Building capacity for material transfer agreements in public health emergencies
Informal consultation
16 December 2016
Institut Pasteur, Paris, France

Meeting report

The meeting was organized under the WHO R&D Blueprint effort, which aims to reduce the time between declaration of a public health emergency and the availability of effective diagnostic tests, vaccines, antivirals and other treatments that can save lives and avert a public health crisis (http://www.who.int/csr/research-and-development/en/).
# Table of contents

Acknowledgements .................................................................................................................. Error! Bookmark not defined.
List of acronyms .......................................................................................................................... 4
Note to the reader .......................................................................................................................... 5
Background .................................................................................................................................. Error! Bookmark not defined.
Executive summary ....................................................................................................................... 6
Opening session ............................................................................................................................. 6
Session 1: Context and ongoing work on MTA development ....................................................... 7
  Discussion.................................................................................................................................. 12
Session 2: The draft MTA guidance tool: a starting point .......................................................... 13
  Discussion.................................................................................................................................. 14
  Engagement and objectives......................................................................................................... 14
  Issues related to commercial models and different beneficiaries ........................................... 15
  Scope and practical issues .......................................................................................................... 15
  The role of WHO ....................................................................................................................... 16
Session 3: improvement of the draft MTA capacity building tool ............................................. 16
  Discussion.................................................................................................................................. 17
  Intellectual property, different use cases and aligning opposing approaches ....................... 18
  Suggested IP solutions ............................................................................................................... 19
  Data sharing ............................................................................................................................... 20
  Fundamental principles ............................................................................................................ Error! Bookmark not defined.
Session 4: development of next steps ....................................................................................... 20
  Discussion.................................................................................................................................. 21
  Suggestions for testing and validating the tool ....................................................................... 21
Annex A: Meeting agenda ........................................................................................................... 22
Annex B: List of participants ...................................................................................................... Error! Bookmark not defined.
## List of acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHIA</td>
<td>Global Healthcare Innovation Alliances</td>
</tr>
<tr>
<td>GSK</td>
<td>GlaxoSmithKline</td>
</tr>
<tr>
<td>ICMJE</td>
<td>International Council of Medical Journal Editors</td>
</tr>
<tr>
<td>IHR</td>
<td>International Health Regulations</td>
</tr>
<tr>
<td>IP</td>
<td>Intellectual property</td>
</tr>
<tr>
<td>KSA</td>
<td>Kingdom of Saudi Arabia</td>
</tr>
<tr>
<td>LMICs</td>
<td>Low- or middle-income countries</td>
</tr>
<tr>
<td>MOH</td>
<td>Ministry/Ministries of Health</td>
</tr>
<tr>
<td>MSF</td>
<td>Médecins sans Frontières</td>
</tr>
<tr>
<td>NIH</td>
<td>US National Institutes of Health</td>
</tr>
<tr>
<td>PHEIC</td>
<td>Public health emergency of international concern</td>
</tr>
<tr>
<td>PI</td>
<td>Principal investigator</td>
</tr>
<tr>
<td>PIP-FW</td>
<td>Pandemic Influenza Preparedness Framework</td>
</tr>
<tr>
<td>R&amp;D Blueprint</td>
<td>A WHO research and development Blueprint for action to prevent epidemics</td>
</tr>
<tr>
<td>UBMTA</td>
<td>Uniform Biological Material Transfer Agreement</td>
</tr>
<tr>
<td>UNCST</td>
<td>Uganda National Council for Science and Technology</td>
</tr>
<tr>
<td>WAHO</td>
<td>West African Health Organization</td>
</tr>
<tr>
<td>WHO</td>
<td>World Health Organization</td>
</tr>
</tbody>
</table>
Note to the reader

The open discussion parts of this meeting were held under the Chatham House rule: in reporting the discussion sessions, neither the identity nor the affiliation of the speaker(s), nor that of any other participant, is revealed.

This report condenses the themes of each session – including the interventions from the floor – according to the themes addressed, rather than attempting to provide a chronological summary of the dialogue.

Summaries of presentations and of points made in discussion are presented as the opinions expressed; no judgement is implied as to their veracity or otherwise.
Executive summary

A prompt response to a public health emergency can depend upon the ability to move relevant samples and data from one place to another. The movement of such samples and data must be as simple and transparent as possible, whilst protecting the interests of the owners of the samples. Increasing awareness of the potential value of certain samples or data has increased the demand for these protections.

Material Transfer Agreements (MTAs) play an important role in enabling transfers and subsequent use by the recipient, whilst protecting the interests of the transferee.

Recent public health emergencies of international concern (PHEICs) with Ebola virus disease in West Africa and zika virus in Latin America have demonstrated the many difficulties of in negotiating MTAs in an emergency context, and showed a clear need for agreed fundamental principles and scalable, sustainable approaches for MTA negotiation.

To address key issues in the development of MTAs, in December 2016 WHO convened an informal consultation on building capacity for MTAs in public health emergencies. The meeting was co-organized and hosted by the Institut Pasteur in Paris, France.

