DISEASES OF THE DEVELOPING WORLD
WORKING TOGETHER TO MAKE A DIFFERENCE

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The Academy of Medical Sciences

MRC Medical Research Council

2006 Science Policy Conference

Diseases of the Developing World: Working together to make a difference

A report of a meeting, co-hosted by the Academy of Medical Sciences, the Medical Research Council, the Wellcome Trust and GlaxoSmithKline.

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***Chairs, Speakers & Panellists**

PREFACE

This report summarises a number of the issues that were discussed at a one-day meeting "Diseases of the Developing World: Working together to make a difference" that was held in September 2006 at the Royal College of Physicians, London.

The conference, sponsored by GlaxoSmithKline, was co-hosted by the Academy of Medical Sciences, the Medical Research Council and the Wellcome Trust. It was the fourth in a series of such science policy meetings organised by GSK in collaboration with the leading UK biomedical research funders and policy-makers. The 2006 conference sought to take forward the general theme of the importance of partnerships in biomedical research, following on from the previous meetings on "The Value of Medicines", "The Case for Clinical Research in the UK" and "Biomedical Research and Public Trust".

For many years diseases of the developing world have been neglected. There are many reasons for this, including the present availability of well-tolerated and inexpensive medicines, that until relatively recently, were highly effective. However, the emergence and spread of pathogens resistant to older agents has created an urgent need to refocus R&D efforts in this area. GSK has long been committed to helping the world's poorest countries benefit from our life-changing products, and in the context of diseases of the developing world we are leading in the development of medicines and vaccines to tackle all three of the "priority" diseases identified by the WHO – HIV/AIDS, tuberculosis and malaria. Despite our renewed commitment in this field we cannot solve the entire problem on our own and therefore welcome the further development of Public Private Partnerships (PPS) which promise a return to a situation where there is a progression of agents coming through to the clinic.

The conference set out to examine more than the significant and growing challenges facing society as it seeks to tackle diseases of the developing world. It also attempted to review some of the challenges faced by neglected populations and diseases. It was important therefore that we were able to discuss the importance of health systems development, the disease burden of mental health within the context of neglected diseases and examine the gaps in knowledge in addressing global child survival from diseases such as pneumonia and diarrhoea.

In bringing this meeting together, GSK and our co-hosts sought to examine some of the efforts being taken by industry, academia, NGOs, governments and others to respond to today's global healthcare challenges. What more can be done by companies, by researchers and by policy makers? What further co-operative efforts by all parties in the public and private sectors can be done to focus financial, human and scientific resources to achieve real advances in R&D and in the delivery of new and effective therapies?

This report on the outcome of the conference can only provide a brief overview of the expert and passionate contributions from the individual speakers and discussants, many of which travelled far to take part. As with our previous Science Policy conferences the participants at the meeting were under no illusions as to the enormity of the subject they were addressing, or as to the many difficulties that will need to be overcome to improve matters significantly. GSK hopes that this report will provide a small contribution to the much-needed ongoing debate on this important topic. There are still many challenges facing the discovery and development of treatments for neglected populations and diseases and new partnership and policy ideas are still needed.

Dr Moncef Slaoui
Chairman, GSK R&D

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SUMMARY OF KEY FINDINGS

The conference identified a number of issues necessary to support future health gains, particularly in the developing world. These include:

- More research on health systems development will help underpin scaling–up of resources;
- In recipient settings, the role of political leadership is vital to ensure maximum benefit can be derived from donor resource allocation policies and global health initiatives;
- The input of target populations and participants in trials needs to be fully respected;
- Further work on international guidance on the conduct of trials would be beneficial;
- Skills development and retention in resource-poor settings is crucial for the developing world;
- A better balance needs to be struck in tackling the disease burden due to communicable diseases and non-communicable diseases, as the latter impact on the achievement of the Millennium Development Goals;
- Partnership approaches need to be further refined for medicines development and for social policy development–particularly on issues which have a direct impact on health–and on strengthening links between academic and other institutions across the globe.

CONFERENCE PROGRAMME

Introduction
Professor Sir Keith Peters,
Academy of Medical Sciences

FIRST SESSION
Setting the scene: What are the real world healthcare challenges faced by neglected diseases and populations?

Chair, Professor Sir Keith Peters,
Academy of Medical Sciences

- Healthcare delivery in the developing world, **Dr Francis Omaswa** (Global Health Workforce Alliance, WHO)
- Is mental health relevant to public health in developing countries? **Dr Vikram Patel** (Goa and London School of Hygiene & Tropical Medicine)
- A Call to Action - Why The Opportunity is Now **Dr Tachi Yamada** (Bill & Melinda Gates Foundation)

SECOND SESSION
What are the challenges for conducting research in developing countries?

Chair, Dr Diana Dunstan,
(Medical Research Council)

- Paediatric medicines research **Professor Zulfiqar Bhutta** (Aga Khan University, Pakistan)
- Clinical research in the developing world: the challenges of capacity building **Professor Wen Kilama** (Africa Malaria Network Trust) **Professor Fred Binka** (In-Depth Network)

PANEL SESSION
What are the ethical issues concerning the conduct of clinical trials in the developing world?

Panellists: Speakers from Sessions 1 and 2 were joined by :
Professor Sandy Thomas (Nuffield Council on Bioethics)
Professor David Kerr (University of Oxford)

THIRD SESSION
Responding to the Challenges

Chair, Professor Janet Hemingway,
(Liverpool School of Tropical Medicine)

- Research for scaling up access to effective interventions, **Professor Sir Andrew Haines** (London School of Hygiene & Tropical Medicine)
- Stimulating links between the academic biosciences community & the developing world **Dr Jimmy Whitworth** (Wellcome Trust)
- Current pharmaceutical responses to neglected diseases and populations, **Dr Moncef Slaoui** (GSK)
- Diagnostic tests for poverty-related diseases in the developing world **Dr Vinand Nantulya** (FIND)
- Will public-private partnerships deliver in the discovery, development and delivery of new medicines? **Dr Chris Hentschel** (MMV)

PANEL SESSION

What new partnerships and policy opportunities are needed to improve health outcomes?

Chair, Professor Gordon Conway, Dept. for International Development

Panellists: Speakers from Session 3 were joined by:
Andrew Jack (Financial Times) **Dr Joanna Rubinstein** (MillenniumProject) **Dr Lynn Marks** (GSK R&D)

Concluding remarks and close of meeting **Professor Martin Bobrow** (University of Cambridge & Wellcome Trust)

CONFERENCE SUMMARY

Introduction
Professor Sir Keith Peters, President, Academy of Medical Sciences

Sir Keith Peters, welcomed delegates formally to the conference. He congratulated the organisers and GlaxoSmithKline, in particular, for convening a strong set of important speakers and inviting an audience representing a wide range of major interests and experience.

Sir Keith explained the importance of focussing on global public health as a means to address the increasing social and economic burden due to communicable diseases, non-communicable diseases and new and emerging diseases. He referred to the enormous challenges that these diseases present for research, capacity and skills development, the delivery of effective and efficient services and the continuation of established links between researchers and qualified health workers in both the developing and developed world. The conference provided an opportunity to explore ways of finding more coordinated approaches to face up to these challenges and to identify options for developing more coherent strategies for future action.

FIRST SESSION
Setting the scene: What are the real world healthcare challenges faced by neglected diseases and populations?

Chair: Professor Sir Keith Peters, Academy of Medical Sciences

Dr Francis Omaswa is currently a Special Adviser to the Director General of the World Health Organisation on Human Resource for Health issues. He was previously Director General for Health Services,Uganda.

