

WHO activities to implement the global strategy and plan of action on public health, innovation and intellectual property, including the quick start programme

1. Resolution WHA61.21, *inter alia*, requested the Director-General "to prepare a quick start programme with adequate budget provision and begin immediately to implement the elements of the global strategy and plan of action on public health, innovation and intellectual property (GSPOA) that fall under the responsibility of WHO."¹
2. In response, WHO undertook an organization-wide exercise to identify ongoing activities that contribute to the implementation. Additional activities initiated in 2008 under the quick start programme fall within the following broad areas: (i) mapping of global research and development activities, identification of research gaps and research priority setting; (ii) supporting research and development and promoting standard setting for traditional medicines in developing countries; (iii) developing and strengthening regulatory capacity in developing countries; and (iv) development of a monitoring and reporting framework.
3. To maximize effectiveness and efficiencies, the quick start programme and the implementation of the broader GSPOA is being mainstreamed and entrusted to departments with the appropriate technical expertise. This approach promotes synergies with existing initiatives, faster implementation, optimal use of existing resources and collaboration across WHO and with partners.
4. Several WHO departments are contributing to the implementation of the elements of the quick start programme that fall under the responsibility of WHO. This document describes some of the activities that have been initiated as part of the quick start programme and the broader implementation of the global strategy and plan of action.
5. Activities in the areas of intellectual property and trade are coordinated with other relevant international intergovernmental organizations, including UNCTAD, WIPO and WTO, and are aimed at capacity building, information sharing, and technical and policy support to Member States. This ongoing work is guided by the actions in the global strategy and relevant Health Assembly resolutions. A report of the Secretariat's work was also presented to WTO's Council for Trade-Related Aspects of Intellectual Property Rights.² High-level meetings between the Directors-General of UNCTAD, WHO, WIPO and WTO have been held to discuss the global strategy and potential interagency collaboration to facilitate its implementation.
6. In line with the elements 3 and 4 of the global strategy and plan of action on building and improving innovative capacity and the transfer of technology, WHO, with the support of the European Commission and in partnership with the UNCTAD and the International Centre for Trade and Sustainable Development (ICTSD), is undertaking a project which involves

¹ WHA61.21, paragraph 4(6)

² IP/C/W/516/Add.1

exploring the main challenges and obstacles to local production of health products and related transfer of technology to developing countries. It comprises a broad consultation of relevant stakeholders, including a screening of existing initiatives and support schemes and identification of specific needs and best practices. The findings of the project will inform evidence-based recommendations on the feasibility and sustainability of local production. The focus of the project is on Type II and Type III diseases and the specific R&D needs of developing countries in relation to Type I diseases.

7. A major new initiative is being developed through the establishment of an African Network for Drug and Diagnostics Discovery and Innovation (ANDI). The initiative is supported by WHO through the Special Programme for Research and Training in Tropical Diseases (TDR) and operates under the framework of the global strategy and plan of action. It builds upon the concept of network-based innovation involving the academic, public and private sectors, which is being developed successfully by TDR, and linking this to capacity and infrastructure building. An inaugural meeting was held in Abuja, Nigeria in October 2008, after which a task force was established comprising technical experts from African institutions, policy advisers and a representative from the African Development Bank. This taskforce is currently overseeing the development of a business plan to share with a broader constituency of stakeholders in South Africa in October, with a view to establishing an Africa-based and African-led organization in 2010. It is anticipated that the organization will serve as a focal point for fostering and facilitating the development of multiple centres of excellence with the capability to collaborate and collectively build research and innovation capabilities across Africa. At this stage, further governmental and intergovernmental public sector engagement and support is being sought, both to meet current budgetary requirements and for its growth and management in Africa starting in 2010.
8. With the aim of increasing vaccine production in developing countries, WHO has been facilitating technology transfer to interested parties. This has included providing awards to developing country vaccine manufacturers, either to develop pilot influenza vaccine production or to establish “fill and finish” capability for influenza vaccine provided by external sources. In 2009, this programme has been expanded to include producers in the following five countries- Egypt, Iran, the Republic of Korea, Romania and Serbia . These were added to the initial group, consisting of producers in: Brazil, India, Indonesia, Mexico, Thailand and Viet Nam. Additionally, WHO is working with a European vaccine producer to establish an egg-based pilot influenza vaccine production process suitable for scaling up and transferring technology to interested developing country vaccine manufacturers. This technology “hub” will also serve as a source of know-how and training to support the efforts of developing countries to increase local vaccine production capacity.
9. Work towards the strengthening of regulatory oversight of clinical trials in developing countries has included development by member countries of the Developing Country Vaccine Regulatory Network of an investigational new drug application-like procedure that is being implemented on a trial basis by Brazil and Indonesia and which other member countries may adapt or adopt at the national level. Countries with an inspectorate are working on a co-inspection programme towards a future mutual recognition of Good Clinical Practice (GCP) inspections. Some countries that are in the process of establishing an inspectorate (e.g. India and Thailand) are also working with other members as mentors to strengthen their GCP inspection activities. Indonesia and South Africa have initiated activities as global training network centres, supporting the development and delivery of courses related to oversight of clinical trials. This is a first step towards designation of WHO regulatory support centres. Indonesia is assisting Asian countries and South Africa is assisting African Vaccine

