing agreements conducted under the IPR Act by publicly funded research institutions between 2008 and 2014 showed that of the 144 licenses negotiated on ALL types of technologies, only 40% were non-exclusive. The review also found an increasing trend of researchers and universities developing start-ups or spin-off companies to commercialise IP held by publicly funded institutes.xxv

Our interviewees were unable to provide any examples of non-exclusive licensing use to promote affordability and accessibility of TB health technologies. This is partially due to the fact that few health technologies for TB have been licensed and commercialised in South Africa. No new TB drugs or vaccines resulting from South African held IP have entered the market to date.

Through our interviews we identified three agreements negotiated to commercialise diagnostic technology from South African held IP, by Wits University, the University of Cape Town and North-West University. All three licensing agreements employed exclusive licensing approaches and involved the creation of spin off companies to develop and market new health technologies. Spin-off companies are private, for-profit start-up companies created to commercialise IP.xxvi

Spin off companies created to commercialise university IP:

- Smart Spot was created in 2016 as a spin-off company of Wits University. The company is licensed to manufacture and sell TB dry culture spots used to validate GeneXpert instruments from IP held by the university. The TB dry culture spot is now used to validate GeneXpert diagnostics in over 24 countries.xxvii
- Antrum Biotech was created in 2008 as a spin-off company of UCT. The company is licensed to further develop and commercialise IP held by the UCT. Antrum Biotech will seek to commercialise test strips for rapid detection of TBxxviii, and for rapid test for TB meningitis which remain under development.xxx
- North-West University formed a joint venture with BGM Pharmaceuticals to further develop and commercialise a mobile and rapid TB test that differentiates between live and dead TB, from IP held by the university. North-West University and BGM Pharmaceuticals subsequently spun off HANKS TB diagnostics to manufacture the diagnostic.

Biomedical researcher Bavesh Kana explained that the decision to grant an exclusive license to the spin off Smart Spot was made after attempts to identify existing companies with the expertise to develop the product were unsuccessful, therefore a new company was created which will collaborate closely with the IP holders to continue to develop the product line and retain manufacturing locally.
A decision was taken by North-West University to pursue a joint venture for the development of a diagnostic able to distinguish between live and dead TB. BGM Pharmaceuticals was selected to allow for commercialisation by the “right” type of industry partner that furthered the growth of small and medium enterprises (SMEs), broad-based black economic empowerment (B-BBEE) and local industry - in line with the goals of South Africa’s national development plan. BGM Pharmaceuticals is a small business based in Gauteng with level 1 black economic empowerment status. Through their joint venture, North-West University and BGM Pharmaceuticals spun off the biotech company HANKS TB Diagnostic. The decision to spin off a new company was made after attempts to collaborate with multinational funders and companies with the expertise to develop the product were unsuccessful. The new company will allow for North-West University and BGM Pharmaceuticals to develop the product line and retain manufacturing locally.

(Approaches used by companies to promote affordability by exclusive license licensors are discussed in section 8.2.)

6.2. Perceptions of delinkage and non-exclusive licensing approaches

In our interviews we explored researchers, technology transfer officers and policy makers’ perceptions of delinkage and non-exclusive licensing approaches. Both approaches seek to allow for competition as a tactic to improve accessibility. The introduction of generic competition in a market typically drives down costs, thereby allowing for improved access.** The United Nations High-Level Panel on Access to Medicines explains that delinkage is a “term used to describe a key characteristic of financing models of innovation characterized by the uncoupling of R&D costs and consumer prices for health technologies”. The uncoupling of R&D investments from medicine prices allows for IP management strategies that facilitate immediate competition, rather than the use of monopoly periods to recoup R&D investment. IP management approaches to promote competition may include funding requirements to not patent IP so that innovations are broadly accessible as public goods, or the use of broad non-exclusive licensing approaches. Exclusive licensing provides a single licensee the rights to commercialise IP in certain territories for certain applications. Whereas non-exclusive licensing provides multiple licensees’ rights to commercialise IP in the same territories for the same applications, thereby allowing for competition between licensees. Non-exclusive licensing approaches may include licenses negotiated directly between patent holders and licensees, or patent pooling approaches – most commonly through the Medicines Patent Pool.

None of the interviewees expressed ideological opposition to delinkage and non-exclusive licensing approaches, however they raised practical challenges to their implementation at international level. Additionally, interviewees raised concerns that requirements for delinkage or non-exclusive licensing as a condition for receipt of public financing at a domestic level could impede their efforts to deliver and commercialise new health technologies. Market exclusivity was seen by most interviewees as an important incentive to attract commercial partners, be it from local or international companies.

6.3 Perception and knowledge of delinkage models

Knowledge of delinkage and specific delinkage-based proposals varied among interviewees with some having followed recent debates closely and others seeming relatively unaware of both the theory of delinkage and recent WHO and UN processes relating to delinkage. The most well-known example of delinkage appears to be the Life Prize (previously known as the 3P project). This is not surprising, given that the Life Prize has enjoyed explicit support from the South African government with the Director General of Health having chaired the Life Prize steering committee.

Amongst those with a good understanding of delinkage, all expressed general support of the principles and specific support for the Life Prize (see more under box 1). This was however almost universally tempered with scepticism as to the viability of finding the money with which to implement delinkage models, including for TB where global funding shortages impede R&D progress. As one interviewee said, “we first have to see where the funding for the R&D is going to come from. It’s very idealistic, it’s beautiful, same with the BRICS commitments – beautiful, but let’s get down to the tangibles when you actually have to start paying for it – where are you going to get the money?”
SAMRC’s Richard Gordon who was involved in the WHO CEWG (Consultative Expert Working Group) process said, “so in the ideal world this sounds like a great idea, however the challenge is aligning this to each country’s strategies and funding agencies”.

Interviewees further highlighted that the scale of funding requirements for delinkage models was not affordable for developing countries and highlighted the need for multilateral funding pools with significant investments from wealthy countries. One interviewee explained “there’s not that many countries who could contribute to the scale that you would need to fund those kinds of awards”. Wits’ Bavesh Kana added that the only plausible way to fund delinkage-based projects is from non-traditional sources of funding, stating “you know having a model like that where you can show a product or a series of product that meets the [target product profile] and then attract donor funding to that, I think is very attractive…. I think if we keep going to the traditional sources of money, we will keep getting what we get, which is not much.”

While interviewees highlighted the need for multi-lateral and wealthy country financial commitments to fund delinkage approaches, several raised concerns that the allocation of funds could be distorted by political power and interests. SAMRC’s Gordon noted “I get very nervous, when we go for these consortia of countries when the countries select the prize projects and purely from a point of view that it becomes political, you know if the innovator is from x country then x country will beplug for it and another country might not be that interested – you might not be funding the best thing. There are several groups seeking to address this globally and it is an interesting developing space”.

In addition to concerns about the feasibility of funding delinkage models and processes for allocation of resources, some interviewees argued that a test-case was required to test the feasibility and efficacy of delinkage approaches. Gordon noted that “until we see the first proper case where it is done, the jury is out”. Another interviewee added that “you will have to have a test case where that’s going to happen and that’s interesting, the TB vaccine might be the first test case”.

It seems unlikely that delinkage would gather much more than general, in-principle support until such time as the concept has been properly tested. Yet, in order to properly test the concept large financial investment is required – thus creating a dynamic that leaves delinkage stalled in a catch 22 situation.

There was also general in-principle support for the idea of multi-national collaboration through mechanisms such as the BRICS TB Research Network or a potential multi-national R&D convention. While some interviewees were mostly positive about the potential of such collaborations, others expressed scepticism, based mostly on the difficulty in aligning the convergent interests of different countries. It appears that differing interests have already created substantial difficulties in the fledgling BRICS TB Research Network. That said, some collaborations, such as a genomics collaboration between South Africa and China are proceeding. Either way, it seems that substantial negotiation, careful planning, and strong political leadership will be required if any large multi-national research projects are to rise above the thicket created by the often-opposing interests of the various countries involved.

What is the Life Prize?

The Life Prize, previously known as the 3P project, was conceptualised by Doctors Without Borders to incentivise R&D for new TB drugs and regimens. The Life Prize is a mechanism for pooling donor funding in order to provide research grants and prize funding for TB R&D. Grants will be used to finance needed research up-front and prizes will be used to reward important milestone achievements. As a condition of funding, all recipients of Life Prize grants and prizes will be required to pool intellectual property arising from funded research. This will allow for immediate generic production and use of medicines developed from Life Prize funded research.

The Life Prize is hosted by the International Union against Lung Disease and Tuberculosis. It has received public support from the South African government and South Africa’s Director General of Health Precious Matsoso chairs the Life Prize Steering Committee. At the time of writing the Life Prize has only received limited funding.
6.4 Perceptions regarding requirements for non-exclusive licensing at a domestic level

Similarly to delinkage, no interviewees expressed ideological opposition to non-exclusive licensing. However, several interviewees argued that domestic requirements for non-exclusive licensing would impede the progress of research and commercialisation of health technologies. Interviewees explained that the scale of funds required for completing research up to the point of drug registration, particularly for drugs and vaccines, was beyond what the South African government could afford and therefore required commitments from industry.

SAMRC’s Richard Gordon explained “when you get to a phase 2 clinical study, we are talking budgets of 30 to 50 million dollars in some cases. That’s almost the entire budget of some government departments in South Africa. So the model has to be that we partner”.

A key concern of some interviewees was that a requirement to make IP a public good, or to require broad non-exclusive licensing, would impede on their ability to raise funds from partners who did not share these principles, in particular industry partners. Andrew Bailey from UCT’s technology transfer office explained “you’ve got no sort of real asset if you haven’t got patents in that area and it’s to try and raise funding off that”. Another interviewee noted “that the moment when [industry] see this thing is going to work, they will bring in their money to pay for the phase 3 and then they want the ownership. So that is why if you want to delink it you actually have to provide the pooled money to do the phase 3 clinical trials... the price cost between phase 2 and phase 3, it’s a hundred-fold”.

Interviewees also expressed concerns that strict requirements linked to public funding would impede their ability to generate investment from industry partners to commercialise new health technologies. UCT’s Andrew Bailey explained “what happens is that because there’s no market protection for the pharmaceutical company... there’s no protection once they have developed the market that somebody else just comes in and sees oh great you’ve developed a market, we are climbing in. So those drugs have not ever made it to the market.” Romanowska (Wits TTO) cautioned that in cases where companies are willing to compete and “take the first step” the companies with the greatest resources would be first to market, which could allow for Big Pharma competitors to crowd out domestic companies.

Another concern highlighted was a perception that the South African market is too small to sustain multiple competitors for certain health technologies and so licensing strategies should consider what the market will bear in order to allow for sustainable growth of local industry.

Given the perceived practical challenges to broad non-exclusive licensing, one interviewee argued that there is a need for enabling legislation that creates room for technology transfer officers and other stakeholders to negotiate the best possible deal for the country while taking into account contextual challenges and opportunities to introducing the specific health technology to market, including the type of health technology, potential suppliers and the size of the market.

While interviewees noted concerns about their ability to raise research funding and commercialisation investment without IP ownership or exclusive licensing approaches, they also highlighted some potential solutions to overcome these challenges. Two interviewees argued that government production could be used to introduce useful health products without granting exclusive licenses to industry. They also noted however that the South African government’s pharmaceutical production efforts remain in nascent stages.

Interviewees also suggested that market analyses demonstrating need and potential buyers, obtaining WHO pre-qualification and/or advance purchasing commitments, could be used to incentivise industry players that do not hold IP or exclusivity to commercialise health technologies. UCT’s Andrew Bailey explained how a health technology produced with philanthropic funding outside of South Africa was commercialised without IP protection: “I said [to the funders] how did you then make it interesting for a company to participate? And for them it was the fact that they had WHO pre-approval for the technology, and they knew exactly the market, who would be buying, how they would buy. So that market knowledge and that pre-approval, those were actually far more valuable than the IP”. On advanced purchasing commitments, Bailey added “it’s actually quite a nice way to get...
competition in that space… where it is hopefully a win win, you get lowest cost because it would have to be to a particular cost target, but then you are getting the surety of supply”.

Advanced purchasing commitments have successfully been used to incentivise commercialisation of new health technologies without granting exclusivity, including dolutegravir fixed dose regimens for HIV. During 2017, the South African and Kenyan governments together with Pepfar, the Global Fund and other buyers used their joint purchasing power to negotiate significantly reduced prices in 92 LMICs from generic suppliers licensed to market dolutegravir regimens through non-exclusive licenses negotiated by the Medicines Patent Pool.

While some interviewees highlighted advanced purchasing commitments as a mechanism to incentivise commercialisation without exclusive licensing, they cautioned that it may not be a feasible mechanism at a country level to incentivise research because governments could not make the long-term funding commitments required. One interviewee highlighted that governments cannot commit to buying interventions in 10 – 15 years time, as policy-makers change over time, as do funding priorities. The interviewee cautioned that in 10 – 15 years, South Africa could face an epidemic in something unpredicted that requires a funding priority shift.

7. Perceptions of public benefit and strategies used to promote it

While the IPR Act requires that IP developed with public funding is commercialised for the benefit of society, it does not provide guidance as to what constitutes public benefit. In our interviews we found that there was general consensus that the role of publicly funded researchers, technology transfer officers and policy makers was to deliver public benefit, as well as broad commitment to doing so. Ela Romanowska from Wits TTO noted that “tax money, it is supposed to be deployed for the benefit of South African citizens not just to line the pockets of an industry player”.

Interviewees broadly agreed on the need to deliver public benefit and noted that there were multiple ways in which public benefit could be achieved, including:

1. delivery of novel health technologies to address unmet health needs;
2. delivery of local solutions for local health needs;
3. delivery of health technologies that are affordable and accessible within South Africa, and LMICs more broadly;
4. growth of the domestic pharmaceutical sector and local manufacturing;
5. creation of jobs in the pharmaceutical sector;
6. employing and retaining biomedical researchers in South Africa; and,
7. delivery of royalties to public institutions.

While interviewees generally agreed that there were a range of different ways public benefit could be delivered, they noted that different stakeholders prioritised different public benefits depending on their mandate. This was also apparent through the types of public benefits stressed by different interviewees. Unsurprisingly, the Department of Science and Technology prioritised local manufacturing, the Department of Health prioritised addressing health needs and technology transfer officers prioritised commercialising technologies and generating royalties for public institutions.

Biomedical TB researcher Valerie Mizrahi highlighted the tension arising from these competing mandates: “It's not clear exactly what government's thinking is around what constitutes a ‘public good'. On the one hand, the thinking seems to be very industry- and products-focused. So, as a grantee, the questions I am asked are how many industry partners do I have? How many patents have I filed? How many drug candidates have I produced? What has my research contributed to the employment of people in the emerging drug development industry in this country? On the other hand, I am also asked how many lives my research is saving? What tends to be under-appreciated is the fact that our research is producing highly skilled people many of whom have stayed in the TB field, contributing in many different ways. In this environment, meeting this mix of high expectations is very challenging”.

