This short document reports on the Operational Research (OR) work conducted over the past 18 months by the Department of HIV/AIDS and the UNICEF/UNDP/World Bank/WHO Special Programme for Tropical Diseases Research and Training (TDR).

It gives information about the overall "learning by doing" strategy regarding the evidence needed to inform treatment and prevention programs. It reports on the activities that were conducted to facilitate priority setting and the involvement of teams from national programs, and on efforts to develop tools for operational research in multiple settings. It also reflects on achievements to date and next steps.

It is hoped that the work done to date in selected countries will be used as a basis to expand to others. The document should be useful to staff in country who are interested in how to gather the evidence needed to improve treatment and prevention programs.

Outline of this Report
1. OR Strategy
2. Defining a framework for OR
3. Priority setting for OR in 5 Countries
4. Generic Tools to facilitate OR
5. Achievements and Challenges

1. OPERATIONAL RESEARCH STRATEGY

The overall Operational Research (OR) strategy adopted by WHO, in collaboration with TDR, seeks to address the longstanding challenge of linking research to policy in the emergency context of the HIV epidemic, and to provide rapid evidence to scale-up and improve programs. Much has been written about operational research and there are numerous definitions of what it is or should be. Rather than engaging in lengthy discussions about exact definitions and terminology, a pragmatic decision was made to draw on the recent US Institute of Medicine's statement, and refer to operational research as the use of analytical techniques to define optimal processes of delivery, achieve better outcomes through evidence-based approaches, and provide more cost-effective care.
Operational research is a central element in the "learning by doing" approach to scaling up treatment and prevention. This notion recognizes that incomplete evidence should not constrain scale-up, provided that efforts are made to actively monitor what is happening in countries, learn from comparisons of different programs and policies, and inform decisions. In line with the "three ones" unified strategy endorsed by WHO and partners, the operational research agenda is collaborative; it involves partnerships among agencies and multiple stakeholders, including national country programs, and associations of People Living with HIV AIDS (PLWHA). It is designed to guide collective efforts, with WHO playing the role of facilitator, convenor, or catalyzer.

Priority is given to research that has direct relevance to programs, and can be applied widely; and while speed of implementation is crucial, the evidence should also make it possible to conduct longer-term evaluation of programs and policies. The research agenda has to be defined in light of the public health approach to treatment and prevention scale-up promoted by WHO: effective and equitable treatment provision to those who need it, especially vulnerable and high risk groups; treatment scale-up in the context of primary and chronic care disease management; simultaneous efforts to scale-up treatment and accelerate prevention; and strengthening, not weakening, existing health systems. In addition, two principles have guided the operational research strategy: that research be multi-disciplinary; and that ownership rest with local partners, especially National Control Programmes who ensure its sustainability and integrate its results into policies and programs. Beyond these principles however, much work is needed to identify the most appropriate methods, formulate questions, implement the research, and ensure that its results help improve programs.

2. DEFINING A FRAMEWORK FOR OPERATIONAL RESEARCH

An expert consultation convened by HIV Department and TDR, in Geneva in July 2004, brought together about 30 participants from different countries and disciplinary backgrounds. It discussed a framework to define priorities for operational research and endorsed a multidisciplinary approach, in recognition of the multiple factors that influence scale-up, and in light of evidence showing that many of the important questions are at the intersection of disciplinary areas.

The scope of the evidence to be generated by OR is defined in light of the objectives of HIV programs, namely:
- Improving treatment and providing medicines to those who need them
- Dispensing ARVs and supporting adherence
- Optimizing the consequences of treatment for individuals and communities
- Strengthening health systems

These objectives cut across disciplinary boundaries, and OR should use joint methodologies that are not discipline-specific, such as rapid appraisal, aimed at identifying problems; repeated household or facility surveys; comparisons of treated/untreated individuals, of different approaches to treatment support, or of treatment outcomes in different groups; triangulation of data from multiple sources, including existing information. Different phases of scale-up call for different research strategies: intensive country projects initially, followed by multi-country initiatives, focused studies in additional countries, and further cross-country comparisons.

