Comments received on the first draft of the global strategy on TB research and innovation

June 2019

Contents

1. NGOs and CSOs

1.1 ACTION/RESULTS

Locator (Page & Line No)	Comment	Suggested Amendment
General	**Comment**: "Accountability" appears once in the document (table 5.1, under political and legal), and is not linked to the WHO multisectoral accountability framework (MSAF). There should be a much tighter integration between this document and the MSAF. WHO has already begun dialogues with countries about implementing the MSAF and so there must be alignment between the two.	**Suggestion** -There should be greater alignment throughout the strategy.
Page 6 Point 5	**Comment:** The paragraph lists the End TB Strategy and the SDGs. This should also reference the commitments made at the UN HLM on TB in September 2018.	**Suggestion** - Reference to the HLM commitments could be added to subsequent paragraphs which recognize that progress has been insufficient. The HLM commitments aim to redress this. For example, Member States committed to diagnose and treat 40 million people with TB by 2022.
Page 6 Point 5	**Comment**: "…a new TB vaccine that is effective both before and after exposure;"	Suggestion - rephrase as: "…new TB vaccines that are effective both before and after exposure, and across the range of age groups and global populations;"

Page 10 Point 23	**Comment**: This point does not reference the multi-sectoral accountability framework (MSAF) despite talking about monitoring the implementation of the strategy.	**Suggestion** - rephrase as: "Moreover, actions need to be monitored regularly, *as outlined in the multisectoral accountability framework,* to ensure that national and global progress will achieve the stipulated targets."
Page 18 Point 51	**Comment**: Include in the opening line that vaccines are both effective and cost-effective.	**Suggestion** - rephrase as: "Vaccines are one of the most successful, effective *and cost-effective* public health interventions to reduce and even eradicate life-threatening infectious diseases."
Point 52	**Comment**: No mention of recent significant successes (M72 and BCG revaccination). M72 mentioned in point 53 in the context of AMR only. The paragraph indicates need for more and novel vaccines in pipeline but does not acknowledge that despite the narrow diversity.	**Suggestion:** Add recent successes to point 52.
Page 19 Point 56	**Comment**: Add in comments of recent Lancet Commission on Tuberculosis (Page 30, 2019) regarding cost-effectiveness.	**Suggestion** - rephrase/add as: "Multiple health economic evaluations have shown that new TB vaccines will be highly cost-effective and will offer substantial cost savings to health systems and society. *The Lancet Commission on Tuberculosis noted that 'the returns even from a partially effective vaccine would be very great.'*"
Page 19	**Comment**: In light of the UNGA-HLM targets and the current overall funding	**Suggestion** - rephrase/add text as:

Point 58	landscape, public and philanthropic funding will have to increase.	"Public and philanthropic support should be directed at improving the full continuum of vaccine R&D, from early-stage research to translational science to clinical trials. *Given overall and longstanding funding shortfalls, investments must increase in line with the UNGA-HLM political declaration on the fight against TB agreed by Member States*."
Page 23 Point 74	**Comment**: Pooling of IP and data can be important to support open collaborative research that facilitates the development of new regimens (as opposed to a new individual drug).	**Suggestion**- rephrase/add text as: "A range of incentives – both financial and nonfinancial – must be initiated and existing initiatives must be strengthened to stimulate innovation, from discovery to diffusion of technologies. Policies that encourage and support new collaborative models for research, data *and intellectual property* sharing and public–private partnerships (PPPs) are key to leveraging the comparative advantages of various actors to foster R&D, and to facilitate equitable, affordable and sustainable access to medicines and technologies. *Such incentives should promote tuberculosis R&D efforts that are needs driven and evidence based and guided by the principles of affordability, effectiveness, efficiency and equity as outlined by the 2018 UN Political Declaration on Antimicrobial Resistance*."
Page 23	**Comment**: National TB research networks have also been established.	**Suggestion** - rephrase as:

Point 75		"…as illustrated most notably through the establishment of the BRICS TB research network *and national TB research networks*."
Page 23 Point 76	**Commen**t: It should be reiterated that both pull and push incentives are needed, and that not all incentives are equally designed to meet patient needs. So, in order to align with the commitments of the 2018 UN HLM on TB political declaration, there is a need to specify that these incentives must build in provisions that ensure that any resulting product is accessible, affordable and available to all who need it. Targeted pull mechanisms are not just volume guarantees or advanced market commitments. Other targeted pull mechanisms that are being considered in TB is the role of milestone prizes throughout the R&D pipeline linked to technical and access criteria – as outlined in The Life Prize. These should be mentioned.	**Suggestion** - Add text/rephrase as: "*Any incentive mechanisms must include provisions for ensuring that the end products are available, accessible and affordable for all who need them.*" "However, more targeted pull mechanisms, such as *milestone prizes awarded on set criteria*[1], volume guarantees or advanced market commitments, would be an important additional incentive mechanism…"
Page 23-24 Point 78	**Comment**: This point is key and should be retained.	**Suggestion** - Add test as: "*Combining patent and data pooling with push and pull mechanisms could contribute to the development of new regimens that are needed in the field of TB to improve current treatments and for multi-drug resistant TB in particular*."

[1] *[ref: Tuberculosis and antimicrobial resistance – new models of research and development needed. Grania Brigden, José Luis Castro, Lucica Ditiu, Glenda Gray, Debra Hanna et al.Bulletin of the World Health Organization 2017;95:315]*

Page 24 Point 79	**Comment**: This point should recognize the burden of DRTB as a proportion of the overall burden of AMR and despite this, many national and global AMR initiatives have thus far excluded TB from their scope of work.	**Suggestion** -rephrase as: "Thanks to the revitalization of TB research over the past 2 decades, the TB field is well positioned to play a leading role in the AMR response. *Despite this, and the fact that DRTB accounts for one third of all AMR-related deaths, many national and international AMR initiatives have thus far excluded TB from their scope of work*." **Suggestion** - Add text in final sentence to the end of the point as: "*TB therefore should be included within national and international AMR policies and programs*."
Page 24 point 80	**Commen**t: There could be an additional point in this chapter on accountability for all the points raised. Or a sentence could be added to point 80. In relation to the commitment to "fair share" contributions to R&D funding, there should be a reference to the GERD target of 0.1% (as outlined by Treatment Action Group) – all countries should spend 0.1% of gross domestic expenditure on R&D on TB R&D specifically.	**Suggestion** - Add text as: "*Further, as outlined in the UNGA-HLM on TB political declaration, accountability mechanisms must be implemented at the national, regional and global levels to monitor and review progress on R&D activities and R&D funding targets committed to in the political declaration*." **Suggestion** - add text as: "This concept needs to be developed and agreed on as a matter of priority. *All countries could agree to spend 0.1% of total spending on R&D on TB R&D, as calculated by the Treatment Action Group*."

Page 25 Point 82	**Comment**: Licensing on public health oriented terms and conditions can be one way to maintain the IP incentive for innovation while facilitating the wide dissemination of the technology through the competitive supply. This approach has been used in HIV and hepatitis C to great success, with multiple generic manufacturers making the new regimens and supplying LMICs at affordable prices.	**Suggestion** - add text in final sentence as: "*Licensing of patented technologies on public-health oriented terms is one way through which IP can be used to promote innovation and facilitate equitable access*."
p. 25 Point 83	**Comment**: It is important that the draft strategy mention human rights in the context of research, but the current text falsely equates the protection of moral and material interests of authors and inventors under ICESCR Article 15 1(c) with intellectual property rights. WHO should ensure that the language in this section mirrors the Committee on Economic, Social and Cultural Rights (CESCR)'s authoritative interpretation in General Comment No. 17 of the difference between the human rights recognized in Article 15 1(c) and intellectual property rights as currently defined by international trade law. In General Comment No. 17 on ICESCR Article 15 para. 1(c), the CESCR clearly states that the protection of moral and materials interests in Article 15 1(c) must ***not*** be equated with intellectual property rights. The core obligation of governments under Article 15 (the right to science) is nondiscrimination in access—access to the benefits of scientific progress for the public, especially marginalized communities, and access to the means, methods, and	**Suggestion** - Replace the first sentence of ¶83 with: *"The international Covenant on Economic, Social and Cultural Rights and the Universal Declaration of Human Rights enshrine the right of everyone to share in scientific advancement and its benefits (i.e, the right to science)."* **Suggestion** – Add a sentence indicating that access is core to the right to science: *"The right to science obligates states to take action to conserve, develop, and diffuse science and its benefits. "A core principle of the right to science is that 'innovations essential for a life with dignity' be accessible to everyone, in particular vulnerable and marginalized populations. This category includes tangible applications of scientific progress such as essential medicines, provision of which is considered a 'core obligation' under the right to health (ICESCR article 12)." Suggested*

	materials of science for scientists themselves. The CESCR writes: "the right to benefit from the protection of moral and materials interests resulting from one's scientific…production seeks to encourage the active contribution of creators to the sciences and to the progress of society as a whole." In short, the protection of moral and materials interests must be interpreted in a manner consistent with the protection of other human rights. This is in keeping with the interrelated nature of human rights and agreement that human rights must be interpreted in relation to each other.	*citation: Shaheed F [2012].* **Suggestion** - Following the above, add a sentence clarifying that the moral and material are not the same as intellectual property rights: *"Where the right to science speaks to the moral and material interests of authors and inventors (ICESCR Article 15 1(c)), states must ensure that these protections are established and interpreted in a manner consistent with the protection of other human rights in the Covenant, such as the right to health (Art 12) or the right to enjoy the benefits of science and its applications (Art 15 1(b)). Importantly, states must not confuse moral and material interests with intellectual property rights. By drawing a distinction between moral and material interests and intellectual property rights, the right to science offers states a framework for reconciling the policy incoherence between the rights of investors, international human rights law, and access to medicines, the subject of the UN Secretary-General's High-Level Panel on Access to Medicines."*
Page 26 Point 86	**Comment**: Enhance the point about PDPs by making clear funding is an issue if PDPs are to function optimally. Reference the UNGA-HLM on TB political declaration which encouraged support for PDPs.	**Suggestion** - rephrase as: "PPPs, including PDPs *which the UNGA-HLM on TB political declaration called on countries to support*, are good examples of collaborative research initiatives, which bridge public and private