At the meeting, experts from a variety of backgrounds discussed key issues in MTAs in a public health emergency context. Participants considered existing tools, resources and methods, analysing and extracting concrete language, options and approaches for an MTA capacity-building tool. There was broad support that such a tool be user friendly, tailored to the needs of countries and stakeholders, in particular lower- and middle-income countries (LMICs), and focused on cases where WHO is not directly involved in sample transfer. It should be developed with the maximum possible engagement of WHO Member States, with a view to advancing public health benefit where need is greatest, and improving preparation for emergencies under the International Health Regulations (IHR).

The meeting was organized under the WHO R&D Blueprint, which aims to reduce the time between declaration of a public health emergency and the availability of effective diagnostic tests, vaccines, antivirals and other treatments that can save lives and avert a public health crisis (http://www.who.int/csr/research-and-development/en/).

It was agreed that a tool could usefully provide:

- An introductory overview of MTAs
- A guide to overarching principles
- Further detail of what is expected in an MTA
- Guidance on how agreements in different areas of an MTA relate to one another.
- The different possible approaches, and how to go about constructing them
- Case studies.

The draft tool will be put out to public comment, reviewed and refined, then tested with the collaboration of Member States. While the R&D Blueprint focuses on emergencies, participants agreed on the importance of not waiting for the next emergency to test it in practice.
Building capacity for material transfer agreements in public health emergencies

The meeting was chaired by Dr Gian Luca Burci, who welcomed the participants and outlined the structure (Annex) and goals of the meeting – stressing this was not a negotiation or a renegotiation, but rather a discussion of process. The meeting was taking place as part of WHO’s larger Research & Development (R&D) Blueprint initiative to build on the lessons of Ebola and zika, and to address them before the next public health emergency of international concern (PHEIC).

Dr Nadia Khelef, Institut Pasteur, welcomed everybody on behalf of the President of the Institute.

Dr Vasee Moorthy of WHO’s R&D Blueprint team introduced the R&D Blueprint (‘the Blueprint’) and provided a short history of the initiative, establishing the Blueprint as a high-level, standing mechanism to look systematically at R&D barriers and opportunities to improve preparation for the future. WHO’s role was described as convening and enabling consultation between different partners. The utility of the Blueprint depends on the extent of consultation between different groups—especially in low- and middle-income countries (LMICs)—and on understanding different groups’ perspectives around the world. Outlining different perspectives is essential to capacity building.

Context and on going work on MTA development

A number of presentations provided context for the meeting.

Dr Moorthy and Piers Millett, also of WHO, explained work to date on the MTA tool. By May 2015, issues around samples originating in West Africa lacked clarity. An initial WHO stakeholder consultation on needs for storage and exchange of samples clarified issues around sample holding and national inventory processes; outlined different models in use around the world for dealing with these issues; and highlighted the central role of MTAs in sample sharing. A further round of consultation in September 2015 showed how WHO’s convening role can catalyse shared objectives. Dr Millett suggested that the ideal new norm would be the sharing of data by default, without which he argued a public health response cannot happen.

Many stakeholders took part in these consultations, which became a global consensus gathering exercise. Journal editors responded immediately, and the International Council of Medical Journal Editors (ICMJE) issued a statement that in emergency circumstances critical information should be shared before publication. During the zika epidemic that followed, a large group of stakeholders came out in support of these principles, and research data sharing around zika has since proceeded more openly. This has not, however, been accompanied by an upsurge in the sharing of surveillance and epidemiological data, leading to the conclusion that a distinction is developing between research data and some other types.
In conclusion, issues in data and sample sharing are complex, and different for different groups. The international public health community is working to clarify different categories of information sharing.

Dr Katherine Littler summarised the relevant work of the Wellcome Trust, which had held a series of meetings relevant to MTAs: in January 2016 they convened a meeting to increase preparedness for managing samples generated by future public health emergencies. This meeting highlighted a need for, and began to develop, principles and issues relevant to Material Transfer Agreements. In May 2016 they convened another meeting in London as part of broader efforts to help build stakeholder capacity for MTAs for the transfer of both biological materials and information. Participants reviewed existing relevant international and national frameworks and the interests and needs of different stakeholder groups, and began to map different approaches to benefit sharing and intellectual property.

Under the umbrella of the Global Research Collaboration for Infectious Disease Preparedness (GLOPID-R), with WHO as an observer, Wellcome Trust is now working to strengthen pandemic response preparation. Within this effort are many working groups, one of which is on data sharing (not sample sharing). This group is developing a decision tree for outbreaks, to identify stakeholders and sharing needs, and looking at a set of principles that ties in with the work of Chatham House (below). While it is commendable that a number of sharing policies now exist, these will do nothing unless implementation challenges are solved. The Wellcome Trust is addressing this need through three work areas: incentives; infrastructure; and addressing the ethical and legal challenges of sharing.

