Dr Tim Hubbard (Head of Human Genome Analysis, Sanger Institute), 15/8/05.

Reply to the comments requested by CIPIH and WHO to the CPTech proposal for a Medical Research and Development Treaty (MRDT)

There have now been four replies to the requests by CIPIH and WHO to experts in the field for comments on the Medical Research and Development Treaty proposal. These have been (in the order received) from Professor Richard Nelson [RN], Prof. Rochelle Dreyfuss [RD], Prof. F.M.Scherer [FS] and Prof. Luigi Orsenigo [LO]. Independently and some months before there has also been a paper published by DiMasi & Grabowski[1] [DG] which comments on the paper published by Hubbard and Love[2] [HL] which outlined many of the principle ideas that later led to the treaty proposal.

These authors raise many questions about the treaty. As one of its architects, I attempt here to provide some clarification of our intentions, where the text of the treaty proposal appear to have been unclear, and expand on how we envision it working in practice. To aid this, I've reproduced a schematic figure from previous presentations to give an overview of the proposed treaty mechanisms. Where I refer to comments by specific authors we use the two letter abbreviations defined above.

[1] There appears some confusion about the status of the patent system under the treaty [e.g. DG]. We envisage a mixed system, as concluded by RD. Part of the confusion arises from treaty clause 14.1 where the HapMap example is given. The objective of the HapMap was to create an unrestricted public resource which other research could be built on. However, during the resources construction it was feared that external users might combine the incomplete public HapMap data with their own data and gain enough insight to preempt the resources completion and gain patents that would inhibit the resources future use. Once the resource was complete and fully in the public domain, there was no risk of such blocking patents, so the restriction was removed. Treaty clause 14.1 seeks to incentivise the creation of such public resources and maximise the global benefits from them by providing narrow temporary protection from opportunistic behaviour during their construction. It does not attempt to restrict follow on patenting that RD was concerned about. Regarding treaty clause 14.2, RD is correct that this is meant to address research exemption issues, though as pointed out it is important that such exceptions are not too broad. The other relationship of the treaty to the patent system is the consequences of holding a patent on a drug that has been approved by authorities (e.g FDA). Currently a marketing monopoly is granted to the patent holder. Under treaty flexibilities a country might implement a different scheme for rewarding patent holders such as granting the right to draw on a large prize fund an amount related to the assessed medical benefit, in exchange for allowing the drug to be generically manufactured.

[2] The treaty creates a legal obligation on each country to support medical R&D while allowing them flexibility in a way that they support it. Some of the authors [e.g. FS] are justifiably sceptical of countries ability to sustain treaty obligations within a continuously

changing political climate. For this reason the treaty creates incentives to comply, penalties for failing to comply and a structure for evaluating compliance. Countries that support medical R&D to the required level (fraction of GDP) are granted flexibility to incentivise R&D innovation through mechanisms other than just marketing monopolies. Countries whose support for R&D is deemed not to meet the required level immediately lose these flexibilities. Decisions on whether a country has complied are made centrally by treaty institutions (figure 1), however countries make their own decisions on R&D innovation policy and no money is collected or distributed centrally. These mechanisms ensure that support for R&D by each country is maintained, without central planning.

Even with compliance mechanisms, a risk of basing evaluation on accounting is that governments will continuously find new creative spending avoidance methods and run rings around the treaty secretariat [FS]. The system could also create pernicious incentives. We accept there are risks, however we believe that economic tools and experience exists to implement such structures rigorously and make them flexible enough to respond to government strategies. Ultimately, success depends on sufficient power, authority and resources being vested in the treaty institutions. For this reason we suggest tying the granting and revoking of the 'flexibilities' referred to, to the TRIPS agreement under the WTO, which already has strong dispute resolution mechanisms. As a weaker 'stick' we also believe, perhaps naively, that there is enough global community acceptance of the importance of supporting healthcare R&D that this can also provide pressure on governments to be seen to be meeting global commitments. For example, we note the desire of governments to be seen to have contributed to the human genome project and other international public domain health research projects. We would hope that openness of evaluation and public reporting by the treaty secretariat of relative contributions and efficiency to R&D outputs by each country would have significant popular impact. For example we note the political impact for governments of countries reported to be performing poorly in global rankings of education standards.

While we have confidence in these proposed structures, no system works perfectly. However, when evaluating their likely efficiency, they should be compared with the efficiency of current system, which is also not fool proof.

[3] Several authors [e.g. RD, LO] have questioned how a mixed system of direct funding and rewards for patented research would be managed. Clearly payments from a prize fund would have to be sufficiently large to make investment in patented R&D attractive. DG worries that prizes will tend to be either too large or too small. However we think that the competitive structure encouraged under the treaty framework should address these issues. Firstly, since the total R&D obligation of a government is fixed it is restricted to choosing the proportion of money that flows into different R&D incentives. Under a treaty compliance regime that evaluates R&D outputs there will also be pressure on governments to optimise this allocation. These constraints on governments should create confidence for investors in the long-term stability of the system. Secondly, rather setting individual prizes for particular targets of predefined size, which many have pointed out is problematic, we advocate rights to draw on a prize fund. The market

should therefore optimise the amount of private investment in R&D to fit the prize fund size.