		sectors to broaden access to new skills, sources of finance, specialized R&D infrastructure and product pipelines, to ensure that the next decade delivers the tools needed to end TB. *If PPPs and PDPs are to function optimally, they must receive sufficient funding.* Maximising contributions depends on governments creating appropriate incentives, guided by the principles of affordability, effectiveness, efficiency and equity."
Page 30 table 5.1	**Comment**: under patent pools The current text reflects the role that patent pooling could have in the field of TB if associated with pull and push incentives, as well as clinical trials data sharing. This is the structure proposed by the Life Prize project. To date, patent pooling has facilitated access to new treatments for HIV and hepatitis C (HCV) in LMICs through the licensing of medicines to multiple manufacturers, thus enabling robust competition and facilitating price reductions. In addition, patent pooling has been used to facilitate the development of new fixed dose combinations (e.g. a recent example is the combination tenofovir/lamivudine/dolutegravir or TLD) or new paediatric formulations needed in LMICs. In 2017, the Medicines Patent Pool also announced a royalty free license agreement with Johns Hopkins University to facilitate the clinical development of TB drug candidate sutezolid to contribute to accelerating its development by facilitating access to the IP by other	*The patent pool box should accurately reflect the work that the MPP currently does for TB, HIV and HCV medications – the current text in the box reflects the potential role that the MPP/Patent Pools could have within an innovative financing model like The Life Prize.* ***Suggested text**: "...Patent pools encourage open, collaborative development through pooling of intellectual property and facilitate access to new medicines through market competition. If combined with push and pull incentives and the pooling of clinical trial data, they could contribute to the development of new needed regimens for the treatment of TB. The Medicines Patent Pool is an example of a mechanism for patent pooling that has played a pivotal role in facilitating access to new medicines in HIV and hepatitis C. It has also supported the development of needed new formulations. It is well positioned to play such a role in TB and could contribute to new innovation models that incentivize the development of new and*

	potential developers, thereby contributing to further innovation.	*improved regimens. It is important that any licensing of intellectual property via the MPP or similar patent pooling structures be oriented on public health terms—i.e., any licenses should be non-exclusive, not exclude certain countries or geographies, and be transparent and available to the public."* *"Innovative financing mechanisms, such as The Life Prize, can create a research enabling environment by linking milestone payments/awards to set criteria with regards to technical, IP access (ideally through the MPP) and data access. The Life Prize is one example of an approach to R&D based on the principle of delinkage, whereby the costs of R&D are delinked from final product prices and volume of sales. The UN HLM political declaration on TB describes the relevance of delinkage for TB innovation (member states stated their support for voluntary initiatives and incentive mechanisms that separate the cost of investment in research and development from the price and volume of sales to facilitate equitable and affordable access to new tools), and delinkage is mentioned as an important objective in the UN HLM political declaration on AMR."*
Page 36 Point 102	***Paragraph 102:*** *"Strengthens existing PPPs and PDPs nationally and globally (and, where necessary, creates new partnerships) to encourage research and development of new medical innovations and*	**Suggestion -** Rephrase as: *"Promotes the role of* PPPs and PDPs nationally and globally (and, where necessary, creates new partnerships) to encourage research and development of new medical

	digital health innovations to improve TB care and prevention." **Comment:** As individual partnerships may form or dissolve depending on the progress of their research, this could be rephrased.	innovations and digital health innovations to improve TB care and prevention."
Page 36 Point 105	***Page 36 - Member State Action*** **Comment**: we recommend an additional paragraph to highlight the need for competition and regulatory improvement in line with the political declaration on TB. This is key to creating an enabling environment for TB R&I.	**Suggestion -** add action item as: *"Promotes competition and collaboration, removes barriers to innovation and improves regulatory processes and capabilities."*
Page 37 Point 111	***Page 37 - International and national partners action*** **Comment:** We recommend adding an additional action to recognize the important role that civil society can play in bridging the gap between researchers and affected communities to make R&I effective and people-centered.	**Suggestion** - add action item after 111 as: *"Civil society should facilitate collaboration between researchers and affected communities during the development and implementation of new technologies to ensure s people-centered approach to R&I."*
Page 37, Point 112	***Page 37 - International and national partners action*** **Comment**: The role of civil society in ensuring accountability should be mentioned.	**Suggestion** - add a line as: *"Civil society should play a role in promoting accountability, monitoring and transparency in development and implementation of TB programs at all levels to ensure access to new tools and technologies."*
Page 37 Point 113	***Page 37 - International and national partners action*** **Comment:** The draft mentions PDPs as good examples for collaborative	**Suggestion** - mention individual PDPs in line 113 as: The pharmaceutical industry should cooperate with PPPS and PDPs *such*

	research but does not give examples of any PDPs.	*as FIND, TB Alliance, IAVI and others* and increase industry's meaningful contribution to their activities."
Page 38 Point 118	***Page 38 - Member State Action*** **Comment**: Domestic resource mobilization is crucial to expanding access to new tool and ensuring UHC.	**Suggestion** - add action after 118: *"Implementing countries should raise domestic revenue and increase health budgets to ensure access to quality, affordable and equitable prevention, diagnosis and treatment tools and provide UHC and social protection for all TB patients."*
Page 38 Point 122	***Page 38 - International and national partners action*** **Comment**: The draft does not include any actions to address the threat of transition on research and innovation to ensure access to new tools. Countries transitioning out of Global Fund face increased risk of critical serious problems including drug stock-outs and poor drug quality.	**Suggestion** - rephrase action 122 as: "International funding agencies and donor assistance organizations should commit to larger-term funding for TB research *in light of imminent donor withdraw* to foster capacity building, *address shortages and stock outs, ensure effective demand forecasts, and provide affordable access.*
Page 39 Point 125	***Page 39 - Member State Action*** **Comment**: we recommend adding language of integration of information systems.	**Suggestion** - Rephrase action 125 as: "Establishes, strengthens and *integrates* national and subnational health information and vital registration systems for the collection of…"
Page 40 Point 137	**Comment:** Drug-resistant forms of TB are a major driver of the global AMR problem and pose a big challenge in the global fight against TB. Drug-resistant TB requires different strategies to address. Currently the draft fails to adequately link DRTB to AMR initiatives. In the 2018 UN High-Level Meeting on	**Suggestion** - add action after line 137 as: *"Strengthens efforts to combat DRTB and actively contributes to the development of national action strategies, plans and capacities for AMR at all levels - global, regional and national ."*

	TB Political Declaration countries committed to "Ensure that TB programmes actively contribute to developing national AMR strategies, capacities and plans and that lessons learned from global, regional and national efforts to combat DRTB inform the design and implementation of both global AMR strategies and national action plans (NAPs) according to national contexts (27)."	*"Promotes synergies and identifies opportunities between national TB and national AMR action plans."*
Page 40 points 141 and 142	**Comment**: These recommendations are limited to low-income and lower-middle income countries.	**Suggestion** - This should be expanded to include all middle-income countries.
Chapter 7, implement ation and monitoring	**Comment**: This section does not recognize the role of civil society in monitoring and reporting on R&D spending, such as the Treatment Action Group's Research Funding Trends report. This is recognized in the MSAF, and this is an example of where closer alignment between this strategy and the framework would be beneficial	**Suggestion -** Point 148 should include reference to the UN HLM on TB commitments alongside the End TB Strategy. It should also include reference to the MSAF. All Member States have committed to implement the MSAF not later than 2019 and WHO has committed to support countries in doing so. Point 150 should include reference to civil society monitoring of R&D spending, specifically the Treatment Action Group Research Funding Trends report.
Page 38 Point 118	**Comment:** The country funding priority for TB R&D (both domestic, and especially international collaboration) should have a long-term investment timeline (more than five years).	**Suggestion –** Global Health R&D should be formal part of the official development

	Changing priorities every few years is ineffective.	assistance of donor countries.

1.2 Filha

Locator (Page & Line No)	Comment	Suggested Amendment
5	The team writing this very comprehensive text has done excellent job! This is a really honest and brave text. I have only one comment: the summary in it's present form is good, but I would appreciate a clear and short list of major suggestions in the text. No more than 10 – 15 most important ones to be highlighted and used. Reading the whole text through is for those who really care and are involved, but those who we will convince about this would probably like a list of the most important issues to be implemented.	A short list of actions needed most during the fortcoming years.