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However, despite apparent tensions, interviewees generally reiterated the importance of other players’ mandates and priorities in addition to their own and felt that for the most part they could co-exist. Department of Health Deputy Director General Yogan Pillay explained that “we need to get all stakeholders on board and moving in the same direction. These include the Department of Health, Department of Science and Technology, the Department of Trade and Industry, the research institutions. This is how we can provide health commodities that are affordable and grow the economy at the same time”

An important area of tension that did emerge however is the extent to which South Africa should pay higher prices to procure health technologies from local producers when local producers' prices exceed those of international producers. Different government departments have taken different positions on this issue and Cabinet and Treasury have played a role in resolving conflicts. One interviewee stated, “It's one of our big fights... we need to look at job creation, local manufacturing, getting down the trade deficit”. Pillay added that “Cabinet had to take a decision about whether or not we pay a higher price and then the question was also where would the money come from if we are paying a higher price for local manufacture and the question was will treasury give us the additional money? If treasury is not going to give us the additional money, then it means we put fewer patients on treatment. So, it's a discussion that has to happen at a higher level because there are competing needs by different government departments and different sectors.”

8. Perceptions of access and affordability and strategies used to promote it

8.1. Perceptions of affordability and access

All interviewees expressed the view that health technologies developed with public financing in South Africa should be affordable and broadly accessible within the country. Some interviewees also highlighted the need to ensure that health technologies are affordable to all LMIC public health systems. Biomedical researcher Valerie Mizrahi stressed that “it is essential that new health technologies for TB are affordable. I would find it deeply troubling to have contributed the development of a new tool for TB control that was not of public benefit on my own continent, in my own country, for reasons of affordability and/or access.”

Biomedical researcher Bavesh Kana highlighted regarding Smart Spot's technology that “before this was a company or even a product that was viewed from the perspective of profit generation, we took the view of whoever needs it needs to get access to it, otherwise it just sits in a laboratory and it’s not very useful.”

While there was general consensus that products should be affordable and accessible, the view was expressed that there is no benchmark or guidance for what constitutes affordable pricing and access. One interviewee asked, “on one level I wholeheartedly agree that we should ensure that health interventions are made accessible to people who would otherwise not access them… but more accessible than what, you know do I have a comparative benchmark?”. Another said that “we want the price to be affordable, but there's no formula for affordability”.

Some interviewees were of the view that excessive pricing was a problem that South Africa faced because of the profit-driven approaches of Big Pharma. There was a perception from some interviewees that local industry holding IP or licensed by IP holders would not pursue excessive pricing practises because of their proximity to the disease and understanding of the need to deliver affordable health technologies to address public health needs. This perception could not be tested as few health technologies for TB have been commercialised from South African held IP. Biomedical researcher from North-West University Anne Grobler explained regarding a commercial partner “it’s a local company, it is doing the right thing… we do want to build manufacturing capacity in this country, they believe the same thing, so I think we’ve got a shared vision and culture… this company is not going to sell at the most expensive price because they live and work in South Africa”.

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Interviewees broadly expressed agreement regarding the need for health technologies to be affordable and accessible, but some researchers also highlighted this as a consideration in raising funding for research. One interviewee noted the need to discuss affordability issues in applications for public funding. Researchers also expressed the perception that because of the market for TB, their technologies would not be utilised if they could not be marketed at affordable prices. Kana explained “when it comes to TB the formula is not complex, it’s got to be cheap, it’s got to be simple and it’s got to be scalable”.

8.2. Strategies employed to promote affordability and access

While all interviewees expressed commitment to delivering affordable and accessible health technologies, there was not a one-size-fits-all approach employed to pursue these deliverables. Rather a range of strategies were employed to deliver affordable and accessible health technologies, outlined below.

Patenting strategies to promote access and affordability

UCT’s Andrew Bailey explained that, as required by the IPR Act, patenting was pursued when IP could deliver societal or commercial benefit. When questioned as to how patents could deliver societal benefits, Bailey explained that they provided leverage for technology transfer offices to negotiate affordable prices for South Africa, and LMICs more broadly noting “the question is whether without patents one would have a situation where someone picks up on your patent or whatever, makes drugs available but they don’t come to South Africa. That would be negative. The other thing would be if it came to South Africa, but it was just ridiculously expensive. So, for us patenting is very much a way of trying to control – you’ve got a tool for negotiating to ensure that there is benefit”.

In addition to patenting as a tool to negotiate access, when filing patents technology transfer offices may choose not to seek patents in jurisdictions in underserved markets where they could inhibit access. It was explained that this strategy also results from the fact that patenting is expensive, and South African universities cannot afford to file patents in all jurisdictions.

Donation of IP to promote access and affordability

Another approach identified to promote access and affordability was donation of IP. Nesri Padayatchi from CAPRISA explained that CAPRISA has a policy not to hold patents and that patents on health technologies that have adequate evidence to proceed into public use resulting from the institution’s research will be donated to the Department of Health. Padayatchi explained that this policy was adopted because CAPRISA is a non-profit institute seeking to address public health needs. Its interest is therefore in addressing public health needs, not in holding patents or earning profits. However, two patents currently held by CAPRISA on tenofovir gel and on a precursor for an HIV vaccine have not been donated to the DoH to date as research has not proceeded into the development of technologies for public use.

Socially responsible licensing practises to promote access and affordability

MRC SHIP and technology transfer offices highlighted the use of socially responsible licensing practises to ensure access and affordability. The MRC SHIP seeks to ensure that socially responsible licensing practises are applied by IP holders when commercialising IP developed with SAMRC funding through including clauses in research contracts requiring engagement of the SAMRC in the establishment of commercialisation and benefit sharing agreements.

A typical socially responsible licensing clause would include requirements for affordable pricing in the public health sectors of LMICs, while allowing licensees to pursue profit driven models in LIMC private health systems and developed countries. Affordable pricing may be defined as at-cost pricing, cost-plus cap pricing, or subsidised pricing that allows companies to subsidise low pricing in LMIC markets through profits gained in other markets. This market segmentation approach has been employed by Smart Spot who offer lower prices to poor countries than wealthy countries. This approach was incorporated into the business model at the outset in “recognition that some countries are not in the same position to pay as wealthy countries”. Another approach to segment markets that may be pursued are requirements for different pricing according to the application of health technologies. This
approach is particularly relevant for diagnostic technologies that may be employed for detection of a range of illnesses in addition to TB, including illnesses for which there are large markets in developed countries.

While socially responsible licensing practises are employed to promote affordability and access, Romanowska of Wits TTO highlighted challenges in monitoring the compliance of licensees with licensing conditions explaining “what I think one needs to bear in mind, is if there is going to be for example preferential pricing to ease access for particular constituencies or countries or communities or whatever, ones got to be very careful how you audit that mechanism because it’s not an easy thing for me as an institution to see whether the company is actually doing preferential pricing for particular stakeholders”.

**Setting target product prices to promote access**

Another approach that has been employed to promote access involves identifying target prices for health technologies and seeking to develop health technologies that can be commercialised at or below the target price. This approach is being employed by researchers at North-West University who are seeking to develop a rapid, portable TB diagnostic that can differentiate between live and dead bacilli. Biomedical researcher Anne Grobler said it will seek to commercialise the technology at under $5 per test per patient. Grobler envisions that this locally-developed technology could replace the current diagnostic tests, such as GeneXpert as the initial diagnostic test employed in public sector algorithms for diagnosing TB. The subsidised price of testing a patient using GeneXpert is $17 per cartridge. Grobler clarified that this pricing target was not required by funders, but rather resulted from the researchers’ own commitment to ensuring that the diagnostic is affordable. To inform their target product price, researchers consulted the Bill and Melinda Gates Foundation. While target product prices can be employed as a tactic to promote affordability, another interviewee cautioned that access or target prices must allow for price reductions over time as production levels increase.

**Minimising the costs of production and use of health technologies**

Finally, in addition to licensing and pricing strategies pursued to promote access and affordability, several interviewees highlighted that concerns around affordability and access were present throughout all research stages, and informed decisions related to the directionality of research. Biomedical researcher Valerie Mizrahi explained that “judicious choices need to be made quite early in the discovery phase of drug development based on the cost of goods because the field is insufficiently resourced to pursue all possible options.”

Smart Spot’s diagnostic verification technology effectively illustrates how researchers can consider and respond to cost considerations when developing new technologies. Recognising that requirements for biosafety level 3 laboratories would pose a cost barrier to the use of their health technologies, the researchers employed biomimicry techniques which allowed them to edit non-contagious bacteria to mimic TB bacteria. Bavesh Kana explained “in thinking about this we thought well how do we reduce the price of the products? And we need to remove the biosafety level containment component of it. And so, then what I did was I developed a second generation of products that are based on biomimicry... this effectively brought the product price down and created a better sustainability model for Smart Spot and it also allows everyone to access the product”.

9. **Recommendations**

The below recommendations are those of the authors of this paper. The recommendations are informed by the various interviews conducted and the materials referenced in this report. While some of these recommendations are supported by people interviewed for this paper, we stress that the recommendations as formulated and presented here have not specifically been endorsed by any interviewees.

9.1. **The South African government must invest more in TB research**
In his 2012 report on the future of the MRC Professor Salim Abdool Karim wrote: “Indeed, the size of the government’s allocation to medical research indicates the extent to which it is not taken seriously as a public good, as a contributor to the knowledge economy and as the principal source of new knowledge to improve the health of our nation. At its current level of funding, the MRC has little chance of being a serious player in the global stage of medical research, this requires investments in clinical research infrastructure, laboratories and the ability to undertake research across the spectrum from the most basic molecular and cellular studies to animal research to clinical investigations to public health projects and to health systems studies and interventions. The MRC, which carries the citizen-mandate for medical research, needs to ensure no one component of this value chain is compromised and starved of resources. This can only be done with adequate resources.”

While substantial increases in funding did follow in 2012 to 2014, funding from the South African government has now stagnated, along with government spending in many areas, and is far below the trajectory mapped out by Abdool Karim. In addition, most interviewees interviewed for this report agreed that medical research, and TB research, does not receive sufficient funding from the South African government.

Increased government funding of TB research is likely to have many benefits. These range from the health benefits that result from the research to the social and economic benefits of training more scientists and increasing research capacity, and the economic benefits of developing and commercialising new products. Increased funding from the South African government will also make South African researchers less beholden to foreign donors, be it regarding what research does or does not get funded, or the access or IP conditions related to their research.

9.2. The South African government should adopt an enforceable access policy building on the existing SAMRC guide for socially responsible licensing

The SAMRC’s existing guide for socially responsible licensing (SRL) meets most of the requirements for SRL guidance and creates a good balance between competing interests, while also leaving significant scope for negotiations to suit specific cases. The guide should be used to establish an enforceable policy for socially responsible licensing, global access and affordability as a condition for receipt of public funding. The development of the guide may be led by the SAMRC but will require inter-ministerial engagement by the Departments of Science and Technology, Health, and Trade and Industry.

The policy should include clear definitions of access and must ensure that socially responsible licensing requirements extend to all LMICs. A challenge in enforcement of socially responsible licensing is the lack of a clear definition for what constitutes affordability. Recognising the significant complexity and difficulty of defining affordability, government should engage with experts and stakeholders on options to define affordability and include enforceable affordability provisions in the policy. Engagements around price affordability should also consider legislative and policy options to require transparency of R&D expenditure (including public contributions) and production costs. This is particularly important as globally companies commonly claim that unaffordable medicine prices are needed to recoup hidden R&D costs.

While an enforceable policy for socially responsible licensing, affordability and access must apply to all university research conducted with public funding, universities should also develop their own access policies for all university R&D informed by the Global Licensing Access Framework developed by Universities Allied for Essential Medicines.

Government funders and publicly funded institutions should create oversight bodies to monitor the implementation of access policies. Additionally, government and universities should ensure transparency of research funding agreements to expand institutional accountability by allowing third party oversight. See more under recommendation 9.6.
9.3. The South African government must increase its support for alternative research funding models such as prize funds

The South African government’s explicit and publicly stated support for the Life Prize and for the principles of delinkage is commendable. This support should continue. However, government should also explore how, alone or in collaboration with other governments, or through innovative forms of funding such as transaction or sin taxes, funds can be raised to support large demonstration projects that tests whether delinkage-based drug or diagnostic development can address urgent needs in TB.

It is concerning that the White Paper does not include language on delinkage or any recognition that existing market-exclusivity-based incentives have proven insufficient to overcome the market failure in TB drug development.

9.4. Greater diplomatic efforts and political leadership are required to support multi-national initiatives such as the BRICS TB Research Network and a potential WHO R&D Convention

The narrow, mostly economic, interests of individual countries appears to be a major barrier both to scaling up initiatives such as the BRICS TB Research Network and to getting agreement on a binding R&D convention. Overcoming these difficulties will likely require careful tailoring and negotiating to ensure that, what is likely to be relatively complex agreements, benefit all parties involved. It will also require the investment of substantial political will and political capital at the head of state level. Despite the recently held United Nations High-Level Meeting on Tuberculosis, indications are that this kind of visionary leadership is still absent. It is hard to see much beyond incremental advances in the TB field without much greater multi-national collaboration and investment.

A critical step toward such multi-national cooperation would be the establishment of a multi-national grant-making entity that is free of political interference. Such independence from political considerations will increase government and public confidence that decisions will be made to fund the best proposals to address the greatest health needs. On the other hand, it could lead to most grants going to countries with greater existing research capacity – an issue that should be addressed explicitly through technology transfer and capacity building between countries and funding for the development of research infrastructure.

9.5. The South African government should develop and then fully fund a national drug development framework

The South African government, including the Department of Science and Technology, the Department of Health and the Department of Trade and Industry, in consultation with researchers, local industry and civil society, should develop a drug development framework for South Africa. This framework should guide government investments in drug development and ensure an optimal regulatory, legal and support environment for drug development in South Africa. It is critical that this framework makes provision for all stages of drug development – from basic research aimed at identifying potential drug targets through to clinical trials and eventual marketing of products.

Such a framework is required in order to maximise South Africa’s existing capacity in this area. A lack of coordination, various gaps in the drug development chain, and a lack of funding for key projects appears to reduce the combined impact of the various research and development projects in the country to less than the sum of its parts. Greater coordination and greater funding in key areas are likely to offer substantial benefits over the status quo.

