Message

The year 2000 was indeed momentous. The dawn of a new century, also marked by the publication of the human genome and the adoption of the Millennium Development Goals. A new dawn also rose in TDR, culminating in the adoption of a new five-year strategy reflecting the changes in the world around the programme. A constructive re-moulding of activities to better fit prevailing needs and changing global economic, political and scientific environments.

I wholeheartedly endorse the creative vision and achievable goals detailed in TDR’s Strategy for 2000-2005. The period covered in this report, 2001-2002, represents the successful initial transference from ideas into practice. TDR’s role is to empower and enable, with the added task of generating, embracing and applying new knowledge. TDR is continuing to play a leading role in discovering and exploring the grand new opportunities opened up by advances in science and technology, particularly in the exciting and highly promising genomics and bioinformatics fields. Moreover, the directed move into implementation research, and a renewed focus on socioeconomic and behavioural research, shrewdly presaged the massive global initiatives which have recently been established in these areas. These moves can ensure that new products generated through TDR’s and others’ product development research can be placed in their appropriate contexts.

Research is not always visible, and often does not have ‘immediacy’. Results may take years to manifest themselves, and I commend the programme and its committed donors for continuing their work. But research remains essential if goals are to be achieved. TDR is an integral instrument in global health. Naturally, the programme’s pioneering history in setting up private sector/public sector collaborations has stood it in good stead, and been a model for others, in establishing innovative, value-added public-private initiatives. Again, in the new century, a new working framework, a collaborative, holistic, multidisciplinary approach, will be essential if we are to achieve the goals that we have set ourselves, upon the achievement of which millions of lives will depend.

To reach our goals, barriers will have to be broken and difficult pathways traversed. We will need to engage those living with and dealing with diseases on a day-to-day basis, to use their intimate knowledge to help set suitable agenda, and help accelerate development of acceptable, appropriate and affordable solutions. To obtain that knowledge, and to use it, apply it and disseminate it wisely and equitably, we will need to make the most effective possible use of information and communication technologies and advances, and TDR has confirmed its commitment to do so in its forward-thinking agenda. We will also need to continue to make best use of knowledge, tools and technologies, wherever they are found or generated.

The Millennium Development Goals call for the creation of a sustainable ‘global partnership for development’. TDR and WHO will continue to be active in such a partnership.

Dr Gro Harlem Brundtland
Director-General
World Health Organization
Foreword

As I write this, looking back at the period covered by this report but mindful of the recent outbreak of the SARS virus, I am reminded of the crucial importance of research in modern-day public health. Someone, somewhere, needs to be continuously working to discover solutions to problems like SARS that we may not yet have encountered, and to devise better means to tackle those health challenges we face on a daily basis. Knowledge remains the greatest power in the search for solutions to public health problems. It is the greatest remedy for any disease. Yet we cannot start research when an epidemic is upon us. We must plan, be pre-emptive where we can, and build up a bank of knowledge and cadre of trained personnel and expertise to bring to bear as and when needed. As this report confirms, TDR has been and remains a leading player in this respect. Without the contributions of TDR, it would have been impossible for control efforts to move four of the programme’s target diseases (Chagas’ disease, leprosy, lymphatic filariasis, onchocerciasis) to the point where they should soon be eliminated as public health problems.

After 27 years we know what TDR can offer. A recognized and well-respected name and trusted status, allowing the programme to bring together partners that may otherwise never collaborate. The power to convene the best minds and ideas in a truly global agenda-setting enterprise. The ability to organize extensive, large-scale field trials in disease-endemic nations. A base of extensive knowledge and profound understanding of its target diseases, and recognition of the need to develop the infrastructure in disease-endemic countries necessary to be able to cope with whatever nature throws at them.

As readers of this report will learn, TDR has revised its working methods, ever cognisant of the needs of its end-users. It has embraced new technologies and novel operating practices, and harnessed some of the world’s best and multidisciplinary minds to help prioritize work in the most cost-effective and high-impact manner possible. This has created a new strategic emphasis model that has been widely embraced by both the scientific community and those who finance public health and the production of public goods.