1.3 Global Health Technologies Coalition

Locator (Page & Line No)	Comment	Suggested Amendment
Page 36 / Line 106 Create an enabling environment for TB research	The WHO can provide effective guidance to member countries on what diagnostic technologies they should adopt through the Essential Diagnostic List. These highly vetted, evidence-based recommendations can serve as an important framework for member countries for tracking priorities for program implementation. We suggest adding a linkage to the Essential Diagnostics List as part of setting the global research & development priorities.	**Suggested Additions:** We urge the WHO and member states to continue to support the efforts to expand the Essential Diagnostic List and ensure that TB remains a primary focus. Diagnostic tests are critical tools for health care, providing vital information that impacts the prevention, detection, diagnosis, treatment, management of disease, surveillance and epidemiology. We strongly support WHO's goal of increasing access to appropriate, affordable, quality-assured and effective TB diagnostics in underserved regions of the world.
Page 39 Promote and Improve approaches to data sharing	This report does not sufficiently address the importance that civil society plays in enabling transparency and ensuring accountability.	**Suggested Additions:** We call for the recognition of the role of civil society in facilitating collaboration and promoting accountability and transparency. Civil society needs to have a more explicit role in helping countries evaluate whether they are following through on their commitments. This includes a more prominent role at the follow up to the High-Level Meeting on TB.
Page 41 / Line 146	There is a need for clear accountability mechanisms	**Suggested Additions:** We call for full implementation, including

Locator (Page & Line No)	Comment	Suggested Amendment
Implementation and Monitoring Progress	when it comes to implementation. We urge the creation of clear structures that allow the country implementation to be evaluated, to ensure it tracks with the political declaration on TB.	adoption at country level, of the WHO Multisectoral Accountability Framework with global high-level review. This high-level review should be through a multisectoral panel chaired by an independent expert, supported by a secretariat and hosted by an existing organization. Among other tasks, this panel should review whether the targets set by countries match up with their share of the targets agreed to at the UN High Level Meeting on Tuberculosis.

Comments are hyperlinked

1.4 International Union Against TB and Lung Disease

1.5 Médecins Sans Frontières (MSF)

1.6 Treatment Action Group

Locator (Page & Line No)	Comment	Suggested Amendment
p. 11 ¶ 27	Section 27, in its entirety, states, "For the pharmaceutical sector, developing country markets are not sufficiently attractive to incentivize the full development of promising diagnostics, treatment and vaccine candidates." This section should be amended to clarify that the above is specifically the case under the patent-based innovation system. Governments of high TB countries could create viable innovation markets by sponsoring prize funds. So far governments have decided not to do so.	Rephrase paragraph 27 as follows: "For the pharmaceutical sector, developing country markets are not sufficiently attractive under the current mainly patent-based incentive system to incentivize the full development of promising diagnostics, treatment and vaccine candidates. Despite this problem, governments have as yet been unwilling to invest in alternative incentives such as prize funds."
p. 14 ¶ 43	The priorities listed for diagnostics development should include a test that can be used to monitor treatment in place of smear microscopy.	Recast sub-point 3: "a point-of-care test to detect pulmonary TB and monitor treatment."
p.16 ¶ 47	Single drugs are already recommended (i.e. rifampin [4R], isoniazid [6H]) or under evaluation for treatment of TB infection (i.e. levofloxacin [VQUIN, TB CHAMP], delamanid [PHOENIX]).	Recast first sentence: "For treatment of active TB disease, it is important to focus on developing wholly new regimens rather than single drugs."
p. 19 58	For TB vaccine R&D, public and philanthropic funding support is especially important for advancing phase III trials given size and cost.	Adjust paragraph to read: "Public and philanthropic sources of funding are essential, especially given the anticipated size and cost of phase III TB vaccine trials. Public and

Locator (Page & Line No)	Comment	Suggested Amendment
		philanthropic support should be directed at improving the full continuum of vaccine R&D, from early-stage research to translational science to clinical trials, and should be considered when setting the price of any vaccine that results from a collective development effort."
p. 23 75	Financial investment (rather than incentives) is the most important intervention to address challenges in TB research and development, which suffers from decades of persistent underfunding.	Recast first sentence: "Financial investment is the most important intervention in addressing challenges in TB research. […]"
p. 23 76	Government commitments to rapidly implement/ adopt new TB technologies and interventions are important, and can be demonstrated beyond volume guarantees and/or advanced marketing commitments to reassure innovators and the public regarding access to the benefits of scientific progress. Additionally, another pull mechanism that should be mentioned is prize funds.	Add prize funds to the list of targeted pull mechanisms: "However, more targeted pull mechanisms, such as prize funds, volume guarantees or advanced market commitments, would be important additional incentive mechanisms."
p. 23-24 78	Section 78 correctly states that access issues should be identified at every stage of the research process. This statement is however too vague to have any meaningful impact on practice. It should state that binding and enforceable access provisions should be included in all research contracts at every stage of the	Add to paragraph 78: "Binding and enforceable access provisions should be included in all research contracts at every stage of the research process."

Locator (Page & Line No)	Comment	Suggested Amendment
	research process. One future area of work for the WHO might be to explore what such enforceable access provisions might look like.	
p. 25 ¶ 82	Intellectual property is incorrectly presented as a policy tool that can facilitate diffusion of technology and access to essential medicines and technologies, and as necessary for governments to safeguard the health of their populations. Section 82 is misleading since it fails to recognize the fundamental fact that the patent system has been highly inefficient in incentivizing TB research (as is hinted at in section 27 of the draft strategy). The extremely low levels of private sector investment in TB research noted in the document illustrate very clearly that current private sector incentives are insufficient. A strategy that does not confront this underlying reality head-on has little hope of addressing the underlying problems in TB research.	Recast paragraph to read: "The intellectual property (IP) system, and the patent system in particular, offer inappropriate and inadequate incentives for innovations for TB and other neglected diseases critical to the health of the public, and can block the diffusion of technology and access to essential medicines, including those that were developed with public and philanthropic funding, and through a collective effort. There is an urgent need to build policy coherence between trade, intellectual property, and health to enable medical innovation that can be accessed by all who need it, and to reinforce and promote support for countries to make full use of the TRIPS flexibilities to ensure access and safeguard the health of their populations."
p. 25 ¶ 83	Specific reference to the right to science (ICESCR Article 15 and UDHR Article 27) in the draft strategy is appreciated. However, the current text misrepresents the nature of state obligations under the right and requires	Recast the first sentence of ¶83 to read: "The international Covenant on Economic, Social and Cultural Rights and the Universal Declaration of Human Rights enshrine the right of everyone to share in scientific advancement and its benefits

Locator (Page & Line No)	Comment	Suggested Amendment
	major revision in order to accurately reflect legal consensus on the normative interpretation and application of the right under international law. The right to science obligates governments to ensure that everyone enjoys the benefits and scientific progress and its applications. Core to the right is the principle of **nondiscrimination in access** (see Shaheed F [2012]; Shaver L [2010]; and Chapman A [2009]). As currently represented, the text of the strategy pits access against intellectual property. This goes against both the spirit and the letter of the right to science. Additionally, as human rights are interrelated, they must be interpreted in relation to one another; rights cannot be read in isolation. The current text of the strategy gives a primacy to individual property protections that would undermine the realization of other rights in the Covenant, e.g., the right to health. This must be corrected. In General Comment No. 17 on ICESCR Article 15 para. 1(c), the Committee on Economic, Social, and Cultural Rights (CESCR) made clear that the protection of moral and materials interests in Article 15 must ***not*** be equated with intellectual property rights as currently	(i.e, the right to science)." Strike the sentence beginning "In brief,…" and ending "…both an individual and a collective level." Replace with a sentence that outlines the obligations of governments under the right to science—e.g., "The right to science obligates governments to take three types of actions. They must act to conserve, develop, and diffuse science and its benefits. In brief, *develop* requires governments to invest in research and create environments that enable research. *Diffuse* means that governments must ensure the availability and accessibility of science and its applications by e.g., publishing results, establishing fair and responsive regulatory systems to evaluate new discoveries, and basing public health programs and policies on scientific evidence. *Conserve* means that governments must ensure that scientific benefits are available not only for people alive today, but also for future generations." Suggested citation: UNDP [2018]; Shaheed F [2012]. Add a sentence that links the right to science to health—e.g.,: "A core principle of the right to science is that 'innovations essential for a life with dignity' be accessible to everyone, in particular vulnerable and marginalized populations. This category includes tangible applications of scientific progress such as essential medicines, provision of which is considered a 'core obligation' under the right to health (ICESCR article 12)." Suggested citation: Shaheed F [2012].

Locator (Page & Line No)	Comment	Suggested Amendment
	defined by international trade law: "The scope and protection of moral and material interests provided for by article 15, para. 1(c) does not necessarily coincide with what is referred to as intellectual property rights under national legislation or international agreements." The CESCR unequivocally stated that: "It is important not to equate intellectual property rights with the human right recognized in article 15, paragraph 1(c)." Instead, "the right to benefit from the protection of moral and materials interests resulting from one's scientific…production seeks to encourage the active contribution of creators to the sciences and to the progress of society as a whole." The emphasis of protecting moral and material interests, therefore, is on access to and participation in the scientific process rather than on setting up exclusionary protections. **Protections of moral and material interests must be established and interpreted in a manner consistent with the protection of other human rights.** We encourage WHO to carefully review and revisit General Comment No. 17 to ensure that the text of the draft strategy is in line with this authoritative interpretation.	Add a sentence that mentions access protections under the right for scientists: "Importantly, access under the right to science not only applies to beneficiaries of science, but also to scientists themselves who have a right to access the means, methods, and materials of science." Suggested citation: AAAS [2013]. Following this, add a sentence clarifying that the moral and material are not the same as intellectual property rights: "Where the right to science speaks to the moral and material interests of authors and inventors (ICESCR Article 15 1(c)), states must ensure that these protections are established and interpreted in a manner consistent with the protection of other human rights in the Covenant, such as the right to health (Art 12) or the right to enjoy the benefits of science and its applications (Art 15 1(b)). Importantly, states must *not* confuse moral and material interests with intellectual property rights, which differ from human rights in several aspects including that they are temporary in nature, can be bought, sold, and transferred to others." Add a sentence acknowledging the importance of participation to the right to science—e.g., "To ensure that scientific discovery addresses human needs, states must create opportunities for people to participate in science. The principle of participation extends beyond scientists themselves to include the intended beneficiaries of research. As such, it is important that research and development initiatives create space for the meaningful