Given relatively low global investment in key areas of interest such as tuberculosis drug development, it is not implausible that South Africa could become a competitive player in the market for diseases such as TB. Thus, even though drug development is a relatively high-risk area in which to invest, the potential exists for great rewards, with substantial implications for industrial development and for South Africa’s trade balance should important drugs be developed. In addition, investment in drug
development is investment in skills that will be of value to the economy more widely – and that would thus benefit the economy even if no important new drugs are developed.

Furthermore, the trend, with only few exceptions, is for foreign donors to fund clinical trials rather than drug development in South Africa. While our very substantial clinical trial capacity in South Africa is an invaluable asset that must be supported and maintained, it is not economically optimal for South Africa to be primarily a testing ground for drugs developed in other countries since the revenue from such drugs will continue to flow to other countries. Greater investment in domestic drug development could help create a better balance in this regard. Such investment in drug development is also in line with South Africa’s stated goals of increased local production of key pharmaceuticals.

Our understanding is that the TB Think Tank and MRC’s TB R&D Plan will have a broader focus than this proposed drug development framework and that the two documents would thus supplement each other.

9.6. The South African government should enable third-party monitoring of access and affordability commitments

A practical concern raised in relation to the use of clauses on access and affordability was the lack of capacity of technology transfer officers and licensors to monitor whether access and affordability commitments are met by licensees. To expand monitoring capacity, government should enable third party monitoring of access and affordability deliverables on publicly funded IP. To enable third party monitoring, government should establish a searchable public database and require IP holders to publicise all data relating to IP ownership and related research and commercialisation contracts. Licensees should also be required to submit annual updates on their efforts to deliver on access and affordability commitments and these updates should be made publicly available.

A similar approach to enable third party monitoring has been used by the Medicines Patent Pool and Unitaid, who publish patent data related to licensed and priority health technologies and related licensing agreements on their public searchable MedsPal database. This data has been used by civil society in South Africa and globally in identifying and highlighting access barriers for key health technologies.

Creating a public searchable database will enable third parties, including civil society, to monitor progress by companies in realising commitments to access and alert licensors and government when commitments are not upheld. However, an anticipated challenge in monitoring licensors efforts to deliver on access and affordability commitments in South Africa is the lack of publicly searchable data on registration applications at the South African Health Products Regulatory Authority (SAHPRA). Without access to this data, it is often difficult to assess whether access challenges in the country arise from company delays or inaction, or SAHPA regulatory delays. To address this challenge and allow for greater monitoring of licenses negotiated on publicly funded IP, as well as Medicines Patent Pool licenses, SAHPRA should ensure that data on pending registration applications is publicly available. Greater disclosure regarding application filings has been recommended to improve transparency at the US Food and Drug Administration, including by the FDA 2010 Transparency Task Force.\textsuperscript{xiii} The European Medicines Agency already publishes some data related to pending applications on its website.\textsuperscript{xiii}

9.7. Multilateral organisations should support research, thinking and engagement on the overlap and tensions between A2M and market shaping strategies

A key obstacle to greater use of non-exclusive licensing are perceptions that the domestic market is too small to bear competition and that companies will not invest in commercialising products without exclusivity. This perception has also arisen globally with regards to neglected tropical diseases, with PDPs often preferring to limit licensing to support economies of scale. Greater scrutiny of these perceptions is necessary.
To date there has been significant thinking from international groups such as the World Health Organisation and United Nations on opportunities to address market failures of the patent system that inhibits medicine access for poor populations and creates ‘neglected diseases’ which fail to attract adequate innovation investment. A 2012 Report from the WHO’s Consultative Expert Working Group on Research and Development and a 2016 Report from the United Nations High-Level Panel on Access to Medicines recommend (among other interventions) greater funding and use of alternative innovation models that do not result in access inhibiting patent monopolies.

There has also been thinking from groups such as UNITAID, the Bill and Melinda Gates Foundation, the Global Fund and others on ways to address market failures and challenges related to commercialisation and supply, such as inadequate incentives for companies to commercialise products, or launch or sustain supply of products in territories not viewed as sufficiently profitable. International groups, including UNITAID recommend the use of market shaping techniques “so that manufacturers and distributors have the appropriate incentives to invest, innovate, and supply quality health products at affordable prices and in acceptable formulations to developing countries.”

Market shaping techniques may include advanced procurement, pooled procurement and long-term contracts. By their nature, market shaping techniques can create monopolies even in the absence of patents by establishing long term commitments from buyers to a limited number of suppliers. At a domestic level, technology transfer offices and policy makers similarly grapple with options to incentivise companies to commercialise health technologies, and commonly use exclusivity to do this.

Careful and collaborative thinking is needed by a broad range of stakeholders, including the WHO and United Nations, to consider tensions and incoherencies between guidance to promote broad generic competition versus market shaping techniques. Importantly, this research should not only consider global procurement approaches, but also country-level approaches for procuring medicines and must engage country-level buyers.

9.8. Further research on the commercialisation of health technologies in South Africa would strengthen evidence for policy making to ensure public benefit

For the most part interviewees perceived that TB health technologies developed from South African public funding would be broadly affordable and accessible. Interviewees believed that actors (researchers, technology transfer offices and industry) would feel obliged to ensure affordability and accessibility of TB health technologies due to their proximity to the disease. Interviewees also perceived that health technologies for TB that were not affordable would not be procured or used. However, this perception can be challenged, given that high cost health technologies for TB developed outside of South Africa, such as the drug bedaquiline, have been procured for use locally. It is also notable that the high price of rifapentine appears to be responsible for a delay in the introduction of rifapentine-based TB preventive therapy in South Africa.

We could not test the validity of interviewees perceptions that health technologies resulting from South African public funding would be made affordable and accessible as few such TB health technologies have been commercialised in South Africa. Further research related to all health technologies commercialised since the adoption of the IPR Act in 2008 by publicly funded institutions could provide greater insight into the practises used to commercialise health technologies and their impact on affordability and accessibility. Research should consider the extent to which exclusive versus non-exclusive licenses are used, whether and if so, how the IPR Act has been applied to ensure public benefit, and the affordability and accessibility of commercialised health technologies – especially in South Africa's public sector. This research would build on the insight gained from the recent review of IP commercialised by publicly funded institutions following the passing of the IPR Act that was conducted by the HSRC and would inform better policy making to ensure public health benefit is achieved from publicly funded biomedical R&D.

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Annexures

Five annexures are provided as separate attachments.

Annexures include:

1. SAMRC’s socially responsible licensing guide for technology transfer offices (2013)
2. Sample socially responsible licensing clauses used by the SAMRC (2018)
4. BMFG Sample Terms and Conditions for Grant Support
5. Survey sent to TB research units in South Africa (2018)


11 Unpublished data shared in 2018 by Treatment Action Group)


21 Email communication with MRC SHIP on 13 November 2018

22 Email communication with MRC SHIP on 13 November 2018

23 Medical Research Council. Socially Responsible Licensing Guide for Technology Transfer Offices. 2013


26 http://smartspotq.com/


SOCIALLY RESPONSIBLE LICENSING GUIDE FOR TECHNOLOGY TRANSFER OFFICES

Adoption and Implementation of Socially Responsible Licensing Practices

Co-ordinators: Rabogajane Busang & Rosemary Wolson
SOCIALLY RESPONSIBLE
LICENSING GUIDE
FOR TECHNOLOGY
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Foreword

This guide seeks to provide technology transfer offices with some guidelines on how to implement Socially Responsible Licensing practices when carrying out their IP management & commercialisation activities. This is an easy to understand guide with examples of clauses provided in the appendices. The aim is to translate the theoretical concept of Socially Responsible Licensing into a more practical, easy to implement concept. We hope that this guide will lead to increased implementation of Socially Responsible Licensing practices in an effort to alleviate the problem of access to healthcare technologies in poorer countries.

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Introduction

Although some papers have been published on the topic of Socially Responsible Licensing (SRL) and the topic discussed at meetings and conferences, there has been very little practical implementation by technology transfer offices and their licensees to date, with the result that SRL remains largely a theoretical issue. Technology transfer professionals who are familiar with the concept of SRL might therefore struggle in trying to implement SRL practices. This document seeks to provide some practical guidance in such implementation. In this guide, the concept of SRL is explained, the benefits for adopting SRL strategies are discussed and various SRL strategies are provided, and practitioners are encouraged to take into account issues such as institutional culture, policy and varied perspectives of stakeholders in their implementation.

The Concept of Socially Responsible Licensing

SRL is the licensing of intellectual property (IP) so as to ensure access to health technologies or products for underserved populations at affordable cost, while also seeking to encourage dissemination of know-how in all relevant markets. SRL is a way to leverage IP to accelerate the development of solutions in a manner that leads to optimised access to medicines and other health technologies by populations most in need. Optimised access includes availability, affordability and acceptability of such technologies by the populations in need.

The SRL approach is not intended to affect business transactions in developed countries where significant profits can still be achieved, but rather makes use of parallel strategies to promote access in developing countries. Technology transfer offices (TTOs) can therefore adopt SRL practices and still maintain the profit incentive of commercialisation. SRL is a free market alternative to compulsory licensing, in that the parties can voluntarily agree on licensing terms that will promote access to medicines.
Why Should TTOs adopt SRL Practices

- To address market failures

In terms of the free market system, everyone is entitled to participate in business, allowing the markets to determine the price. An alternative option is price regulation by government authorities. In the pharmaceutical industry, the market price of drugs takes into account R&D investment, regulatory and marketing costs, quality control and risk, but it has been alleged that in some instances, excessive prices have been charged. The free market system therefore sometimes leads to inaccessibility of some important drugs in poorer countries, which cannot afford to procure the drugs at the market price. Although generic companies produce cheaper versions of branded products, they are also subject to market forces. Time to market for the introduction of generic alternatives may be increased, and quality may be adversely affected in some cases. Also, companies will most likely not enter markets where there is no perceived economic benefit.

A further aggravating factor is that research priorities are often guided by potential commercialisation benefits. This leads to projects with good prospects of commercialisation being selected that are not necessarily addressing the health needs of poorer countries. Consequently certain types of diseases are not given attention and become what is known as ‘diseases of the poor’ or ‘neglected diseases’. The adoption of SRL practices can serve as one of the means to address these market failures. The concept of SRL attempts to balance issues of economic, social and environmental impact, which are important for ensuring the sustainability of businesses while simultaneously meeting the needs of underserved market segments.

- To ensure that society benefits from the research outputs of publicly funded research and increase the impact of such research

Universities and other public research institutions access public funds used to carry out research that is relevant to and addresses the needs of their communities. Publicly funded research should, as far as possible, be in line with the needs of society and commercialisation of such research should also be aimed at addressing these needs. Hence, by adopting SRL practices, universities and public research institutions can increase the impact on society of their research outputs by ensuring that they do not only generate revenues for the institutions and their licensees, but also address societal needs.
• **To adhere to legislative requirements and contribute to overall corporate social investment**

Some countries and funding agencies have legislative or policy requirements that seek to promote SRL practices.¹ For recipients of applicable funding, an SRL approach must be followed. Even where such regulation is lacking, one can also argue that considering the needs of society and putting in an effort to commercialise technologies in a socially responsible manner is the right thing to do. It is an ethical imperative which should be adhered to. If the health needs of society are addressed, the quality of life will be improved and there will be a larger and more productive workforce to build economies, thereby increasing the level of sustainability of communities and companies.

• **To create alternative models of commercialisation and increase the uptake of technologies**

A two-pronged approach to commercialisation can be taken whereby IP is licensed to generate profit for certain territories or market segments, and to address health needs in other territories or market segments, typically in developing countries. In this way, institutions will continue to generate income and recover some of their R&D costs, without preventing licensees from pursuing commercially viable business models, while at the same time increasing the impact of the technologies concerned on society. Methods of commercialisation need to be adapted with changing times and needs. By developing and adopting SRL practices, TTOs will be contributing to the shaping of global innovation systems and providing new ways of working together. Collaboration partners and companies with a higher interest in technologies with social impact will be encouraged to enter into licence or collaboration agreements with the institution adopting SRL practices.

• **To create enhanced reputational goodwill for institutions and their licensees and increase sources of funding**

By ensuring that health technologies are licensed in a manner that addresses the health needs of society, institutions will reap reputational benefits and most likely increase their chances of securing more funding from their existing funders and/or philanthropic funding sources. Also, this approach will respond to concerns from student activists and other interest groups trying to promote the public interest. This will further serve as motivation for researchers working for the public good and wishing to see evidence of the impact of their work on society.

¹ One example is the South African Intellectual Property Rights from Publicly Financed Research and Development Act of 2008 (IPPFRD Act).
Potential Benefits to the Licensee

• **Addressing unmet needs and accessibility issues**

Licensees accepting SRL clauses stand to benefit from entering markets where there is an unmet need and can gain a good market share in these territories, creating new distribution channels, which they can use for other products. By making their products more accessible, such licensees are able to increase the awareness of their brand and create goodwill. These companies can, later on, benefit from the increased positive brand awareness by making more products available in the market, which customers will recognise and buy due to the brand reputation. They can provide non-essential drugs at market-related prices and essential medicines at cost plus a small mark-up and continue to reap the benefits of commercialisation of their products in poorer countries.

• **Mechanism for corporate social investment and enhanced reputation**

Companies are increasingly required to take the triple bottom line approach when doing business. This entails taking the economic, social and ecological considerations into account. Hence, a lot of companies have adopted corporate social investment (CSI) programmes. By adopting SRL clauses companies can meet their CSI obligations and build a positive global reputation. Companies adopting SRL practices also stand a chance of developing or strengthening relationships with policy makers in developing countries, enabling them to have an opportunity to make an input in policy issues they would otherwise have not had.

• **New business models**

Adopting SRL practices can provide the licensee with an opportunity to explore and develop new models of doing business which provide the company with a competitive advantage.

• **Access to regional and national disease expertise**

Regional and/or national experts in particular disease areas are likely to be more willing to collaborate with the licensee if they see that the licensee is committed to creating social impact. Such collaboration will be highly beneficial to the licensee, providing valuable know-how in the particular disease areas and a deeper understanding and prior experience of the local context.
• Affirmation of industry as responsible steward of IP

By adopting SRL practices, licensees will affirm that industry is a responsible steward of IP and potentially improve the reputation of industry among global society. A lot of criticism has been directed at industry for only pursuing profits and ignoring the needs of the poor. Adopting SRL practices will demonstrate that industry can champion the process of ensuring that IP monopolies are also used to benefit the less advantaged.

Business Models

Academic research is funded primarily by public or sovereign granting agencies in pursuit of their missions of teaching, research and public service. Technology transfer programs of academic research institutions operate within their institutional missions and pursue several goals when managing institutional IP rights, such as:

» Encourage the practical application of research and research results by the industry sector for the broad public benefit,
» Honour commitments to sponsors of research and other stakeholders,
» Build research relationships with industry to enhance education and research opportunities,
» Stimulate translation of research results through commercial uptake, investment, and deployment,
» Stimulate economic development,
» Ensure appropriate returns on taxpayer and other stakeholder investments that support the research enterprise.

