

***Oxford Conference on Innovation and
Technology Transfer for Global Health:
Bridging the Gap in Global Health
Innovation – From Needs to Access***

Oxford

9 -13 September 2007

Conference Proceedings¹

***A conference generously supported by
The Bill and Melinda Gates Foundation***

¹ Written by Rachelle Harris and Sarah Miller, based on transcriptions of the conference proceedings which were recorded throughout. The correct citation is Harris, R. & Miller, S. (Eds.) June, 2008: *Conference Proceedings: The Oxford Conference on Innovation and Technology Transfer for Global Health: Bridging the Gap in Global Health Innovation – From Needs to Access. 9 -13 September 2007.* Please address any comments or queries to andrew.farlow@economics.ox.ac.uk.

TABLE OF CONTENTS

| | |
|---|-----------|
| PREFACE | 1 |
| 1. INTRODUCTION | 2 |
| 1.1 Report Structure | 2 |
| 1.2 Global Health & Access - Background | 2 |
| 1.3 Considerations for a Future Research Agenda | 4 |
| 2. PLENARY LECTURE: HEALTH INNOVATION: THE NEGLECTED CAPACITY OF DEVELOPING COUNTRIES TO ADDRESS NEGLECTED DISEASES | 4 |
| 3. DIMENSIONS OF THE CHALLENGES | 7 |
| 3.1 Free Market Strategy in Healthcare: Key to achieving Product Availability and Access: Dr Stephen Mallinga, Minister of Health, Uganda | 7 |
| 3.2 New Solutions for Global Health Challenges: Ms. Patricia Atkinson, Bill & Melinda Gates Foundation, USA | 8 |
| 3.3 Innovation, Access and Public Health: Dr. Harold Jaffe, University of Oxford, UK | 9 |
| 3.4 Challenges to Vaccine Financing and Systems Support: Rebecca Affolder, GAVI Alliance, Switzerland | 11 |
| 3.5 The Intergovernmental Working Group: Dr. Howard Zucker, WHO, Switzerland | 12 |
| 3.6 Who is Listening to Those in Need?: Prof. Peter Ndumbe, University of Buea, Cameroon | 13 |
| 4. STRATEGIES FOR SECURING PRODUCT AVAILABILITY AND ACCESS | 14 |
| 4.1 The Development of Paromomycin IM for Visceral Leishmaniasis: Ms. Katherine Woo, Institute for One World Health, USA | 15 |
| 4.2 On-the-horizon Developments in Biotech and Nanotechnology: Ms. Dianna Derhak, DNA International Consultancy, Ukraine | 15 |
| 4.3 Pharmaceutical Industry initiatives: Dr Richard Barker, Association of the British Pharmaceutical Industry, UK | 15 |
| Private-Sector Case Studies | 16 |
| 4.4. The Case of Merck: Dr. Diana Lanchoney, Merck, USA | 16 |
| 4.5 The Case of Ranbaxy and ARVs: Dr. Arun Purohit, Ranbaxy, India | 17 |
| 4.6 The Case of Eli Lilly MDR: Dr. Gail Cassell, Eli Lilly, USA | 17 |
| 4.7 The Case of Pfizer – Dr. Robert Mallett, USA | 18 |
| 4.8 Discussion | 19 |