Regulatory Forum (AVAREF) countries in various regulatory activities relevant to clinical trial oversight.

10. In December 2008, WHO unveiled a new research and development agenda for children as part of its campaign, *make medicines child size*. The agenda targets a range of medicines — including antibiotics, asthma and pain medication — that need to be better tailored to children's needs. It calls for further research and development of combination pills for HIV/AIDS, TB and malaria, as well as appropriate child therapy for a number of neglected tropical diseases. At the same time, WHO released the first international list of essential medicines for children.
11. In line with element 4 of the global strategy and plan of action that includes a Specific action on possible new mechanisms to promote the transfer of and access to key health-related technologies, WHO is collaborating with partners to define the need for new fixed-dose combination antiretroviral treatment in the context of a medicines patent pool being initiated by UNITAID. WHO is contributing to the ongoing activities linked to the UNITAID patent pool through its participation in the expert taskforce and through provision of technical guidance on fixed-dose combinations. The Expert Committee on the Selection and Use of Essential Medicines has endorsed the need to identify priority missing essential medicines based on clinical need and also to meet the needs and challenges of resource-limited settings.
12. The global strategy and plan of action has also been presented, discussed and included in the declarations of a number of high-level fora and meetings including the Global Ministerial Forum on Research for Health (Bamako); the WHO Congress on Traditional Medicine (Beijing); Eurobio 2008 (Paris); *Esenciales para la vida* (Zaragoza); First International Seminar on Access to High Cost and Limited Source Medicines (Brasilia); Global Hospital Pharmacy Conference (Amsterdam); Afro-European Medical and Research Network (Bern); Pharmaceutical Sciences 2020 (Amsterdam); and the International Workshop on Innovation and development in Health (Florence).
13. A key step towards the implementation of the plan of action has been the development of a proposal by TDR to expand its work to respond to the GSPOA, particularly related to elements 1 to 3. This has been reviewed by TDR's governing Joint Coordinating Board (JCB) and approval has been given to work towards a detailed and budgeted plan and assess the potential for raising the necessary funding.

THE QUICK START PROGRAMME

Component 1. Mapping of global R&D activities, identification of research gaps and research priority setting (Specific actions: 1.1(a), 1.1(b), 1.1(c), 7.1(c), 7.2(a), 7.2(b), 8.1(e))

14. Mapping of R&D priorities for infectious diseases of poverty is part of TDR's new strategy and business plan. A major objective is the production of a biennial report on the global status of research on infectious diseases of poverty, with the first of these to be published in early 2011. There are opportunities to deepen this activity and expand it to cover a broader range of diseases should additional funding become available. The activity is being coordinated through a series of expert reference groups in collaboration with departments at WHO

headquarters and regional and country offices. The endeavor will also be informed by broad stakeholder consultations at country, regional and global levels.