Piers Millett then elaborated the goal of the meeting, which was to build on existing work and use WHO’s convening power to sketch out a way to move forward in the same direction. The aim was not to solve problems, but to capture different views and seek out practical examples, and to try to increase understanding of different contexts and parameters affecting MTAs and the use of samples.

Attempts would be made to gather examples of language from existing MTAs that could then be incorporated into a tool. Mr Millett provided an overview of the meeting background document, which examined: general and cross cutting issues distilling earlier discussions; when MTAs will be needed; what comes out of sample sharing and the different types of outputs; chains of custody; use of third parties in MTAs and the nature of WHO’s role; the nature of the sample (e.g. clinical samples versus isolates); specifying who has the authority to sign up to MTAs; and the overarching principles.

He highlighted a number of areas in which views previously expressed were particularly divergent. Different stakeholders have different, conflicting views of ownership. This cannot be solved, but rather must be recognised in order to develop a tool that accommodates different points of view. The meeting would also try to capture and assess the different approaches applicable to questions of benefit sharing and intellectual property (IP).

Dr David Harper then presented the work of Chatham House in this area. Since February 2014, they have been running a tool development project funded by the Bill and Melinda Gates Foundation,
focussed on strengthening the sharing of routine surveillance data for public health. The tool is an easily updated web-based guide to sharing agreements that bring as many resources as possible together into one place. It includes high-level principles, and it has an application further afield than MTAs. For example, it may be usable in emergencies and between organisations, rather than only between national governments. The development process has been “very inclusive”, managed from the point of view that the process might be at least as important as the product. The tool has been piloted in a number of locations in Africa and South East Asia with a web developer as an integral part of the team, and has been re-coded a number of times in response to feedback.

Dr Harper underlined the importance in tool development of conceding how the real world works. The tool's template section provides a particular example: many users have said that in a resource-limited context people will simply download and use templates from the web; and while there are qualifiers on the site stating that it only provides a model, and is not intended to work for all contexts, the real world can work differently. It is therefore important that tool development should have a number of strong underlying ethical principles.

For data sharing, Chatham House experiences suggest the role of the tool is now relatively clear: helping create the right environment for data sharing, providing case studies, and identifying good practice. MTAs are a new initiative, and Chatham House wants MTA efforts to benefit from its data sharing work. Some of it is directly applicable, but there are differences. The goal is to help people see where they need expert advice, and show them the resources available.

The tool can be customised to providers, recipients, state or non-state parties, users experiencing emergencies or not, etc., including tailoring the overarching principles. It will be piloted at a meeting in Abuja with the West African Health Organization (WAHO) countries in the first quarter of 2017. As it is web-based, the tool will be updatable and will be improved continuously.

Julie Barnes-Weise and Ana Santos Rutschman of Duke University then outlined the work of the Global Healthcare Innovation Alliances (GHIA) project, which was originally funded to map the response to Ebola and the emerging alliances and agreements. The process has been inclusive, starting with interviewing parties to the alliances but expanding to include people not directly involved in those alliances, such as funders and experts.

During the Ebola epidemic there were a number of interesting developments —for example, GlaxoSmithKline (GSK) formed a multi-party consortium to develop an Ebola vaccine candidate. Normally a two party development agreement is difficult to negotiate in under a year; in this example, alliance of over 15 parties came together in several months. GHIA spent a year and a half analysing successes, failures and contextual factors affecting this work, in order to enable more innovative alliances in global healthcare. Issues identified included: ownership; data sharing and safety; liability; the structure and management of consortia; and funding and access to vaccines for less developed countries.
Other lessons learned included the GSK consortium’s need to obtain clinical trial insurance, as the US PREP Act reducing liability does not exist in other countries, in particular in the countries in which the clinical trials were conducted. Addressing IP issues also took several months, which it was suggested, led to insufficient enrolment in clinical trials.

The GHIA team had gathered provisions from healthcare alliance agreements, templates and examples in use on these key issues and had organised them into a master chart. The resulting resource enables users to determine what has been applied in other contexts and what the alternatives are. They are not intended as model agreements or templates, but as examples of what has been used in the past to deal with specific issues. This document is continually updated and the issues addressed are being expanded.

GHIA noted that access issues have been difficult to map because ‘access’ means different things to different people; however GHIA is working to develop clear frameworks and language to address access issues, on which others can build.

GHIA has also examining issues related to biobanking, health data and precision medicine. Language addressing this wider set of issues is not yet collected; but efforts to expand the Guide are on going, as is work to develop frameworks for use both in emergencies and in chronic disease situations.

For an MTA tool, clarity is needed on the goal, potential use and applicability, and next steps. A number of different types of MTAs will need to be collected and annotated for use in different situations. Ultimately the goal would be a resource similar to the Chatham House tool, open for all to use.