Even as they use discipline-specific concepts and methods, OR projects should consider the multiple dimensions of scale-up, specifically:
1. Individual, community and social factors
The involvement of individuals and communities is a critical component of ART and prevention programmes. Evidence is needed on health resources and therapeutic networks; the social implications of guidelines for treatment and prevention; the quality of services as seen from the point of view of patients; the factors that facilitate or hinder the uptake of testing and adherence to recommended regimens; the influence of stigma; and the critical link between prevention and treatment.

2. Economic questions
The question of incentives—broadly defined as the prices, costs and benefits, that influence decisions by providers and patients—defines a rich agenda for economic analyses, including how to promote compliance with treatment and prevention guidelines on the part of providers and patients; the cost of ARV programs; the impact of expanded treatment on household economics; the differential access of some individuals and groups to medicines, care, and follow-up; and the cost-effectiveness of different clinical guidelines, care strategies, and interventions.

3. Health systems concerns
The integration of treatment into primary health care systems raises questions of human and financial resources, task shifting, as well as changes in the quality of services, and impacts on other disease programs and the health system as a whole. Evidence is needed to assess the implications of these changes and on the extent to which access is expanding while quality is maintained. Periodic comparisons of different parts of the system and different sorts of public-private partnerships are also needed.

4. Clinical regimens
As ARV regimens are implemented in diverse settings, it is necessary to assess the appropriateness of guidelines for treatment initiation and switching and for the management of opportunistic infections, toxicity and comorbidities. This is especially important since diagnosis, counseling, initiation of treatment and patient monitoring often have to be done at primary health facilities, and in conditions of scarce human and material resources.

3. PRIORITY-SETTING FOR OPERATIONAL RESEARCH IN 5 COUNTRIES

A key principle that has guided work on operational research (OR) for HIV is to encourage country ownership and to embed OR activities in National Control Programmes. The process of priority setting should be informed by inputs from multiple players, including national programmes, national research institutes, international donors, technical agencies, academic institutions, and NGOs, including PLWHA associations. Multi-stakeholder workshops should be initiated before research begins and subsequently take place at periodic intervals, with the goal of adapting the research agenda, sharing the interpretation of results, and jointly deciding on action. As research capacity in many member countries is limited, capacity has to be built and technical assistance provided, particularly in the early phases of the work.

Thus, the second phase of the OR project sought to involve teams from selected countries into the process of defining priorities, along with other partners. A pragmatic approach was adopted in view of available resources, and a decision was made to select five African countries and begin implementation. The countries selected for the first phase are Burkina Faso, Malawi, Tanzania, Uganda, and Zambia, a choice that was based on a number of factors, including discussions by WHO, TDR and UNAIDS, the presence of an HIV officer in the WHO country office, geographic and linguistic diversity in Africa, and local capacities to undertake OR. While recognizing that no process of selection could be perfect, it is hoped that these countries represent the first wave, and that work will expand to other countries after the approach is refined and further resources obtained.

A workshop organized in Kampala by HIV Department, TDR and UNDP, in December 2004 brought together teams representing national programs and non-governmental organizations in
the selected countries; experts who would act as facilitators; and partners who would be interested in supporting operational research. The objectives of the workshop were to set priorities and to start the development of OR proposals. In the course of the meeting, each of the country teams began to draft the elements needed for a proposal, while experts acted as facilitators.