• The virtuous cycle

The patent system provides incentives for entities to invest in risky and protracted R&D expenditures. Where profits from the investment are both feasible and expected, the traditional approach to licensing IP rights based on academic research involves finding a licensee with the right qualifications, and requiring them to diligently commercialise goods and/or services so that consumers, including taxpayers (who help fund the academic research enterprise) can benefit. The licensor (research institution and IP rights owner) typically benefits under this strategy through financial remuneration (through license fees and royalties) and its stakeholders (inventors, research departments, institution) also receive a portion of net revenues, thus creating a cycle of investment, invention, deployment, and reinvestment.
• **Market failure and models to traverse gaps in translation**

Where traditional profits are lacking, however, market economics do not drive investment, resulting in market failure. For example, the IP system alone does not induce investment in new innovations for neglected diseases (that afflict many who cannot afford to pay for treatment) and rare diseases (that afflict few, thus comprising a small customer base). When consumers cannot pay for a product, investment is lacking and investment in translational research to develop basic discovery into products does not occur.

The gap between discovery and translation of research results (often referred to as the “Valley of Death”) can be bridged by push and pull mechanisms, not all of which are sufficient to bring a given technology to those in need.

New business models, including creative financing, and modified IP management strategies can traverse R&D gaps by finding ways to share risk and apportion rewards.

• **Technologies with applications in the developed and developing world**

How can academic TTOs address situations where a new technology can be licensed into a traditional, profit-driven market and a non-traditional market where profits are not possible to achieve? Such “dual use” technologies can have standard terms and conditions covering products to be sold in developed economies, and modified “humanitarian” terms and conditions for low- and middle income countries. Under the traditional “push model” of academic tech transfer it is difficult, indeed, to stimulate and sustain commercial investment in an early-stage technology under the best market conditions, so the addition of “new” and unfamiliar terms and conditions at the time of IP rights licensing can be difficult to insert. Those developed or co-developed under a “pull model” are more applicable to such tailored contract terms, and/or do not require negotiation of the terms, due to prior arrangements in contracts that precede an IP license (such as collaboration and sponsored research agreements and letters of intent).

Contract terms to implement humanitarian use of a technology in developing countries include:

Definitions of licensed field of use (defining “humanitarian” or “charitable use”):

- royalty sharing,
- attribution,
- selective patent rights coverage (to encourage generic drug manufacture and other forms of competition to achieve competitive pricing),
- “claw-back” terms (mandatory sublicensing to address unmet needs and/or achieve target price),
humanitarian reservation of rights,
royalty-free sales (requires informed consent of inventors),
separate treatment of for-profit markets from non-profit markets,
tiered pricing within a given country (including conversion options),
favourable pricing (such as “free or at-cost” terms),
“no profit, no loss” definitions,
non-assertion.²

• **Bifurcated business models and dual commercialisation strategies**

Sometimes a single licensee (or a partnership among licensees) serves both markets, under different obligations to the licensor, following a bifurcated business plan pursuing different commercialisation strategies. One pursues for-profit sales (in developed markets) and the other operates under an “at cost” or “cost plus” cap on the sale of products, or operates under a “no profit, no loss” basis (in developing markets). Another form of bifurcation or dual commercialisation strategy achieves enough benefit for a commercial investor from one strategy to offset and justify the lack of profit from the other. For example, profits from developed markets can pay for market entry into developing markets with the aim of deriving a long-term benefit. Examples of these include opening of markets, development channels and distribution networks, navigation of in-country regulatory regimes, access to local know-how, receipt of “incentive vouchers” such as the U.S. Food and Drug expedited review voucher and the U.S. Patent and Trademark Office priority review voucher.

In short, two forms of de-linkage can be used to achieve humanitarian objectives such as affordable pricing including:

1. dissociating the cost of R&D from the sales price
2. deriving an ancillary benefit from a “humanitarian” strategy

Some examples of partnerships that have achieved these objectives are described below:

• **Collaborations and partnerships to traverse funding and R&D gaps**

Basic academic research is sometimes not translated due to several reasons, the largest of which is lack of funding. The risk: reward ratio is highly skewed against commercial applications that do not provide sufficient profit incentives, resulting in non-investment as described above in the description of market failure. In recent years collaborations between academics and those in other sectors have improved the risk: reward ratio by advancing R&D projects through public-private partnerships, public-public partnerships and product development partnerships (PDPs) that share and leverage resources, to focus on translational R&D.

² See for example, “Guidance and Clauses” at: [http://ipira.berkeley.edu/socially-responsible-licensing-ip-management](http://ipira.berkeley.edu/socially-responsible-licensing-ip-management) - refer to Appendix B
In doing so, the progression from discovery to development and deployment is advanced, the value proposition is improved, and translation is “de-risked.”

- All such partnerships address:
  - The partnership structure, including, who are the parties and whether they are for-profit, non-profit or both
  - Financing of the partnership
  - Alignment of goals, including finding and retaining incentives
  - Treatment of property rights, including IP rights
  - The coordination and timing of participation – how do the various partners enter and exit the partnership?
  - Which partners are involved in which stages?
  - What are their respective roles?
  - How many and what types of contracts are needed?
  - What are the specific terms and conditions?
  - How are results delivered, measured and put to use?

In recent years PDPs have arisen in the medical field that are focused on medical solutions for developing countries such as therapeutics, vaccines, and diagnostics. Medical PDPs bridge important gaps in translation by partnering “upstream” with academics and “downstream” with biotechnology and pharmaceutical companies. They are primarily funded by public funders and philanthropic foundations and thus, have missions and goals similar to those of academics in basic research institutions. They bring vital funding, drug, vaccine and device development expertise to partnerships, thereby facilitating translation and expediting commercial outcomes. Other PDPs are focused on agricultural biotechnology outcomes, such as improved crops.

To optimise collaborations between academic researchers and PDPs (and other partnerships) support is needed in terms of both organisational structures (infrastructure, policies) and values (aligning benefit outcomes). Academic norms and academic cultures are slowly changing to reflect a growing desire of researchers (and their institutions) to focus their research results with relevance to global health needs, and ultimately help those in need. Streamlined material transfers, data sharing and access to knowledge and know-how through publications and personnel exchange can all facilitate collaborative research and dissemination of good public assets for public benefit.

Constructs such as the Clinical and Translational Science Award (CTSAs) in the US and dedicated translational research institutes light a way to the future. Relevant “needs-based” research involves a “pull model” of innovation as opposed to the traditional IP rights “push model” and requires at a minimum, institutional contracting offices that go beyond licensing and also include expertise in industry sponsorship and collaboration agreements, plus insight into strategic alliances.
Overview of SRL Strategies

• **Technology selection**

SRL is generally appropriate to certain types of technologies. Those most suited to this approach are technologies which offer solutions to problems in underserved markets, including:

• **Healthcare**
  » Vaccines, drugs, diagnostics, formulations, cold chain distribution
  » Agriculture
  » Renewable/distributed energy
  » Potable water

• **IP management strategies**

An SRL approach should aim to reduce IP barriers in the target markets where the licensor wishes to see the technology made available. Patent filing strategies should therefore be guided by whether patent protection is likely to promote or hinder availability and accessibility of a technology in a particular market of interest.

**Motivation for not filing patent applications**

In some cases, choosing not to file patent applications in certain territories can promote availability and affordability of products.

1. Often there is little value to be obtained by patenting in least developed countries.
   » Where markets are unlikely to be lucrative enough to attract developed country producers to enter, domestic companies can then, in the absence of patent protection in their own country, make use of patent information from other countries as well as other literature, to develop the technology themselves (provided sufficient information is publicly available and that the companies concerned have the necessary capacity).
   » Where local companies do not have the capacity to take a product to market independently, absence of patent protection can then pave the way for importation of affordable generic drugs.

2. Where technologies are ‘enablers’ for further R&D, and/or can be used without requiring significant further downstream investment (which is likely to be forthcoming only in exchange for exclusive exploitation rights), patents are often not necessary. Examples where this might apply include:
   » Research reagents
   » Drug targets
   » Certain other research tools
Motivation for filing patent applications

However, in many cases (notably in respect of healthcare technologies), lack of patent protection could in fact hinder uptake of technology by industry and prevent it from reaching its intended market.

Where substantial investment is required for further development and marketing of a technology, patents are often essential, to give licensees an opportunity to recoup their investment before competitors enter the market.

- For those developing countries with domestic innovative and manufacturing capacity, patents are often necessary to incentivise local companies to invest in developing and marketing a technology, thus creating a barrier to entry for potential competitors. Where such companies export in addition to serving local markets, patents become even more important.

- Patents can be used as bargaining chips (e.g. via cross-licensing) to gain access to IP belonging to others, which might be necessary to use a particular technology or to add value.

- By licensing patent rights, the licensor is in a stronger position than it would be in the absence of patent rights, to impose conditions on the licensee to make technologies available in target markets, and have a means of enforcing such conditions contractually.

Complementary approaches to consider
1. In those countries that recognise ‘petty patents’, such protection can be considered for technologies that meet the relevant requirements.

2. Open and proprietary mechanisms can and do co-exist. One can therefore choose to protect certain elements of a technology to provide a necessary competitive edge, while putting associated information into the public domain; this could be of value to other researchers, but would not hinder the ultimate commercialisation of the technology.

- Licensing frameworks

SRL licences aim to promote availability and affordability of technologies in underserved (typically developing country) markets. In order to achieve this, a balance must be struck between providing adequate incentives to attract licensees with the capacity and willingness to take technologies to these markets, and building in suitable measures to ensure access of technologies on affordable terms in the markets of interest.
Licence terms to consider

Various provisions may be considered for inclusion in licence agreements to assist in achieving SRL objectives. These should be selected on a case-by-case basis; such decisions to be informed by the business model for taking the technology to market, which in turn will be influenced by the nature of the technology, the stage of development (and by implication the further steps required to achieve a marketable technology), the needs of the licensee, the structure and demands of the market, etc. A range of licensing terms promoting SRL objectives are suggested here, but should not be considered an exhaustive list. Different combinations of terms can be used, as appropriate. Overall, it must be borne in mind that licence terms found to be (individually or in combination) excessively restrictive on licensees could prevent a technology from reaching the market at all, and licence negotiations must ultimately produce a feasible outcome.

1. Market segmentation

Where a dual market business model is proposed, differentiated terms for various market segments can be applied.

Examples of different market segments:
- Developed vs developing countries
- Identification of regional blocs
- Public sector vs private sector
- Differentiated fields of use or industry sectors
- Humanitarian use or charitable objectives
- Appropriate definitions are important to avoid misuse

Examples of differentiated terms, which might apply in the specified market segments:
- Exclusive vs non-exclusive rights vs non-assert provisions/waivers
  - Note that in the case of non-asserts/waivers, liability to IP holders may be reduced, as they do not take on many of the positive obligations of the licensor. However, non-asserts can also raise concern about product diversion from the target SRL market to other markets where exclusive rights are in place.

- Exclusive rights in more profitable markets coupled with guarantees for underserved markets
  - Milestones can be set for the markets of interest e.g. minimum sales, date of first sale
Tiered pricing models – favourable pricing in specified markets
- Subsidisation in certain markets – typically by a not-for-profit third party
- Sales to be made ‘at cost’ in certain markets
- Set limits on allowable mark-up (‘cost-plus’ pricing)
- Price reduction facilitated by licensor taking a royalty sacrifice (in whole or in part, subject to prior consent of affected stakeholders, including inventors at a research institution)

2. Diligence/performance clauses
Provisions need to be included to encourage compliance with SRL terms, and to allow for alternative measures to be taken by the licensor to ensure that the SRL objectives are met in the event of non-compliance with the relevant provisions by the licensee.

- In the event of non-compliance with stipulated milestones or other SRL performance clauses, the licensee may require that exclusive licensed rights (which might include those for developed country markets) be converted to non-exclusive rights, or that the license be terminated (in some or all of the licensed territories)

- Mandatory sub-licensing clauses can be included in terms of which the licensee is obligated to sub-license to a third party in the event that the licensee itself is failing to develop the technology and/or satisfy market demand
  » It should be noted that licensees often view such provisions unfavourably as they are concerned about the extent to which this limits their freedom to do business

- ‘Walk-in rights’ can be used to allow the licensor or a third party (e.g. a government or not-for-profit funding agency) to take over the licensed rights in those markets that are not being satisfied
  » These rights may be built into grant and funding agreements from certain agencies under relevant national legislation or funding agency policy

- Performance clauses are of course of little value unless performance can be monitored and enforced and relevant terms should be incorporated to ensure that this can be done, to the extent possible.
3. **Research use licenses retained by licensor**

Efforts should be made to build in license terms to ensure that further R&D based on the SRL technology is restricted as little as possible.

- At a minimum, the licensor should ensure that it has a royalty-free license to continue its own non-commercial R&D

- Preferably, such rights should also be extended for use by other public research organisations for non-commercial R&D purposes

- In some cases, such rights might be extended even to companies, with appropriate conditions or limitations in place (e.g. for work on neglected diseases and subject to certain undertakings to ensure that ultimately, products are made available in the markets that need them)

4. **Benefit-sharing with communities & providers of plant genetic resources and/or traditional knowledge**

Where technologies are developed as a result of traditional knowledge and/or plant genetic resources provided by communities or traditional knowledge holders, licence agreements need to build in provisions for benefit sharing with such parties.

- Under the Convention on Biological Diversity, several countries have legislation governing access and benefit-sharing, resulting from bio-prospecting. But even where such activity is not formally regulated, a licence agreement for relevant technologies should provide for this.

- Both monetary and non-monetary benefits should be considered and incorporated wherever possible.

5. **Providing for unforeseen or changed circumstances**

SRL agreements should attempt to build in some flexibility to allow for unforeseen or changed circumstances (e.g. where a new use for a drug is discovered that addresses unmet needs and could have a substantial impact). Such provisions might not always be binding and are typically difficult to enforce, but nonetheless can assist in creating good faith expectations.

- The agreement can obligate the licensee to consult with the licensor to renegotiate in the event of certain stipulated circumstances occurring.
  
  » Depending on the language, this will often be considered ‘an agreement to agree’ and as such, not be legally binding.

- Wherever possible, license fee and benefit-sharing provisions should be crafted sufficiently broadly to cover all developments enabled by the license.
  
  » There are, however, limitations in terms of how far the licensor is able to ‘reach-through’ to future developments, especially where these are not anticipated at the time that the license agreement is drawn up.
Support for innovation and industry in developing countries as a component of SRL

For TTOs in developing countries, building local innovation capacity and strengthening local industry (particularly innovation-based companies) achieves many social and policy objectives. Local licensing technologies may play a role in creating new industries and employment opportunities and ensure that the benefits of the technologies concerned are harnessed locally. In cases where international licensing ultimately provides better prospects for increasing impact and ensuring that technologies reach their intended markets, provisions can nonetheless be drafted to ensure that benefits to the local economy and to local innovation efforts are achieved.