| | |
|---|-----------|
| 5. THE INTERFACE OF SCIENCE, TECHNOLOGY TRANSFER AND ACCESS | 21 |
| 5.1 Biotechnology Companies and Innovation: James Geraghty, Genzyme Corp. | 21 |
| 5.2 Improving Access to Existing Global Health Solutions: Dr Devi Sridhar, Global Economic Governance Programme, University of Oxford | 23 |
| 5.3 A Technology Driven Anti-counterfeiting Approach to Counterfeiting: Dr Prabuddha Ganguli and Dr Praful Naik of Bilcare, India | 24 |
| 5.4 The Power of Networks for Innovation: Dr. Rafael Rangel-Aldao, Simon Bolivar University | 25 |
| 5.5 New Initiatives in Japan: Prof. Katsuya Tamai, University of Tokyo | 25 |
| 5.6 ICBG Program and its Impact in Academia, Conservation and Drug Discovery in Latin America: Prof. Barbara Timmermann, University of Kansas | 26 |
| 5.7 Implementation of Biomedical and Information Technologies in Developing Countries: Prof. Eva Harris, University of California | 27 |
| 5.8 Discussion | 28 |
| 6. PARTNERSHIPS IN PROMOTING INNOVATION AND MANAGING RISK | 29 |
| 6.1 Strategies for Product Innovation: the PDPs: Dr. Mary Moran, The George Institute | 30 |
| Public-Private Partnership Case Studies | 32 |
| 6.2 The Aeras Foundation: Achieving Access: Dr. Jerald Sadoff, Aeras Global TB Vaccine Foundation | 32 |
| 6.3 Potential New Approaches to Scientific and Financial Innovation in PDPs - the example of AIDS Vaccines: Mr. Labeeb M. Abboud, IAVI | 34 |
| 6.4 PDVI – What is the End Game?: Dr. Harold Margolis, PDVI | 35 |
| 6.5 The PATH Strategy: Dr. Michael Free, PATH | 35 |
| 6.6. The South African Malaria Initiative: Jane Morris, African Centre for Gene Technologies | 36 |
| 6.7 MMV - Moving to Access: Dr. Chris Hentschel, Medicines for Malaria Venture | 37 |
| 6.8 IPM Case Study: Dr. Zeda Rosenberg, International Partnership for Microbicides (IPM) | 38 |
| 6.9 The Evolution of PDPs: Best Practices: Dr Adrian Towse, Office for Health Economics | 40 |
| 6.10 Desa Siaga – A Strategy for Health Investment: Siti Sundari, Ministry of Health, Indonesia | 40 |
| 6.11 Universities-Private Sector Relationships in Developing Countries: Dr. Jose Miguel Flores, Flores & Asociados, Universidad de Concepción | 41 |
| 6.12 From Recruitment to Implementation of Contemporary Research in Traditional Environments: Ms. Paulette Baukol, Mayo Clinic | 42 |

| | |
|--|-----------|
| 7. MANAGING INTELLECTUAL PROPERTY FOR HEALTH AND AGRICULTURAL INNOVATION | 43 |
| 7.1 The WTO TRIPS Agreement and Public Health: Ms. Jayashree Watal, World Trade Organisation | 43 |
| 7.2 TRIPS. Did the Sky Fall?: Prof. Keith Maskus, University of Colorado | 44 |
| 7.3 IP and Agricultural Innovation: Prof. Magdy Madkour, Bibliotheca Alexandria, Egypt | 45 |
| 7.4 IP, Pharmaceuticals and Foreign Direct Investment: Dr. Douglas Lippoldt, OECD | 46 |
| 7.5 Case study: ICMR: Dr. K. Satyanarayana, Indian Council for Medical Research | 47 |
| 7.6 IP, Innovation and Access – New Insights from the MIHR/PIPRA Handbook: Dr. Anatole Krattiger, Arizona State University | 48 |
| 7.7 Discussion | 49 |
| 8. FINANCING FOR INNOVATION AND TECHNOLOGY TRANSFER | 50 |
| 8.1 Who Really Pays?: Prof. Adrian Towse, Office of Health Economics | 50 |
| 8.2 Axios Partnership in Tanzania: Dr. Anne Reeler, Axios International | 50 |
| 8.3 The Chile Foundation, Mr. Marcos Kulka, Chile Foundation Case Study | 51 |
| 8.4 The Intersection of Economics and Access: Mr. Andrew Farlow, University of Oxford | 52 |
| 8.5 Funding for Biotechnology in Africa: Prof. Diran Makinde, African BIO | 53 |
| 8.6 Discussion | 54 |
| 9. CLOSING DISCUSSION | 55 |
| <i>APPENDIX A: AGENDA</i> | 58 |
| <i>APPENDIX B: DELEGATES LIST</i> | 62 |
| <i>APPENDIX C: SANJAYA LALL FELLOWS</i> | 65 |
| <i>APPENDIX D: GLOSSARY</i> | 66 |