Locator (Page & Line No)	Comment	Suggested Amendment
		participation of communities affected by TB and civil society representatives. This participation should extend to each stage of the research progress, from setting research agendas to overseeing the conduct of clinical trials to translating results into policy and practice." Suggested citation: GPP-TB [2012].
p. 25 ¶ 85	The strategic approach should also make sure that collaborations with industry include safeguards for governments to ensure their citizens benefit from investments and scientific progress.	Add to end of sentence: " […] and safeguard governments' abilities to ensure citizens benefit from public investments and scientific progress."
p. 26 ¶ 86	See previous comment	Add safeguards after incentives: "Maximizing these contributions depends on governments creating appropriate incentives and safeguards, guided by the principles of affordability, effectiveness, efficiency, and equity."
p. 28 table 5.1	A critical key fiscal feature currently missing from among the examples of enabling environments for TB research and innovation is delinkage.	Add key enabling feature: "Investing in TB R&D according to the principles of delinkage, whereby the cost of R&D is delinked from the sales prices of medicines and diagnostics."
p. 29 table 5.1	Other government enabling actions should be listed under the political and legal section of the table.	Add: "Making full use of TRIPS flexibilities to ensure equitable access to the benefits of research and scientific progress" and "providing support and empowering regulatory authorities to expedite registration of generic products".
p. 30 table 5.1	Regulatory incentives offered to stimulate innovation and R&D should	Strike " or extended patent periods of data exclusivity" from the "illustrative government

Locator (Page & Line No)	Comment	Suggested Amendment
	not compromise access by allowing patent extensions.	enabling actions" under "Orphan product legislation."
p. 33 ¶ 105	Intellectual property laws can prevent data sharing, promote inefficient use of resources, and block new knowledge from being put to use. This section should specify that national intellectual policy laws should support country level contribution to national and global policy-making and discovery, prevent duplication of efforts/ improve TB R&D efficiency, and expedite diffusion and impact of new knowledge.	Recast: "National laws should be designed to facilitate these objectives, and to protect the privacy and confidentiality of research participants."
p. 34 ¶109	The generics industry has also been important to reducing the prices of products that are not yet off patent, including through voluntary licensing.	Strike "of off-patent products" from paragraph 109.
p. 34 ¶113	In addition to support for national regulatory channels, in certain countries there may be a need for support for policy change to enable access to the global market when domestic funds are used to procure medicines and other health products.	Add to last sentence in paragraph 113: " […] biomedical interventions for all people, or for policy changes to enable access to the global market using domestic funds."
p. 36	The listed potential measure of effectiveness doesn't specify the target of meaningful engagement in research networks and PPPs for TB research and innovation. If the target is government, this should be made clear.	Specify "extent of government engagement in research networks and PPPs for research and innovations…"
p. 40	Add The Report of the UN Secretary	Add: "[…] as highlighted in the Global Strategy

Locator (Page & Line No)	Comment	Suggested Amendment
¶ 135	General High Level Task Force on Access to Medicines as a reference for how to address access and innovation simultaneously.	and Plan of Action on Public Health, Innovation and Intellectual Property, and the Report of the UN Secretary General High Level Task Force on Access to Medicines."
p. 40 ¶ 139	Objective 4 is focused on ensuring equitable access to the benefits of research and innovation, yet section 139 suggests the secretariat consult with the World Trade Organization and the World Intellectual Property Organization, both of which promote policies that prevent equitable access. The secretariat should instead be providing support to Member States to make full use of the TRIPS flexibilities to ensure equitable access to the benefits of research and innovation.	Recast paragraph 139: "Collaborates with other relevant international and regional organizations (e.g. the World Trade Organization, the World Intellectual Property Organization, the United Nations Development Program, the United Nations Conference on Trade and Development, the Office of the High Commissioner for Human Rights [OHCHR], and the South Centre) to provide, upon request, technical support to Member States on public health and human rights related aspects of intellectual property and trade policies, including to support Member States to make full use of TRIPS flexibilities to promote equitable access to the benefits of research and innovation."
p. 40 ¶ 141	Pharmaceutical companies should also reduce the prices of essential TB medicines and technologies in high-income countries, where underfunded public health programs are responsible for baring these costs.	Recast section 141: "Pharmaceutical companies should reduce prices of essential TB medicines and technologies in all countries, especially where there are high numbers of poor patients, and/or where public health programs are chronically underfunded and without access to generic, more affordable equivalents."
p. 40 ¶ 142	Developing country markets are not sufficiently attractive under the current mainly patent-based incentive system to incentivize the full development of promising diagnostics, treatment and vaccine candidates for TB.	Recast paragraph 142: "The patent-based incentive system has failed to incentivize sufficient private-sector investment in TB research. Pharmaceutical companies should engage governments regarding alternative incentives, and encourage them to consider

Locator (Page & Line No)	Comment	Suggested Amendment
	Pharmaceutical companies should engage governments regarding alternative incentives such as prize funds.	investing in TB R&D according to the principles of delinkage, whereby the cost of R&D is delinked from the sales prices of medicines and diagnostics. Delinkage-based R&D is particularly well-suited to the TB field given that the dominant patent-based innovation system has proven to be particularly inefficient in this area. One concrete way in which governments could make such investments is through prize fund mechanisms such as the Life Prize.”

1.7 TB Proof

Locator (Page & Line No)	Comment	Suggested Amendment
Page 9 point 18	Interventions should also be available in people's local languages so that they can understand adequately. "Socially desirable" does speak to it in a sense, but not in a clear way.	Policies for health innovation must align with the demands of health systems, to ensure that innovations can be made available equitably and sustainably, taking into account that most people with TB disease are in low-resource settings, including in middle-income countries. Mechanisms for promoting health system research that gear innovation to strive towards sustainability, ethically acceptable, and socially desirable interventions (communicated effectively in the affected community's local language) in a systematic way must be improved.
Page 12 point 32	Stigma and discrimination are major barriers to accessing care.	32. The TB field still suffers from lack of equitable access to medicines and technologies, and low use of services by populations that need them most. The challenges include lack of legal and regulatory mechanisms for introducing new medicines and technologies, and negotiating price reductions; weak health system infrastructure, and social care; stigma and discrimination that limits access to overall care; inadequate financing for health care and medicines; local costs that drive up the price of medicines (e.g. taxes and tariffs on pharmaceutical products); gaps in

Locator (Page & Line No)	Comment	Suggested Amendment
		procurement and supply chain frameworks; regulatory deficiencies; and lack of awareness of opportunities to obtain care
Page 12 point 33	Affected communities should be informing what is needed to strengthen the health system.	Strong health systems are a prerequisite to achieving the goals and targets of the End TB Strategy. If health systems have misaligned capabilities in key areas (e.g. the health workforce, drug supply, health financing and information systems), it will not be possible to respond adequately to TB. There is a need for a strong body of knowledge, from stakeholders including affected communities, on effective strategies for strengthening health and social care systems, to ensure that available technologies in TB deliver the maximum impact
Page 13 point 39	Could specifically mention community health workers as they could offer TB tests in a person's own house.	From a patient perspective, a major limitation is the lack of a rapid test to detect (or at least rule out) TB in all populations, including self-testing, as well as tests for those who are difficult to diagnose with currently available tools. Most TB tests require a good sputum specimen, which some patients (e.g. children and people living with HIV) have difficulty producing. Tests on more easily accessible samples (e.g. urine, blood or breath) are urgently needed. Moreover, there is no point-of-care test that can be

Locator (Page & Line No)	Comment	Suggested Amendment
		used at the most peripheral levels of the health system, such as the primary care clinics where most patients first present for care or at household-level when community health workers do TB screening.
Page 20 point 59	Infection Prevention and Control should be mentioned- N-95 respirators are often unavailable or surgical masks can be unavailable in resource-limited settings.	59. TB is not only a biomedical and a public health problem, but also a disease associated with several adverse social forces. Many people get ill and die from TB, owing to underlying socioeconomic determinants of transmission, as well as ineffective implementation and use of existing interventions that result from socioeconomic barriers (including stigma, poverty, poor housing conditions and malnutrition), weak health system infrastructure , inadequate implementation of infection prevention and control measures and insufficient human resource capacity in health systems
Page 20 point 63	“affected” communities	Analysis of the TB care continuum between diagnosis and cure confirms the need for collaboration with other health services, and with prevention and infection control measures, to maximize TB elimination efforts (with special attention to the needs of vulnerable populations1) to deliver affordable, quality health services. Examples of other

Locator (Page & Line No)	Comment	Suggested Amendment
		health services are those for people who smoke; people with HIV, diabetes, chronic lung disease, cancer and alcohol-use disorder; prison health systems; and immigration, mental health and substance abuse services. Analysis of the TB care continuum also highlights the need for engagement and collaboration with affected communities, civil society and private care providers.
Page 30	In Table: Sociocultural	Perhaps replace “supporting” with “prioritising” or “recommending” or “ensuring” (a stronger word).
Page 34 point 107	Add stigma and discrimination	In many parts of the world, patients go without the necessary treatment or receive poor quality services and treatments because of poor access to and use of new technologies and medicines. Reasons for this situation include financial cost, limited or unpredictable availability of medicines by manufacturers, regulatory challenges that result in complex and lengthy product evaluation and registration procedures, weak national procurement processes, inadequate health and social service availability, stigma and discrimination and slow adoption or poor adherence to the International Standards of TB Care (45)

Locator (Page & Line No)	Comment	Suggested Amendment
Page 35 point 114	Specific mention of creating platforms.	114. Civil society and affected communities can have a valuable role in providing a public interest perspective on issues of equitable access and affordability; hence, meaningful engagement strategies are needed to include this knowledge base in discussions about access policy. Platforms should be created where affected communities can advocate at key stakeholder meetings.
Page 27 Point 92	Thank you for prioritizing the role of affected communities and civil society. General: where possible at other key points, please add affected communities as key stakeholders to participate in research.	