15. The mapping of R&D activities is supported by a new web-based knowledge management system (www.tropIKA.net), which ensures broad sharing of expert group discussions and commissioned studies and democratise the process by enabling web-based participation and comment on documentation by all interested in the issues associated with research for health. By generating a document that combines expert analysis with broad stakeholder ownership it is anticipated that the documented output of this activity will achieve broad acceptance and will inform the priority setting processes of those involved in related research activities. Through a grant from the European Commission, the European Union has formally engaged in this effort as a partner with a view to using the output of the activity to inform its priority decision making. Other formalized governmental and intergovernmental public sector engagement and financial support is being sought to meet existing plans and further extend them to a broader range of diseases.
16. An innovative North-South drug discovery platform based on networks and partnerships with public and private sectors in developed and developing countries has been recently launched. These networks and partnerships: manage drug screening, medicinal chemistry, pharmacology and drug target networks for Type I and II diseases; proactively source compounds from industry and academia for screening; and have established an open source drug and diagnostics target database for Type I and II diseases (www.tdrtargets.org). Additional funding is being sought to further expand this work. This platform will also need to be expanded and sustained. Plans are underway to extend this to regions as part of regional networks for innovation. Training has begun for postdoctoral fellows from developing countries as part of this project.
17. As an example of a partnership initiative with the private sector, a drug discovery agreement between WHO/TDR, a pharmaceutical company and the National Center for Drug Screening (NCDS) China was concluded. The company has transferred its compound library of over 300,000 compounds to the NCDS to support screening for infectious tropical diseases covered by WHO/TDR (details are available in TDR annual reports and on the website-www.who.int/tdr or <http://apps.who.int/tdr/svc/news-events/news/chinese-drug-screening>). In addition, fellows from Africa will be trained in China as part of this project. This is the first time such a large amount of compound has been transferred to a developing country in support of drug discovery for neglected diseases. This activity has the potential of being expanded and extended to other regions.
18. In January 2009, WHO received support from the Bill & Melinda Gates Foundation to work with UNICEF to conduct crucial research in children's medicines. The initiative will focus on determining the optimum dosage forms for paediatric medicines, developing dosage guidelines, and developing guidelines for testing, treatment and use of medicines in children. In addition, the WHO International Clinical Trials Registry Platform (ICTRP) launched a website on clinical trials in children to improve awareness and make it easier to access accurate, up-to-date, understandable information relevant to the conduct of clinical trials in children.

Component 2. Supporting R&D and promoting standard setting for traditional medicines in developing countries (Specific actions: 1.3(b), 1.3(c), 1.3(d), 1.3(e), 3.4(c), 3.4(d), 3.4(f))

19. In November 2008, WHO organized the first WHO Congress on Traditional Medicine in Beijing, China. Representatives of over 70 Member States attended and shared national experiences and information. The "Beijing Declaration" was adopted, promoting the safe and effective use of traditional medicine. The Declaration calls on WHO Member States and other stakeholders to take steps to integrate traditional medicine/complementary and alternative medicine into national health systems. It states that research and innovation on traditional medicine should be further developed in line with WHA61.21. Subsequently, in May 2009, the 62nd World Health Assembly passed a resolution which, *inter alia*, urges Member States to consider adopting and implementing the Beijing Declaration on Traditional Medicine.
20. Over the course of the last year, WHO's work in traditional medicine has emphasized capacity building, technical guidance and coordination. For example, this has included:
- Training and technical guidance on clinical research in traditional medicine and initiation of work on a WHO technical guide on clinical research in traditional medicine
 - Developing guidelines on basic training in various types of traditional medicine/complementary alternative medicine, as well as training on regulation and qualification in this area
 - Promoting international cooperation and the ethical conduct of research in traditional medicine. This includes supporting selected countries in the development of a national inventory of medicinal plants for preservation and protection of traditional medical knowledge
 - Supporting South-South cooperation in information exchange and research activities. For example, the development of: WHO monographs on selected medicinal plants; subregional/regional WHO monographs on medicinal plants commonly used in the concerned subregion/region; and a WHO subregional handbook on selected medicinal plants for primary health care
 - Supporting and promoting standard setting to ensure the quality, safety and efficacy of traditional medicine. This includes developing WHO guidelines and technical documents, as well as collating and providing of information on national regulatory and legislative frameworks to facilitate information exchange
 - Facilitating the international regulatory cooperation for herbal medicines (IRCH). To this end, the 3rd annual meeting of IRCH took place in February 2009. The strategic plan of action for IRCH for the next three to five years was developed. Additionally, membership increased from 18 (May 2008) to 22 (May 2009)
 - Developing a technical document on safety of herbal medicines with reference to interaction with other medicines
 - Preparing a WHO technical review on the use of traditional medicine in healthcare. In this regard, WHO convened a WHO working group meeting on clinical studies on phytotherapy in Italy in March/April 2009 that discussed key technical issues for the development of the review document
 - Supporting pilot research on malaria