The diversity of topics selected by the country teams reflects the particular concerns of national programs, for example the fact that in both Burkina and Uganda, there is a multiplicity of providers of ARVs, with the resulting potential for fragmentation and uneven quality of care; the shortage of health workers and the problem of silence around HIV in Malawi; and the missed opportunities to provide testing and treatment at existing entry points, as is the case in Zambia. At the same time however, some themes were shared by all proposals: the adaptation of clinical regimens to various populations and in the context of overburdened health systems; the need to measure adherence and support it; improving access and the quality of testing and care as a basis for scaling-up; making better use of various entry points and coordinating the different services that can contribute to scale-up; and obtaining a clear view of how the system as a whole functions around HIV treatment. Also common across country proposals is the effort to consider medical and socio-economic factors in an integrated way, and the preference for phased approaches to implementation, starting from situational analyses, and later focusing on specific themes.

Following the workshop, a Product Development Team (PDT) was formed, consisting of national program managers, researchers with expertise in HIV in multiple settings, and partners who may have an interest in funding operational research. The team's mission is to provide oversight and support, promote cross-country exchanges, review final proposals, advise on disbursement of funds for OR activities, and discuss cross-cutting issues, including the need for capacity building and the next steps of this initiative at the level of the 5 countries and beyond.

Between December 2004 and April 2005, the 5 country teams worked to develop full proposals, a process that required a broad consultation of stakeholders within each country, the provision of technical support on the part of WHO, and the facilitation of exchanges between experts and country team. The PDT found that the submitted proposals were at different levels of advancement, and required different sorts of inputs in order to be suitable. Proposals were approved pending the presentation of revised protocols by the country teams, in light of the consolidated comments sent to the principal investigators. Revised proposal were subsequently reviewed by members of the PDT and went through the ethical review process at the national level and at the WHO Ethics Review Committee. By the end of 2005, all proposals were revised, and funds were disbursed for four projects, with the fifth about to obtain final clearance.

- Burkina Faso developed a participatory research project on treatment and care practices, aiming to improve coordination between NGOs and public healthcare facilities providing care for HIV positive persons
- Malawi's objective is to improve uptake of voluntary counselling, testing and treatment by healthcare professionals in a country where lack of human resources is a bottleneck to scale up;
- Tanzania's operation research effort will focus on adherence to ARV treatment, with the objective of developing a national tool to routinely evaluate adherence and determinants;
- Uganda will study adherence and prevention support in the different models of care provision co-existing in the country, with the aim to identify and generalize good practices.
- Zambia seeks to identify constraints to ART uptake in TB and ANC clinics, in order to facilitate access in these settings.
The process of proposal preparation has brought together colleagues who would not otherwise have had the opportunity to work collectively on HIV treatment scale-up. The project has linked program managers, researchers, and NGOs. It has mobilized their energies to define issues that would help improve programs, and encourage discussion of the needs for evidence and the best way to collaborate to obtain the needed information and feed it back to programs. Participants in this project have conveyed their satisfaction that WHO was taking the lead in this area and was proposing a way to proceed that was technically sound and attentive to country concerns. Country teams recognized the value of the priority-setting exercise and the relevance of other countries' proposals to their own national situation. They valued the fact that the proposed OR agenda accommodated both country specificity and common themes, and that it would provide an opportunity for exchanges with colleagues from other countries.

While it is clear that many more countries need to be brought into the process, the work done thus far holds the promise that expansion will be easier and faster when the project is taken to other settings.

4. GENERIC TOOLS TO FACILITATE THE IMPLEMENTATION OF OR IN COUNTRIES

To support operational research in the selected African countries, and to expand it beyond these five countries, it is essential to enhance local ability to collect and analyze data on key topics related to scale-up. In addition, the "learning by doing" approach requires that public health strategies to scale-up treatment and prevention be reviewed, evaluated, and revised in light of the circumstances in different settings, and that comparisons across settings be carried out in order to measure the impact of ongoing initiatives and identify problems and "best practices." One of the main stumbling blocks to the implementation of OR is the lack of tools to collect and analyze data. Numerous individuals and groups have developed instruments on a variety of topics relevant to HIV, but these have not been systematically reviewed and compiled. Most countries therefore do not have readily accessible ways to collect and analyze information to improve programs, and comparisons across settings are limited. Thus, support is needed to define the essential information to be collected, formulate the best methodologies for operational research, and provide technical support during implementation and analysis. To facilitate countries' efforts in this area and foster comparative analyses, WHO has initiated a process to produce a set of tools that are informed by the latest research, cover essential questions, and at the same time, can be adapted to country circumstances.