Dr Omaswa observed that Africa is lagging behind other parts of the world in achieving the targets set in the Millennium Development Goals (MDGs). He referred to the the high level of HIV/AIDS prevalence in sub-Saharan Africa and the link with changes in life expectancy, the very high levels of maternal mortality, the low level of health spend *per capita* and the low numbers of health workers per population in Africa in comparison with other regions of the world. He referred also to external factors which impinge on national planning, such as the involvement of donors and global initiatives. These external initiatives influences can offer high level of support, but in order to deliver benefits, they nearly always require new and more sophisticated structures within national health systems. Studies conducted in Uganda into the link between poverty and health show that poor health is a contributor to poverty and that poverty is exacerbating health status.

Dr Omaswa proposed that the challenges posed by new emerging diseases can be met if national governments show leadership, undertake stewardship and accept accountability. This requires a clear vision for securing health improvements, building up mutual trust with partners in all sectors which impact on health; establishing mechanisms for effective dialogue within government, with NGOs, industry and with native populations. Monitoring and analysis ability to take account of research outcomes and improved ownership and commitment, particularly at sub-national levels. In particular, he stressed the importance of a better managed approach, both to human and financial resource planning. He underlined the importance of:

- Devolution of responsibility for the provision of services;
- Cross–government reforms can reinforce the contribution of effective health services;
- Global health initiatives need sustainable financing for more than for a limited period;
- Macro-economic and political stability;
- Competition from sectors other than Health for sustainable support;
- Human Resources for Health, as set out in the World Health Report 2006, describes a 10–year action plan with close links to the achievement of the Millennium Development Goals–particularly the four health specific goals.

Challenges of working with Global Health Initiatives

- Duplication in planning/accounting/procurement and M&E systems undermines the harmonisation efforts that have been built over the last 5 years, and have been noted to lead to a more efficient sector
- GHI funds have the potential to displace GoU budget funds - are the GHIs funds as efficient as the goverment budget??
- Unpredictability of GHI/project funds
  - How long will these be available (sustainability)
  - The predictability of disbursement

Dr Vikram Patel is a Reader in International Mental Health and Wellcome Trust Senior Clinical Research Fellow in Tropical Medicine at the London School of Hygiene & Tropical Medicine.

Dr Patel underlined the disease burden of mental health (and other chronic and non-communicable diseases), within the context of neglected diseases. He made clear that there is no health without mental health. Securing improvements in mental health requires a greater understanding of the public health significance of mental disorders, sharing good practice on what works and what is cost-effective and scaling–up resources to support mental health services. Whilst the prevalence of mental health disorders varies between settings and conditions, about 10% of adults suffer from such a disorder. Mental health disorders are present in 30% of primary care attenders with depressive and anxiety disorders and substance abuse (including alcohol and drugs) amongst the most common; up to 2% of all adults suffer from a chronic, severe mental disorder and 1 in 10 children suffer from a childhood mental disorder.

Dr Patel explained how some 75% of mental disorders have their onset during youth–the most productive years of life. He described how mental health is intimately associated with the attainment of many Millenium Developed Goals (MDGs). For example, MDG 1 is about poverty alleviation and the vicious cycle of poverty and poor mental health is evident. Factors such as economic insecurity and indebtedness lead to depression, anxiety, physical ill-health and substance abuse. These conditions in turn reduce the available resources to support the family, through diminished productivity, higher levels of disability and higher health costs. MDG 2 is about promoting universal primary education. Mental disorders are risk factors for learning under-achievement and school-drop out. Vulnerable children, such as orphans, child soldiers and street children, have increased rates of mental disorders and education failure. MDG 4 is about reducing child mortality;

depression in mothers is strongly associated with child undernutrition, which in turn is a risk factor for mortality. MDG 6 concentrates on improving the health of people with HIV/AIDS; suffering from this condition is strongly associated with mental disorders such as depression, suicide, substance abuse and dementia. Mental disorders can reduce the efficacy of HIV treatment, through reduced adherence, or be worsened through the side-effects of treatments.

MDGs 1 eradicate poverty

- Poor people have more mental illness
- Poverty is a risk factor for mental illness
  - Social change and urbanization
  - Material stressors, e.g hunger, indebtedness
  - Noisy, crowded, polluted and unsafe living conditions
  - Higher burden of physical ill-health
  - Inadequate access to good health care
- Mental illness worsens poverty
  - Impairs educational achievement
  - Impairs working ability
  - Increases costs of health care

Source: Patel & Kleinman, Bull WHO 2003 Patel et al, Trop Med Int Health 2006

Dr Patel explained the evidence emerging from trials in developing countries aimed at tackling mental disorders. Antidepressants and group psychological interventions have been found to be efficacious in community and primary care settings for depressive and anxiety disorders. Antipsychotic drugs combined with community-based rehabilitation have been shown to be effective interventions for chronic schizophrenia. Brief GP-delivered psychological interventions are effective in tackling alcohol problems, and cheap anticonvulsants dramatically improve the control of epilepsy. All these interventions are low-cost and utilise locally available resources. Recent economic analyses found that the cost–effectiveness of treating depression is the same as that of diabetes and other chronic diseases. Despite this evidence base on effective treatments, the vast majority of persons with mental disorders in developing countries receive no treatment or inappropriate treatment; many, particularly those suffering from severe mental disorders, suffer appalling abuses of basic human rights.

Dr Patel suggested that the major priority for addressing mental health needs in developing countries was scaling-up and evaluating affordable and feasible evidence-based treatments. Examples of such scaled-up interventions are: strengthening community-based services for severe mental disorders such as developmental disabilities in children; schizophrenia in adults and dementia in elders; strengthening primary health care services for depressive disorders and substance abuse; and integrating mental health interventions in other programmes such as the 3 by 5 initiative for HIV/AIDS and the IMCI initiative for maternal and child health. Such interventions would not only benefit public health through direct effects on improving mental health, but also through the impact that improved mental health will ultimately have on physical and social health outcomes.

Dr Tachi Yamada President of the Global Health programme of the Bill and Melinda Gates Foundation and former R&D chairman at GSK discussed the range of opportunities which favoured action at the current time.

Dr Yamada outlined the scale of the global health problem – the death of 11 million babies every year, four million deaths before the age of five, one million deaths from malaria and 14 million children living with one parent with HIV/AIDS. Life expectancy in sub-Saharan Africa is 46 compared with 79 in the developed world. Against this background, Dr Yamada identified grounds for optimism. The interest in global health rather than more specific medical specialities is growing, with qualified doctors switching to global health and more medical students selecting global health for their careers. More companies are interested in working out how they can support efforts to improve global health. Successes include vigorous and rigorous application of new interventions, the eradication of smallpox, polio on the brink of eradication and considerable advances with river blindness and lymphatic filariasis. The Global Alliance for Vaccines and Immunisation (GAVI) has been very successful in increasing the availability and targeting of vaccines. 14 million children have received vaccines for diphtheria, pertussis and tetanus, 18 million children have been vaccinated against Hepatitis B, 13 million children have been vaccinated against yellow fever. In the drug pipeline, there are nine vaccines and a further 20 medicines for malaria and exciting trials for TB and HIV. Millions of lives have been saved and prospects for continuing improvements are very encouraging.