- Providing technical support in R&D and good manufacturing practices
- Organizing interregional/subregional workshops, including on regulation and quality assurance of herbal medicines, including Good Agricultural and Collection Practices, Good Manufacturing Practices, and expertise required at a quality control laboratory in handling herbal medicines and traditional medicine

Component 3. Develop and strengthen regulatory capacity, including safety, efficacy, quality and ethical review (Specific actions: 3.2(a), 6.2(a), 6.2(b), 6.2(c), 6.2(d), 6.2(g), 6.2(h))

21. WHO, through several of its co-sponsored research programmes, including the Special Programme of Research, Development and Research Training in Human Reproduction, the Initiative for Vaccine Research and TDR, is helping coordinate and support research that evaluates the use of existing products in real-life situations as a basis for supporting regulatory and policy decisions. This is occurring for drugs, vaccines, diagnostics and other medical products and is primarily directed at the use of products against high-burden diseases in resource-poor settings. Where there is limited regulatory experience, for example, in the field of diagnostics, guides for evaluation are being developed for certain diseases as a basis for multi-country based evaluations (e.g. rapid diagnostic tests for malaria) and to assist authorities in assessing the value of the products. Increasingly this work includes cost-effectiveness assessments to inform policy. Resources are needed to further globally coordinate this activity and promote associated capacities in developing countries to extend and lead these efforts.
22. WHO, through TDR, is supporting the strategic initiative for developing capacity in ethical review (SIDCER). This network-based initiative, built upon regional and national forums and discussion, is grounded in national and regional ownership. It has already been successful in South-East Asia and the Western Pacific, in supporting the establishment and development of ethical review committees in collaboration with national authorities. Systems are now in place that recognise the competency of ethical review boards and legislative changes to protect human subjects in research have been enacted in several countries. More resources are required, in particular to assist other regions, such as Africa, to scale up similar efforts.
23. The GSPOA calls for the strengthening of WHO's Prequalification Programme. The WHO Medicines Prequalification Programme has grown in output, with the total number of prequalified products assessed by the Programme being close to 200. Several workshops were organised for both national drug regulatory authorities (NDRA) and manufacturers in resource-limited countries. Scientific advice and technical assistance were provided for manufacturers with the aim of supporting the improvements of quality of their products.
 - During 2008 the first ever fixed-dose combination tablets of antiretroviral medicines designed for use in children to treat HIV/AIDS and the first fixed-dose combination tablets of artesunate and amodiaquine to treat malaria, were prequalified.
 - A total of six quality control laboratories were prequalified in 2008. Countries that were recipients of drug donations benefitted from three comprehensive medicines sampling and testing programmes during 2008.
 - To increase the transparency and accountability of prequalification performance, the procedure for the prequalification of medicines has been revised and updated (more

http://www.who.int/medicines/publications/pharmprep/pdf_trs953.pdf#page=145).