An illustrative example of in field MTA support was provided by Institut Pasteur. They detailing their work on MERS-CoV where they supported data and samples access efforts. They assisted in the development of relevant agreements, were set up to offer support on the ground and answer key questions at the beginning of the outbreak. In this context, Insitut Pasteur had had internal discussions of the types of investigations conducted at the start of an outbreak, and efforts to generate research protocol templates for field investigations. They felt templates to be important to countries and felt they must be adaptable, yet must contain building blocks and essential elements. Internally, the Institut Pasteur has also discussed legal, ethical, and regulatory issues pertaining to investigations conducted under local leadership (where an outbreak occurs). They highlighted challenges in establishing a set method for engaging countries and stressed the need for tailored approaches. Institute Pasteur also noted that leadership and personnel changes, common in emergency settings, complicated efforts to undertake sustained activities.

Institute Pasteur is developing open-access, standardised research protocols for epidemic pathogens as well as MTAs building on existing protocols. Their goal is to have investigations use a standardised approach whereby data is used first for action to stop an outbreak, then shared. Data sharing is about getting the right information to the right groups for a specific purpose; it is not necessary to have every single data point available online.
An important general lesson highlighted by Institute Pasteur was that while many incredible efforts around MTAs are underway worldwide, they remain separate, and WHO can provide help bring them together.

**Dr Linda Kahl** then explained the work of the **BioBricks Foundation**, in collaboration with the Open Plant Initiative (UK), to create an OpenMTA in the context of engineering biology, or synthetic biology. This is a simple, standardised tool that allows groups to share materials. The process started by bringing together those who would be involved and those who would be signing the MTA, and the needs and design goals were defined over the course of a year before any legal language was drafted. The design goals were access; attribution; reuse; redistribution (and reporting back); and non-discrimination. Dr Kahl noted the Uniform Biological Material Transfer Agreement (UBMTA) had been a useful a starting point. The project identified language and provisions consistent with the collaborators’ design goals. They removed any language that was not consistent. A draft was assembled and, in a second stage, shared with stakeholders. They then helped in refining the language. Dr Kahl presented a table comparing the different provisions and restrictions of different MTAs.

The goal of this project was to eliminate or reduce transaction costs; provide an avenue for researchers to be credited for making materials available; support collaboration across institutional and international boundaries; facilitate the translation of resources; provide access to materials for researchers in less privileged institutions or regions; and to empower small groups to solve problems for themselves, making sure they have the materials they need. A website has been set up—OpenMTA.org—which further explains the genesis and motivation for creating the OpenMTA.

**Ms. Hellen Naluyima Opolot** of the **Uganda National Council for Science and Technology (UNCST)** then provided some insight into the Ugandan context. The country has comprehensive guidelines for research involving humans, of which MTAs are a well-developed component. The guidelines were developed in July 2014 and involved a number of stakeholders. Their main objective was to provide a coherent regulatory framework for research involving humans without compromising their rights.

Under national guidelines, MTAs are signed between the legally authorised heads of the receiving and providing institutions, with the principal investigators (PIs) signing as witnesses. Components of the guidelines include the parties providing and receiving; descriptions of materials; their purpose; where they will be stored; who will be the users at receiving institution; locations for transfer; the period of use; the disposal plan; ownership of any derivatives; ownership of any resulting product, commercial rights and rights to publication; obligation to inform providers of any secondary use; and termination of MTA. The MTA is developed under the governing laws of both countries with regard to liabilities and warranties. In addition, data sharing agreements should be set out clearly between the providing and receiving institutions before work is started. The MTAs currently cover samples that are not human in origin.

---

UNCST registers up to 100 MTAs annually which, it was suggested, is outstripping current capabilities. Help is needed from partners and WHO to build the capacity of researchers in country, including training staff, providing laboratory capacity, etc. The more preliminary research which can be done in Uganda, the fewer samples leave the country and the lighter the demand for MTAs.

Representatives of Médecins sans Frontières (MSF) then outlined their experiences, highlighting three types of MTAs, covering three different scenarios:

- Normal medical care when treating patients, confirming diagnostics etc.
- Engaging in research with partners
- Data sharing policies that potentially include samples, for which there is a specific MTA.

MSF suggested compliance with rules and ethics in countries of origin around secondary use are particularly challenging. They noted legal advisors from recipient countries have reported difficulties in knowing the rules in the country of origin. MSF highlighted that failing to address secondary use can result in harm at community level. They stressed the important of acknowledging this and for all parties to work to and it is their duty to know them.

There is a need to find the right balance between conservation of samples and blocking them forever. The challenges of agreeing the optimal use of valuable samples, for example through a common research agenda, could potentially prevent important research from being undertaken. It is necessary to be creative in this area, and explore different options.

MSF implements a policy for sharing: no IP is conferred unless requested, in which case the burden is on the recipient to make clear their ambitions for the IP. There are many good questions about how to go about this in emergencies, but very few answers. The timing of prolonged negotiations on benefit sharing or IP is incompatible with emergencies, where a case-by-case approach may be impossible. When not in an emergency setting, having master agreements between selected institutions would be useful innovation.