Preface

The Bill and Melinda Gates Foundation generously granted \$139,725 to support a conference gathering together key policy makers and practitioners to examine innovation and technology transfer issues that impact on global health goals, with a particular focus on downstream access. The aim was to define an action agenda for further research and to disseminate findings following the conference. This document summarises the proceedings of the conference, entitled *'The Oxford Conference on Innovation and Technology Transfer for Global Health - Bridging the Gap in Global Health Innovation – From Needs to Access'*. The conference was held in Oxford from 9 -13 September 2007.

The conference emerged from the 'Gordon Conferences' model and brought together a diverse group of practitioners to address a range of issues related to technology transfer in health and global access to health. The conference commemorated the contributions of the late Professor Sanjaya Lall whose work, writings and presentations were instrumental in developing the whole field of technology transfer, foreign direct investment and corporate development. His work has guided research in this area for several decades and lies at the root of much that was discussed at this conference. In recognition of this, the conference organisers inaugurated a Sanjaya Lall Fellowship, a competitive award allocated to 32 individuals from the developing world. Representing policy makers and thought leaders from countries in Africa, Asia and Latin America, the Lall Fellows made up over thirty percent of the conference. Their financial support was thanks to the generosity of the Bill and Melinda Gates Foundation.

The conference focused on issues relating to access to health systems in developing countries, financing of research and development, and a range of initiatives aimed at enhancing developing countries' ability to deliver essential health interventions. The meeting's primary aim was to help develop the research agenda in this area and to explore means of influencing policy related to health product innovation and integration for the world's poorest populations. The conference also

examined questions of governance, accountability, institutional and policy design and ways to address them. The relationship between science, policy and management – both in business and healthcare - was at the heart of the discussions. It was accepted that the concepts of healthcare, technology and innovation extend beyond a narrow definition of these subjects. These issues raise challenging questions that are increasingly being transformed into concerns at an academic, business and policymaker level.

The conference was novel for several reasons. Among them, it aimed to identify actionable outcomes that were both commercial and non-commercial in nature that would have an impact on a practical level. Additionally, it sought to consider how business can help address the major social questions of the 21st century. The conference was structured to feature a large number of short presentations which consequently reserved a large amount of time for discussion. The conference speakers had a good gender balance; and both they and the discussants represented institutions in the UK, US, Australia, Japan, India, Switzerland, Sri Lanka, India, Uganda, South Africa, Chile, Bangladesh, India, Senegal, Namibia, Lesotho, Tanzania, Venezuela, Indonesia and Kenya among others. Participants included university researchers, representatives from donor agencies, biotechnology and pharmaceutical firms, senior managers from public-private product development partnerships, and others involved in programmes seeking to improve access to health products² and the treatment and prevention of disease for poor people in developing countries.

² "Health products" hereafter should be understood to include vaccines, diagnostics, medical devices and medicines

1. Introduction

One hundred participants took part in a four-day conference to assess the challenges and opportunities that impact on access to health products and healthcare by the world's poorest populations.

The discussion focused on:

- Dimensions of the Challenges
- Strategies for Securing Product Availability and Access
- The Interface of Science, Technology Transfer and Access
- Partnerships in Promoting Innovation and Managing Risk
- Managing Intellectual Property for Health and Agricultural Innovation
- Financing for Innovation and Technology Transfer.

1.1 Report Structure

The document structure reflects the structure of the conference. A short description is provided at the beginning of each section. An overview of each presentation is given in the main text and some of the key discussion points are highlighted in boxes throughout the report. Where relevant, additional discussion themes are noted in the final part of each chapter. This report was written based on transcripts taken of the entire conference. While every effort was made to keep the summaries of presentations and discussions as true to detail as possible, it is possible that through the interpretation of the transcripts the text here may not exactly replicate the conference proceedings.