The notion of generic tools refers to standardized approaches to data collection and analysis (tools refer to the entire process, which includes preparation, training, adaptation, and support, while instruments refer to the actual data collection and entry devices, for example questionnaires or records, or observation checklists). Tools are developed in light of global advances in research, and are designed to foster unified approaches to data collection and comparisons across settings. They take into account local circumstances and lend themselves to country-specific adaptation. They combine quantitative and qualitative items, and include core and country-specific sections. Based on previous discussions of OR priorities with experts and with colleagues in countries, several issues have been identified, which are pertinent across settings and call for the development of generic tools. They include:

1. Adherence
Measures of adherence to ART, investigations of its determinants and its association with clinical outcomes are key in order to formulate appropriate interventions to ensure high adherence. This in turn requires the collection of socio-economic, behavioral and, when possible, biological and clinical data among patients on ART; it also requires ways to elicit the perspectives of the patients.
themselves. Much work has already been conducted on the measurement and determinants of adherence, and this is an opportune time to identify the essential information needed, and the most efficient ways to collect it.

2. Equitable access to care, treatment, and prevention
Ensuring that available resources are provided equitably and follow national agreed-upon criteria requires information on the extent to which different populations avail themselves of existing testing and counselling, treatment, and prevention services. Analyses of the determinants of uptake—whether they result from economic or social factors, or from the characteristics and quality of health services as a whole—will help throw light on the extent to which different models of care provision contribute to scaling up. Household level data can help assess the burden represented by the cost of HIV infection and its treatment, the impact of treatment at the individual and household levels on employment and other social and economic activities, and the incentives that influence the use of services.

3. Links between treatment and prevention
This is a multi-layered topic that can be examined at the level of individuals, health facilities, and the community. Specifically, several issues can be investigated: the extent to which risk behavior differs among those who know their status compared to those who do not, and among those on ARV treatment compared to those who are not; the degree of integration among testing, treatment, and prevention services; the extent to which the increased availability and use of testing and treatment services is associated with changing risk behavior.

4. Costing of treatment and prevention
The economic information generated at health facility levels complements that obtained through existing 'top-down' resource tracking mechanisms such as National Health Accounts. The regular collection of information on the use and cost of HIV therapeutic, laboratory, and preventive services makes it possible to estimate costs at the level of health facilities, to aggregate them at sub-national and national levels, and to estimate working budgets at these three levels of the health system. Regular comparisons of the disbursements, expenditures, and requirements can facilitate the measurement of the cost-effectiveness of selected interventions, programs and health services.

Some of these questions require data collection at several points in time, but they can all be examined using similar sources of data: surveys of the general population, vulnerable groups, users of services, or health care personnel; surveys on HIV+ individuals and the general population to investigate reported changes in perceptions and behaviors; and health facility surveys to assess the extent to which services for treatment and prevention are integrated, functioning, and effective.

On January 16-18th 2006, a meeting was held in Geneva, on Generic Tools for Operational Research on Scaling-up HIV Treatment and Prevention. The meeting brought together about 45 individuals, including representatives from countries, NGOs, and PLWHA, international bi- and multi-lateral organizations, academic institutions in countries of the North and South, and organizations that develop and/or support the development of data collection and analysis tools. Participants worked mainly in working groups to clarify the scope of the necessary information on the topics that were selected as key, namely adherence, access to treatment care and prevention, links between treatment and prevention, as well as the costing of services. They also began to draft questions that would be part of instruments, and considered the implementation of OR using generic tools by countries. Following the meeting, a report will be produced, including the revised instruments, recommendations regarding key components and questions, and guidance to those who wish to conduct operational research.
5. ACHIEVEMENTS AND CHALLENGES