These may include the following:

» Commitment from the international licensee to collaborate in and/or support further R&D at the licensor organisation and/or other local institutions

» Support for human capital development
  • Exchange programmes
  • Funding of scholarships
  • Hosting and training researchers

» Providing knowledge and technology transfer

» Commitment to manufacture/produce locally (possibly in addition to doing so elsewhere), whether complete products or certain components

Further examples of SRL terms and strategies are provided in the appendices. Also, the Association of University Technology Managers (AUTM) website provides more examples of clauses: http://www.autm.net/AM/Template.cfm?Section=Global_Health&Template=/CM/ContentDisplay.cfm&ContentID=8010

Metrics

Appropriate metrics for measuring the success of such activities include: numbers and types of partnerships, diversification of funding sources, collaborative “fitness” (sharing of data, materials, personnel, reciprocity on IP terms or other property treatment), efficiency of translation, and importantly, the social impact of the activities, including use of research results, enablement of follow-on improvements, inducement of co-investment, recruitment of personnel for public good goals, and humanitarian metrics such as alleviation of poverty, health improvements, and infrastructure (such as sanitation, clean water).
Underlying Considerations

• Institutional culture and top management expectations
To allow easy adoption of SRL practices it is important for technology transfer practitioners to get buy-in from top management. This will ensure that there is alignment between expectations of senior managers and those of technology transfer personnel. If top management expects the TTO to only generate profits for the institutions, this might affect the choice of projects by technology transfer personnel and the type of licenses they may enter into. This could encourage the technology transfer personnel to pursue projects with potentially high financial returns and ignore those with potentially high social impact but low financial returns. Also, the licensing models adopted by technology transfer personnel might be geared to generating high profit margins instead of social impact. Hence, if top management buy-in into SRL practices is not obtained, it might be difficult for technology transfer personnel to implement these practices. Where the culture of the institution is such that it does not support projects with high social impact, this will also make it difficult for the adoption of SRL practices. It is important that TTOs work with other stakeholders to instil a culture inside the technology transfer office, of adopting projects and commercialisation models, which lead to high social impact and advocate broad buy-in within the institution. Incentives to technology transfer personnel should therefore not only be based on the profit generated by the TTO: recognition and incentives should also be provided for the social impact that the TTO has helped facilitate.

• Institutional policies
For effective adoption of SRL practices, institutional policies should explicitly support this type of licensing activity. For example, an institutional IP policy could provide for licensing for social impact. Enshrining SRL practices in institutional policies will provide the TTO with extra ammunition during negotiations with outside parties. Institutional policy promoting SRL will also provide clear guidance and extra motivation for the TTO, whose actions will be supported by policy.

• Multiple perspectives
Since SRL affects multiple stakeholders, both within the institution and externally, there will exist many different perspectives on how things should be done. In adopting SRL practices the TTO will have to effectively manage these different perspectives on technology transfer models and the purpose of the TTO. (e.g. some stakeholders might view the TTO as a vehicle for generating profit and expect it to be self-sustainable. Some inventors might view it as a vehicle to generate their future riches. Others might wish to make their technologies available in the public domain. Potential licensees might fail to see the benefits that an SRL approach might bring them.)
It is important that the TTO is able to handle these different perspectives and manage the expectations of the different stakeholders. For example, the TTO will need to build awareness in order to gain buy-in from the inventors with regard to commercialising technologies for social impact. This will ensure that there are no tensions between the inventors and the TTO when commercialised technologies do not generate income, which might otherwise have been expected by the inventor.

**Conclusions**

We believe that the adoption of SRL practices by TTOs is critical to improve access to healthcare technologies in underserved markets. By adopting SRL practices, TTOs can address market failures, ensure that society benefits from the research outputs of publicly funded research, increase the impact of publicly funded research, adhere to legislative and/or policy requirements, contribute to overall corporate social investment, create alternative models for commercialisation, increase the uptake of their technologies, create reputational goodwill for their institutions and increase sources of funding. It is clear that there are many incentives for TTOs to adopt SRL practices. Various SRL strategies can be followed when carrying out IP management and commercialisation activities to ensure greater societal impact. Successful SRL will be dependent on obtaining buy-in from top management and ensuring that institutional policies and culture are supportive of and aligned with the implementation of SRL practices. The approaches that have been described here are not intended to be an exhaustive catalogue – instead, technology transfer practitioners are urged to consider crafting new solutions tailored to the circumstances of their own deals, and to share these with the technology transfer community on an on-going basis, thereby helping to expand options in this fledgling field, ultimately increasing adoption of SRL for appropriate technologies.
References


Appendix A

Examples of SRL clauses developed by Medical Research Council when entering agreement for intellectual property funded by the South African AIDS Vaccine Initiative (SAAVI):

Company A, 2001
* MRC hereby grants to Company A (i) a royalty-free, non-exclusive license to make, have made, use and sell HIV Collaboration Vaccine and/or Cocktail Vaccine to the Public Sector in Developing Countries, and (ii) a royalty-bearing non-exclusive license to make, have made, use and sell HIV Collaboration Vaccine and/or Cocktail Vaccine to other than the Public Sector in Developing Countries. For the avoidance of any doubt this includes Private Sector in Developing Countries and both Public and Private Sector in Developed Countries.

Company B, 2002
* Company B hereby grants to MRC an exclusive perpetual fully-paid up license to make, use and sell products within the continent of Africa, without the right to export such products from Africa, that are covered under any Company B Background Invention and/or any Joint Invention that is utilized with any MRC nucleotide sequences in the Study with the right to sub-license such rights (Company B retains the right of first refusal and the first right to negotiate an exclusive license for North America and Europe).

Institution C, 2002
* Institution C grants the MRC a non-exclusive license under any and all of its intellectual property rights in vector X to manufacture and distribute HIV vaccine which incorporates the said vector or parts thereof together with the MRC HIV gene sequences.
* The license shall be world-wide and royalty-free for Developing Countries (list provided from World Bank classification) for the term of this Agreement.
* For Developed Countries (list provided from World Bank classification) the license granted to MRC shall for the term of this Agreement be world-wide and provide a royalty to Institution C (the royalty is only payable once the MRC has recovered all its reasonable direct costs expended on the development, manufacture and distribution of the HIV vaccine).
* Upon the MRC’s written request, Company D will, as promptly as commercially reasonable, manufacture and deliver to the MRC up to a maximum of five thousand (5,000) doses (the “Doses”) of Vaccine for use solely in clinical trials. The total amount payable to Company D for manufacture and delivery of such Vaccine shall be equal to Company D’s Manufacturing Cost (defined) of the Doses plus ten percent (10%). If Company D declines to supply Commercial Product to the MRC (for use in the Territory) on the terms set forth in the term sheet, then the MRC shall be permitted to enter into an agreement with a Third Party on the terms set forth in the term sheet and such other terms and conditions as are commercially reasonable under the circumstances..... Company D shall enter into an agreement with such Third Party Manufacturer pursuant to which Company D will grant a license and transfer its technology to such Third Party (with royalty provision) as required to enable such Third Party Manufacturer to manufacture and supply Vaccine to the MRC.... Company D shall make seed stock of the Vaccine available to the MRC and Third Party Manufacturer and the Third Party Manufacturer shall be permitted to use such seed stock to manufacture and supply Vaccine to the MRC (or its nominated distributor) for use solely within the Territory.

* Territory shall mean the sub-Saharan African countries listed in the exhibit (48 countries).
Appendix B

http://ipira.berkeley.edu
Carol Mimura
Memo: Updated August 17, 2010

Guidance and sample clauses for use in developing strategies, licenses, research and collaboration agreements in IPIRA's humanitarian/ socially responsible licensing program (SRLP) at Berkeley.

Please remember that even before discussing contract terms we should discuss with all parties (including inventors and authors of creative works) not patenting or not patenting in certain geographies, patent pools, technology trusts, commons (such as for software), open source licenses, and other incentives to achieving the goal of social impact, access and affordability through our initiatives.

Licenses grant rights to existing IP. Research agreements and collaboration agreements state our intention to deploy rights when they arise under sponsored research or through joint efforts. When prior IP exists and continuing development is funded under a research or collaboration agreement with charitable purposes, an option to license the original IP can be coupled with the research agreement and access terms under the SRLP can be applied to both.

Sample clauses:

In the recitals:
LICENSEE is capable of developing safe, effective, and affordable new [medicines] for people in the developing world afflicted with [infectious diseases], including [ ]. BERKELEY and LICENSEE wish to have LICENSED PRODUCTS marketed in the LICENSED TERRITORY as soon as possible [and at cost] so that products resulting therefrom may be available for public use and benefit.

In the definitions section:
PROJECT INVENTIONS are defined in the RESEARCH AGREEMENT. The research underlying PROJECT INVENTIONS is expected to be fully funded by [foundation or other grant source name, or use “LICENSEE” if licensee is the charitable funding source]. If PROJECT INVENTIONS arise, however, that are funded entirely or in part by grants from U.S. Government agencies, BERKELEY will grant to the U.S. Government a non-exclusive royalty-free, non-transferable, and irrevocable license to practice or have practiced the PROJECT INVENTIONS for, or on behalf of, the U.S. Government throughout the world (35 U.S.C. § 203) and this Agreement will be subject to those
rights. (insert as applicable for exclusive license) Moreover, this license will be subject to 35 U.S.C. § 204 (preference for U.S. industry) and March-in rights (35 U.S.C. § 202(c)(4)).

“LICENSED TERRITORY” means countries listed in Appendix A (note: this varies widely but has typically included low and middle income countries and/or least developed countries. Or, Economically Disadvantaged Countries (EDC) vs. non-EDC. See World Health Organization site, Doris Duke Charitable Foundation site for examples) of the RESEARCH AGREEMENT provided that, any development or manufacture of LICENSED PRODUCTS for the purpose of sale or distribution thereof in the LICENSED TERRITORY shall be deemed to have occurred within the LICENSED TERRITORY, whether or not such development or manufacture occurs in the LICENSED TERRITORY.

“HUMANITARIAN PURPOSES” means (a) the use of LICENSED PRODUCTS and LICENSED SERVICES for research and development purposes by any nonprofit organization or other third party, anywhere in the world that has the express purpose of developing the LICENSED PRODUCTS or LICENSED SERVICES for use solely in an EDC, and (b) the use of the LICENSED PRODUCTS or LICENSED SERVICES by any nonprofit organization or other third party for SALE solely in an EDC at or below cost.

Reminder, define “HUMANITARIAN OBJECTIVE” in research agreement and attach GLOBAL ACCESS STRATEGY in addition to the scope of work (corresponding to budget) as an appendix.
Reminder, define Field of Use in research agreement if a present grant such as “means the conduct of the [project] in accordance with the scope of work and the GLOBAL ACCESS STRATEGY and implementation of the HUMANITARIAN OBJECTIVE.
Reminder, define ECONOMICALLY DISADVANTAGED POPULATIONS (EDP) for tiered pricing requirements.

In the Grant clause section:
Subject to the limitations set forth in this Agreement and subject to potential licenses granted to the U.S. Government in the future, BERKELEY hereby grants and LICENSEE hereby accepts an [exclusive/nonexclusive/co-exclusive], royalty-free license [with right to sublicense, if exclusive] under BERKELEYS' PATENT [could be copyrights] RIGHTS to make, have made, use, offer for sale, import, and sell [or for copyrights, reproduce, prepare derivative works, distribute copies, perform publicly, or display publicly] LICENSED PRODUCT(S) and to practice LICENSED METHOD in the LICENSED FIELD OF USE in the LICENSED TERRITORY.
This grant is further subject to receipt by BERKELEY of written, informed consent of its inventors [or authors]. Written consent for the license terms in this AGREEMENT has been received from BERKELEY employees who will receive funding under the RESEARCH AGREEMENT. If one or more inventors or authors with an obligation to assign his or her patent rights to BERKELEY is named an inventor [author] on a future patent application or patent within BERKELEY’s PATENT RIGHTS has not received funding under the RESEARCH AGREEMENT, then this grant will be subject to that future inventor(s)’ written consent.

**In termination article:**

After typical terms for termination by BERKELEY stating that if a material breach is not cured within six months after written notice has been received by LICENSEE Insert for nonprofits: OR, shall terminate immediately if a) LICENSEE ceases to be designated a 501(c)(3) non-profit organization, or; b) if LICENSEE’S CHARITABLE OBJECTIVE changes.

Sublicensing: consider expansion to geographical unmet need, not just new uses. Note that “free or at cost” can be substituted for “new use” to drive the licensed product price lower.

**Mandatory Sublicensing Clause**

The concept is that when the University grants a broad exclusive license then we must have a mechanism to ensure that the market demand is met. As future, perhaps unanticipated, new uses arise we have an obligation to fill new market niches for the public good. This is especially important when our inventions are developed using federal funds. If we become aware of a new use that our licensee is not addressing, or if a third party approaches us for the (licensed) rights in order to develop a new use or other unmet need then we ask our licensee to tell us within 90 days if it will: (a) develop the new application on its own, or (b) grant a sublicense to the third party. If the licensee chooses to develop the new application then it must diligently undertake the new development (and report such progress to us).

**Suggested language:**

“If REGENTS (as represented by the actual knowledge of the licensing professional responsible for administration of U.C. Berkeley Case No.: xx or if a third party discovers and notifies that licensing professional that the INVENTION is useful for an application covered by the LICENSED FIELD OF USE but for which LICENSED PRODUCTS have not been developed or are not currently under development by LICENSEE, then the REGENTS, as represented by the Office of Technology Licensing, shall give written notice to the LICENSEE, except for: 1) information that is subject to restrictions of confidentiality with third parties, and 2) information which originates with REGENTS personnel who do not assent to its disclosure to LICENSEE.”
Within ninety (90) days following LICENSEE’s receipt of REGENTS’ notification
LICENSEE shall give REGENTS written notice stating whether LICENSEE elects to
develop LICENSED PRODUCTS for the application.

If LICENSEE elects to develop and commercialize the proposed LICENSED
PRODUCTS for the new application, LICENSEE shall submit a progress report
describing LICENSEE’s commercialization efforts in developing the new application
every six months to REGENTS pursuant to Article xx herein. (this language if this
paragraph is used in an option agreement: pursuant to the appropriate paragraph in
the LICENSE AGREEMENT).