There is a common adage: ‘Science discovers, Industry develops, People implement.’ With its new steps into implementation research, TDR is now facilitating research and training across almost the entire spectrum of health sector activities. You will read in this report the story of miltefosine, a prime example of how the system can and does work, to produce, in this case, a novel, highly-appropriate therapeutic drug for one of the world’s neglected diseases, leishmaniasis. Like anything else, however, the system does not operate where there is no power to drive it. And the resource-poor,
marginalized communities who suffer the heaviest burden from infectious diseases have little empowerment. TDR helps to give them a voice. Helps to ensure a comparatively few but nevertheless essential resources are devoted to their problems; helps them to influence global agenda; helps identify research that holds the greatest promise for producing urgently needed practical and applicable tools. And in the case of community-directed treatment (ComDT) for onchocerciasis and lymphatic filariasis, helps them to devise solutions to their own problems, take their health care into their own hands, and pay for it themselves. Indeed, ComDT heralds a possible revolution in primary health care in Africa, and TDR is pressing ahead to see if the goal can be realized.

The example of miltefosine shows how TDR is eminently capable of taking an idea and, mustering the competitive advantages of selected partners, shepherding it through the discovery, development and implementation stages, to finally provide a novel, greatly-needed health intervention tool that is acceptable, appropriate and affordable. Miltefosine is not the first such example. And it will not be the last. This report confirms that there are many more in the pipeline.

In the foreword to the 15th Programme Report, I mentioned TDR’s first ever resource mobilization meeting in Paris, 2001. The promise and enthusiasm expressed by all who attended that meeting have not yet been translated into suitably increased resources for the programme, and TDR must redouble its efforts in an ever-increasing competitive environment to secure the funds it needs to do justice to its well-considered plan of work. TDR will need to continue to work hard to retain the level of support from its long-term donors. It may have to proactively investigate options for expanding its co-sponsorship base and other innovative partnerships. Moreover, it will need to reposition itself in relation to new ‘competitors’ on the global stage in light of the funding strategies and largesse of new non-governmental, private sector funding agencies.

Finally, I cannot but return to the example of the SARS outbreak. While control methods can and will be found for almost all infectious diseases at some point, we can also depend on the fact that diseases will change their manifestations according to social and environmental circumstances. Threats to our health are, and will be, inescapable. One of the world’s most renowned scientists, Louis Pasteur, once remarked “Chance favours the prepared mind”. Through its research and training activities, as this report shows, TDR is helping to prepare a collective of minds, skills and technologies, giving us the opportunity to put knowledge and capability to good use when it is most needed.

David L Heymann
Executive Director, Communicable Diseases, World Health Organization

Threats to our health are, and will be, inescapable.
Introduction

The 2001-2002 biennium was an intense period for TDR. The TDR strategy for 2000-2005, endorsed by the Joint Coordinating Board in June 2000, had to be implemented and this would mean profound changes in the structure and management of TDR:

- starting activities in the new areas of implementation research, tuberculosis and dengue, while keeping the traditional areas of work on track.
- moving from process-oriented to results-driven planning, budgeting, management and evaluation.
- adopting a disease-function matrix management, requiring the active participation of, and constant interaction between, functional coordinators and disease research coordinators.
- moving the Research Capability Strengthening area (RCS) to programmatic, research-driven training and capacity building.
- evolving the scientific guidance of Intervention Development and Evaluation (IDE) from eight task forces to two steering committees (Proof of Principle and Implementation Research).

The strategy had indicated the new directions for TDR but detailed workplans, roadmaps and timelines still needed to be worked out. Therefore, no wonder this represented a major challenge to the Special Programme and its staff.