In describing a "Call for Action", Dr Yamada identified three key areas:

Investment in Information technology – Dr Yamada cited a malaria study in southern Mozambique where the introduction of IT has enabled the collection of accurate data, but has also empowered the local population to take a greater interest in their health as well as enabling the providers of health-care and programmes to better target their work. Information is important to donors, foundations and governments, to enable them to better plan the way in which they disburse their resources. Investment in IT is likely to be both easier in the developing world and reap more benefits, as it is often easier to introduce new systems and better target investments to need.

Education – Backing up the investment in IT is the need to ensure the data can be interpreted accurately. Education and training is needed for policy-makers to make better use of the information generated, for implementers to be able to convert the science into practical approaches and for the deliverers to be better involved in the knowledge-generation and implementation processes. It is no longer justifiable for northern scientists to tell southern governments what they should be doing. Investment in skills and education helps smooth the way forward.

Logistics – It is estimated that US$ 25-70 billion is needed to fully achieve the MDGs. Foundations and governments are committed to $10 billion at present. Others need to be better involved and this will require changes in attitudes. It will mean moving from the relative comfort of doing the easy things which may yield instant and rewarding success, to doing the hard things and thinking long-term. It will mean being prepared to fail. History has shown any number of schemes and policies which have floundered, but excellent solutions to difficult healthcare problems are inevitably the result of learning the lessons from failures.

During the questions following on from the presentations, reference was made to the ability to deliver products, particularly to remote areas of developing countries. The "success" of baby milk and soft drinks had shown the possibilities, but there was no similar track record for medicines and vaccines. Reference was also made to the role of civil society and the importance of improved inter-sectoral co-operation. Migration of health professionals within countries and between the public and private sectors was noted as elements of the health professional migration agenda, which need to be addressed even if these were matters for national administrations. Coordination at a global level was important to eliminate duplication and overlap. This requires all sectors to be involved.

In addition, the role of women and women's networks need to be supported to help provide local solutions. Military logistic specialists are another source of expertise which could be beneficial to the health sector. The effective co-ordination of multinational donors and their ability to make informed decisions, particularly in relation to non-communicable diseases, was also acknowledged, along with the importance of who, where and how decisions are taken in these circumstances. This effort needs to take full account of the cultural, racial and gender sensitive issues of the situations where the policies will be applied.

KEY THEMES

- Political Leadership is vital;
- Need for better coordination between donors and receiving countries;
- Growth in burden of non-communicable diseases;
- Role of IT and market-based approaches.

SECOND SESSION

What are the challenges for conducting research in developing countries?

Chair: Dr Diana Dunstan, Director of Research Management at the Medical Research Council.

Dr Dunstan introduced this session which looked at the challenges for conducting research within countries of the developing world. The first session set the scene on healthcare challenges. This was followed by a look at research needs and how research could best make an impact. The speakers reflected on their experiences of doing research in the developing world to highlight the lessons for strengthening the research base.

Professor Zulfiqar Bhutta is Chairman of the Department of Paediatrics and Child Health at the Aga Khan University in Karachi.

Professor Bhutta spoke about the link between research and global child health policies, the ethical challenges of research and the link with the poverty reduction agenda. Over 90% of the 10.6 million child deaths globally is found in 42 countries in the world. 90% of the global prevalence of stunting is found in 31 countries, whilst 55 million children with symptoms of wasting are found in South East Asia. Many countries are making progress with meeting neonatal targets but progress is too slow, particularly in countries of South East Asia and in sub-Saharan Africa. Wide variations within countries also need to be addressed.

Professor Bhutta raised issues around gaps in knowledge and the role of research in addressing child survival. The big killers are pneumonia, diarrhoea and new born deaths (in the first week). They account for almost 75% of child deaths. Some 55% of all child deaths can be saved using currently available interventions including, oral rehydration, breastfeeding, zinc as a prophylactic and as treatment for diarrhoea, insecticide - treated bed nets, complementary feeding, antibiotics for sepsis and pneumonia, Hib vaccine and clean delivery. In addition to having sufficient numbers of appropriately-trained health workers, ethical issues around child health research are a main consideration, particularly in respect of prioritisation and funding.

Professor Bhutta went through a number of issues affecting children. Neonatal sepsis is responsible for 40-50% of all neonatal deaths. The current treatment regime includes injectable penicillin and gentamicin. Yet few pilot studies are conducted in primary care settings and almost no microbiological data are routinely collected. There are no strategies for treating resistant neonatal infections. The global average R&D investments per DALY for all diseases is US$ 73.0. For diarrhoea, the corresponding figure is $0.32. The main treatment for diarrhoea is via rehydration therapy. Oral rehydration therapy was established in the early 1980s. Evidence suggests that WASH strategies, use of rotavirus vaccines and probiotics, low osmolality oral rehabilitation therapy, antibiotics for drug resistant dysentery and the use of new drugs such as nitrozoxanide, are effective. The efficacy of the use of zinc as a treatment regime was generated by research in the 80s and 90s. Systematic reviews in 1999-2000 established the impact on mortality. WHO and UNICEF adopted the use of zinc as a global standard of care in 2004, yet only one major industry supplier has been identified to date and only one country programme has been able to introduce zinc for diarrhoea treatment. This illustrates one of the ethical challenges where research has indicated the efficacy, yet implementation has lagged far behind.

Other ethical issues in child research, particularly in terms of therapeutic work, include the use of placebos, issues around informed consent in various cultural settings as well as in health systems research more generally, standards of care, prior agreements and benefits, assured availability of products of research and variations in capacity and standards to conduct an ethical review of research. In relation to standards of care, a major source of disquiet has been the debate between best proven therapy versus established effective therapy. Finding mechanisms to bridge the gap between research information and implementation, is crucial.

In conclusion, Professor Bhutta explained that there remains considerable global and within-country inequities in rates of child survival, despite all efforts and a strong focus on the health needs of children. The major causes of death are well known, as are many of the solutions. However universal implementation of effective policies is patchy. He noted the variations in research funding, the capacity to tackle priority issues and the importance of targeting research to activity at community level. It is at this level where most benefit is likely to be achieved. He concluded by referring to the immense effort needed to secure the MDG 4 target for child mortality, as present indications suggest the timetable will slip.

Professor Wen Kilama is Founder and Managing Trustee of the African Malaria Network Trust (AMANET).

Professor Kilama spoke about the practical issues facing AMANET and the findings emerging from the work of the Trust. He explained how Africa had many research institutions but that there is a wide variation in the quality of work between those institutions, some of which had links with institutions in the northern hemisphere. He identified the need to strengthen skills-capacity across Africa, addressing the skills migration issue and improved accountability as the most important issues. Partnerships had a key role to play, but along with financial flows, these need to put on a long-term sustainable basis.

Based on his experience in working with AMANET, Professor Kilama identified the following areas where capacity building would help in facing the challenges in malaria vaccine development:

- Strengthening capacity needs to focus on personnel and their skills development;

- Meeting the challenge of the significant training demands needs to combine a speciality focus – particularly in terms of financing accountability and needs assessment - with more general health care training;
- Identifying the financial resources needed to conduct capacity-strengthening programmes to enable effective trials to be conducted;
- Recognising the full costs of product development;
- Increasing the frequency of monitoring and other oversight procedures;
- Accepting that African R&D institutions can undertake trials to internationally accepted standards;
- Maintaining sites between trials and particularly the need for increased capacity between Phases 1b to 2b;
- Facilitating the transfer of technology from the north to the south.Building trust especially between donors and with researchers in the north.