If LICENSEE elects not to develop and commercialize the proposed LICENSED
PRODUCTS for use in the new application, REGENTS may seek (a) third party(ies)
to develop and commercialize the proposed LICENSED PRODUCTS for the new
application. If REGENTS identifies a third party, it shall refer such third party to
LICENSEE. If the third party requests a sublicense under this Agreement, then the
LICENSEE shall report the request to REGENTS within thirty (30) days from the date
of such written request. If the request results in a sublicense, then LICENSEE shall
report it to REGENTS (this language if this paragraph is used in an option agreement:
pursuant to the appropriate paragraph in the LICENSE AGREEMENT).

If the LICENSEE refuses to grant a sublicense to the third party, then within thirty (30)
days after such refusal the LICENSEE shall submit to REGENTS a report specifying the
license terms proposed by the third party and a written justification for the LICENSEE’s
refusal to grant the proposed sublicense. If REGENTS, at its sole discretion, determines
that the terms of the sublicense proposed by the third party are reasonable under the
totality of the circumstances, taking into account LICENSEE’s LICENSED PRODUCTS
in development, then REGENTS shall have
the right to grant to the third party a license to make, have made, use, sell, offer for
sale and import LICENSED PRODUCTS for use in the LICENSED FIELD-OF-USE at
substantially the same terms last proposed to LICENSEE by the third party providing
royalty rates are at least equal to those paid by LICENSEE.

ALSO ADD THIS TO THE REPORTING REQUIREMENT in both an option agreement
and a license agreement:
(b)LICENSEE’s progress in developing any applications of the REGENTS’ PATENT
RIGHTS elected for commercial development by LICENSEE pursuant to Article 4.5 of
this Agreement.

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Humanitarian Use Tiered Pricing License Terms
For a Research Agreement or Master Agreement

Summary
The following, sample Humanitarian Use License approach may be included in a research agreement. The terms provide conditions for a non-exclusive, royalty free license to inventions arising in the course of an industry sponsored research project. This sample language may be used in research agreements or in master agreements with separately executable project schedules, as in the case below.

Four concepts are notable in the terms below. First, the terms are oriented toward the information technology sector, while most humanitarian use terms are applied in the biomedical sector. Section 2.E addresses the fact that in the IT sector, many intellectual property rights may be incorporated in a single product, and products may be bundled or merged. Second, the usual country-level definition of licensed territory (usually defined as economically disadvantaged country, or “EDC”) is defined more granularly at a population level (economically disadvantaged population, or “EDP”). Third, to address possible anti-competition issues, a “Conversion” clause is introduced which provides for automatic conversion of a non-exclusive, royalty-free license to a Commercial License if any of three conditions arise, as described in Section 2.G. Fourth, many cases of offering humanitarian use clauses involve a nonprofit licensee with a charitable focus. In the case below, the sponsor and prospective licensee is a multinational, for-profit corporation with a clear commercial purpose even as it exercises its own social impact goals. We recognize this fact in the recitals and in associating the exercise of Humanitarian Use License with the company’s Corporate Responsibility unit provided the company has its own social impact goals and criteria related to the university’s public good mission. The fourth provision may not be feasible in all cases.

Recital
The Parties agree that provisions for humanitarian use license rights, as further described in Section 2 herein, are intended to address economically disadvantaged populations (“EDPs" as defined Article 1), and to induce investment and create markets for such populations where: i) there is strong potential for social impact in EDPs; ii) Company’s business potential for specific University Foreground is unclear and therefore lacks a natural home within a Company business unit except for use by Company Corporate Responsibility; and iii) University’s provision of Humanitarian Use License to Company for such University Foreground would motivate uptake and use by Company Corporate Responsibility in EDPs. University supports the social impact goals of Company Corporate Responsibility and encourages Company’s offer in EDPs of Humanitarian Products incorporating University Foreground under Humanitarian Use License (the “Humanitarian Objectives”).
1. Definitions

“Company Corporate Responsibility” means Company’s corporate responsibility program. “Conversion” means a conversion of Humanitarian Use License to a Commercial License if Company offers Humanitarian Products: a) at market rate according to GAAP within EDPs, b) at EDP Rate in populations not listed in or added by amendment within sixty (60) days of notice to the relevant license, or c) if a given EDP graduates from its applicable EDP status. Financial terms and diligent development requirements may apply.

“EDP” shall be defined as: a) countries recognized by either the United Nations as “least developed countries” (“LDCs”) or by the World Bank as countries with extreme or moderate poverty; and b) populations within a country living below the generally accepted poverty line in non-LDCs. For (b), populations in the United States will be identified using the standard of populations below the U.S. federal government poverty line according to the U.S. Census, and for other non-LDCs, a generally accepted poverty line of the given country which is substantially similar to the U.S. poverty line relative to the given country.

“EDP Rate” means the offer of Humanitarian Products by Company in EDPs for free, below market rate, or at cost, but not at market rate according to generally accepted accounting practice (“GAAP”).

“Humanitarian Objective” means the social impact goals of Company Corporate Responsibility and University and the offer in EDPs of Humanitarian Products incorporating University Foreground under a Humanitarian Use License.

“Humanitarian Products” means Company products and/or services incorporating University Foreground licensed under any Humanitarian Use License granted pursuant to Section 1.

“Humanitarian Use License” A non-exclusive, royalty free license, as outlined in Section ____, for University Foreground which shall be granted to Company when Company intends to incorporate into Humanitarian Products offered within EDPs to meet Humanitarian Objectives and satisfied criteria outlined in Section 1.

“LDCs” means countries defined by the United Nations as “least developed countries.”
“OTL” means University’s Office of Technology Licensing.
“Commercial License” means a license for commercial use with terms described in Section __[standard IP section].
“Project Schedule” means a project schedule agreement using the form in Appendix 1 to this Agreement that is signed by an authorized representative of each of the Parties, and that describes a research or collaboration project by the Parties. [Note: These terms are part of a master agreement, and a Project Schedule is separately executable under the master agreement.]

2. Humanitarian Use Terms

2. Conditions for Royalty Free, Non-Exclusive Humanitarian Use License. A Humanitarian Use License shall be granted to Company if Company satisfies the conditions outlined below and provides written, supporting documentation to University’s OTL. Upon submission of written documentation, University’s OTL shall respond in writing to Company within thirty (30) days as to whether it will accept or challenge Company’s assertion that conditions for a license granted pursuant to this Section 1 have been satisfied. A license granted pursuant this Section 1 shall automatically be offered, without further documentation, upon such acceptance from the OTL.

A. Company shall manage its exercise of the Humanitarian Use License or offer of Humanitarian Products under its Company Corporate Responsibility unit.

B. Company shall offer Humanitarian Products solely within EDPs, for Humanitarian Objectives. Such EDPs shall be listed in any Humanitarian Use License and anticipated if possible by listing in the Project Schedule.

C. Company’s offer of Humanitarian Products shall be made available at the EDP Rate in the EDPs listed in the Project Schedule or license, as applicable.

D. While not limiting Company’s exercise of any other rights under this Agreement, Company’s offer of Humanitarian Products shall be restricted to populations in which it is presumed Company or its competitors do not expect to make a near term profit under GAAP with respect to such Humanitarian Products, whether or not Company operates in such markets. The probable effect on other markets may be taken into account in determining this exclusion.

E. To satisfy the Humanitarian Objectives, for any (i) offer of products and services incorporating University Foreground under a Humanitarian Use License, and (ii) any Humanitarian Products coupled or packaged with other products or services necessary to use Humanitarian Products, such offers shall be offered together at an EDP Rate.
F. Company shall provide to University's OTL a separate annual report of products and services provided under Humanitarian Use Terms and listed by EDP and EDP Rate.

G. A Humanitarian Use License is convertible upon six months' written notice by University to a Commercial License if Company offers Humanitarian Products:
   a) at market rate according to GAAP within EDPs, b) at EDP Rate in populations not listed in or added by amendment within sixty (60) days of notice to the relevant license, or c) if a given EDP graduates from its applicable EDP status. In the event of conversion, financial terms and diligent development requirements may apply. The Conversion shall not occur if Company cures the identified event within the six month period and reports such cure to University within at least thirty days before the end of the six month period.

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Humanitarian Reservation of Rights
Text for license agreement, modify for research contract
x.x "HUMANITARIAN PURPOSES" means (a) the use of LICENSED PRODUCTS and LICENSED SERVICES for research and development purposes by any nonprofit organization or other third party, anywhere in the world that has the express purpose of developing the LICENSED PRODUCTS or LICENSED SERVICES for use solely in an EDC, and (b) the use of the LICENSED PRODUCTS or LICENSED SERVICES by any nonprofit organization or other third party for SALE solely in an EDC at or below cost.

x.x Nothing in this Agreement will be deemed to limit the right of UNIVERSITY to:

a) publish any and all technical data resulting from any research performed by UNIVERSITY relating to the INVENTION, and to make and use the INVENTION, LICENSED PRODUCTS, and LICENSED SERVICES and practice LICENSED METHOD and associated technology for its educational and research purposes, and to allow other educational and non-profit institutions to do so for their educational and research purposes, and;

b) license the UNIVERSITY PATENT RIGHTS to any third parties solely for HUMANITARIAN PURPOSES. Such licenses for HUMANITARIAN PURPOSES shall (i) expressly exclude the right of the third party licensee to export or SELL the LICENSED PRODUCTS from an EDC into a market outside of the EDC where LICENSEE has introduced or will introduce a LICENSED PRODUCT and where UNIVERSITY PATENT RIGHTS exist (such markets, the "LICENSEEMARKETS") and
(ii) require the third party licensee to create and maintain distinctive trade dress and trademarks ("EDC Trademarks and Trade dress") that clearly distinguish third party LICENSED PRODUCTS or LICENSED SERVICES from LICENSEE’S LICENSED PRODUCTS or LICENSED SERVICES, (iii) require such third party licensee’s SALE of LICENSED PRODUCTS or LICENSED SERVICES in such EDCs at or below cost. For avoidance of doubt, such third party licensee may be permitted to export LICENSED PRODUCTS from the EDC of origin to other EDCs and all other countries mutually agreed to by The UNIVERSITY and LICENSEE.

Notwithstanding the foregoing:

i. prior to issuance of any such license to UNIVERSITY’ PATENT RIGHTS to a third party, the UNIVERSITY will notify LICENSEE of its intention to grant such license so that LICENSEE may have the opportunity to fill the anticipated market need itself and/or to engage in discussions for a sublicense with such third party in accordance with the procedures set forth in Section 4.8; and

ii. in the event any LICENSED PRODUCT SOLD in any EDC by any such third party according to the provisions of Section 3.3(b) is exported, re-SOLD or otherwise introduced in any LICENSEE MARKET, LICENSEE will provide the UNIVERSITY with written notification thereof, and if such exportation, re-SALE or introduction does not cease within ninety (90) days after the date of such notice, then an amount equal to the retail price of LICENSED PRODUCTS so exported, re-SOLD or introduced to such LICENSEE MARKET shall be deducted from any royalties due to THE UNIVERSITY hereunder
Building a healthy nation through research
Socially Responsible Licensing Clauses

Definitions:

“Global Access” means the provision of meaningful access to the Licensed Product(s) for those most in need, specifically the public sector in low and middle income countries, where meaningful access means the Licensed Product(s) is made broadly and quickly available at costs that are reasonable in each country context;

“Global Access Markets” means the public sector in the low and middle income countries included in the Licensed Territories;

Clauses on benefit to SA required in terms of the IPR Act:

The South African Government may acquire certain rights in the event of the Licensed Technology and/or Licensed Products not being commercialised for the benefit of South Africa, and/or not being commercialised within a reasonable period, if applicable, which rights include the right to require the granting of a licence in any field of use to any third party on reasonable terms.

The South African Government is entitled to an irrevocable, royalty-free license to use/have used the Licensed Technology and/or Licensed Products throughout the world, for South Africa’s health, security and/or emergency needs.

Global access clauses:

The Licensee shall use its best efforts and endeavour in good faith, either directly or through sub-licensees, throughout the term of this Agreement and in the execution of its obligations in terms of this Agreement as they relate to the marketing, distribution and supply of Licensed Product, to achieve Global Access to the Licensed Products in Global Access Markets.

More particularly, in the furtherance of Global Access objectives, the Licensee shall:

- employ methods of market segmentation within Licensed Territories, including by applying tiered pricing for the Licensed Products between wealthier consumers and the Global Access Markets in Licensed Territories and, where necessary, investigating alternate distribution or implementation channels in Global Access Markets;

- make reasonable efforts to market the Licensed Products in Global Access Markets and pursue the conclusion of the necessary tenders and contracts for such purpose;

- ensure timely and adequate supply of Licensed Products to meet the reasonable needs of Global Access Markets.

Should the Licensee be unable or unwilling to address the needs of any of the Global Access Markets included in this Agreement then it shall notify the Licensor of such. The Licensor shall then be free to exercise or to license any third party to exercise rights to the Licensed Technology for the purposes of making the Licensed Products available in the applicable markets. Such rights shall be in addition to the rights of the South African Government in terms of clauses ............
If the Licensee is unable or unwilling to serve or develop a potential market or market territory (including a Global Access Market) in the Licensed Territory for which there is a company willing to be a sub-licensee, the Licensee will, at the Licensor's request, negotiate in good faith a sub-license with any such sub-licensee.

In the event that the Licensor has determined that the Licensee has failed to achieve Global Access in one or more Global Access Territories and:
- the Licensee has been provided with written notice of the basis for its determination; and
- the Licensee has been provided with 60 days from the date of the written notice to demonstrate to the Licensor that it has remedied the Global Access deficiency or will be able to do so within a reasonable period of time; and
- the Licensee has not provided the Licensor with a written response within 60 days or the Licensor is not satisfied with a received written response that the Global Access deficiency has been remedied, or will be remedied within a reasonable period of time;
the license in the affected Global Access Territories may be revoked by the Licensor.

In the event of exercise of rights by the Licensor or the South African Government in terms of clauses ............., respectively, the Licensee shall employ best efforts and endeavour in good faith to assist in obtaining the required marketing approvals and/or product registrations, including by providing such technical documentation, information, data, and assistance as may be required in the circumstances.
Global Access Policy

BACKGROUND

Grand Challenges Canada is dedicated to supporting Bold Ideas with Big Impact® in global health. We are funded by a variety of governments and organizations ("Funding Partners") and we primarily fund innovators in low- and middle-income countries (LMICs) and Canada. The bold ideas we support integrate science and technology, social, and business innovation – we call this Integrated Innovation®. We focus on bringing successful innovation to scale, catalyzing sustainability and impact. We have a determined focus on results, and on saving and improving lives.

The objective of this Global Access Policy is to ensure that the successful innovations we support and the vital knowledge we help create will have the greatest possible impact for those most in need.

GUIDING PRINCIPLES OF GLOBAL ACCESS

Grand Challenges Canada's Global Access Policy is grounded in the following three principles:

1. Solutions to grand challenges in global health that are supported by Grand Challenges Canada funding or that are developed through funded activities ("funded solutions") should be made broadly and quickly accessible and affordable in the relevant context and setting.