2. Private sector

2.1 Johnson & Johnson

Comments are hyperlinked

3. Other organizations, partnerships and professional associations

3.1 International AIDS Society

Locator (Page & Line No)	Comment	Suggested Amendment
Not linked to any comment	Increase profile of service delivery research methodologies to increase quality of services	Could be referred to in the section of enabling environments: operational research for models of care, patient engagement models, demand creation, differentiated care in TB and TB/HIV, etc.
3.1 Developing new TB diagnostics: needs, challenges and opportunities	Developing diagnostic tests with other biological samples	Urine, saliva, blood, etc
	Developing pan TB regimens that are suitable for co-treatments with ART	
	PKs and dosing schemes for pediatric new drugs formulations (FDCs for DRTB, new drugs for DRTB)	
	Developing a save TB vaccine for high burden HIV populations.	

3.2 International AIDS Vaccine Initiative (IAVI)

Locator (Page & Line No)	Comment	Suggested Amendment
Page 5	In final paragraph, change "can" to "must": countries committed in the HLM declaration to do so; it is question of how much they contribute rather than whether they choose to do so.	"All countries that have committed to the political declaration on the fight against TB must contribute,"
5	Regarding: "…a new TB vaccine that is effective both before and after exposure;"	: "…new TB vaccines that are effective both before and after exposure, and across the range of age groups and global populations;"
16	Regarding: "…challenges both new (e.g. missing people with TB) …"	Is this challenge "new" or rather "newly recognized"?
19	"It would cost only a modest amount to increase investments in TB research and innovation, and to create the necessary policy reforms to enable research and innovation to thrive, when that cost is measured against the anticipated morbidity and mortality and associated economic tolls from TB." The sentence is unclear; of course, adding *any* amount would increase investments but it also implies that only a modest amount is needed. The Lancet Commission on Tuberculosis (2019, Page 31) states that investment in R&D for new tools "represents an excellent	"Investment in TB research and innovation and the necessary policies that enable research and innovation to thrive, will bring significant societal and economic returns when measured against the anticipated morbidity and mortality and associated economic tolls from TB."

Locator (Page & Line No)	Comment	Suggested Amendment
	return on investment".	
31	The point notes DR-TB deaths and future projections but should also include that TB already accounts for a third of AMR-related deaths making the epidemic's current impact clear.	"About a quarter of a million people die annually from drug-resistant forms of TB, representing a third of all global deaths attributable to antimicrobial resistance."
51	Include in opening line that vaccines are both effective *and cost-effective.* Comment regarding BCG - 'Nevertheless, BCG averts thousands of cases of paediatric TB mortality annually; sustaining this progress requires production capacity to be maintained'.	"Vaccines are one of the most successful and cost-effective public health interventions to reduce and even eradicate life-threatening infectious diseases." 'Nevertheless, BCG averts thousands of cases of paediatric TB mortality annually; to sustain and improve on this progress requires production capacity to be significantly enhanced'.
52	No mention of recent significant successes (M72 and BCG revaccination). M72 mentioned in point 53 in the context of AMR only. The paragraph indicates need for more and novel vaccines in pipeline but does not acknowledge that despite the narrow diversity.	Add recent successes to point 52.
53	Regarding: "Further development and validation of the candidate vaccine is conditional on collaboration between people infected with TB, research funders, governments, PDPs and the pharmaceutical industry."	Suggested amendment: "Further development and validation of the candidate vaccine is conditional on collaborations among people uninfected and infected with TB, research funders, governments, PDPs, affected communities

Locator (Page & Line No)	Comment	Suggested Amendment
		and the pharmaceutical industry."
54	Regarding: "From a scientific perspective, the greatest challenge is the lack of biomarkers that can act as prospective signatures of the risk of developing TB or as correlates of protection."	Suggested amendment: "From a scientific perspective, the greatest challenge is the lack of validated, predictive animal models of TB infection and disease and the lack of biomarkers that can act as prospective signatures of the risk of developing TB or as correlates of protection."
55	'Industry engagement in TB vaccine development is low, owing to the lack of market incentives to invest in a disease that is concentrated in low- and middle-income countries, and that disproportionately affects the poor'. I get where they are coming from but all 3 big efficacy studies have had significant industry support from GSK, Sanofi, and Emergent.	While there has been some significant support from industry, engagement is low…
56	Add in comments of recent Lancet Commission on Tuberculosis (Page 30, 2019) regarding cost-effectiveness.	"Multiple health economic evaluations have shown that new TB vaccines will be highly cost-effective and will offer substantial cost savings to health systems and society. The Lancet Commission on Tuberculosis noted that 'the returns even from a partially effective vaccines would be very great'."
58	Note that in light of the overall funding landscape, public and philanthropic funding will have to increase.	"Public and philanthropic support should be directed at improving the full continuum of vaccine R&D, from early-stage research to translational science to clinical trials. Given overall and longstanding funding shortfalls, investments must increase in line with the UNGA-HLM political declaration

Locator (Page & Line No)	Comment	Suggested Amendment
		on the fight against TB agreed by Member States."
79	Recognize that in many policy discussions TB is siloed from AMR despite synergies between the two.	Add at the end of this point: "TB therefore should be included within national and international AMR policies and programs".
86	They acknowledge the usefulness of PDPs - enhance this point by making clear funding is an issue if PDPs are to function optimally. Reference the HLM political declaration which encouraged support for PDPs.	"PPPs, including PDPs which the UNGA-HLM political declaration called on countries to support, are good examples of collaborative research initiatives, which bridge public and private sectors to broaden access to new skills, sources of finance, specialized R&D infrastructure and product pipelines, to ensure that the next decade delivers the tools needed to end TB. If PPPs and PDPs are to function optimally, they must receive sufficient funding. Maximising contributions depends on governments creating appropriate incentives, guided by the principles of affordability, effectiveness, efficiency and equity.
97	Note that existing funders must increase investments as well as new funders, as well as highlighting that this need is urgent.	"Declining investments by industry and flat expenditures from existing major funders point to the urgent need to bring new resources into the TB research field from both existing and new funders, and to develop innovative, flexible and collaborative mechanisms for advancing the science needed to end TB.
98	Include the HLM commitment (paragraph 42) on vaccines, not only on drugs and diagnostics.	Add: "and 'delivering, as soon as possible, new, safe, effective, equitable, affordable, available vaccines'."
102	Note that PDPs need the support and	"Strengthens, by supporting and funding,

Locator (Page & Line No)	Comment	Suggested Amendment
	investment of Member States to function optimally.	existing PPPs and PDPs nationally and globally (and, where necessary, creates new partnerships) to encourage research and development of new medical innovations and digital health innovations to improve TB care and prevention."
117	Note that research funding must increase	" Implements the commitments on TB research financing that have been made in the political declaration of the UNGA-HLM on TB by increasing investments so that the global funding gap is closed, and…"

3.3 Medicines Patent Pool

Comments are hyperlinked

3.4 Research Institute of Tuberculosis, Japan

Locator (Page & Line No)	Comment	Suggested Amendment
Page 5	drug-sensitive	drug-susceptible
Page 13, #36	The current WHO TB diagnostic algorithm without new tool still works in many studies. The reason why new diagnostics are really necessary is always unclear in many recent WHO literatures.	It will be necessary to persuasively describe the needs of new diagnostics to mobilise the international budgets.
Page 19, 55	Like industry engagement, scientific/bacteriological background engagement is poor, so that many vaccine candidates failed in last decades.	It shall be re-emphasised to conduct basic bacteriological study for finding optimal targets of vaccine. One section shall describe this inconvenient truth.
Page 33	To produce/share the high-quality data for the development of TB research, we must consider the very basic laboratory capacity to detect and isolate M. tuberculosis for further studies. If the laboratory network, including national/supra-national reference laboratories, is poor, we never have reliable data which will be the basis of any advanced researches.	It will be recommended to touch the current laboratory network system strengthening. Otherwise, any reliable materials for good researches never been obtained. We must remember that the high quality data never be produced automatically.

3.5 TB Alliance

Locator (Page/ Line No)	Comment	Suggested Amendment
Page 5, starting on line 8	"*Reaping the benefits of innovation at the global and national levels requires governments and other stakeholders to undertake the investments, innovative partnerships and policy reforms necessary for accelerating innovation."* -We think it is important to include a separate sentence in the summary specifically on the need for multilateral collaboration and joint investments	Add "The foundation for a successful public health focused global TB R&D strategy rests on multilateral collaboration and joint investment, as only leveraging and combining resources across all types of stakeholders will lead to high-impact innovations."
Page 17, line 8	"*Sustaining the pipeline through the basic discovery of TB drugs and increased clinical trial site capacity for the testing of these medicines.*" -We think it is important to note that while the pipeline for new drugs has improved, it is still not sufficient. Rather than sustaining the pipeline, we need to see growth.	replace sentence with… "While the pipeline for new drug candidates has expanded over the last few years, it is critical to sustain and grow the pipeline *through the basic discovery of TB drugs and increased clinical trial site capacity for the testing of these medicines. "*
Page 17, end of paragraph 50	"For example, in 2016, WHO published the target regimen profiles for TB treatment, to help drug developers to identify important features of new regimens for rifampicin-susceptible TB, RR-TB and pan-TB treatment" - Given that we've seen research goals and target regimen profiles (TRPs) that were too aspirational become a hurdle to do research on and introduce (incrementally) improved therapies, we would like to emphasize that TRPs should be aspirational goals, while still allowing for improvements to occur incrementally if needed. Although we need	"However, it is important that strategic research goals and the target regimen profiles are understood as aspirational goals, allowing for and promoting incremental (sometimes significant) improvements to therapy, and do not become a hurdle to introducing improvements toward an ideal target." We suggest this additional sentence be added at the end of paragraph 50.