- Guidelines and standards to facilitate global quality assurance activities, including pharmacopoeial monographs and chemical reference standards continue to be developed and updated.
 - Prequalification is expanding to include zinc and recently a generic influenza product has been prequalified. The process for the prequalification of reproductive health products has been initiated.
 - In response to the AH1N1 influenza outbreak, prequalification for the antiviral oseltamivir from one generic manufacturer was finalized with a positive outcome. The product has been included in the WHO list of prequalified products and the details may be found at <http://apps.who.int/prequal/>. An additional Expression of Interest process for prequalification of the antiviral zanamivir was initiated.
24. To strengthen capacity, regulatory personnel from resource-limited countries have participated in a three-month full-time post at WHO with an aim to create links, establish a network between WHO and the countries involved and facilitate information exchange. Assessors from less resourced regulatory authorities continue to participate in prequalification assessment sessions, as well as inspectors who are now invited to take part in WHO inspections as observers. At the global level, WHO continues to perform its normative role and this will expand due to the priority areas identified in the action plans and in response to priority diseases. At the regional/country level, an African regional national drug regulatory authority conference was launched in partnership with donors that will introduce measures to harmonise regulatory requirements and facilitate access to needed medicines. The group will also facilitate accreditation visits by content and training experts and provide additional training courses.
25. Three teams dealing with vaccines are coordinating efforts to ensure vaccine access and delivery, development and quality, including: EPI (access and delivery), IVR (vaccine development) and QSS (quality, safety and standards). WHO is continuing its ongoing work in assessing national regulatory systems of countries producing prequalified vaccines, as well as for capacity building in Africa. This has included work on:
- Strengthening regulatory capacity for oversight of clinical trials through global training network courses on Clinical Trial Authorization (CTA) and good clinical practice inspections through the developing country vaccine regulators network (DCVRN) regulatory support centres in Asia (Indonesia) and Africa (South Africa)
 - Strengthening regulatory oversight of clinical trials through regulatory networks
 - Technical support to selected countries for the prequalification of vaccines to be purchased by UN agencies, such as through: meetings with developing country NDRAs; prequalification of vaccines for public health emergencies; laboratory tests of quality for prequalification; and prequalification of immunization-related devices and equipment
 - Planning and conducting country NDRA assessments, action plans and follow-up in developing countries, firstly, for those countries producing prequalified vaccines, and secondly, for capacity building in Africa
26. New NDRA assessment tools have been developed and are accessible through a WHO website. In 2008-2009, some 14 countries were using them and their use is expected to be

expanded gradually to include all vaccine producing countries (48 countries) by 2011. To this end, priority countries are vaccine exporting countries, including those that have prequalified vaccines. Additionally, a quality system is being developed which includes standard operating procedures for planning assessment, conducting assessment, and using the assessment tools.

27. Out of the 27 countries that have prequalified vaccines as of 2009, WHO has planned several reassessments. In preparation for reassessment, several pre-visits have been planned and conducted, including in Belgium, France, Hungary, Japan, Mexico, the Netherlands, the Philippines, the Russian Federation, Serbia and South Africa.
28. Two in-country training courses have been developed on risk-based inspections and product evaluation, which were field tested in India. Further field testing will take place in Brazil, Egypt, Indonesia and Thailand. To build the capacity of developing countries in vaccine evaluation using the common technical document format, a parallel review of vaccine and evaluation is ongoing between Canada and India. This initiative is funded by USAID and WHO, with the technical assistance of the NDRA Canada.
29. Full reassessment for prequalification of countries has been completed in Brazil, Cuba, India and Thailand. In 2009, follow up reassessments are taking place in: Algeria, Bangladesh, the Democratic People's Republic of Korea, Egypt, India, Indonesia, Iran Senegal, Thailand and Viet Nam.
30. With the aim of monitoring progress of regulatory systems, providing oversight on global production and supply and to better assuring the quality of vaccines, a data management website was established in 2008. The website provides data and analysis on assessments and training conducted since 1996. To this end, data has been compiled, such as in relation to countries': regulatory functions; sources of vaccines; training and staff; budget; expertise; and NDRA websites. In addition, data on activities and technical support since 1996 have been compiled for some 356 WHO country visits and 101 country assessments and re-assessments, including follow up visits. This information will be published as a global NDRA atlas of regulatory systems and selected success stories from Algeria, Brazil, China, Croatia, Cuba, Egypt, India, Iran, Senegal, Thailand, Tunisia and Viet Nam.
31. Joint reviews of clinical trials of meningitis and malaria vaccines have been conducted and coordinated by WHO. Good Clinical Practice inspections of clinical trials have been conducted for meningitis A vaccine. As a result, all trials in Africa for the Conjugate Meningitis A vaccine have been authorized by the national regulatory authorities and all sites have been inspected. In 2008, AVAREF members endorsed a plan to integrate ethical review, regulation and registration of clinical trials, as well as to harmonize clinical trial regulation. This involves clinical trials of medicines, including drugs and vaccines. The project is moving forward through the concerted effort of several partners.
32. WHO, in coordination with the Pediatric Dengue Vaccine Initiative (PDVI) and ASEAN Vaccine Chapter, is organizing a Workshop on Regulatory Pathways for clinical trials of dengue vaccine.
33. WHO has planned additional safety training in the context of its work on strengthening pharmacovigilance relative to vaccines. In this context, WHO is enhancing risk management of vaccines safety, including through activities that are planned in support of vaccine prequalification. With respect to standard setting for vaccine safety, WHO plans to develop