More broadly, benefit sharing should not only cover access to medical countermeasures. MSF would like to go further—for example, giving countries of origin/communities a say in prioritising research. This approach is complex, but the principle is important: prospective not retrospective community input.

**Discussion**

During the discussion which followed, a number of points and opinions were expressed, including:

- Even before medical care and confirming diagnosis, there is a need for MTAs in connection with outbreak investigation. This includes for efforts to sequence pathogens – as well as for surveillance. The latter may be more to do with data material access, but materials may also be relevant.
• A model exists for prospective community input, not in relation to infectious disease but for traditional biobanking. It is based on an IT platform that communicates with donors of samples and continues to do so over time, including in discussions of subsequent use. Donors are consulted both as a community and as individuals. This demonstrates that the idea is not impossible—though internationally it is more complicated.

• Another interesting initiative regarding secondary use is the H3 Africa initiative. Here, three biobanks have an established process for sending samples with related ethics clearance, meaning trail should follow each one. There are existing mechanisms and methods to make sure ethics follow the samples. They have been fed into wider WHO work on sample access and biobanking. They can be hard to negotiate in practice: often pro bono research is done on the understanding that there will be on going benefit for researchers. Initiatives are needed on framing master agreements for secondary use, clarifying what requires ethical clearance from countries of origin.

• There is a current proposal for a liability regime that could apply to MTAs, which takes a tort figure and brings it into IP.

A WHO MTA capacity-building tool

With the presentations having showcased the many established frameworks, participants considered how to flesh out existing models and options and discuss concrete language, options and approaches for a MTA capacity-building tool. The desire for such a tool originates from a shared objective of advancing public health, in particular building capacity and sharing public health benefits where the need is greatest. Building capacity for MTAs can contribute to improving preparation for future emergencies.

Participants felt that such a tool would be valuable and that it should be user friendly, tailored to the needs of countries and stakeholders, in particular lower- and middle-income countries (LMICs), and focused on cases where WHO is not directly involved in sample transfer. It should be developed with the maximum possible engagement of WHO Member States, with a view to advancing public health benefit where need is greatest, and improving preparation for emergencies under the International Health Regulations (IHR).

This work is framed within the R&D Blueprint, which focuses on severe emerging diseases with PHEIC potential that have no current solutions, and thereby frames research through a public health lens. There have been internal discussions at WHO about templates, but the need to take into account all different users, sample types and contexts means that—while there have been calls for templates—such an approach would be challenging.

It was agrees that a tool could usefully provide:

• An introductory overview of MTAs
A guide to overarching principles
Further detail of what is expected in an MTA
The different possible approaches, and how to go about constructing them
How agreements in different areas of an MTA relate to one another.

Such a tool should allow the user to take their own path through the material. Additional functionality might include letting them work their way through an MTA, choosing the approaches best suited to them and compiling them into an illustrative single text (though this would not be intended as a template, and it would have to be underlined that anything it produced would need expert legal review). The work of Chatham House is an excellent example of the level of interactivity required.

Dr Millett explained the projected development process: the first stage was to capture a range of approaches (this meeting). The results would be compiled into a bigger text that examined in turn all the different components of an MTA. This compilation would then be put out for public comment. It would be reviewed, revised and developed into a draft text. The text would then be converted into a digital tool, providing the levels of desirable functionality. In collaboration with Member States and possible end-users, the tool would then be field-tested.

Development of such a tool has been integrated into the R&D Blueprint, which provides appropriate reporting structures and an oversight mechanism for Member States. Participants noted that this consultation took place at the same time as the work of the PIP Framework review group, Conference of Parties to the Nagoya Protocol, and other relevant initiatives. This highlighted contemporary relevance to policy makers of access to samples and data, and the role of MTAs.

Discussion
Engagement and objectives

- The perfect should not be the enemy of the good. It is important to make swift progress – moving from talking about MTA needs to provide tools for use. It is important to have an MTA ready for emergencies in advance of the next event, as there will be little time for discussion or consultation with ministries. GHIA efforts in this regard were duly noted.

- **Involvement of Ministries of Health** (MOH) at operational level is a priority, and engagements from Member States should take place during the entire development process, not only in the testing phase. A process that does not engage MOH will be hard to implement.

- While the next emergency cannot be predicted, some **pre-positioning of MTA agreements** might be usefully attempted, including for specific pathogens (such as the List of Priority diseases under the Blueprint) or for specific at-risk countries. Dialogue with such partners should take place in advance of a major disease outbreak.

- There is need to think carefully about different **levels of engagement**. So far the work of
Chatham House, for example, has been high level—through WAHO and ministries—but engagement at institutional level is also important.

- Ultimately a decision must be made about whether the **objective for the MTA process** is to make it smooth, fast and efficient; or to ensure that it is maximally beneficial to those who most need it. While objectives for an MTA will differ widely, the best outcome will take both goals into account and create a balance that responds to different needs and communities.