Some Lessons Learnt

- Capacity strengthening should cover personnel, equipment and other infrastructures;
- Training demands great, need to focus yet spread out;
- Capacity strengthening costly;
- Product development costlier;
- Frequent site monitoring and oversight;
- Strengthened African R&D inst. can undertake trails at internationally acceptable standards;
- Site maintenance grants between trails, also increased needs Phase 1b to 2b;
- N-S technology transfer essential
- Delays in product availability common
- Build trust (with donors, northern researchers)

Source: www.amanet-trust.org

Professor Fred Binka, is Executive Director of INDEPTH network and Project Director of the Malaria Clinical Trials Alliance (MCTA).

Professor Binka summarised the work and projects of the INDEPTH network. He emphasised the importance of developing capacity to enable effective clinical research to be undertaken within the developing world. WHO had reported in 2006 that "the present capacity for conducting clinical trials is insufficient or even non-existent in virtually all countries in sub-Saharan Africa". This state of affairs had persisted despite Africa having been involved for some time in clinical trials. However, the problems lay with the trials being conducted on a piecemeal basis, demanding a more serious and concerted effort to ensure the selection and conduct of clinical trials a priority for the research agenda in Africa. Clinical research in developing countries should be focussed on local health needs in disease endemic countries, with the use of different population groups and healthcare settings to satisfy national and international regulatory requirements.

Professor Binka reported on how INDEPTH is using its network of 37 sites in 19 countries to harness the the collective potential of the world''s community-based longitudinal demographic surveillance initiatives. This helps provide better empirical understanding of health and social issues and to use this understanding to alleviate the most severe health and social challenges. INDEPTH provides added-value through its ability to harmonise and improve approaches, share good practises, help raise the level of competences and support the use of data for policy formulation.

Based on this experience Professor Binka identified three key areas:

- investment of significant resources – human and financial – to expand the limited number of clinical trial sites in Africa;
- assistance to developing countries to strengthen their regulatory infrastructure;
- develop sustainable partnerships between drug and vaccine producers, clinical trial sites, regulatory authorities, training institutions and donor partners.

Professor Sandy Thomas is Director of the Nuffield Council on Bioethics.

Professor Thomas summarised the key issues to emerge from the first two sessions.
She noted that all research has to deal with ethical issues. In resource-poor settings, participants in clinical trials are most vulnerable, linked to cultural issues and the application of the fundamental principles of clinical research. She listed four of specific areas of challenge:

Consent – Relative consensus has been achieved on producing international guidelines, but disagreements remain in their application, particularly in the areas of information-sharing and the obligations for those conducting the trials to be sensitive to the participants.

Standard of care – Despite the availability of universal guidelines, there is increased awareness of the need for flexibility to meet the demands of different settings.

Post research issues – There are a range of issues involving the role and expectations of participants, the responsibilities of community services in respect of the participants, particularly if the trials are not related to their main health needs and recognising the different demands of chronic and communicable disease trials which may demand a case by case assessment.

Ethical review - The potential for conflict of interest over seeking and using resources is considerable, but there is also an obligation on donor supporters of clinical trials to play due attention to supporting health systems development.

International guidance on the conduct of trials has been revised. Such international guidance was not legally-binding although some countries are using it to introduce national legislation. Standards still vary between settings which make it difficult for researchers to draw up protocols for the conduct of trials. The onus is on governments, partners and donors to have a clear understanding of the standards to be followed. Some trials, which attracted very significant resources, had had to be curtailed because of ethical disputes. These unfortunate circumstances must not be repeated.

Panel Session

Professor Thomas was joined by the previous speakers and by **Professor David Kerr** (Rhodes Professor of Clinical Pharmacology and Cancer Therapeutics at Oxford University and conductor of cancer-related studies in India) for further comment and to take questions from the floor.

Dr Vikram Patel referred to the particular concerns around clinical trials in India. Three specific concerns were raised. Firstly, questions are raised regarding the ultimate beneficiaries of trials, i.e. whether they will include the participants in the trial and their fellow countrymen or whether trials are being conducted primarily to secure regulatory approval in other parts of the world. Second, trials in public healthcare settings raise specific ethical issues around informed consent because, typically, the physician obtaining consent is the only person who is offering free or subsidised treatment to the patient. Economic compulsions can limit choices for poorer patients. In a hierarchical health system, informed consent in response to an

invitation from a patient's doctor to enrol in a trial is unlikely to be truly free and fair. Thirdly, the role of the private sector is another concern. Financial incentives can interfere with the due process of obtaining informed consent in environments where there are weak regulatory systems for private healthcare.

Dr Francis Omaswa spoke about the need to look at the big picture, based on his experience as Director General for Health in Uganda. In particular he underlined the importance of having a national structure to oversee research and for research to be included in the development of health- sector plans to better enable research to be linked with routine clinical work. Research centres often stand alone. There needs to be a mechanism for sharing the output of research more widely within a country and with neighbouring countries. Implementing research outputs requires political leadership and the involvement of all sectors including technical managers and civil society.

Dr Tachi Yamada supported the big picture approach. Clinical trials in a developing country tend to be based upon the approaches adopted by a developed country and needs to reflect a common standard. Precisely what constitutes a standard of care needs to be agreed to avoid micro-ethics getting in the way of macro-ethics.

Professor Zulfiqar Bhutta urged that standards of care need to be seen in the context of health system research and the involvement of the private sector. He referred specifically to the potential dilemma of a patient accepting a government-approved antibiotic, when better treatment is available in the private sector. He supported the involvement of sub-national government and community leaders to enable agreement to be reached with donors about the flexibilities linked to the acceptance of a universal standard of care to meet the cultural and social needs of the setting for the trial. The question of efficacy versus effectiveness needs to be addressed.

Professor Wen Kilama noted from his work with AMANET that there had been significant improvements in the conduct of research in Africa and the involvement of ethical review committees had played an important role as well as the more widespread use of Standard Operating Procedures (SOPs). The SOPs need to be supported by research institutions in the face of competing priorities for limited resources. Professor Kilama also spoke about the dilemma faced by African research institutions when approached by donors to conduct research which is not amongst their top priorities. It is very difficult for these institutions to turn away funds. Product development needs to be backed in a sustainable manner so that the outcome of trials can be made available to the wider communities of those taking part. Without this commitment, there is a real danger of Africa creating a market for northern research.

Professor Fred Binka underlined the importance of continuous monitoring and review of research institutions in resource-poor settings. This was necessary to ensure all lessons are learnt from these experiences in order to develop a more solid research base for the future.

Professor David Kerr referred to the increasing global cancer burden, with 16 million new cancer cases expected globally by 2020, with two thirds of these in the developing world. Annual cancer rates are outstripping mortality from HIV/AIDs and malaria combined. In responding to this need, Professor Kerr explained the steps taken in India and the ethics of building infrastructure to support the conduct of clinical trials in India's six top cancer centres, linked to Oxford University and supported by GSK. 100,000 new cases are seen each year and the value of the approach has enabled Indian patients to participate in global trials but treated by Indian doctors and accessible to the ideas and drugs from the GSK pipeline which are relevant to the disease prevalence in India. The result of this partnership approach has been the support of the Indian Government, India's senior experts and the patients.

A further issue was in the area of training and education. Professor Kerr cited the example of greater access to human tissues. Training of specialists in India to analyse tissue taken from tumours had been extremely beneficial and had helped reduce diagnostic times.

Professor Kerr noted that there were some similarities in the conduct of trials between his work and the malaria studies in Africa. There was a danger of disease-specific research being compartmentalised. It is important to learn from all research experiences in such areas as the design of trials. The work of AMANET and INDEPTH provide some useful insights in to the design of cancer trials particularly in sub-Saharan Africa.