definitions for vaccine safety. Additionally, WHO has undertaken efforts to put in place a framework and support structures for a new network of countries which have recently introduced prequalified vaccines and to study the safety of these vaccines as they are introduced into national immunization programmes. This has included consultation with key partners in the proposed network, including selected network member countries, WHO's Collaborating Centre for International Drug Monitoring, WHO Regional Offices and the UNICEF Supply Division. As a result, agreement was obtained on the main operational terms of the network. The network's *Operational Manual* has been developed and critical elements of an activity workplan for the network in 2008-2009 are being implemented. In particular, a number of key technical/data issues were identified and are being addressed. Other activities include establishment of a network management group and technical oversight committee. The operational phase of the network, defined by the onset of data submission and analysis with related in-country operations, is now in process.

34. Two activities have been planned in support of standard setting and regulatory preparedness for biologicals, both for vaccines and copy products. These activities include support of GMP standards for biologicals by facilitating developing country NDRA participation in the standard setting process and development of standards to monitor human papillomavirus (HPV) vaccines.
35. With respect to implementation of standards for biologicals, both for vaccines and copy products, WHO has ensured the participation of developing country NDRAs and national control laboratories. Activities to date include consultations which have covered: (i) development of new WHO guidelines on lot release of virus vaccines; and (ii) revision of the current WHO technical specifications on cell substrates used for production of virus vaccines. In both cases, it is anticipated that documents will be submitted to the WHO Expert Committee on Biological Standardization in 2009 and 2010 respectively.
36. WHO is strengthening pharmacovigilance for vaccines by building country capacity in this area, as well as by providing training on investigations of adverse events following immunization and causality assessments. WHO is addressing risk management of vaccine safety through: networks for pharmacovigilance of vaccines; development of collaborative platforms for vaccine safety; and development of crisis management skills and capacities in countries. WHO is continuing to support developing country NDRA participation in the standard setting process for vaccine safety, as well as for monitoring vaccine effectiveness. WHO is supporting implementation of new standards for monitoring vaccine effectiveness by providing support to the HPV lab network, and the pneumo serology WHO laboratories.
37. With the aim of increasing and sustaining the global supply of quality vaccines, WHO is: monitoring country road maps and institutional development plans; developing and delivering training to implement regulatory functions; organizing and conducting international WHO NDRA assessments; and developing the 2nd phase of e-governance, which deals with harmonizing electronic requirements to assist in the development of regulatory management systems and the sharing of information. Additionally, through the global training network on vaccine quality, WHO is providing training courses on vaccine quality for developing countries, including the development of e-learning materials. Finally, WHO is promoting regulatory exchanges and harmonization through development and management of confidentiality agreements and regulatory exchange programs.
38. Activities have included those towards implementing the WHO International Clinical Trials Registry Platform (ICTRP), which aims to ensure that a complete view of research is

accessible to all those involved in health care decision making. To this end, ICTRP improves research transparency and ultimately strengthens the validity and value of the scientific evidence base. Work in this area has included the following: expansion of the existing HIV/AIDS, Tuberculosis and Malaria Clinical Trials Registry to the Pan African Clinical Trial Registry (PACTR); development and implementation of national clinical trial databases to linked with PACTR; and development and implementation of the African Common Clinical Trial Guidelines by all AVAREF countries.

Component 4. Establishing monitoring and reporting systems (Specific actions: 8.1(a), 8.1(b))

39. The WHO Secretariat developed and submitted progress indicators which were considered and accepted by the 62nd World Health Assembly. The indicators will form the basis for regular reporting to the Health Assembly on performance and overall progress made over a two-year reporting period, as well as inform the evaluation of the strategy at the end of four years. Each element has a set of indicators that measure results achieved with respect to key objectives relevant to that particular element. In addition, two overarching indicators have been developed for measurement of overall progress. Where the indicators are quantitative, the Secretariat will provide additional complementary information on the implementation of the specific actions.
40. Monitoring and evaluation activities are currently underway. This involves: ongoing consultations to track outputs contributing to implementation; systematic collection of data; and a database tool that enables easy data collection in a standardized way and transfer of data from Member States to the WHO Secretariat at headquarters.