Locator (Page/ Line No)	Comment	Suggested Amendment
	breakthroughs, the perfect should not be the enemy of the good! For example, even if a Pan TB regimen would be ideal, significantly reducing the mortality and disease burden for MDR TB (even if a regimen requires medical monitoring) is important and should thus never be ignored.	
Page 25, paragraph 85	*"Ideally, the strategic approach should ensure that researchers, public research institutes and higher education institutions have incentives and opportunities to collaborate both among themselves and with industry, in order to expedite discovery, increase capacity-building, ensure equitable access and enable knowledge transfer, particularly to low- and middle income countries."*	Add "… and with industry and not-for-profit product developers, both nationally as well as in multinational collaborations, in order to…."
Page 29, "expedited and predictable process for TB research protocol review" row	*"Regulatory frameworks that allow for expedited and predictable timelines for research protocol review processes (including for clinical trials), considering the urgency of the end TB response. Delayed or unpredictable research protocol review processes significantly reduces the incentives for research."* -It should be emphasized that harmonizing research and approval in one process (at least for high burden countries) will save time, money, and lives. We should ensure that we don't have multiple separate approvals for every high burden countries, taking extra time and money when it could all be harmonized and worked on simultaneously.	add: "Regulatory harmonization among key high burden countries would allow both research and new product approvals to be done in one single process, saving enormous amounts of time, money, and most importantly, lives and is therefore called for."

4. Individuals

4.1 Professor Brook K. Baker

Institution: Northeastern U. School of Law, Program on Human Rights and the Global Economy; and Health GAP (Global Access Project)

City, Country: Boston, Massachusetts, United States of America

Locator (Page & Line No)	Comment	Suggested Amendment	Internal Use Only [blank]
p. 25 ¶82	The proposed paragraph incorrectly states the success of existing intellectual property rules on incentivizing innovation. There is a wealth of scholarship and findings within the GLOBAL STRATEGY AND PLAN OF ACTION ON PUBLIC HEALTH, INNOVATION AND INTELLECTUAL PROPERTY and THE REPORT OF THE UN SECRETARY GENERAL HIGH LEVEL TASK FORCE ON ACCESS TO MEDICIINES documenting that the current IP system does incentivize sufficiently targeted resources toward so called neglected diseases and neglected populations, including, most relevantly for this document, tuberculosis. Moreover, there is continuing evidence of insufficient research activity on antimicrobials, certain vaccines, and preventative medicines more generally. In addition to the IP system being far from perfect in terms of incentivizing needed medical R&D, the IP system affords substantially misdirected incentives in in the form of IP exclusivities that drive investments towards me-too medicines, minor changes designed to evergreen exclusivities through secondary patents, and patent-thickets that can actually interfere with follow-on innovation. Finally, high prices linked to IP exclusivities are creating access/rationing problems not only in	**82. The intellectual property (IP) system, and the patent system in particular, ~~can~~ play a ~~pivotal~~ partial but incomplete role in incentivizing innovation in the pharmaceutical field and ~~as a policy tool to facilitate~~ can actually act as barriers to the diffusion of technology and access to essential medicines and technologies. ~~Conversely, p~~Poorly structured IP systems with insufficient adoption and use of permissible flexibilities ~~, with an inappropriate balance between innovation and access, c~~an hamper the ability of governments to safeguard the health of their populations. Instead of relying solely or primarily on IP-based exclusivities and supra-competitive prices to incentivize needed medical research and development, there should be exploration and gradual adoption of alternatives such as delinkage, especially in neglected disease areas such as tuberculosis.**	

Locator (Page & Line No)	Comment	Suggested Amendment	Internal Use Only [blank]
	low- and middle-income countries but increasingly in upper-income countries as well (diabetes, hepatis C DAAs, cancer medicines, and biologics more generally are key example) . Given the impacts of IP on affordability and the lack of evidence of meaningful diffusion of innovation and pharmaceutical manufacturing capacity to LMICs, it is highly erroneous to state that IP leads to the diffusion of technology and access to medicines. Instead of relying solely or primarily on IP as the incentive system for medical R&D, even as it is currently highly subsidized by government and charitable resources, the WHO and other global health entities should be promoting exploration and gradual evolution to new, better targeted systems such as delinkage that prioritize research towards health needs and access based on competitive pricing.		
p. 25 ¶82	Although this paragraph properly cites the relevant human rights provisions, it inaccurately puts the material interests of the author on par with the right to the benefits of scientific advancement and it inaccurately conflates protecting the interests of the author as being dependent on intellectual property regimes. Again, multiple sources have confirmed the primacy of rights to health and of access to medicines as being superior to intellectual property rights. Similarly, the interests of authors (and arguably inventors though they are not directly mentioned) do not equate with IP exclusivities. Stated differently, authors and innovators can be socially supported in materials way through a wide variety of mechanisms that fall far short of IP monopolies.	**83. Although ~~T~~the International Covenant on Economic, Social and Cultural Rights and the Universal Declaration of Human Rights specify that Member States that have ratified or acceded to these instruments "recognize the right of everyone" both "to enjoy the benefits of scientific progress and its applications" and "to benefit from the protection of the moral and material interests resulting from any scientific, literary or artistic production of which he is the author" (31, 32), the rights to the benefits of scientific progress are generally superior to the material interests of authors and the interests of authors can be protected through social supports other than intellectual property. ~~In~~**	

Locator (Page & Line No)	Comment	Suggested Amendment	Internal Use Only [blank]
		~~brief, these instruments articulate that the type and level of protection afforded under~~ ~~a~~Any intellectual property regime must directly facilitate and promote scientific progress and its applications, and do so in a manner that will broadly benefit members of society on both an individual and a collective level.	

4.2 Dr. Anne G. Kasmar

Title: Program Officer, TB Vaccines

Institution: Bill & Melinda Gates Foundation

Locator (Page & Line No)	Comment	Suggested Amendment
Page 26 lines 89 and 91	The lack of 89 (in-country TB R&D champions) is a root cause of the failure of 91 (uptake of effective innovations at the country level).	Aggressive investment in cultivating in-country TB R&D champions and local expertise is a key prerequisite for the ultimate discovery, development and effective deployment of new tools to END TB.
Page 31 line 93	$2 billion required annually to discover and develop new tools for TB	The evidence base for this very large number is essentially absent. Please work with Price Waterhouse Coopers or other financial group with R&D expertise to put in place a logical, evidence-and-experience based framework to rationally justify a number that the global TB advocacy community can then mobilize on our behalf.
Page 37 line 110	“national/regional/global networks of TB research”	Recommend linking National TB plans to locally-driven, national research plans that address key needs of that particular country/region’s TB epidemic/health care delivery system/economics. Some high TB burden countries like China will contribute both to systems approaches and new tools, others have capacity to trial new interventions and still others represent the ultimate target audience all groups should be making tools for.
Page 38, line 122	“Longer-term funding for TB research to foster capacity building and allow discoveries to mature”	Could not agree more; need to change ALL funders views on this.
Page 38, line 124	“those funding TB care programmes, should consider earmarking a budget for TB research”	Absolutely! These groups fund the implementers who will be using new tools or training country experts to use them. Toolmakers should be accountable to them and empowered by them to make effective tools that can easily be used to end the epidemic.

4.3 Dr Christian Lienhardt

Institution: Institut de Recherche pour le Développement (IRD)

City: Montpellier, France

Locator (Page & Line No)	Item	Comment and Suggested Amendment
Page 9 – para 20	**Objective 1:** Create an enabling environment for TB innovation.	Create an enabling environment for TB **research and** innovation.
Page 11, para 24	24. **Linking research to innovation is demanding and costly**, and the road from discovery to the market or the intended beneficiary needs to include several support points, to expedite the availability of life-saving innovations	This is a confusing statement. The essence of health research is to improve understanding of pathophysiological processes with the view to lead to solutions that include (among others) the development of suitable products. It is not the link from research to product development that is costly – but the full process. I would rephrase as: *The road from discovery to development of health products or strategies is demanding and costly, and needs to include several support points, to expedite the availability of life-saving innovations to the intended beneficiary.*
Page 11, para 25	25. Great efforts have been made to replenish the R&D pipeline for TB in the past decade…	Should include *Ref 13*
Page 11, para 28	28. Most national TB programmes have little capability to innovate or absorb innovations, weak links to public research institutes and universities, and **few incentives and resources for innovation**. Coupled with weak research infrastructure, few academic researchers and performers, and a heavy reliance on foreign funding for research in many high TB burden countries, this has slowed the pace of local innovations.	I think it is wrong to start the argument stating the little capacity of TB control programmes for innovation – since their role would be primarily to get the capacity to **implement** innovation – in the absence of such capacity, scale-up is simply impossible. I would rephrase as: *Most national TB programmes have limited capability to implement innovations, as well as weak links to public research institutes and universities, and few incentives and resources*