Points raised in discussion covered the debate between effectiveness and efficiency and particularly the potential tension between use of efficiency data in resource-poor settings. It was noted that there is insufficient debate about the running of trials to support scaling-up of evidence-based interventions. Continuing dialogue between governments, multinational bodies and donors was mentioned as one way of seeking to overcome the current difficulties. On the question of north-south organisation and conduct of research, there was general agreement on the importance of strengthening collaboration between research institutes through the establishment of a code of conduct. This would not only help support vaccine development but would also help clarify issues around the ownership of the data collected and the outcome of the trials. The experiences of INDEPTH and AMANET indicated the value of this approach. The effectiveness of the code would depend on ensuring that appropriately trained staff were in place to support implementation and monitoring of the code. Shortage of skills around intellectual property, pay scales and improved reimbursement policies were important issues in Africa,which could inhibit a code's implementation.

KEY THEMES

- International guidance on the conduct of trails is beneficial;
- Improved development of sustainable parterships is desirable and would help protect skills drain;
- Call for better sharing of information about the conduct of trails across diseases and on-line evidence-based interventions.

THIRD SESSION
Responding to the Challenges

Chair: Professor Janet Hemmingway

Professor Janet Hemmingway – Director of the Liverpool School of Tropical Medicine – chaired the session which focussed on options for policy and partnership development to strengthen research and health status in developing countries.

Professor Sir Andrew Haines is Director of the London School of Hygiene & Tropical Medicine.

Professor Haines' presentation concentrated on research to enable global health goals to be met, by improving coverage of existing interventions which had shown to be efficacious and effective in large-scale trials, and how these interventions can be scaled up in populations. Data in the child health area shows that take-up of interventions varies dramatically between countries. There are significant variations between the highest and lowest quartiles in the use of health services in developing countries and countries with economies in transition. Scaling-up

effective procedures requires a functioning health-system and needs to overcome the wide variations in access within some countries. Similar inequities apply between countries, which can inhibit knowledge and technology transfer as a result of trials.

Professor Haines identified a number of common barriers and challenges to improving service delivery emerging from reviews of major initiatives on maternal health, child health, TB, malaria and HIV/AIDS. These include demand-side barriers, multiple providers with a mixture of private and public provision, human resource issues, drug supplies and supply systems more generally. Other issues were management capacity, financial constraints and resource allocation policies, limited or lack of coordination between programmes, weak monitoring systems and poor use of information.

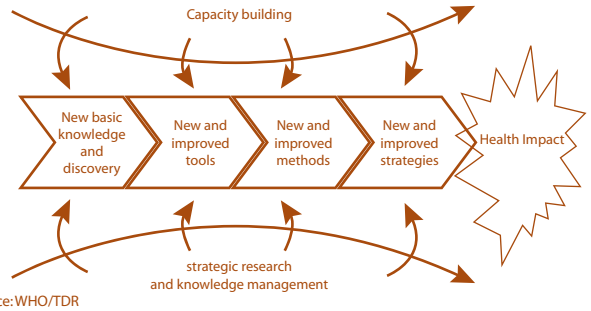
The key response to these challenges is the development of better knowledge about how to improve health systems. A growing number of effective interventions are now available and increasing amounts of resources are now being made available to support research. But scaling-up of services is being handicapped by fragile and fragmented health systems. Reasons why research for scaling-up has not been attractive include the lack of visibility in the issues. Also health systems work is less emotive than child survival work. Long time-frames, limited capacity, lack of sustainable resourcing and weak linkages between research and policy are other issues.

Community-based health insurance is one option for improving access to health care in low-income settings. It is being promoted as a solution to "out of pocket" expenses. Although some countries such as Rwanda are making progress in scaling-up access to community-based health insurance, the evidence shows that many schemes are very small and the poorest tend to be under-represented. Other problems include the tendency for the sickest to join first which can skew the costs, low enrolment and variable quality of clinical care. Research needs to address what are the appropriate subsidy policies by donors and governments to support scaling-up, along with the appropriate mechanisms for promoting strategic purchasing of quality health services.

There is very limited evidence from resource-poor settings on how to bridge the gap between research and practice. For example, two out of 18 studies in the Cochrane review on educational outreach visits were in low-income countries. Four out of 32 studies in the systematic review on continuing education and one out of 21 studies on the role of mass-media interventions were conducted in these same countries.

Scaling-up research requires large-scale studies and population. Resources for evaluation need to be embedded alongside the programmes being rolled out from such sources as the Global Fund and other major donors to ensure that evaluative research is an integral part of scaling up such activities from the outset. Valid and transferable research is required and this needs to

Innovation to impact-ensuring that evaluative research is built in to major programmes



Source: WHO/TDR
Nature Medicine 2004, 10, 1-4

take a multidisciplinary approach involving, in addition to epi-demiologists, health economists, anthropologists and sociologists, to ensure the work is appropriate to the cultural setting and that important contextual factors such as acceptability, site selection, human resources and socio-economic profile are adequately documented.

Research on effective interventions and effective delivery strategies needs to be an iterative process between policy-makers and researchers from an early stage. Information dissemination strategies are important and will help ensure that research is an intrinsic part of policy formulation. It is also important for there to be a mechanism for feeding back when implementation for research finds fails and in this way "research to policy to practice" becomes a cyclical process.

Dr Jimmy Whitworth is Head of International Activities at the Wellcome Trust.

Dr Whitworth addressed the conference on stimulating links between the academic bioscience community and the developing world. He outlined some key principles for supporting global health research the importance of scientific excellence but limited resources, inequity of skills and access. He supported the development of an international strategy to help broaden the base of scientific evidence and the further development of international networks. He noted that much research focussed on communicable disease but a better balance with chronic and non-communicable disease is desirable. Strengthening health research capacity is important and links and partnerships had key roles to play both in stimulating research but also its implementation

Dr Whitworth referred to a number of barriers to conducting research in developing countries. These included a lack of quality education, particularly in science, a lack of clear career opportunities and pathways, competing factors both within countries and externally such as opportunities to work with multinational agencies, limited facilities and funding. There was also a need for stronger government and ministerial commitment and support.

Partnerships are one way of stimulating links. These require joint funding arrangements, sharing of resources, providing in-kind support and advocacy and influence. Partners include governments, research funders, industry, universities, charities and NGOs. The benefits to be derived from this approach are the added-value of joint approaches, increased leverage to influence external factors which impact on the conduct of research, enhanced synergy between partners and shared goals. Other benefits included maximising the available financial resources, reducing risk exposure and duplication of effort, as well as broadening out the available networks, expertise and infrastructure.

There are a number of models for partnerships. These include joint funding for one-off initiatives such as the Wellcome Trust and the Gates Foundation's support for work on the genetics of protective immunity against malaria, protection against HIV infection and drugs for treatment of latent TB infection. Other mechanisms are parallel funding, but with either separate decision-making or with a single decision-making body, interde-pendent funding partnerships such as the International Collaborative Research Grants; and consortium-funding arrangements. There was also joint-venture approaches such as the Medicines for Malaria venture, hybrid arrangements and strategic alliances.

Dr Whitworth noted that the parts of the world with the highest disease rates were in the poorest countries and covered a third of the world's population. In high-income countries, chronic non-communicable diseases were the major diseases

whilst the disease burden of these diseases and that of communicable diseases were roughly the same in low-income countries. Capacity building was the key and Dr Whitworth outlined some of the approaches which were being supported by the Wellcome Trust. There is a focus in human resources though support for International Senior Research Fellows. This scheme supports training in basic science in countries where there already exists a foundation on which to build. Further support is being given to programmes and networks in South East Asia and, in conjunction with the UK's Department for International Development and with IDRC from Canada, the Trust is supporting health-research systems development in Kenya and Malawi. The aim is to use capacity building to improve the use of evidence-based decision making, whilst supporting talented individual scientists, equipping institutions and facilitating and enabling an environment where research can flourish.