1.2 Global Health & Access - Background

The WHO constitution states that the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being³. Despite this, the benefits of biomedical science and advances in public health have not been available to everyone. For low and middle income countries combined, almost a third of deaths are due to preventable or treatable conditions of communicable diseases, maternal and perinatal conditions and nutritional deficiencies.

Around 2.5 million children die every year from diseases that can be prevented by currently available or new vaccines. In addition, there are currently an estimated 40 million people living with HIV/AIDS worldwide, most of them from sub-Saharan Africa or South-Eastern Asia and the disease is the leading cause of death in that part of the world. Additionally, TB causes about 1.6 million deaths a year and is the leading cause of death in HIV infected people. For TB and a number of other drugs, multiple drug resistance (MDR) and extreme drug resistance is increasing, posing additional challenges to the biomedical research and product development communities who are seeking new treatments and preventative approaches for such diseases. For the diseases which are the major causes of child mortality, such as pneumococcal pneumonia, there is a lack of effective preventive vaccines and there is still no vaccine for malaria, to prevent HIV or to prevent the majority of TB cases.

A decline in life expectancy has a direct impact on a nation's economic well-being. The WHO Commission on Macroeconomics and Health (2001)⁴ made a compelling argument that disease impedes economic well-being, and accordingly global commitments to improved health are featured in the Millennium Development Goals (MDGs)⁵ agreed by the world's heads of governments in 2000, and make an explicit link between poverty reduction and investments in health. An unprecedented level of effort and investment is congruently going into prevention and treatment of some of the major diseases affecting the developing world, such as TB, AIDS and malaria.

Product development pipelines are being replenished and the pursuit of new, risky avenues of research in challenging scientific areas are being made possible through the efforts of a range of public-private product development partnerships (PDPs), thanks to the financial support of large foundations such as the Bill and Melinda Gates Foundation (BMGF) and governments; the technical inputs and good-will of private firms and the

³http://www.who.int/governance/eb/who_constitution_en.pdf

⁴<http://www.who.int/macrohealth/infocentre/advocacy/en/investinginhealth02052003.pdf>

⁵ <http://www.un.org/millenniumgoals/>

commitment of developing world researchers and policy-makers. Where products already exist but were previously unaffordable, various initiatives have enabled the drastic lowering of prices to ensure that procurement agencies and public health bodies can afford to supply products to the poor.

Despite the lower cost and increased availability of many life-saving medicines compared with those of a decade ago, however, developing country health systems have an uneven capacity to deploy proven and emerging interventions⁶. They are often insufficiently resourced to be able to treat millions of patients for chronic diseases⁷ without adversely impacting existing public health services. In order to alleviate the extreme poverty faced by many populations in these regions, it is imperative that disease prevention is given priority. In addition, it is also essential that appropriate and affordable treatments are made available both through the development of new medicines and the effective delivery and integration of existing medicines. Both areas require a range of technological, economic, social and political interventions.

The overarching challenge is to construct incentives to engage public and private institutions in a range of areas including:

- Research and development (R&D) behavioural research to ensure adoption of and adherence to health solutions
- Human, technical and physical resources for health care delivery
- New mechanisms that improve the outcomes and relevance of policy making for global health⁸

⁶ Eiss, R, Plenary Lecture, AUTM Annual Conference, March 2007, unpublished.

⁷ Now that affordable, appropriate medication exists, HIV/AIDS has become a chronic disease that can be managed for many years. While lengthening life expectancy, this places an enormous burden on health systems which already face difficulty in treating patients and has led to a redirection of resource away from other areas of need, such as childhood diarrhoea and respiratory health (Jaffe).

⁸ Eiss, R., Plenary Lecture, AUTM Annual Meeting, March 2007, unpublished.

This raises issues around the following areas of concern, among others:

Product Development:

- Funding, prioritisation and incentivisation of product development and blue skies research⁹
- Technology transfer and commercialisation
- Regulatory harmonisation
- Clinical trials capacity
- Risk and liability
- Capacity building and coherent national policies and public sector investments into developing country manufacturing of essential medicines and vaccines.