Challenges, however, are opportunities for change and evolution. Although TDR was recognized as an efficient and performing Special Programme, we knew it still had enormous and untapped potential for growth and improvement. The implementation of the new strategy, therefore, was not dealt with as a routine operation; it rather triggered an unparalleled period of reflection, analytical work and discussion that generated the intellectual and operational bases for the present phase of TDR’s life.
TDR belongs to Pasteur’s quadrant

In his seminal work, Donald Stokes re-examined the role of basic science in technological innovation and the perceived tensions between understanding and use as goals of research. He challenged the post World War II paradigms emanating from Vannevar Bush’s famous report to the President of the United States, which implied an inherent separation of basic and applied research and saw basic research as the pacemaker of technological progress. Stokes questioned this linear paradigm saying “It is no longer believed that a heavy investment in pure, curiosity-driven basic science will by itself guarantee the technology required to compete in the world economy and meet a full spectrum of other societal needs”.

Stokes found it impossible to draw a sharp line between basic and applied research. He elected Pasteur as the example of a scientist whose work encompassed both “pure” and “applied” science and therefore could not be located on the classical one-dimensional basic-applied spectrum. He proposed a new model – the “two dimensional conceptual plane” – to rescue the importance of “use-inspired basic research”, or strategic research. Stokes’ plane is divided into four quadrants delimited according to whether the research and development (R&D) addresses understanding [yes/no] and use [yes/no]. To illustrate his thesis, he correlates each quadrant with a person whose work symbolizes the type of research proper to that space of the plane: Niels Bohr [quest for understanding? yes; considerations for use? No], Louis Pasteur [yes;yes], Thomas Alva Edison [no;yes] and Roger Tory Peterson, author of a well-known bird catalogue [no;no] (Fig 1).

The TDR strategy for 2000-2005 firmly locates the Programme in Pasteur’s quadrant, where it needs to address both the understanding and use of research, and where it is strategically located to interact with the two forces coming from neighbouring quadrants:

- **Push:** scientific discoveries and technological breakthroughs relevant to the development of new health interventions, generated by universities and/or R&D institutions working in Bohr’s quadrant, where the priority is the understanding of biological phenomena.
- **Pull:** disease control needs for new interventions, methods and approaches, requested by ministries of health and health systems working in Edison’s quadrant, where the priority is on the use of R&D findings.

---

1 Morel CM. Reaching maturity – 25 years of the TDR. *Parasitology Today*, 2000, 16(12):522-528


Considerations of use?

- **NO**
- **YES**

<table>
<thead>
<tr>
<th>Quest for understanding?</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NO</strong></td>
<td>Niels Bohr</td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td>Louis Pasteur</td>
</tr>
<tr>
<td><strong>NO</strong></td>
<td>Roger Tory Peterson</td>
</tr>
<tr>
<td><strong>NO</strong></td>
<td>Thomas Alva Edison</td>
</tr>
<tr>
<td><strong>YES</strong></td>
<td></td>
</tr>
</tbody>
</table>
TDR priority-setting: the strategic emphases matrix

Any organization funding R&D, no matter how large or small its budget, should have clear ideas and guiding principles on how to establish its priorities. During the 2001-2002 biennium, TDR developed a new approach to priority-setting, summarized in its “strategic emphases matrix” (Fig. 2), which addresses two dimensions:

- The disease: the ten diseases in the TDR portfolio were categorized into three groups according to epidemiological trend and appropriateness of existing interventions.
- The functional area of work: TDR R&D activities were distributed in four areas corresponding to the main stages of the R&D pipeline – knowledge generation, development, testing of new interventions, implementation of new interventions.

This disease-function matrix provided a platform for the priority-setting process. The published matrix was the result of analytical work carried out during the biennium and involving the TDR functional coordinators.
and disease research coordinators as focal points while tapping into the expertise of TDR scientific committees and disease control programmes. The final version, approved by TDR’s Scientific and Technical Advisory Committee (STAC), lists the R&D priorities for each disease and stage of the R&D pipeline, and took into account, inter alia:

- **The disease category**: diseases of group I, which lack cost-effective interventions, require more emphasis on the upstream stages of the R&D pipeline; diseases of group III, on the contrary, require more attention on downstream R&D, e.g. how to make better use of the available tools.