The lessons learnt from Wellcome's input to these partnerships are that it is important to be clear about the expectations and objectives of all partners from the outset. There is a risk of loss of control, reducing flexibility and adding complexities to the working relations and the slowing down of decision-making. There is a need for partnerships and host institutions to be committed to capacity development and to recognise that exit strategies and sunset clauses may be required to enable donors to withdraw their support without completely undermining the research. Building in evaluation and review from an early stage is essential as well as developing strategies for sharing outcomes, disseminating results and engaging and influencing policy development and its implementation.

Partnerships: lessons learnt

- Be clear about expectations and objectives of all partners from the onset
- Potential loss of control
  - Less flexibility, additional complexity in working arrangements
- Risk of slowing down decision making
- Need for partnership with host institutions:
  - developing capacity
  - exit strategies, sunset clauses
- Build in evaluation and review from an early stage
- Consider how to share outcomes, disseminate results, and influence policy and practice

Dr Moncef Slaoui is Chairman of Research and Development for GlaxoSmithKline.

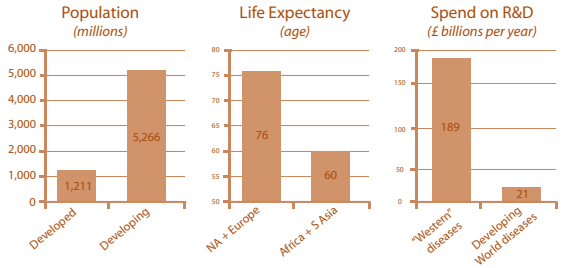
Dr Slaoui reviewed the Pharmaceutical R&D responses to neglected diseases and and the impact of these diseases on populations in the developing world. The conference had identified many of the critical issues which stand in the way of scientists, individuals and physicians in their quest to make access to healthcare throughout the world an equal opportunity for everyone. This is one of GSK's commitments to society and the company's R&D focus is dedicated to the discovery and development of drugs and vaccines for the disease burden in the developing world.

The majority of the world's population facing the worst of the disease burden is in the developing world. Life expectancy figures show the impact of these diseases. The disproportionate R&D expenditure in the developing world highlights one of the gaps in the fight against neglected diseases. The scientific community in general, over the last several decades, has to some extent tended to neglect basic research into the understanding of the basic biology and pathophysiology of a number of complex pathogens, such as malaria and leishmaniasis, and complex viruses, such as dengue virus.

These are some of the major diseases in the developing world. So the hurdle for discovering new drugs and vaccines in terms of scientific understanding is higher for these diseases than many others, yet the level of scientific knowledge is more limited.

There are multiple facets to the problems of bringing forward new therapies for diseases of the developing world.At an operational level, clinical trial infrastructure and governance, as well as quality and ethical issues, are critical aspects for the development of new drugs. Registration and approval procedures are also important. Financial issues are also important for pharmaceutical companies, like GSK, which are public companies that face market pressures and an accountability to deliver returns to shareholders. These multifaceted problems require a multifaceted solution. A major element of the solution will be working in partnership with an assortment of dedicated parties, such as NGOs, healthcare systems, and governments.

stark need... ...disproportionate effort



2006 UK Science Policy Conference
Royal college of Physicians, London, 7th Sept
Source: 2005 World Population Data Sheet, WHO commissioned study by UC Berkeley & Univ of Delhi

GSK's strategy for developing new drugs and medicines for neglected diseases is based on seeking to work in partnership to maximise scientific expertise, to value the input of local knowledge, know-how and resource availability and to make a long-term commitment to ensure the drug developments reach their target populations. Underpinning this strategy are two dedicated initiatives: GSK's Diseases of the Developing World (DDW) Drug Discovery Centre in Spain, with more than 100 scientists (chemists and biologists) dedicated to the work, with an annual budget of £20 million per year. GSK's Infectious Disease Medicines Development Centre is committed to the clinical development and production of all DDW medicines, working with many partners and involved in trials with more than 1000 patients, mainly in the developing world. Dr Slaoui referred to two DDW examples which underlined GSK's commitment to public health. He referred to the Chlorproguanil/Dapsone/ Artesunate combination therapy for the fight against malaria. This has been developed with a number of partners and is currently undertaking Phase III trials. This drug has been developed in line with WHO's "Roll Back Malaria" recommended combination therapy and its development has underlined the benefits to be derived from a partnership approach. The second example was Sitamaquine used in the treatment of leishmaniasis. Dr Slaoui referred also to the work of GSK Biologicals in Brussels , which has a long history of uninterrupted work on DDW, with 8 ongoing clinical programmes for vaccines. This has contributed greatly to the programmes of WHO, UNICEF, GAVI and PAHO. He explained the 26 year history of GSK's malaria vaccine programme. This has contributed greatly to the understanding of which malaria antigens should be used in the vaccines and had supported developments in vaccinology and immunology over the years.

A number of challenges remain. On the discovery of new medicines, the pharmaceutical industry has faced problems with fragmented approaches and a dilution of effort. Scientists have never had sufficient resources to fully undertake their work. Clinical development is being hindered because of the requirement of clinical infrastructure for large trials and the requirement for effective clinical governance. Capital infrastructure and investments for developing a drug along with effective pharmacovigilance are key elements for ensuring sustainable implementation.

Turning to the need for new partnerships and policy ideas, Dr Slaoui highlighted three areas:

Discovery of new drugs – It is important to find ways of breaking down the barriers of competition with the formation of consortia as one means of this being achieved.

Clinical development – Greater involvement by multinational organisations such as WHO, governments and NGOs is important. This will help ensure good quality clinical trials are being conducted with the necessary infrastructure, governance, regulation and skills training addressed. Coordination and sharing information with other parts of industry is important so that duplication and overlap is reduced.

Sustainable development – The key challenge is to find an appropriate mechanism for funding agencies, governments and industry to create credible and sustainable market conditions to enable research and development to flourish and to focus on reducing the burden of diseases in the developing world.

Dr Vinand Nantulya is currently with the Foundation for Innovative New Diagnostics (FIND) and was previously with The Global Fund to fight AIDS, Tuberculosis and Malaria.

Dr Nantulya made a strong case for the importance of effective diagnostic tests for tackling poverty-related diseases in the developing world. He reminded the conference that diagnostics in Africa tend not to play a significant role in treatment. There are a number of reasons for this. Laboratory facilities are poor and the quality of diagnostic results is poor. The absence of quality control is another major factor. Diagnostics are central to the fight against diseases of the developing world and there are consequences for the individual and to public health if there is no accurate diagnosis. The absence of diagnostics makes physicians rely on syndromic treatments. This is not satisfactory for the patient and is a misuse of public health resources.

The microscope remains the fundamental tool for diagnostics today as it was more than a hundred years ago. Taking the example of TB in Africa, there are nine million new cases per year, yet only 25% cases are detected using sputum microscopy. This takes about five days in Africa, in comparison with diagnosis in the western world taking only four hours, by using more sophisticated techniques. What is needed are simple, accurate, rapid and affordable diagnostics. They must be able to respond to the needs at all different levels of the health system – at health posts, hospitals and at district levels. Diagnostics must be brought closer to the patient rather than taking the patient to the diagnostic services.