2. Knowledge gained through funded research should be broadly and quickly disseminated between related projects and to the global scientific community.

3. Commercialization of funded solutions is encouraged, as long as the first two principles are respected.

REQUIREMENTS OF GLOBAL ACCESS

The following requirements apply to funded solutions and to other outputs of work undertaken with funds from Grand Challenges Canada.

1. **Broad dissemination of knowledge.** All research-related outputs of Grand Challenges Canada-funded projects, including results, data, and reports, must be shared with Grand Challenges Canada and its community of researchers and related institutions, and must be disseminated as quickly and broadly as possible to the scientific community. Dissemination of research-related outputs may be delayed for a reasonable period of
time – typically no more than 12 months after project completion but subject to extension in appropriate circumstances – if necessary to prepare and submit materials for publication, to file intellectual property applications, or to enable successful commercial implementation of funded solutions.

2. **Open access publication.** Publications arising from funded research must be immediately openly accessible under a Creative Commons Attribution (CC BY) or equivalent license and must be discoverable and accessible online.¹ The financial costs of open access publication may be included in proposed project budgets and will be subject to review and approval.

3. **Open access to data.** As further elaborated in Grand Challenges Canada’s Data Access Policy, data from funded projects must be made openly accessible.

4. **Commitment to achieving global access.** Funding recipients must work with Grand Challenges Canada to achieve their objectives in compliance with this Policy during the funding process and throughout the subsequent implementation of funded solutions. Innovators that receive Grand Challenges Canada funding to transition their solutions to scale must develop action plans to achieve access and affordability in the relevant context and setting. Grand Challenges Canada will monitor implementation of these access plans.

5. **Development and protection of intellectual property.** Funding recipients may apply for and maintain intellectual property protection for funded solutions, but must administer their rights in a manner that will not impede achievement of access and affordability in the relevant context and setting. Generally, ownership and control of intellectual property shall remain with the funding recipient, subject to applicable laws and policies.

6. **Commercialization that promotes meaningful access.** Funding recipients are encouraged to commercialize funded solutions but must do so in a manner that promotes access and affordability consistent with the Guiding Principles. Funding recipients may satisfy this requirement directly or by way of partnerships, license agreements, or other arrangements with for-profit or not-for-profit entities.

7. **Grand Challenges Canada and Funding Partners’ access to funded solutions.** To ensure that the Guiding Principles will be achieved, funding recipients must provide Grand Challenges Canada with a limited right of access to funded solutions that may be exercised in the event the funding recipient is unable to achieve access and affordability in the relevant context or setting. The details of this limited access right will be specified in each funding agreement. The right may take the form of a non-exclusive license to intellectual property rights or a distribution agreement in the relevant territory and, if triggered, it must be sub- licensable or assignable by Grand Challenges Canada, including to its Funding Partners or an appointee thereof. Funding recipients must

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¹ Grand Challenges Canada’s open access publication requirement is aligned with the Bill & Melinda Gates Foundation Open Access Policy (http://www.gatesfoundation.org/How-We-Work/General-Information/Open-Access-Policy).
ensure that their agreements with third parties do not conflict with the above access rights. Third parties that own core intellectual property rights in funded solutions may also be required to provide access commitments to Grand Challenges Canada and its Funding Partners.

8. **Global Health Emergencies.** Where applicable, in order to ensure global health emergencies can be quickly and adequately addressed, some funding recipients may be required to grant, upon request and in the event that the World Health Organization declares a Public Health Emergency of International Concern, a non-exclusive license to funded solutions to Grand Challenges Canada or an appointee of the Funding Partner. Funding recipients must ensure that their agreements with third parties, or any third party intellectual property rights in the funded solutions, do not conflict with the above global health access rights.

9. **Revenues from commercialization.** Generally, revenues generated from the sale of funded solutions shall remain with the funding recipient, subject to applicable laws and policies and the collaborative process described above, including any arrangements between the funding recipient and other individuals or institutions. Grand Challenges Canada may, however, require repayment of funds from innovators that it supports at transition to scale in the form of a loan or a success-based royalty.

10. **Due diligence.** Grand Challenges Canada will conduct due diligence to determine the viability of a project and to ensure that the project conforms to this Policy. This due diligence may include inquiries into important background technologies and how they will be accessed; the intellectual property landscape and how intellectual property rights will be accessed, managed and/or allocated; and what collaborations may be involved and how these collaborations will be managed.

11. **Reporting.** Funding recipients must provide periodic reports on progress in achieving global access, including after completion of the funded project.

Last updated: May 16, 2018
SAMPLE TERMS & CONDITIONS
PROJECT SUPPORT GRANT AGREEMENT

This document contains a list of standard terms and conditions frequently included in our project support grant agreements. This is not an exhaustive list and is subject to change from time to time in our sole discretion. This list is provided for informational purposes only and does not imply an award, agreement, or offer to contract.

GRANT AMOUNT: The Foundation will pay You the total grant amount specified in the Reporting & Payment Schedule below. The Foundation’s Primary Contact must approve in writing any Budget cost category change of more than 10%.

REPORTING & PAYMENT SCHEDULE: Payments are subject to Your compliance with this Agreement, including Your achievement, and the Foundation’s approval, of any applicable targets, milestones, and reporting deliverables required under this Agreement. The Foundation may, in its reasonable discretion, modify payment dates or amounts and will notify You of any such changes in writing.

REPORTING: You will submit reports according to the Reporting & Payment Schedule using the Foundation’s templates or forms, which the Foundation will make available to You and which may be modified from time to time. For a progress or final report to be considered satisfactory, it must demonstrate meaningful progress against the targets or milestones for that investment period. If meaningful progress has not been made, the report should explain why not and what adjustments You are making to get back on track.

PROJECT DESCRIPTION AND CHARITABLE PURPOSE: The Foundation is awarding You this grant to carry out the project described in the Proposal Narrative and Results Framework and Tracker (collectively, "Project") in order to further the Charitable Purpose. The Foundation, in its discretion, may approve in writing any request by You to make non-material changes to the Proposal Narrative and/or Results Framework and Tracker.

USE OF FUNDS: You may not use funds provided under this Agreement ("Grant Funds") for any purpose other than the Project. You may not use Grant Funds to reimburse any expenses You incurred prior to the Start Date. At the Foundation’s request, You will repay any portion of Grant Funds and/or Income used or committed in material breach of this Agreement, as determined by the Foundation in its discretion.

INVESTMENT OF FUNDS: You must invest Grant Funds in highly liquid investments with the primary objective of preservation of principal (e.g., an interest-bearing account or a registered money market mutual fund) so that the Grant Funds are available for the Project.

GLOBAL ACCESS COMMITMENT: You will conduct and manage the Project and the Funded Developments in a manner that ensures Global Access. Your Global Access commitments will survive the term of this Agreement. “Funded Developments” means the products, services, processes, technologies, materials, software, data, other innovations, and intellectual property resulting from the Project.

INTELLECTUAL PROPERTY REPORTING: During the term of this Agreement and for 5 years after, You will submit annual intellectual property reports relating to the Funded Developments, Background Technology, and any related agreements using the Foundation’s templates or forms, which the Foundation may modify from time to time.

SUBGRANTS AND SUBCONTRACTS: You have the exclusive right to select subgrantees and sub contractors to assist with the Project.

RESPONSIBILITY FOR OTHERS: You are responsible for all acts and omissions of any of Your trustees, directors, officers, employees, subgrantees, subcontractors, contingent workers, agents, and affiliates assisting with the Project and ensuring their compliance with the terms of this Agreement.

ANTI-TELEVI SION: You will use funds provided under this Agreement, directly or indirectly, in support of activities (a) prohibited by U.S. laws related to combating terrorism; (b) with persons on the List of Specially Designated Nationals (www.treasury.gov/sdn) or entities owned or controlled by such persons; or (c) with countries against which the U.S. maintains comprehensive or targeted sanctions (currently, Cuba, Iran, Syria, North Korea, and the Crimea Region of Ukraine), unless such activities are fully authorized by the U.S. government under applicable law and specifically approved by the Foundation in its sole discretion.

ANTI-CORRUPTI ON AND ANTI-BRIBERY: You will not offer or provide money, gifts, or any other things of value directly or indirectly to anyone in order to improperly influence any act or decision relating to the Foundation or the Project, including by assisting any party to secure an improper advantage. Training and information on compliance with these requirements are available at www.learnfoundationlaw.org.
LOBBYING AND ELECTIONEERING PROHIBITION

You may not use Grant Funds to influence the outcome of any election for public office or to carry on any voter registration drive. You acknowledge that the Foundation has not earmarked Grant Funds to support lobbying activities or to otherwise support attempts to influence legislation. Activities will be conducted consistent with the private foundation lobbying rules and exceptions under Internal Revenue Code Section 4945 and related regulations. You confirm that the Budget (or the combined project budget if there are multiple funders) accurately reflects that You will expend at least the amount of the Grant Funds on (a) non-lobbying activities in the project year, or (b) for multiple year projects, the total non-lobbying portion of the project.

OTHER LOBBYING, GIFT, AND ETHICS RULES

You agree to comply with any national, state, local, or other lobbying, gift, and ethics rules applicable to the Project. The Foundation is not retaining or employing You in engaging in lobbying activities.

PUBLICITY BY THE FOUNDATION:

The Foundation may include information about the award of this grant, including Your name, in its periodic public reports and may make such information available on its website and as part of press releases, public reports, speeches, newsletters, tax returns, and other public disclosures.

PUBLICITY BY YOU:

You must obtain the Foundation’s prior written approval before: (a) issuing a press release or other public announcement regarding this grant; and (b) any other public use of the Foundation’s name or logo. Please email Your request to: grantee.comms@gatesfoundation.org two weeks in advance to provide the Foundation an opportunity to review and comment. Detailed guidelines are available at: www.gatesfoundation.org/grantseeker/documents/guidelines_communications_for_grantees.doc.

PUBLICITY BY OTHERS:

You and Your subgrantees, subcontractors, contingent workers, agents, or affiliates may not state or imply to third parties that the Foundation directly funds or otherwise endorses their activities.

COMPLIANCE WITH LAWS:

In carrying out the Project, You will comply with all applicable laws, regulations, and rules and will not infringe, misappropriate, or violate the intellectual property, privacy, or publicity rights of any third party.

RELIANCE:

You acknowledge that the Foundation is relying on the information You provide in reports and during the course of any due diligence conducted prior to the Start Date and during the term of this Agreement. You represent that the Foundation may continue to rely on this information and on any additional information You provide regarding activities, progress, and Funded Developments.

TERM:

This Agreement commences on the Start Date and continues until the End Date, unless terminated earlier as provided in this Agreement. The Foundation, in its discretion, may approve in writing any request by You for a no-cost extension, including amending the End Date and adjusting any affected reporting requirements.

TERMINATION:

The Foundation may modify, suspend, or discontinue any payment of Grant Funds or terminate this Agreement if: (a) the Foundation is not reasonably satisfied with Your progress on the Project; (b) there are significant changes to Your leadership or other factors that the Foundation reasonably believes may threaten the Project’s success; (c) there is a change in Your control; (d) there is a change in Your tax status; or (e) You fail to comply with this Agreement.

RETURN OF FUNDS:

Any Grant Funds that have not been used for, or committed to, the Project upon expiration or termination of this Agreement must be returned promptly to the Foundation, applied to another Foundation-funded project (current or under consideration), or applied to another mutually-agreed upon charitable purpose, as directed in writing by the Foundation. Any Income that has not been used for, or committed to, the Project must be either applied to another Foundation-funded project (current or under consideration) or applied to another mutually-agreed upon charitable purpose, as directed in writing by the Foundation.

RECORD KEEPING:

You will maintain complete and accurate accounting records and copies of any reports submitted to the Foundation relating to the Project. You will retain such records and reports for 4 years after Grant Funds have been fully spent. At the Foundation’s request, You will make such records and reports available to enable the Foundation to monitor and evaluate how Grant Funds have been used or committed.

SURVIVAL:

A Party’s obligations under this Agreement will be continuous and survive expiration or termination of this Agreement as expressly provided in this Agreement or otherwise required by law or intended by their nature.

ENTIRE AGREEMENT AND AMENDMENTS:

This Agreement contains the entire agreement of the Parties and supersedes all prior and contemporaneous agreements concerning its subject matter. Except as specifically permitted in this Agreement, no modification, amendment, or waiver of any provision of this Agreement will be effective unless in writing and signed by authorized representatives of both Parties.

NOTICES AND APPROVALS:

Written notices, requests, and approvals under this Agreement must be delivered by mail or email to the other Party’s primary contact specified on the Agreement Summary & Signature Page, or as otherwise directed by the other Party.

SEVERABILITY:

Each provision of this Agreement must be interpreted in a way that is enforceable under applicable law. If any provision is held unenforceable, the rest of the Agreement will remain in effect.

ASSIGNMENT:

You may not assign, or transfer by operation of law or court order, any of Your rights or obligations under this Agreement without the Foundation’s prior written approval. This Agreement will bind and benefit any permitted successors and assigns.

COUNTERPARTS AND ELECTRONIC SIGNATURES:

Except as may be prohibited by applicable law or regulation, this Agreement and any amendment may be signed in counterparts, by facsimile, PDF, or other electronic means, each of which will be deemed an original and all of which when taken together will constitute one agreement. Facsimile and electronic signatures will be binding for all purposes.

The following clauses will be included in project support grant agreements if relevant to your project, as determined by the Foundation. These terms are non-negotiable.

EVALUATION: [Included in all U.S. Program grants.] You agree to notify the Foundation and provide copies of any reports or findings if You conduct or commission any research or evaluation regarding the Project. If You are selected to participate in Foundation-funded research or evaluation relating to the Project, You agree to: (a) designate a primary point of contact; (b) cooperate with the Foundation’s evaluation partner as reasonably required to implement an evaluation plan; (c) provide or facilitate the collection of data as reasonably required; and (d) permit dissemination of resulting reports or findings.
GLOBAL ACCESS MILESTONES: [Included if the foundation requires that Global Access commitments be further defined.] To further define Your Global Access commitments, You are required to complete a Global Access Strategy and any other Global Access activities and documentation listed in the Reporting & Payment Schedule. The Global Access Strategy should address the following concepts with respect to all Funded Developments: (a) identification of Background Technology associated with the Project and any Funded Developments created during the Project and specific strategies to ensure access to such Funded Developments and Background Technology; (b) agreements and/or procedures for transfers of materials and data among Project Collaborators or third parties relevant to the Project; (c) reporting processes for the creation of Funded Developments to both the Project management team and the Foundation as well as the publishing and dissemination of the knowledge and information gained from the Project; (d) strategies to secure, manage and allocate intellectual property rights associated with the Funded Developments or Background Technology in a way that ensures Global Access while providing incentives for future potential private sector participation; and (e) anticipated development, commercialization and sustainability strategies during and after the Project to ensure that Global Access can be met.