Locator (Page & Line No)	Item	Comment and Suggested Amendment
		for innovation…
Page 16, para 45	45[…] The main challenges in treatment of TB infection and disease are the duration and complexity of treatment regimens, difficulties in adherence, toxic side-effects, drug resistance...	This is not really true anymore for the treatment of LTBI with the widely recommended 3HP regimen and the potential 1HOP regimen. The sentence should be revised
Page 16, para 47	*TB preventive treatment:* The first-ever clinical trials of MDR-TB prophylaxis for contacts of MDR-TB patients with TB infection are underway, with a regimen that includes the new drug delamanid or the repurposed drug levofloxacin (22). Long-acting drug formulations for preventing TB disease need to be developed to improve adherence and safety …	Why starting this paragraph with MDR-TB prevention – which is a part of larger TB preventive treatment ? In addition, this is the only place in the whole document where specific products in trials are cited while results are not yet known. This would need revision
Page 16, para 47	*DS-TB treatment research:* Researchers are following a number of novel approaches to improve DS-TB treatment, but the overriding focus is still on reducing the duration of therapy.	Yes, but it is essential to keep *efficacy* high !
Page 18, para 51	… BCG provides moderate protection against severe forms of TB in infants and young children …	BCG provides moderate **to good** protection against severe forms of TB in infants and young children,
Page 18, para 53	53. An effective vaccine would also play an important role in tackling DR-TB, since new vaccines are likely to be equally effective against both DR-TB and DS-TB. By preventing disease, vaccines would reduce the need for antibiotics, an essential step for curbing AMR. Therapeutic vaccines, used in combination with drugs, could also reduce treatment duration and the risk of recurrence, thus reducing the development and spread of AMR (18). Recently, an experimental TB vaccine candidate (M72/AS01E) was found to be significantly protective against TB disease	This whole section is illogical and inconsistent – it provides a series of very different messages that should not be grouped under the same goal (i.e. an effective vaccine) since these relate to widely different indications, approaches, strategies, and potential beneficiaries. I suggest splitting and re-arranging this section and use the DR-TB argument last, since it concerns a minor part of the full TB burden.

Locator (Page & Line No)	Item	Comment and Suggested Amendment
	in a Phase IIb trial conducted in Kenya, South Africa and Zambia, in individuals with evidence of LTBI (25). Moreover, the study showed that a proof-of-concept human trial on the prevention of pulmonary TB in adults – the most relevant clinical outcome when considering public health need – is possible (26). Further development and validation of the candidate vaccine is conditional on collaboration between people infected with TB, research funders, governments, PDPs and the pharmaceutical industry.	
Page 22, para 53	Advancing basic science research	This is a weak section overall, with no major references. This would need to be revised, deepened and cite major review references.
Page 28, Table 5.1	Grant funding: Upfront financing awarded through competitive, peer-reviewed processes ….	This is not a fiscal measure. This should be placed under 'political and legal'. Alternatively, for better consistency in the whole category, replace 'fiscal' by 'financial'
Page 30, Table 5.1	Priority review vouchers	This strategy has been established by the US FDA for a couple of years. Before recommending it, are sure that this has been properly evaluated ? *See in particular:* - Kerr KW, Henry TC and Miller KL. Is the priority review voucher program stimulating new drug development for tropical diseases? PLoS Negl Trop Dis. [Online]. 2018 Aug https://doi.org/10.1371/journal.pntd.0006695 - https://msfaccess.org/open-letter-jj-calling-affordable-access-critical-tb-drug-bedaquiline
Page 32,	99. Collaborative financing is an important	Methods for establishing *collaborative*

Locator (Page & Line No)	Item	Comment and Suggested Amendment
para 99	way to "do more" with existing resources, by joining forces to conduct high-impact multisite and multidisciplinary studies. In particular, collaborative funding for large, late-stage clinical trials is urgently needed, to create pull incentives and reduce the lag time for bringing promising breakthroughs to the approvals stage.	*financing* should be indicated.
Page 36, ***Obj. 1***	**Potential measure of effectiveness**: Extent of meaningful engagement in research networks and PPPs for TB research and innovation, and extent of time it takes to process regulatory approvals for clinical trials and product evaluation.	It is unclear how this "meaningful engagement" will be measured and quantified…
Page 36, ***Obj. 1***		Caution: mistake in numbering sections (does not follow from previous page)
Page 36, para 101	101. Develops country-specific TB research agendas and strategic plans that are aligned with the national health research strategic plan, to expand and accelerate TB research at the country level through capacity-building and collaboration among actors in the innovation system (particularly in the national science, technology and development sectors).	This statement should be first in the MS recommendations.
Page 36, para 102	new medical innovations and digital health innovations to …	Caution: repeat *new* and *innovation* digital : first time mentioned here; this is quite specific – why in the same sentence ?
Page 36, para 109	109. Facilitates collaborations between TB researchers in different countries around common research goals, and promotes multisite and multidisciplinary research. This will rely on existing or new international TB research networks and consortia dedicated to discovery, preclinical, clinical, operational/implementation, health	Not sure how this can be achieved by the secretariat – who should rather have a role in monitoring these collaborations and networks.

Locator (Page & Line No)	Item	Comment and Suggested Amendment
	system and social science research.	
Page 39, ***Obj. 3***	**Potential measure of effectiveness**: Extent of contribution of and access to quality research data through global data-sharing mechanisms in a timely and consistent manner to guide global policy decision-making processes and development of new tools for TB	This is a complex measure to quantify. How will contributions and access be quantified ? There is an element of caution to consider here: one has to be careful about universal promotion of data sharing as multiple platforms do exist, that are not all compatible with recommendations from national legal committees on data policy and privacy. In addition, this has a potential ethical impact since consent forms from patients are usually for a specific study – not for a succession of studies using patients' data.
Page 39, ***Obj. 4***	**Potential measure of effectiveness**: Proportion of people with TB and at risk of TB with affordable access to the best proven standard of diagnosis, treatment and prevention	This is also a complex measure to quantify. How will it be measured ?
Page 41, para 148	148. Systematic monitoring and evaluation of efforts, appropriate to each country's context, is needed to ensure that the necessary policy changes are being made and implemented, and to track whether the implemented policies are having an impact that is linked to achieving the goals and targets set in national TB strategic plans and the End TB Strategy.	Not clear whether this is a recommendation to MS to undertake this monitoring or if it is a more general recommendation that the WHO should undertake.
General comments		1. Overall, this is a good document, but it is not clear from the start whom the **audience** is for this important strategy. In the *summary*, the audience is defined as "all stakeholders" and "governments and other partners". In the *Scope* section, MS are clearly defined as key actors, as well as "research policy-makers, funders, civil society and other relevant actors". Then in the *strategic recommendations*, MS are clearly designated for specific actions, while all other

Locator (Page & Line No)	Item	Comment and Suggested Amendment
		stakeholders are grouped in a mixed bag of "International and national partners' action". This will not, in my opinion, generate great enthusiasm for all these 'other partners', all of which are key in their respective roles. So I would add a section, or a Summary table listing properly all the expected actors of this Global TB Research Strategy and specifying what their specific roles would be, since they will all contribute to its success, in full collaboration with the MS. (Paragraph ***23***). 2. *Measures of effectiveness*: this is well defined and measurable only for Strategic Objective 2. Others are rather vague, undefined or not measurable – this needs major revision. 3. More should be said on proposed new strategies for novel financing mechanisms as well as on new mechanisms for collaboration.

4.4 Mrs. Maryam Bibi Rumaney

Institution: www.mbrumaney.co

City: Cape Town, South Africa

Locator (Page & Line No)	Comment	Suggested Amendment
Page 6, line 5	This paragraph needs to take the barriers to clinical management of TB into consideration.	Innovative therapies will address barriers such as a lack in need of cold-storage and technical expertise.
Page 8, line 15	What is meant by implementing a joint strategy? Which parties are we referring to?	Please clarify.
Page 9, line 20	Are the objectives listed in order of importance?	If the objectives are listed in order of importance, then I would swop objective three and four. Objective four should rank higher than three because equitable access is more important than data sharing.
Page 10, line 22	Long-term sustainability is an important part of operational research. Academic research for publication is not necessarily driven by measurable outcomes.	Long-term sustainability is an important part of **operational** research;
Page 14, line 44, point 2	How often will the diagnostic portfolio be evaluated?	Indicate a time period for regular review of the diagnostic portfolio.
Page 39, lines 131 and 132	Who will monitor this progress?	An additional point should be made: A task team will be formed composed of local and international expertise to oversee the implementation and the monitoring of points 131 and 132.

Locator (Page & Line No)	Comment	Suggested Amendment
General comment	Include a diagram that shows the current TB diagnostic pipeline.	Include a diagram that shows the current TB diagnostic pipeline.
General comment	Include an education document. TB knowledge among the general public in endemic regions are still lacking.	Include a civil society and patient education document.

4.5 Professor Jens Seeberg

Institution: Aarhus University

City, Country: Aarhus, Denmark

Locator (Page & Line No)	Comment	Suggested Amendment
21, 67-68	As a social scientist, working in the TB field, with working experience from WHO and with RNTCP in India, I am happy to see that due attention is given to social science contributions to TB control in the revised strategy. However, it is a somewhat disillusioning to note that the substantial body of social science studies on TB carried out in recent decades in various fields, including e.g. medical anthropology, has not informed the strategic thinking the way it could have. For example, this research has pointed to the need to focus not only at the clinical, local and national levels of service implementation and social barriers to service delivery, but also to critical studies of national and global structures that impact on spread of DR-TB and hamper treatment and prevention efforts. Such research should include studies of dynamics between local and national treatment practices and activities – and sometimes conflicting priorities – of significant global health actors, such as Gates Foundation, Global Fund, and key pharmaceutical companies. Without research-based knowledge on such dynamics, the	68. Acknowledging that TB control efforts are not only driven by national authorities but also influenced by global health actors, the complex dynamics between global, national and local actors constitute an important social science research agenda. This includes e.g. interdisciplinary studies to understand structural drivers and barriers of global governance and policy translation regarding DR-TB.