FIND – a public private partnership – is proposing that what is needed is an integrated technology platform. At the level where only symptoms and signs are used for diagnosis, followed by treatment and where 60% of patients go for help, lateral flow technology is needed as a platform for developing other diagnoses. Popularly known as dipsticks, it is possible to use this approach for malaria, for TB, and in other diseases for the detection of antigens and antibodies, whichever applies.

This is a qualitative, simple and rapid "yes" or "no" test which can easily be used at the lower levels of the health system and in patients' homes.

At the level where microscopy is used, where 25% of patients attend, molecular technology tools are needed. FIND is working with a Japanese company that has allowed this technology to be used royalty-free, to help develop diagnostic tools for diseases of the poor. It is applicable to malaria, TB and sleeping sickness. The same instrument is used for all of the diseases with only the primer needing to be changed. Presently efforts are being made to bring this technology to the health post.

Dr Chris Hentschel is President and Chief Executive Officer of the Medicines for Malaria Venture (MMV).

Dr Hentschel traced the development of Public-Private Partnerships (PPPs) for improving health and the options for their further development for the delivery of medicines in resource-poor setting. PPPs are a means to support developments which would not be possible if depending entirely on market forces.

R&D funding is split between the public and private sectors – with the split almost being 50-50. Almost all products are developed in the private sector so that the public sector is more about enabling research. PPPs vary between single product organisations, managed portfolios, exotic diseases and delivery responses.

The mission of PPPs can be simply stated: to discover, develop and deliver affordable appropriate and accessible treatments. Doing this is difficult. Affordability is a key issue for poverty-related diseases. Developing antimalarial drugs is relatively simple from a technical point of view, but it is extremely difficult to make these affordable. Many projects fail because of the need to meet the low price requirement.

PPP projects can now be diverse geographically yet are still managed by a small group based in Geneva. Drug research is becoming more modular over time and the key is to tie particular modules of research together. For example, clinical research on malaria is carried out in Africa and Asia, but other modules such as toxicology and medicinal chemistry are done elsewhere and can be accessed from all round the world. Provided there is an understanding of the science and what is being achieved, it is possible to pull these strands together.

Dr Hentschel quoted the example of the development of a synthetic form of the drug of Artemesinin. Originally this work was carried out by Roche to produce synthetic molecules with some activity. Roche subsequently closed down this activity, but the person engaged on the work moved to WHO, and encouraged some academic scientists around the world to do some further medicinal chemistry work and who started to produce some other compounds. One group in Nebraska came up with some interesting compounds which were tested in Switzerland. MMV then became involved and introduced greater funding and soon more partners were involved around the world. A pharmaceutical company then became involved in the development and soon a single project spanned the globe, managed as a virtual R&D project.

In MMV's experience, projects with pharmaceutical companies are carried out to the same standards and using the same facilities as their "for profit" work. The number of pharmaceutical companies involved with PPPs is limited. GSK is involved, but the industry base needs to be expanded. Results to-date show that whilst there are a number of failures, there is nothing about PPPs which is contrary to their public company responsibilities.

PPPs have attracted significant attention in recent years with Science Magazine suggesting this approach was the "Science breakthrough of the year" in 2004. Harder data had been collected by a study carried out by the London School of Economics and funded by the Wellcome Trust in 2005. This empirical study looked all the R&D into neglected diseases. Some performance indicators were developed and the findings concluded that 75% of global drug R&D (not diagnostics or vaccines) was now being managed as a PPP. The pipeline had increased dramatically with eight to nine new drugs expected to be registered by 2010 against a history of only three new drugs being registered in the past 25 years. This suggests that PPPs deliver results faster than in the public sector, are overall cheaper than R&D within a company, and provide good value for money.

Challenges for the future centre on funding and particularly on the rising costs of development elements. There will always be a funding gap, but successful mechanisms will always be attractive to potential contributors. The "not for profit" sector and PPPs could benefit if the tax environment was more conducive to philanthropy. Several innovative funding mechanisms are being introduced. These include the International Financing Fund (IFF) for vaccines, the French proposals UNITAID which makes use of funds derived from air travel taxes, securitization and Advanced Market Commitments. Other challenges are around the delivery of low-cost products. This depends on a low-cost manufacturing base, with China and India as leading countries where this is happening. In India there are more than 2,000 manufacturing operations yet a high proportion operate at lower than internationally agreed (usually EU) standards. Raising quality standards is a high-cost enterprise. Standards in China need also to be closely monitored and improvements could be assisted by knowledge transfer as partnerships develop.

Delivery of products can be highly complex in resource-poor settings. The public market tends to be well regulated through initiatives like the Global Fund. The private market tends to be well run in capitals but more chaotic in other areas. Forecasting market needs is often poor or non-existent for several neglected diseases in the endemic countries. Reliable data collection and dissemination of information would help attract private-sector participation.

Dr Hentschel summed up his presentation by concluding that PPPs will really deliver in the discovery, development and delivery of new medicines in resource-poor settings. PPPs are still in development and the process has still to reach maturity. However, the signs are encouraging, although there is scope for further development which will benefit the access of new medicines in resource-poor settings.

KEY ISSUES

- More research on health systems development needed to underpin scaling-up of resources;
- Partnerships can help overcome barriers to research, education deficits, career opportunities, improved facilities and joint funding arrangements;
- Market forces must support drug and clinical development;
- Improved diagnostic testing will benefit treatments;
- Public Private Partnerships have delivered but the process has still to reach maturity.

PANEL SESSION

What new partnerships and policy opportunities are needed to improve health outcomes?

Chair: Professor Sir Gordon Conway

Professor Sir Gordon Conway is Chief Scientific Adviser to the UK's Department for International Development. He was joined by the speakers from the third session with **Dr Lynn Marks** – Senior Vice-President, Infectious Diseases at GSK. **Andrew Jack** – Senior reporter on pharmaceuticals and health care for the Financial Times – and **Dr Joanna Rubinstein** – Director for Global Health and Science Initiatives of the UN Millennium Development Project – also joined the panel.

Professor Conway began the session by taking questions on diagnostics and PPPs.

The issue of how PPPs address affordability of medicines was raised in given that the majority of support is coming from private foundations. Whilst it would be encouraging to see a bigger proportion from the public sector, there have been suggestions that PPPs are undemocratic and do not represent the public interest. From a private sector perspective, large pharmaceutical companies are not expecting any financial return in this area, but it is possible that some of the smaller companies from Asia make small profits from private sector sales.

The underfunding of National Drug Regulatory Authorities in resource-poor countries was raised. This can lead to these Authorities being marginalised and easy to bypass. As a result drugs are being imported into these countries without control. Regulation needs to be strengthened at the national level of the importing country and at the same level in the exporting country.

It was suggested that there is no point in scaling-up on those areas which do work, if in the background there is a huge volume of drugs and medicines which don't work and the market is flooded with cheap or counterfeit alternatives. Some research is being carried out to develop technology to detect counterfeits. This technology will need to be portable and transferable and made widely available. Other approaches include enforcing sanctions against those who import counterfeits and improving the delivery of drugs through the public sector. A number of countries, particularly in the EU, are taking steps to improve their regulatory controls for exports and this approach needs to be more widely applied. The Wellcome Trust has experience in South East Asia where its researchers worked on the anti-malaria drug, Artemesinin. They produce a newsletter about the latest drugs to give information on what is being made available. However, several generations of the same drug make it difficult to know if they are genuine. The factories producing these have been identified, but they are well-protected from prosecution.