You may not materially change the plans and strategies contained in any Global Access documents after they have been approved by the Foundation without the Foundation’s prior written approval. You will provide the Foundation with updates to the Global Access Strategy during each year of the Project describing any new or modified approaches with respect to Funded Developments and Background Technology, and related agreements, taking into account new or modified Funded developments and/or market information. “Global Access Strategy” means a written document, subject to the Foundation’s approval, describing how You intend to achieve Global Access given the particular circumstances of the Project. “Project Collaborators” means all current and future subgrantees, subcontractors, partners, agents, affiliates, or other parties who provide any input to the Project.

GLOBAL ACCESS COMMITMENT AGREEMENT: [Included if foundation requires a Global Access Commitment Agreement.] In order to further define Your Global Access commitments, You agree to the terms and conditions set out in the Global Access Commitment Agreement set forth in Attachment C. You may not materially change the plans and strategies contained in any Global Access Commitment Agreement without the Foundation’s prior written approval. Upon request of the Foundation, You will provide the Foundation with progress updates evidencing the progress to attain Your Global Access Commitments.

HUMANITARIAN LICENSE: [Include if foundation requires a license to Funded Developments in order to further Global Access.] Subject to applicable laws and for the purpose of achieving Global Access, You grant the Foundation a non-exclusive, perpetual, irrevocable, worldwide, royalty-free, fully paid up, sublicensable license to make, use, sell, offer to sell, import, distribute, copy, create derivative works, publicly perform, and display Funded Developments and Essential Background Technology. “Essential Background Technology” means Background Technology that is: (a) owned, controlled, or developed by You, or in-licensed with the right to sublicense, and (b) either incorporated into a Funded Development or reasonably required to exercise the license to a Funded Development. You confirm that You have retained sufficient rights in the Funded Developments and Essential Background Technology to grant this license. You must ensure this license survives the assignment or transfer of Funded Developments or Essential Background Technology. On request, You must promptly make available the Funded Developments and Essential Background Technology to the Foundation for use solely under this license. If You demonstrate to the satisfaction of the Foundation that Global Access can be achieved without this license, the Foundation and You will make good faith efforts to modify or terminate this license, as appropriate.

COMPLIANCE WITH REQUIREMENTS: [Included in all US Programs, Global Policy and Advocacy, and Communications grants.] You will conduct, control, manage, and monitor the Project in compliance with all applicable ethical, legal, regulatory, and safety requirements, including applicable international, national, state, local, institutional, and school district or school network standards (“Requirements”). You will obtain and maintain all necessary approvals, consents, and reviews before conducting the applicable activity. As a part of Your annual progress report to the Foundation, You must report whether the Project activities were conducted in compliance with all Requirements.

If the Project involves:

a. any protected information (including personally identifiable, protected health, or third-party confidential), You will not disclose this information to the Foundation without obtaining the Foundation’s prior written approval and all necessary consents to disclose such information; and/or
b. children, students, or vulnerable subjects, You will obtain any necessary consents and approvals unique to these subjects.

Any activities by the Foundation in reviewing documents and providing input or funding does not modify Your responsibility for determining and complying with all Requirements for the Project.

COMPLIANCE WITH REQUIREMENTS: [Included in all Global Health Program and Global Development Program grants.] You will conduct, control, manage, and monitor the Project in compliance with all applicable ethical, legal, regulatory, and safety requirements, including applicable international, national, local, and institutional standards (“Requirements”). You will obtain and maintain all necessary approvals, consents, and reviews before conducting the applicable activity. As a part of Your annual progress report to the Foundation, You must report whether the Project activities were conducted in compliance with all Requirements.

If the Project involves:

a. any protected information (including personally identifiable, protected health, or third-party confidential), You will not disclose this information to the Foundation without obtaining the Foundation’s prior written approval and all necessary consents to disclose such information;

b. children or vulnerable subjects, You will obtain any necessary consents and approvals unique to these subjects; and/or

c. any trial involving human subjects, You will adhere to current Good Clinical Practice as defined by the International Council on Harmonisation (ICH) E-6 Standards (or local regulations if more stringent) and will obtain applicable trial insurance.

Any activities by the Foundation in reviewing documents and providing input or funding does not modify Your responsibility for determining and complying with all Requirements for the Project.

INDEMNIFICATION: [Note: Included in all Global Health Program and Global Development Program grants.] If the Project involves clinical trials, trials involving human subjects, post-appraisal studies, field trials involving genetically modified organisms, experimental medicine, or the provision of medical/health services (“Indemnified Activities”), You will indemnify, defend, and hold harmless the Foundation and its trustees, employees, and agents (“Indemnified Parties”) from and against any and all demands, claims, actions, suits, losses, damages (including property damage, bodily injury, and wrongful death), arbitration and legal proceedings, judgments, settlements, or costs or expenses (including reasonable attorneys’ fees and expenses) (collectively, “Claims”) arising out of or relating to the acts or omissions, actual or alleged, of You or Your employees, subgrantees, subcontractors, contingent workers, agents, and affiliates with respect to the Indemnified Activities. You agree that any activities by the Foundation in connection with the Project, such as its review or proposal of suggested modifications to the Project, will not modify or waive the Foundation’s rights under this paragraph. An Indemnified Party may, at its own expense, employ separate counsel to monitor and participate in the defense of any
Claim. Your indemnification obligations are limited to the extent permitted or precluded under applicable federal, state or local laws, including federal or state tort claims acts, the Federal Anti-Deficiency Act, state governmental immunity acts, or state constitutions. Nothing in this Agreement will constitute an express or implied waiver of Your governmental and sovereign immunities, if any.

INSURANCE: [Included in all Global Health Program and Global Development Program grants.] You will maintain insurance coverage sufficient to cover the activities, risks, and potential omissions of the Project in accordance with generally-accepted industry standards and as required by law. You will ensure Your subgrantees and subcontractors maintain insurance coverage consistent with this section.

MONITORING, REVIEW, AND AUDIT: The Foundation may monitor and review Your use of the Grant Funds, performance of the Project, and compliance with this Agreement, which may include onsite visits to assess Your organization’s governance, management and operations, discuss Your program and finances, and review relevant financial and other records and materials. In addition, the Foundation may conduct audits, including onsite audits, at any time during the term of this Agreement, and within four years after Grant Funds have been fully spent. Any onsite visit or audit shall be conducted at the Foundation’s expense, following prior written notice, during normal business hours, and no more than once during any 12-month period.

INTERNAL OR THIRD PARTY AUDIT: If during the term of this Agreement You are audited by your internal audit department or by a third party, You will provide the audit report to the Foundation upon request, including the management letter and a detailed plan for remedying any deficiencies observed (“Remediation Plan”). The Remediation Plan must include (a) details of actions You will take to correct any deficiencies observed, and (b) target dates for successful completion of the actions to correct the deficiencies.

LEGAL ENTITY AND AUTHORITY: You confirm that: (a) You are an entity duly organized or formed, qualified to do business, and in good standing under the laws of the jurisdiction in which You are organized or formed; (b) You are not an individual (i.e., a natural person) or a disregarded entity (e.g., a sole proprietor or sole-owner entity) under U.S. law; (c) You have the right to enter into and fully perform this Agreement; and (d) Your performance will not violate any agreement or obligation between You and any third party. You will notify the Foundation immediately if any of this changes during the term of this Agreement.
1. Welcome!

The purpose of this survey is to gain greater insight into the TB innovation landscape in South Africa, the role of public financing in driving and supporting innovation, as well as expectation of public returns (i.e. affordable, user friendly health technologies) and strategies for ensuring public returns.

Thank you for taking the time to complete this survey. The results of our analysis will be used to inform ongoing global and local discussion regarding opportunities and challenges to ensuring innovation approaches and public financing for R&D maximise health return and public benefit. The results of our analysis may also be used to inform future advocacy and grant making strategies to support expanded use of innovation approaches that maximise public and health returns.

2. Please provide the following personal and organisational details. Please note that at the end of this survey you will be given the opportunity to select whether you would like your responses to be openly attributed to you, or if you would like your identity and organisation to remain unidentified (confidential) in any findings published from this survey.

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<thead>
<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Title</td>
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<tr>
<td>Organisation representing</td>
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<td>Preferred mode of contact (Email, Tel, WhatsApp, Skype)</td>
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<td>Contact info</td>
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3. In the table below select the type(s) of TB research your organisation is undertaking. For each type of research, please indicate the stage(s) of your research underway. Please select each box that applies.

<table>
<thead>
<tr>
<th>TYPE OF RESEARCH</th>
<th>STAGE OF RESEARCH</th>
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<tbody>
<tr>
<td>Basic science</td>
<td>Pre-clinical</td>
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<td>(Pre-clinical basic science R&amp;D)</td>
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<td>Phase I</td>
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<td>(Phase I basic science R&amp;D)</td>
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<td>Phase II</td>
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<td>Diagnostics</td>
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<td>Drugs</td>
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<td>Vaccines</td>
<td>Pre-clinical</td>
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### DEFINITIONS FOR ‘TYPES OF RESEARCH’ AND ‘STAGES OF RESEARCH’

The definitions provided are sourced and adapted from the Treatment Action Group\(^1\) and the U.S. Food and Drug Administration\(^2\).\(^3\)

#### Types of research:

**BASIC SCIENCE:** “Undirected, investigator-initiated research to discover fundamental knowledge about MTB and closely related mycobacterial organisms” to inform the development of health technologies to prevent, diagnose or treat TB.

**DIAGNOSTIC:** “Preclinical and clinical [research on] diagnostic technologies and algorithms”

**DRUGS:** “Preclinical and clinical research on treatments and treatment strategies for MTB infection and TB disease” (includes novel drug development, drug repurposing and regimen optimization)

**VACCINES:** “Preclinical and clinical research on TB vaccines, including both preventive and immunotherapeutic vaccines”

**OPERATIONAL:** “Operational research may include randomized trials, surveillance, and epidemiological and observational studies” to inform or evaluate the implementation of new or existing TB health technologies.

#### Stages of research:

**PRE-CLINICAL:** In vitro or in vivo research underway toward the development of a new health technology, prior to testing conducted on human subjects.

**PHASE I:** Small scale studies to establish the safety and recommended dosage of a new health technology, that are generally undertaken on healthy volunteers.

**PHASE II:** Medium scale studies (up to several hundred people with the relevant disease/health condition) to assess the safety and efficacy of a new health technology.

**PHASE III:** Large scale studies (up to several thousand people with the relevant disease/health condition) to assess the safety and efficacy of a new health technology, including whether the health technology provides a statistically significant health benefit in a specific population.

**PHASE IV:** Ongoing research and surveillance regarding the safety of health technologies (diagnostics, drugs and vaccines) following their registration.

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4. **Do you receive funding from the South African government to undertake TB R&D?**

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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If you receive funding from the South African government please indicate the source(s) of this funding (i.e. the Department of Science and Technology (DST), National Research Foundation (NRF), Department of Health (DoH), Medical Research Council (MRC) or other)?

Is funding received from the South African government directed at any specific types or stages of TB R&D, or can it be applied broadly across all your TB R&D underway?

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\(^2\) [https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405658.htm](https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405658.htm)

\(^3\) [https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm](https://www.fda.gov/ForPatients/Approvals/Drugs/ucm405622.htm)
5. In addition to any funding received from the South African government, please indicate your other sources of funding for TB R&D and estimate the percentage of funding that each source provides towards your overall budget for TB R&D.

<table>
<thead>
<tr>
<th>Source</th>
<th>Please tick each funding that source applies</th>
<th>Please estimate the percentage of your overall funding for TB R&amp;D received from each source</th>
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<td>Local public funding</td>
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<td>Foreign public funding</td>
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<td>Pharmaceutical industry funding</td>
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<td>Other industry funding</td>
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<td>Philanthropic funding</td>
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<td>Product development partnerships</td>
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<tr>
<td>Other</td>
<td>Please describe</td>
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**Definitions:**

**Local Public Funding:** Funding received from the South African government directly or via an affiliated body (i.e. the Medical Research Council, the National Research Foundation, the Department of Science and Technology).

**Foreign Public Funding:** Funding received from a foreign government or affiliated body (i.e. the US’s National Health Institute, Pepfar, Dfid).

**Pharmaceutical Industry Funding:** Funding received from a pharmaceutical company.

**Other Industry Funding:** Funding received from a private, for-profit entity (excluding pharmaceutical companies). Funding sources may include the banking, investment, mining and other industries.

**Philanthropic Funding:** Funding received from a non-governmental, non-profit organization that makes donations towards social and developmental causes in line with its priorities (i.e. the Bill and Melinda Gates Foundation).

**Product Development Partnerships:** Funding from organisations and alliances of multiple partners seeking to accelerate innovation for neglected diseases (i.e. TB Alliance, TB Vaccine Initiative, Stop TB, DNDi etc.)

6. Does your research unit or organization employ any strategies to ensure the affordability and accessibility of health technologies developed from your research unit for low income populations and developing country healthcare systems? If so, please describe the strategies employed.

*Note: Strategies to ensure affordability and accessibility could include a range of tactics such as non-exclusive IP licensing, use of patent pools, requirements for transparency of R&D and production costs, cost agreements (including profit or price caps) donations, etc.*

For research that is co-funded by the South African government are there additional requirements or strategies employed to ensure affordability of products and their accessibility within the public health system? If so, please describe.

At what stage of your research are affordability and access strategies generally established?

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<tr>
<th>Stage</th>
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<td>Pre-clinical</td>
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<td>Phase II</td>
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<td>Phase IV</td>
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</table>
7. To date, have any diagnostics, drugs, vaccines or other health technologies been commercialized resulting from research undertaken by your research unit? If so, please list them.


Are these health technologies currently provided through South Africa's public health system?

If not, why not?

8. Can you comment on the challenges that research units and/or government face in ensuring the results of their research efforts and investment are affordable and accessible to low-income populations, including through South Africa’s public health system?

Do you have any recommendations or comments on how research units and/or government could better ensure that health technologies developed with public investment are affordable and accessible to low-income populations, including through South Africa’s public health system?

Do you have any additional comments or insights that you would like to share?

9. Thank you for taking the time to complete this survey. We may contact you with follow up questions or queries regarding your answers, or to request a telephonic or in-person interview.

Please indicate how you would like your responses to be attributed to you in any findings published from this analysis. (Select below)

- I am willing to be openly identified by my name, title and organisation’s name
- I am willing to be identified as a representative of my organisation, but would like my name and title to remain confidential
- I would like my name and title, as well as my organisation’s name to remain confidential