- It is important that the MTA process establishes a level of **trust among the participants** where they feel their needs are recognised in the text. This is important also to prevent populations from fearing or misunderstanding research and pushing back; and to prevent stigmatisation of communities. Issues around stigma, violence cannot be ignored.

- While a tool is needed, the **importance of templates** should not be overlooked, and they could be important in an emergency.

### Issues related to commercial models and different beneficiaries

- While in emergencies it is admirable to want to share information and samples, if commercial entities are involved it is unclear how willing they might be to do so. For emergencies a **non-commercial model should be the template**. Subsequent commercial use would require additional negotiation, possibly after the emergency is over. Some participants felt this model would be attractive to most actors. Other participants noted key institutions may be restricted by funders or commercial partners because of pre-existing commitments on commercialization.

- **Non-commercial secondary use is more likely to be widely acceptable**, but there are regulatory issues in many jurisdictions regarding uses of human tissue.

- There is a need to **balance contributions and benefits** - a human sample alone is useful, but a sample linked to clinical data, or part of a series of samples over time, or which is linked with epidemiological data, can be more valuable. The MTA process should ensure that the greater the cost to the donor, the more benefit they receive.

- Concerns were also expressed that if a single laboratory is allowed unrestricted secondary use and attendant IP, then they could potentially effectively define the research agenda.

- Participants felt that the background materials prepared for the meeting reflected the many options for dealing with ownership and licensing of IP, including the possibility of mutual decisions to not seek patent protection for some subject matter.

### Scope and practical issues

- Given its positioning within WHO, the **scope of the MTA tool** might initially focus on the
diseases connected to the R&D Blueprint.\(^2\) This does not include diseases for which there are sizable dedicated programmes, such as influenza, HIV/AIDS, or yellow fever.

- Participants recalled that the Ebola PHEIC taught that while research projects do not start on day one of an epidemic, diagnostics work does and diagnostics means moving a great number of samples. MTAs are therefore important for diagnostics samples. Some participants felt that rapidly reaching agreement on the terms of an MTA for diagnostic samples might be more likely to be problematic than research samples.

- The tool should take into account all possible activities in early investigations, not just surveillance.

### The role of WHO

- The issue of third party beneficiaries provoked some discussion. It was suggested that WHO could play a more active role in mediating or supporting MTA negotiations. The role played by WHO in developing MTAs for the Ebola PHEIC was discussed. It was noted that WHO has limited capacity in this regard and cannot be everywhere to broker negotiations all the time.

- WHO affects MTAs – Participants recalled occasions where WHO and MOH had strongly influenced the use of a particular laboratory for diagnostics. This pre-judged the outcome of (or ability to conduct) specific MTA negotiations.

### Content of a MTA capacity building tool

This session set out to gather a list of specific texts on which the new MTA tool might draw. Suggestions included the following:

- Provisions on managing IP and access to information, including third parties, such as from the Innovative Medicines Initiative (IMI).
- MTAs drawn up by the US National Institutes of Health (NIH) for work during the zika outbreak. Duke University undertook to provide examples.
- Components for developing MTAs from the UN CST website.
- WHO’s own MTA templates, particularly around the Pandemic Influenza Programme (PIP).
- MTAs from Gates Foundation research programmes, and relevant information from its global map project.
- WHO’s on going work on sample sharing agreements as part of the Global Health Security Initiative.
- Wellcome Trust Sanger Institute MTAs.

Participants also consider the use of the creative commons model whereby a legal text is accompanied by layman’s text and simple iconography—a layered approach to making legal text accessible and comprehensible.

Discussion

Fundamental principles

- Practically speaking, the use of MTAs in emergencies is determined by how an outbreak starts. Samples might be needed to identify a pathogen; next use would be surveillance or community screening; then clinical use; then research. **Involvement of countries is important.**

- WHO could consider including narrative on principles as to how certain entities behave in emergency contexts, aiding institutions in considering everything they need to know for negotiations. A helpful approach could be to illustrate different options with case studies or simple examples, but pointing out the most widely used and effective approaches.

- Care must be taken working with organisations that lack the capacity to review contracts. They should be encouraged to take **independent legal advice.**

- **Ethical issues** should not be overlooked. Samples should not be used for research without consent of the communities—that is to say, the patients or family or their legal representatives, or the surveillance population (it could also be argued that the ‘community’ is the local population or even up to national level). The purpose of sample taking is usually not explained to the people in an emergency setting.

- The notion of ‘ownership’ was also discussed. Agreements often contain clauses where ‘ownership’ remains with the country, but some participants suggested this was effectively meaningless. They suggested it is important to differentiate ownership from consent and ethical clearance. It was also noted that when the IP or the samples themselves reside elsewhere, the country of origin claiming ownership led to few tangible benefit being shared.

- There unique challenges to taking, using or sharing samples in an emergency setting, in particular in those associated with informed consent. It may not be practical or possible to go back to the same groups or individuals later to retroactively seek that consent. In emergencies contexts, country level ethical committees should always be consulted in accordance with the Helsinki Declaration.