- **The scientific opportunities**: scientific and technological advances have to be continuously monitored as they can lead to new interventions, e.g. the sequencing of the *Plasmodium falciparum* genome allowed Jomaa and collaborators to discover the antimalarial action of the herbicide fosmidomycin.7

---


5 Group I: African trypanosomiasis, dengue, leishmaniasis; Group II: malaria, schistosomiasis, tuberculosis; Group III: Chagas disease, lymphatic filariasis, leprosy, onchocerciasis (see Remme et al 2002).

6 Area A: New basic knowledge; Area B: New and improved tools; Area C: New and improved methods; Area D: New and improved strategies and policies.

The matrix, which will be revised annually by STAC, should be seen and used as a roadmap or city plan that helps the decision-making process but does not impose one unique path or indicate one place to visit. Once the matrix is ready, additional elements have to be considered during the next steps of the priority-setting process:

- **Available resources:** the budget level and availability of human resources are basic determinants of the projects that TDR can fund and manage.
- **The disease burden:** the TDR budget is shaped towards a direct relationship between level of R&D investment and burden of disease.4
- **TDR comparative advantage:** TDR should concentrate its actions in areas where it can make a difference, where there are no other players, or where its leadership can mobilize the expertise needed for a given project.
- **Product development time frame:** the TDR product portfolio should be balanced and include projects of short, medium and long-term duration, a requirement for a healthy and sustainable R&D pipeline.
- **Capacity building and institution strengthening opportunities:** emphasis is given to projects that will “leave something behind” – which our trainees and principal investigators refer to as a characteristic of TDR action – in terms of human resources and institutions of disease endemic countries.

---

*Immunology laboratory, Pasteur Institute, Tehran: research students with Dr Sima Rafati (centre back), a leading TDR-supported researcher who was recently awarded a UNESCO medal in recognition of her outstanding work.*

*Photo: WHO/TDR/Crump*
A results-driven organization

The priority-setting exercise finally translates into a programme budget based on the individual products or processes that TDR will finance in a given biennium and which are described in electronic Product Master Sheets and databases carrying the following information:
- detailed description of the product or process
- disease addressed and respective disease control needs
- critical success criteria and indicators
- milestones
- responsible officer
- supervising Steering Committee or Product Development Team
- total cost
- funding status.

A bird’s eye view and analysis of the budget allows the generation of tables and graphs of the distribution of resources by disease, functional area of work, and type of funding. There are several advantages of such a budget structure:
- a clear view of the overall directions of the Programme
- increased accountability and transparency of TDR operations
- easier mobility of the funds in case of interruption or discontinuity of a given project (e.g. a “no-go” decision based on unacceptable results of toxicity tests of a drug candidate)
- more effective fundraising for not-yet-funded priority projects
- more efficient planning of the capacity building component of individual areas.

The migration of TDR from a process-driven to a results-driven organization also involved the reorganization of its Research Capability Strengthening (RCS) component to reallocate 60% of RCS funds into “programmatic capacity building”, also known as “R&D driven” or “RCS-plus”. In this “learning by doing” approach, TDR supports strategic priorities involving researchers from disease endemic countries who have comparative advantage within a specific R&D project.

The present programme report is organized according to TDR’s new strategy and highlights some important results obtained by the Special Programme in all seven (A➔G) “Expected Results” areas. From the conclusion of the Anopheles gambiae genome project8 or the registration of miltefosine, the first oral drug against visceral leishmaniasis,9 to the demonstration of reduction of severe malaria morbidity by early treatment of childhood fevers with pre-packaged antimalarials10 or the accomplishments of RCS initiatives such as the Forum of African Medical Editors (FAME), the Health InterNetwork Access to Research Initiative (HINARI), and the RCS-plus on bioinformatics, this sixteenth programme report aims to share with you the results of the hard work undertaken by TDR and its partners during 2001-2002 – undoubtedly a very good vintage biennium. Enjoy it!

Geneva, June 2003

Carlos M. Morel
Director, TDR

---

8 See the special section published in Science, vol 298 (October 2002).