Professor Conway referred to the UK Government's 3rd White Paper on international Development. It contains a large number of commitments to health as well as to increased funding. Further funds will be found to support national health services, 10 year plans in Africa, the replenishment of the Global Fund, Roll Back Malaria and support for AMCs. Funding for Partnerships will increase to £100 million per annum with £20 million for PPP product development and expenditure on science and technology research will double by 2020 with £220 million per year to be spent on research covering agriculture and climate change as well as on health.

Professor Conway reflected on a number of issues emerging from the conference discussions. He identified a range of tensions. These were:

- The tension between western medicine and traditional medicine and how much reliance is placed on one or the other;
- The tension between supporting hospitals and advanced clinics in an urban setting with community health services in rural areas;
- The tensions between vertical and horizontal programmes;
- The tension between supporting a vertical programme rather than health systems research;
- The tension between top-down and bottom-up approaches;
- The tension between what the "experts" believe is good and what the people in poor settings say they want;
- The tension between capacity-building and actual delivery.

A number of different partnerships had been identified. Parties enter these for a variety of reasons, but complementarity is a strong incentive. Partnerships are an essential prerequisite for the delivery of the PPPs' mission statements. Donor harmonisation is another important issue to be developed further.

Professor Andy Haines suggested new forms of relationships needed to be established between northern and southern academic institutions. Too often they have been seen to be fragmented, short-term and exploitative. Clear guidance and long-term incentives and support structures are needed to help institutions improve each others strengths in a mutually-advantageous fashion. The aim should be to leave the southern partner in a stronger position and in a sustainable fashion.

Initiatives are needed to strengthen links between policy makers, including the donor community, and researchers, to ensure research evidence is central to the development of policies. There appears to be insufficient understanding within the donor community of the full spectrum of research on health policies and systems, which leads to insufficient demand from this community for the research evidence which the academic sector is capable of producing. This could help the donor community use their contributions more effectively.

Dr Joanna Rubenstein referred to the universal commitment to the achievement of the MDGs. An implementation road-map has been produced which is now leading to the production of national development strategies. Partnerships are needed to strengthen the harmonisation between donors and for closer working with governments. Health requires an integrated approach. Delivery and the health work-force are key stumbling blocks. Insufficient numbers of doctors and nurses are being trained to meet the need. More community health workers, training and continuous education programmes are required to produce a new cadre of health professionals who will become a part of the health system. In this way health systems can be strengthened. Action plans which change national policies are needed to bring this into effect.

Dr Jimmy Whitworth urged the promotion of south-south networks building using the examples of AMANET and INDEPTH. These demonstrated the value of joint courses on ethics and other training to make full use of each other's strengths. The Wellcome Trust is engaged in some research in South East Asia where the main clinical management expertise for avian flu is located. There are issues of sharing information between countries of different WHO regions. The Turkish outbreak led to western experts becoming involved despite lacking the practical experience of their South East Asian counterparts.

On the policy side, there is a need for further discussions on ethical issues of public health research, cluster-randomised trials and health services research. There are no clear guidelines at present. Problems with the efficacy of an intervention might not be in doubt but more needs to be known about the effectiveness, either alone or as part of a package of health services. A second issue in the context of a cluster-randomised trial of health services is the feasibility for an individual not to consent if they are part of the cluster. It would be helpful to have agreed guidelines to help answer questions of a practical and policy relevance.

Dr Chris Hentschel proposed the need for a partnership to have responsibility for capturing the information which drives the markets. It is extremely difficult to obtain accurate information about what products are in the informal market, who produces them and who sells them. This kind of market information is fundamental to the decision-making process of private companies for making their investments. A second partnership might focus on advocacy. Given the predictions of the high levels of money expected to be available over the next 30 years, global public health needs to act in a more coordinated fashion in order to attract its share of this money for a common cause.

Dr Vinand Nantulya emphasised the critical importance of diagnostics and the scope for a partnership at the global level which brings together donors, industry and researchers to develop new products. At regional level there is scope for enhancing the evaluation of these products taking place in laboratories at sites with good clinical practice. This would provide an opportunity to link networks such as AMANET and INDEPTH and universities and researchers in developing countries, with the evidence providing a pathway into policy making. New tools, new medicines, new vaccines and new diagnostics will make a difference only if access is assured. At country level this can be achieved by developing partnerships involving opinion formers, civil society, policy makers, government, implementers, local professionals,patient organisations and the media.

Dr Lynn Marks referred to the WHO report at end of 2004 which identified pharmaceutical R&D gaps with six out of the top 10 being infectious diseases. PPPs exist for several of these and are operating successfully. They provide the basis for further partnership work. In addition GSK is in partnership on 28 collaborative clinical studies in resource poor settings linked to HIV/AIDS. Eight of these focus on mother to child transmission. A new partnership might focus on further prevention measures such as the development of oral microbicides. Other areas for partnership are; the development of medicines and vaccines for pandemic influenza, building on the work already in hand, further development of sitamaquine and on antibacterial resistance targets– the number one gap in the WHO report.

Andrew Jack identified six challenges. It is crucial to create real PPPs as most are neither "public" nor "private" but rather non-profit driven–with the Gates Foundation behind most of them. This creates two problems – the monopolisation of ideas and direction and the possible intimidation of potential donors who feel that Gates is already occupying the space. More pharmaceutical companies could be engaged in PPPs whilst developing countries' government expenditure on health is still far too low. The "partnership" element could also improve. There is a tendency for academics to think that drug development can be achieved in an academic setting, whilst the pharmaceutical companies pay excessive attention to intellectual property rights and the secrecy that goes with it.

Costs need to be reduced particularly for late-stage clinical trials for drugs for the developing world even before implementation. There is a great deal of duplication and considerable scope for rationalisation, to make better use of limited resources in the developing world

A great deal more needs doing to evaluate and respond to evaluations. More money is coming in, particularly from the Global Fund, but there are huge issues about the effectiveness of its projects on the ground. Very simple benchmarks for allocating grants exist but the bottom-up bidding process needs to be reviewed in the light of experience to reflect that in some settings the projects are less effective and more expensive than elsewhere.

Mr Jack's final three challenges related to strengthening the local regulation and ethics procedures and recognising the need for flexibility in international guidelines to reflect local circumstances, notably the relative risks and benefits of drugs. The social science challenges are at least as great as the medical ones, and need to be recognised to ensure effective implementation reflecting broader political and social issues. The final challenge is the need to improve the advocacy for global health and to clearly establish how far improved health results in improved economic outcomes. Health faces strong competition for development support from other social policy areas. Health advocacy is too often fragmented and would benefit from a more coordinated approach.

Concluding Remarks

Professor Martin Bobrow – Governor of the Wellcome Trust

Professor Bobrow expressed the need for more quality implementation research and provided a couple of personal observations, based on the day's discussions. Humans can be fallible. The evidence of counterfeit drugs and their sales is a testimony to this. Some forms of social control are needed, but care needs to be taken to avoid excessive bureaucracy. Lessons need to be learnt from the Intellectual Property process. A possible theme for a further conference could be to look at drug regulatory processes to see if the right balance has been struck between safety, efficacy and cost and the portability of such mechanisms from developed to developing countries.

Issues around the export of technology fade in comparison to the development of social structures which allow implementation. All stages of this process are dependent on well-motivated people, which makes skills training and fellowship programmes in general such an important exercise.

Professor Bobrow expressed his appreciation to the contributors both for their factual content and the number of constructive and interesting ways forward which have been presented to the conference.