- **Access** discussions occur repeatedly in the context of MTAs. Concepts of ‘access’ should be examined closely. Like many of the terms in this discussion there is no universal understanding as to their meaning. Access, for example, is connected to affordability, research input, research outputs, and product development. Access might mean lower prices for countermeasures developed using a sample. It can also be connected with fewer IP barriers to generate more innovation, and greater product possibilities. Access issues are intertwined with the IP issues.
• The tool could usefully help to define the types of intended investigations or activities to be conducted with the samples. Participants noted a grey area between surveillance and clinical trials. When samples are being used to enhance surveillance, it will be important to carefully define exactly what activities the outbreak investigations will include.

• Differentiation of commercial versus non-commercial MTAs can be difficult. Some participants felt that it might not be clear from the outset the possible value or utility of a sample.

Intellectual property, different use cases and aligning opposing approaches

• The actual use of some models can be surprising: the example was given of a pharmaceutical company MTA that explicitly excluded IP because it chose not to deal with the associated issues and costs. It is important to analyse what people actually use, then fit the tool to that.

• A specific MTA is needed for emergencies. There should be minimal elements for MTAs in first line emergency uses, and these must include reference to IP, perhaps enabling subsequent negotiations on benefit sharing and IP for any secondary use. This should also address donor communities.

• Options for dealing with IP issues include directly opposing approaches: the supplier retaining all IP, and the recipient retaining all. It would be useful if an MTA tool could help a user understand when differing IP approaches were most suitable. The approach taken so far to aligning competing positions has been to lay out the comparative strengths and weaknesses of different approaches as candidly as possible: for example, saying that while suppliers may want to retain IP, this involves costs, and it requires a budget line and a well-developed IP system at country level. The MTA tool will not to resolve this issue but give countries and users a candid assessment that helps them take their own decisions.

• IP is a means not an end. The choice of benefit sharing agreement can be determined by the desired output, which might be publication; validating a diagnostics device; priority access to diagnostics; etc. IP is only one such benefit, where a commercial benefit is involved. Even if a negotiation is not desirable in an emergency situation, the necessary material should be contained in the tool because it is useful in settings where Member States lack the capacity to address all these issues. It could form a ‘beginners guide’ to IP in this space.

• For secondary use, transparency is a first priority. As it is impossible to predict what IP may be developed later. Some participants suggested that the burden should be shifted. A party wishing to retain IP could be required to explain how it, and the associated benefit sharing, will be managed.

• Secondary use also produces derivative samples or samples outside research. Further consideration of the potential coverage of these samples is warranted, as well as exploration of questions around keeping and preserving such samples.

• Users must address what is most likely to happen with a sample. For example, will it be
maintained separately or be mixed in with other samples subject to different rights and ownership? Several participants felt the former scenario more likely than the latter in an emergency situation. This resulted in sample sets with different donors, possibly from different locations, drawn by different institutions, and even taken under different agreements.

- **Creative approaches** are essential - since the entry into force of the Nagoya Protocol, dealing with benefit sharing is unavoidable. Some participants noted the potential commodification of research, and the detrimental impact this might have on samples sharing, even for public health emergencies. Others suggested that putting off dealing with benefit sharing candidly in a public health context further enhances the asymmetry between some countries, which may lack crucial capacity, and incoming partners which might greater resources at their disposal.

- **Detailed individual informed consent** takes a long time to implement and is impossible an emergency context. There is a need to find a balance between being able to take samples rapidly, and protecting the interests of the donor. Further discussion is required about the correct level of consent and how to obtain it during a public health emergency. Future MTA work must consider how benefits will flow back to the donors.

**Suggested IP solutions**

- There was a suggestion that a given percentage of samples might be stored untouched for potential future uses, without delaying necessary research in the short term.

- Some participants felt that with so many conflicting views, needs, and potential scenarios, it will be difficult to develop an MTA tool that encompasses them all. They suggested that it might be better to focus an MTA tool for emergency purposes. It might also make use of generic terms that everyone knows and understands.

- There is a need to consider retrospective permissions for secondary use, possibly introducing a relevant clause into a tool for emergencies. Some participants suggested that WHO leadership in this regard would help enshrine this as a new norm.

- There was a call to explore approaches used by consortia, where IP is not addressed in the MTA but there is an overarching understanding that although in many cases IP issues may not arise, that all parties will negotiate in good faith if it does. Some participants suggested establishing a panel of expert advisers to mediate any dispute.

- There were suggestions it was not necessary to address IP in an MTA for certain activities — for example, storage of samples. Any secondary use could be submitted to ethics reviews and additional consultations between the signatories over any resulting IP. Some participants suggested that the only IP likely to be generated by activities in the early stages of a public health emergency might be patent protection for the gene sequence of a pathogen. There was broad support for an agreement not to seek IP protection on these sequences. This would require a bright line between what parties are authorised to do and any potential secondary
use, including developing diagnostics. It would be important for relevant parties to come together early and create specific agreements as to what will be done with the samples.