Product Integration:

- Absorptive capacity of health systems, typically under-resourced and skewed by dependence on external support
- The need for product development partnerships to integrate with national health systems
- Social behaviours and integration of modern medicines into communities that typically favour traditional medicine, and
- The need to better recognise traditional medicine and its interactions with modern medicine.

Effective linkage between policy-makers, scientists, donors and communities is essential and dependent on sustainability of funding, of political will, of human resource, and of infrastructure. Success will require commitment, learning and participation from developed and developing country governments, NGOs, pharmaceutical companies, university technology transfer offices and the product development public-private partnerships.

⁹ This includes intellectual property rights, legislative instruments such as the Orphan Drugs Act and funding mechanisms such as GAVI, the IFFIm and the AMC, among others

1.3 Considerations for a Future Research Agenda

- How to drive the Paris agenda in practice, and support developing countries in establishing their own priorities, avoiding the North/South colonial approach? Which developing countries have the capacity to set their agendas, and who listens to these? Examples of good practice should be shared.
- How to drive improved performance in the access and delivery area? PDPs should collaborate to formulate proposals and actions.
- How to establish effective national systems of innovation in developing countries?
- How to avoid silo approaches and institute 'diagonal approaches'?
- How to achieve sustainable financing and coherence of approach?
- What do we know about neglected populations which include pastoral and nomadic groups and their needs?

2. Plenary Lecture: Health Innovation: the neglected capacity of developing countries to address neglected diseases

A plenary lecture given by Dr. Carlos Morel, Director, Center for Technological Development in Health, Oswaldo Cruz Foundation (FIOCRUZ), examined the challenges in science and innovation faced by developing countries. National systems of innovation and modes of technological upgrading distinguish leaders from laggards. Investment into research and development (R&D), 'active' learning, innovation and entrepreneurship should enable translation of research outputs into health innovations that benefit the poor and aid economic growth.

Developing countries are not homogenous – they have different needs and different interests. As Peter Hotez, Jeffrey Sacks and others demonstrated in a recent study¹⁰, several diseases can impact the poor simultaneously and represent a significant burden of disease in developing countries.

Cancer today kills more people in developing countries than HIV and diabetes is on the rise. Triple epidemics of chronic diseases will soon be prevalent

The advancement of science, technology and production to address these health challenges in developing countries may be held back due to what Francisco Sagasti¹¹ calls the 'Sisyphus challenge'^{12, 13}. In developed countries science, technology and production are very intimately connected and interact and complement each other, leading to innovative outcomes and, through functional markets,

¹⁰ Hotez et al, Control of Neglected Tropical Diseases. *N Engl J Med*, 357:1018-1027, 2007

¹¹ Francisco Sagasti. Knowledge and innovation for development. The Sisyphus challenge of the 21st century, Cheltenham, UK; Northampton, USA:Edward Elgar, 2004

¹² Krauskopf M, Krauskopf E and Mendez M, "Low awareness of the link between science and innovation affects public policies in developing countries: The Chilean Case" *Scientometrics* 72(1):93-103, 2007

¹³ In Greek mythology Sisyphus had to carry stones from the mountain, but the stones kept returning back to where they started forcing him to endlessly keep repeating the action.

affordable prices. In the Southern Hemisphere, these activities are treated as separate because governments have been slow to recognise science as a tool for development. Consequently, there is a disconnection between scientific production and transformation of this knowledge into practice.

“Developing countries share disbelief about the benefits of the endogenous production of science as a tool for economical growth. Hence, public policies to strengthen science and technology and promote the culture of innovation are, in general, weak and sometimes incoherent”¹⁴.

Entrepreneurship is essential to transform science and technology into innovation and ultimately economic development but it is lacking in several developing countries. Jensen *et al* (2007) describe two modes of innovation: one based on science, technology and innovation (STI), which is based on scientific and technical knowledge and is codified know-what and know-why knowledge, and is considered global knowledge because everyone can access it. The second form of knowledge is what they call doing, using and interacting (DUI), because it relies much less on the formal process of learning and more on experienced-based know-how and know-who¹⁵. While developing countries often do have many of the components of health innovation systems, Eduardo Viotti found that different approaches to knowledge generation, acquisition and management have radical impacts on a country's outputs¹⁶. Countries can be classified into two groups: those engaged in active learning and those engaged in passive learning. Brazil is an example of a country engaged

in passive learning, while Korea has been much more involved in active learning.