The implementation of the OR agenda over the past 18 months reflects the challenges that are inherent in collaborative, multi-disciplinary projects. On the positive side, it has been possible to bring 5 country teams into the process of priority-setting, proposal development, revision, and ethical review. Teams have been put together, and have engaged in broad multi-stakeholder discussion of OR priorities and implementation, and Ministries of Health in the respective countries have shown greater interest in, and support for, OR. Clear plans have been developed and agreed upon, bringing together colleagues from ministries, research institutions, international organizations, and non-government organizations.

The process however, has not been as rapid as hoped, especially in view of the urgency of putting in place mechanisms to keep track of what is happening to treatment and prevention in countries. Some of the challenges that delay the implementation of OR for HIV are similar to those that limit the conduct of research in general and multi-disciplinary research in particular: in resource-poor settings, capacity is limited, access to tools is difficult, incentives are negligible, so that proposal preparation, team mobilization, and ethical clearance inevitably take a long time. Delays also reflect the need to build local capacity and to weave links among local stakeholders. Constraints on human resources, both at Headquarters and in countries, make it difficult to focus energies single-mindedly on OR, when other urgent tasks compete for priority time. Sustaining efforts over time will require creative solutions to the human resource constraints faced by all. While funds have been secured to kick-start a process in 5 countries, additional resources are needed to sustain the momentum in these countries and to expand to others. To scale up OR, it is also necessary to foster the exchange of knowledge across settings, to support activities to disseminate lessons across countries, and to encourage comparative analyses. These will, in turn, require human and financial resources that need to be identified.

In order to discuss priorities and future directions for OR, an informal three-hour consultation was held in November 2005, with selected members of the Department and others within WHO HQ working on OR in HIV, including Stop TB, Child and Adolescent Health, and representatives of The Global Fund and TDR. The discussion and recommendations from individual attendees suggested that WHO's comparative advantage is that it supports countries, is trusted to play a convening and normative role, and can successfully bring together country and international expertise. The group also reviewed a number of individual projects that could be considered in the next phase of the work. All participants concurred that WHO should play a role in facilitating OR both within countries and through cross-country comparisons. They also recognized the need to balance priority setting from HQ with attentiveness to country concerns, and the limited resources in countries to develop an agenda and implement OR. Multi-country protocols and generic tools are seen as a promising way to facilitate country efforts while making it possible to learn from comparative analyses about best practices.

The demand for OR appears to be growing, both in countries, and as expressed by international organizations: for example, the Global Fund has made support for OR an explicit part of proposals, and the US government supports Targeted Evaluation in the countries that are part of the PEPFAR initiative. Given the multiplicity of frameworks, approaches, and tools, there is a clear role for WHO to bring together different players to agree on the essential information that is needed and the most appropriate methods to collect and analyze it. The Generic Tools project is designed to contribute to this goal. But greater clarity and more resources are needed to ensure that OR is systematically included in global initiatives and is implemented by countries, and that
some standards are agreed upon so that these efforts yield projects of acceptable quality, and results can be compared across settings.

How to ensure that the OR agenda continues to reflect global and local priorities represents another important challenge over time. There is an acute need for evidence to compare different service delivery models and assess the relevance of guidelines to scale-up treatment and prevention (many of which are based on expert opinions only). This calls for OR that is not directly tied to individual country context. Moving forward on this global OR agenda, while at the same time sustaining the collaborative process of implementing OR for country priorities calls for a delicate balancing act, as well as greater resources and the support of multiple partners. It is however, a necessary condition to ensure the continued relevance of Operational Research to HIV treatment and prevention.

For further information about the Operational Research work of the HIV Department, please contact Dr Yves Souteyrand souteyrandy@who.int.