- Several participants felt that addressing IP was not as simple as whether it was present or not but that a the tool should present a range of options for address IP issues. A two-step process was suggested: the first step would be to conclude an MTA in the case of emergencies covering no secondary use or IP provisions; the second, separate step would be to discuss further use and IP. Other participants argued that countries might not agree to this, as there were cases where researchers have often failed to act in good faith in the past.

- Alternative IP solutions must be sensitive to any disadvantages suffered by LMICs.

Data sharing

- There was a general understanding that WHO has legitimacy in the area of data sharing in public health emergencies that nobody else does. The meeting heard of separate streams of ongoing activity within WHO. WHO is also considering several different types of data relevant to public health emergencies. WHO will be working on data transfer agreements (DTAs) as well as MTAs. Several participants suggested it might prove more straightforward to develop a DTA template than a MTA template.

- There was also broad support to ensure that any MTA must recognise that there will be data associated with physical material. As a result, work on DTAs and MTAs will are closely connected, and at some point will surely converge, but are separate topics. There was an understanding that this consultation would not address data sharing in the absence of physical samples.

- A number of participants noted, however, that it would be unwise to decouple respective discussions of data transfer and material transfer completely and that thinking about data and samples must remain connected. MTAs can be used to transfer clinical data for samples already given. They could also theoretically be used to transfer data only, for example covering Genome Sequence Data. Data aspects should therefore be covered by MTAs.

Next steps

WHO will use the opinions expressed during this consultation, the output of earlier consultations on the topic, as well as inputs provided by interested parties (such as additional materials highlighted in this report) to develop an initial draft of a MTA capacity-building tool. This draft will be released for public comment. A revised draft will be fed into and reviewed by a WHO consultation on biobanking and sample sharing, planned for 2017. A second round of revision may be required after this consultation. The resulting tool will be ‘beta tested’ with potential end users.
While the R&D Blueprint focuses on emergencies, participants urged WHO not to wait until the next emergency to try the tool out in practice. They stressed the importance of seeking feedback from end users and Member States as soon as possible. This, they noted, will probably mean initial use in non-emergency situations. Appropriate language, text and approaches suitable for use outside emergency settings will be useful.

Discussion

Suggestions for testing and validating the tool

- The draft tool should undergo an ethical review – a review by the WHO Ethics Team was suggested, as were the review boards of African countries—both those accustomed to research, like Uganda, and those less so.

- There should be test runs in different countries and institutions, in order to acknowledge all different contexts in which a tool might be used, such as financial ties, different oversight systems, etc.

- Testing of the tool should prioritise research that has an impact on the patients treated and their communities.

- There must be careful consideration of how to advance dialogue without forestalling the political acceptance of the tool. One approach would be to draft guidelines, principles and timelines, and to include expositional text about the emergency context.

- Some participants highlighted risks associated with jumping the gun. They warned against attempting to develop template MTAs without a strong enough tool. The stronger, more inclusive and more robust the tool, the greater confidence there will be in any MTA it generates.

The meeting closed with brief statements from Mr Burci and Dr Khelef.
Annex: Meeting agenda

08.30-09.00 Registration & coffee

09.00-09.30 Opening Session
09.00-09.15 Welcome remarks (Institute Pasteur)
09.15-09.30 Introduction to the informal consultation and overview of goals for the day (WHO)

09.30-10.45 Working Session 1: Context and ongoing work on MTA development
Review of the process to date and introducing background material (WHO)
Review of past meetings (Wellcome Trust)
Review of template development (Chatham House)
A guide to global health alliance agreements (Duke University)
MTAs in practice (Institut Pasteur)
OpenMTA (BioBricks Foundation)
Directed discussion

10.45-11.00 Coffee

11.00-12.30 Working Session 2: A draft MTA guidance tool: a starting point
Issues and challenges in MTA formulation during public health emergency
Group discussion on:
- Gaps/challenges to be addressed in MTA formation during a public health emergency:
  - Capacity of the parties, national legal systems, emergency circumstances, diversity of partners, etc.
- What went wrong, what can we do?
- What steps should be taken to address these?

12.30-13.30 Lunch

13.30-15.00 Working Session 3: improvement of the draft MTA capacity building tool
Group discussion on how to present practical options in the MTA tool and make linkages to the following areas:
- Ownership and custodianship of samples and materials
- Benefit sharing
- Intellectual property
- Onward use
- Derivatives
- Access to eventual products
Summary – validation of approach

15.00-15.30 Afternoon tea

15.30-17.00 Working Session 4: development of next steps
Group discussion on:
- How the MTA tool will be used
- Existing examples of language/principles for MTAs
- Building acceptance of principles before the next public health emergency
- Making the MTA tool useful to developing country partners
- Concept for pilot testing of MTA tool in select countries
- IT / multimedia architecture for MTA tool

17.00-17.30 Closing Session
Concluding remarks