Morel discussed three types of failures that have radical impacts on access to medicines. The first is the *failure of science*, where there is insufficient knowledge and vaccines or cures for certain diseases do not yet exist. To address this, more research, innovation and new products are needed. *Market failure* is the second type where the product exists but is often too expensive and out of reach of the poor. To address this, cheaper production, new funding strategies and health policy strategies such as budget increases or negotiations to obtain lower prices are needed. Failures of public health systems also exist, where for instance a product may be free to distribute but does not reach the population due to lack of good government, corruption or social and behavioural factors may prevent acceptance of a drug¹⁷.

Countries can be classified into a number of groups, including industrialised, least developed countries and the intermediate level countries, such as those known as BRICS (Brazil, Russia, India, China, South Africa) or IDCs (Innovative Developing Countries)^{18,19}. All classes can make different contributions to address knowledge gaps, resource gaps, or best practice gaps, to support the development of the innovations needed.

Health innovation can be seen as dependent on six components or determinants - good R&D activity, regulations for ensuring safety and efficacy, manufacturing capabilities that meet international quality standards, authoritative IP management and licensing, domestic delivery of immunisation services and international procurement and trade²⁰. In order to

¹⁴ Krauskopf M, Krauskopf E and Mendez M, “Low awareness of the link between science and innovation affects public policies in developing countries: The Chilean Case” *Scientometrics* 72(1):93-103, 2007

¹⁵ Jensen MB, Johnson B, Lorenz E, Lundvall BA: Forms of knowledge and modes of innovation. *Research Policy* 36:680-693, 2007

¹⁶ Viotti E “National Learning systems: A new approach on technological change in late industrializing economies and evidences from the cases of Brazil and South Korea” *Technological Forecasting and Social Change* 69: 653-680, 2002

¹⁷ Mahoney, R and Morel, C “A Global Health Innovation System (GHIS)” *Innovation Strategy Today* 2(1):1-12, 2006

¹⁸ Morel et al, “Health Innovation in Developing Countries to Address Diseases of the Poor” *Innovation Strategy Today* 1 (1): 1-15, 2005

¹⁹ Morel et al, “Health Innovation in Developing Countries to Address Diseases of the Poor” *Innovation Strategy Today* 1 (1): 1-15, 2005

²⁰ Morel et al, “Health Innovation in Developing Countries to Address Diseases of the Poor” *Innovation Strategy Today* 1 (1): 1-15, 2005

realise these components successfully, there must be dynamic linkage and partnerships. Health innovation networks involving developing countries can strengthen their ability to address neglected disease through these partnerships²¹.

Since the turn of the millennium, there has been an increase in networking and we have seen the rise of product development partnerships and public-private partnerships (PDPs and PPPs). These partnerships have varied foci and differing operating models. Some are product based and some are product-development based, sometimes engaged in building capacity and also preparing the people in developing countries²². There are also different types of global health partnerships, some focusing on public health and capacity building, some focusing on reducing financial risks of drug development.

IP protection is one of the key determinants of innovation. The evolution of protection of IP is such that both very rich and very poor countries have strong IP protection. Typically, poorer developing countries face external trade pressures which force them to be very protective of IP. Later, IP protection decreases as national IP policies develop²³. Countries in transition like Brazil and Thailand sometimes have to negotiate hard IP rights with industry to obtain lower fees on licenses in order to avoid high healthcare costs.