Locator (Page & Line No)	Comment	Suggested Amendment
	research agenda remains incomplete. I propose that a new para 68 is inserted, and subsequent paras are renumbered accordingly.	
22, 69	The first para in the basic research section implies that basic social science does not exist, and this is wrong. On the contrary, the recognition of basic social science could serve to substantially qualify important discussion in TB control. Basic social science is concerned with understanding and developing core concepts to understand social and cultural dynamics. A good example is the concept of 'stigma'. In spite of a substantial social science body of work on this concept, a speaker at the recent Union conference in the Hague insisted that the TB community needs to know more about what this means and asked, 'if anybody knew of such social science work'. While the attention increasingly being given to stigma is important, the concept is generally poorly understood in the context of TB. It needs to be studied to what extent stigma and discrimination (the two are related but different) of TB patients in particular contexts are caused by their having TB or the myriad of other possible causes of stigma, such as being low-caste, black, poor, uneducated, woman, etc. Understanding such dynamics is necessary to develop effective interventions, but the first step is to understand the phenomenon as	Likewise, basic social science research is required to develop new theoretical and conceptual models to understand key biosocial processes that may eventually inform TB control strategies, policies and practices.

Locator (Page & Line No)	Comment	Suggested Amendment
	such. Another basic social science concepts that has informed TB control is 'social capital', a concept that is often mistakenly understood to mean 'social network' but that nevertheless points to social practices that play a central role for risk of primary DR-TB development. A basic social science research agenda for TB control could help implementers better understand key social dynamics. This is also true for cutting-edge interdisciplinary research on multi-species interaction, e.g. between MTB/M.bovis, humans and animals such as cattle.	

4.6 Professor Ulrika Simonsson

Institution: Dept of Pharmaceutical Biosciences, Uppsala University

City, Country: Uppsala, Sweden

Locator (Page & Line No)	Comment	Suggested Amendment
p. 16 & 48	Since development of new drugs is very time - and cost - consuming, it is also of importance to improve the existing treatment regimens. One way to enhance cure rates is personalized treatment through therapeutic drug monitoring (TDM). TDM leads to outcomes with higher efficacy, lower toxicity and less development of drug resistant TB [1] [2]. Another approach to improve current treatment is the exploration of exposure-response relationships of TB drugs with non-linear mixed effects modelling (pharmacometrics). With this strategy it is for example possible to choose the dose with the best benefit-risk-ratio or to investigate the efficacy of regimens with higher doses in order to shorten treatment length. It has been shown that model-based approaches allowed detection of that higher rifampicin exposures lead to greater early bactericidal activity [3] which was undetected using conventional statistics [4]. Furthermore exposure-response was identified for rifampicin based on modelling of time to stable sputum culture conversion (TSCC) data [5]. References: 1) Davies Forsman L et al. Plasma concentrations of second-line antituberculosis drugs in relation to minimum inhibitory concentrations	I recommend to add one extra bullet point: • improving current treatment regimens, e.g. through personalized treatment such as TDM, investigation of exposure-response relationships for TB drugs or enhancement of patient's adherence.

Locator (Page & Line No)	Comment	Suggested Amendment
	in multidrug-resistant tuberculosis patients in China: a study protocol of a prospective observational cohort study. BMJ Open 2018; 8. 2) Niward K et al. Distribution of plasma concentrations of first-line anti-TB drugs and individual MICs: a prospective cohort study in a low endemic setting. J Antimicrob Chemotherap 2018; 73: 2838-2845. 3) Svensson RJ. Greater Early Bactericidal Activity at Higher Rifampicin Doses Revealed by Modeling and Clinical Trial Simulations. J Infect Dis 2018; 218: 991-999. 4) Boeree MJ et al. A Dose-Ranging Trial to Optimize the Dose of Rifampin in the Treatment of Tuberculosis. Am J Respir Crit Care Med Vol 2015. 191: 1058-1056. 5) Svensson EM et al. The Potential for Treatment Shortening With Higher Rifampicin Doses: Relating Drug Exposure to Treatment Response in Patients With Pulmonary Tuberculosis. Clin Infect Dis 2018; 67: 34-41.	
p. 16 & 46.	Besides the development of new candidate products, enhanced clinical trial performance is also crucial. Particularly many TB Phase IIa trials fail to identify drug effects or differences between different doses of the same drug using current design and statistical analysis [1] [2]. Thus many trials read out as uninformative and inconclusive which leads to irrational decision-making with a risk of dropping promising candidates too early or continuing the development of bad candidates. Clinical trial simulations with the help of nonlinear mixed effects modelling is an effective tool to substantially improve clinical trial design and analysis of the outcome. Furthermore, modelling assists to identify clinically relevant drug candidates in early stages of development and	"However, the high attrition rate in drug development – and the requirement to treat TB using multidrug regimens – means that a greater number of novel experimental compounds are needed to ensure progress." **Besides the discovery of new candidate products, enhanced clinical trial performance using pharmacometric assistance is also crucial for a cost- and time-effective drug development.**

Locator (Page & Line No)	Comment	Suggested Amendment
	therefore contributes to a cost – and time – effective drug development. This strategy allows developers to mitigate risk and increase the likelihood of regulatory success [3] [4]. References: 1) Donald PR & Diacon AH. The early bactericidal activity of anti-tuberculosis drugs: a literature review. Tuberculosis (Edinb) 2008. 88 Suppl 1:S75-83. 2) Gosling RD et al. A multicentre comparison of a novel surrogate marker for determining the specific potency of anti-tuberculosis drugs. J Antimicob Chemother 2003. 52: 473-476. 3) Svensson RJ et al. Improved power for TB Phase IIa trials using a model-based pharmacokinetic–pharmacodynamic approach compared with commonly used analysis methods. J Antimicrob Chemother 2017. 72: 2311-2319. 4) Muliaditan M et al. The implications of model-informed drug discovery and development for tuberculosis. Drug Discov Today 2017; 22: 481-486.	
P. 22 & 71	The currently common biomarkers focus mainly on multiplying bacteria, ignoring dormant or non-replicating bacteria quantification. For instance, no drug effect was found in an early bactericidal activity study of clofazimine. In contrast, during long term treatment, the drug has shown to be able to shorten treatment duration, hinting that the biomarkers used to quantify drug effect does not reflect long term efficacy [1–3]. Well-validated efficacy predictors are essential	"Possibly the most important consequence of advances in basic research is the opportunity to understand the mechanism of disease development and the associated host or pathogen predictive biomarkers or surrogate end-points associated with disease progression and cure." **Such an understanding could decrease the risk of rejecting effective drugs in**

Locator (Page & Line No)	Comment	Suggested Amendment
	to capture the complexity of the disease, and potential drug effects. Moreover, with a good biomarker the data from early clinical development can be utilized using nonlinear mixed effect modelling to predict long-term efficacy and thus optimize the clinical drug development of tuberculosis medicines. References: 1. Diacon AH, Dawson R, Von Groote-Bidlingmaier F, et al. Bactericidal activity of pyrazinamide and clofazimine alone and in combinations with pretomanid and bedaquiline. Am J Respir Crit Care Med 2015; 191:943–953. 2. Tang S, Yao L, Hao X, et al. Clofazimine for the treatment of multidrug-resistant tuberculosis: Prospective, multicenter, randomized controlled study in China. Clin Infect Dis 2015; 60:1361–1367. 3. Van Deun A, Maug AKJ, Salim MAH, et al. Short, Highly Effective, and Inexpensive Standardized Treatment of Multidrug-resistant Tuberculosis. Am J Respir Crit Care Med 2010; 182:684–692.	**early clinical development that would have shown efficacy in long-term treatment or in combination [1–3]. With usage of modelling and simulation, information from early clinical trials can be used to predict and optimize late-stage clinical trials.**
P. 16 & 47	Many early bactericidal activity studies focus on monotherapy efficacy of new drugs. Such framework is not expected to capture synergy of the drug with potential companion drugs [1]. References: 1. Bonnett LJ, Ken-Dror G, Koh GCKW, Davies GR. Comparing the efficacy of drug regimens for pulmonary tuberculosis: Meta-analysis of endpoints in early-phase clinical trials. Clin Infect Dis 2017; 65:46–54.	"For TB treatment, it is important to focus on developing wholly new regimens rather than single drugs to treat LTBI, DS-TB, MDR-TB and XDR-TB forms of the disease." **It is of importance to test drug combinations in early clinical development, to capture synergistic effects of drugs. Such strategies can reduce the risk of rejecting drugs that are efficacious in combination, but not in**

Locator (Page & Line No)	Comment	Suggested Amendment
		monotherapy [1].
p. 14 & 42	It is suggested, based on modelling and simulation tools, that one biomarker, e.g. CFU, TTP in MGIT, or MBL, is not enough to capture all mtb subpopulations. Using two biomarkers at the same time does seem to improve bacterial population detection and is thus recommended.	"The improved application of traditional biomarkers and the discovery of additional markers will be critical to guide the development of a rapid, easy to use and affordable diagnostic tool that can be used at point of care in low-resource settings." **Whenever possible, two biomarkers are recommended to be used to have a better detection of the bacterial population.**