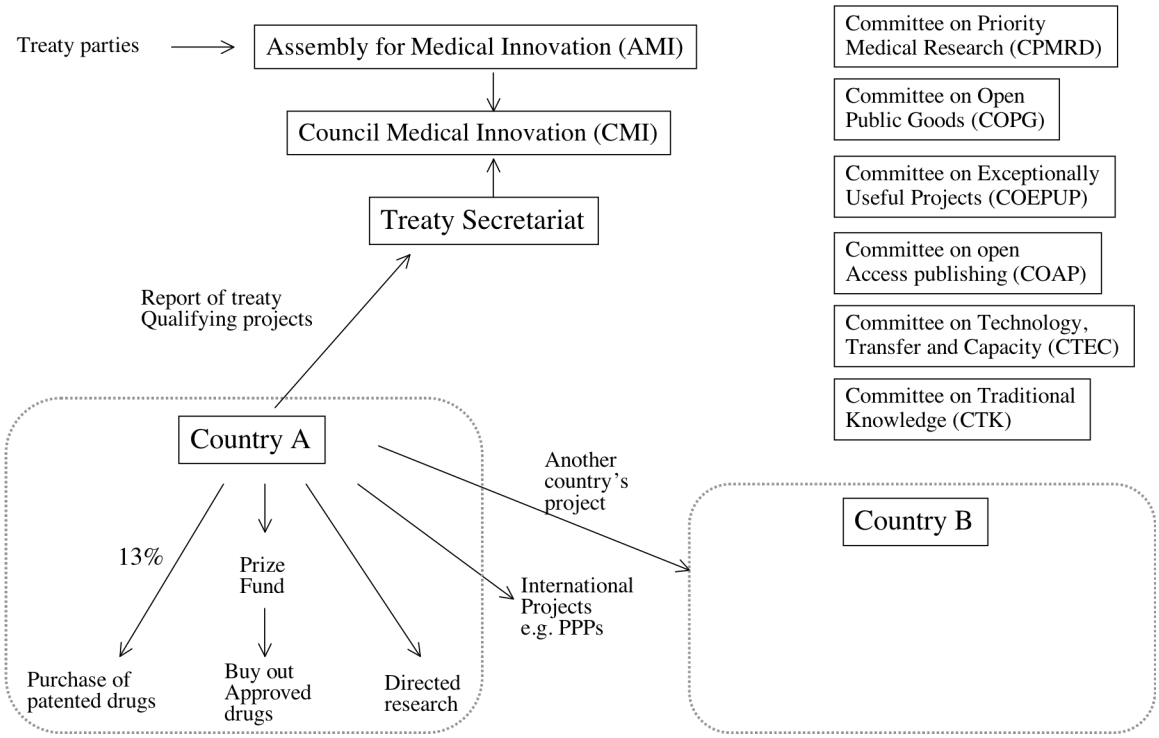
[4] There was some worry that the proposed obligation (0.15% GDP) might actually lower overall spending on medical R&D [FS & LO] as in a few countries basic biology research funding is sufficiently high that governments might claim significant parts towards their obligations. The GDP numbers proposed are based on estimates of spending on directed (principally commercial) drug development[2], which the treaty is specifically designed to address. Since the treaty compliance mechanisms decide what research qualifies towards a countries obligation this should ensure that support for the 'D' component of R&D is maintained appropriately, although we recognise the difficulties deciding what qualifies.

It should be emphasised that treaty levels are minimums and we don't think they should be set on the basis of current spending by outlier countries. However, the CIPIH commission might want to recommend different guideline GDP figures, to those proposed here, on what they think countries should spend on basic, directed or for priority research.

[5] FS suggested that sections of the treaty imply a direction away from granting exclusive licenses and imply that this could harm translation. However agencies with a mandate to improve public health, such as National Institutes of Health and Wellcome Trust, are already using a range of different approaches to ensure that research discoveries are developed into treatments, only one of which is exclusive licensing. Our view is that a mixed approach is likely to be the most successful, but that new open access approaches should be encourage where appropriate. Recent evidence suggests that the selective creation of public research resources (e.g. human genome sequence), which are of wide utility to other researchers, stimulate research activity more than any lose of potential exclusivity. More widely, encouraging researchers to be more proactive in sharing their data and research results, under open access research initiatives, also appears beneficial[3].

[6] Finally, many of the authors are sceptical of the political feasibility of the treaty proposal. It is clear that getting it adopting in full would be hard, since it would represent a significant change to the existing system. However, for priority research, some new mechanism to support priority research is urgently required as there is none at present at an appropriate scale. Just now have a lot of research progress in these areas, largely as a result of the new PPP that have recently been set up. However, unless a sustainable source of resource to support these efforts is found soon, these efforts will not be able to translate their research into treatments and the efforts will wither. We consider that one of the major benefits of the treaty is being able to address this issue on a long term basis.

Figure 1



Each treaty country is required to record its direct and indirect spending on medical R&D and report this to the Treaty Secretariat. The Secretariat is advised on what expenditure qualifies against a country's obligations by CMI and a number of specialist committees. If the secretariat deems that a country has not met their obligations it advises the WTO that the country's TRIPS flexibilities under the treaty are void. The secretariat would also assess the impact of each country's expenditure on R&D outputs and publish an appraisal of which countries incentive regimes are most effective. A county's obligations, framed around fraction of GDP, would over time also be linked to R&D outputs, to provide incentives to create the best regime.

References

1. DiMasi, J. A. & Grabowski, H. G. Patents and R&D Incentives: Comments on the Hubbard and Love Trade Framework for Financing Pharaceutical R&D. http://www.who.int/intellectualproperty/news/en/Submission3.pdf (2004).
2. Hubbard, T. J. & Love, J. A New Trade Framework for Global Healthcare R&D. *PLoS Biology* **2**, 147-150 (2004).
3. OECD. Promoting Access to Public research Data for Scientific, Economic, and Social Development. http://dataaccess.ucsd.edu/ (2003).