As countries evolve, they begin to see the merit of protecting their own innovations. For example, India is protecting traditional knowledge through a digital library linked to international patent classification to increase accuracy and accountability in the IP system. This system has been accepted by 170 member nations of WIPO and may help to avoid some of the distortions that exist in the IP system. Innovation is dependent on the transfer of technology from the laboratory (usually in

the public sector) to industrial partners who can scale inventions up to testing, manufacture and commercialisation. To assure technology transfer occurs in this way, developing countries need to train human resources and strengthen their institutions in the area of IP management and licensing. Exchange programmes such as those recently established by FIOCRUZ and MIT can strengthen human capacity in this area. Another instrument that may be useful to developing countries is the *Handbook of Best Practice in Health and Agricultural Innovation*²⁴.

International organisations are also engaging in developing IP to ensure innovation and developments in public health. In 2005, the Commission for Intellectual Property Rights, Innovation, and Public Health (CIPRH) published a report, which revealed the divides in thinking about this area. The World Health Assembly created the IGWG (the Inter-governmental Working Group on Public Health, Innovation and Intellectual Property), whose mandate is to follow up the report of that commission and to shape global strategy and a plan of action specifically securing and enhancing a stable base for needs-driven, essential health R&D particularly for diseases that disproportionately affect developing countries. In May 2008, the plan was to be presented to the World Health Assembly (WHA). A final product should go beyond this resolution – long term vision and strategic thinking is required to move the field of neglected diseases forward. The “Global Strategy and Plan of Action” will need to be developed and characterised by expertise in neglected disease R&D, good interface with industry and PDPs and balanced governance involving developing and developed countries.

Financing is a further key determinant of innovation, technology transfer and ensuring access to medicines. Financing may be required at differed stages - for supplies and incremental innovation, for technological innovation (seed money) or for autonomous social and economic development. Interesting examples to illustrate some of the challenges of financing technological innovation are

²¹ Morel et al “Health Innovation Networks to Help Developing Countries Address Neglected Diseases” *Science* 309: 401-405, 2005

²² Chon, M., personal communication

²³ Chen Y, Puttitanun T: Intellectual property rights and innovation in developing countries. *Journal of Development Economics* 2005, 78:474-493

²⁴ *IP Handbook in Health and Agricultural Innovation*, Krattiger et al., 2007

seen in programmes for vaccines. With WHO and UNICEF supporting the Expanded Programme for Immunisation (EPI) prices for vaccines can be significantly reduced. Mahoney *et al*²⁵ showed that EPI vaccines, which are based on very common, old technology) are very cheap (c. 35 cents per dose), making it possible to immunise a child with USD \$1.50. However, new vaccines cost ten times more than this, so to fully immunise a child \$13 is needed. The impact of this pricing on national programmes and health budgets of some countries is enormous and places many new vaccines out of their reach. The Global Alliance for Vaccines and Immunisation (GAVI) tries to address the pressure that this places on many national health budgets. However there are many different ways of funding and the money may typically come from different sources.

Financing has to be supported by a number of other approaches. Brazil is well known for its success in dealing with HIV due to the public sector's response to the epidemic, strong civil society participation, mobilisation and a comprehensive approach to prevention, treatment and human rights.

In conclusion, Morel²⁶ shows that countries can move out of stagnation if they recognise and address the dichotomy gaps between R&D, production and innovation.

The formation of a working group to share best practice and assist developing countries in the formation of national innovation system frameworks is recommended

²⁵ Mahoney et al. "The Introduction of New Vaccines into Developing Countries II" *Vaccine* 18: 2625-2635, 2000

²⁶ Morel et al "The Road to Recovery". *Nature* 449: 180-182, 2007

3. Dimensions of the challenges

An introductory session chaired by John Kilama of the Global Biosciences Development Institute, USA, looked at the challenges that policy makers face in relation to global equity and access to medicines.

Despite the unequal distribution of access to healthcare particularly in the developing world, there have been tremendous achievements in global health in the last twenty years. These include an unprecedented response to HIV, TB and malaria and also commitments to address problems related to neglected diseases (such as trachoma, river blindness, and guinea worm) and chronic diseases (such as cancer, diabetes, hypertension and childhood respiratory illness). Now that these issues are firmly on the political agenda, debate on prioritisation of issues and movements to increase advocacy for interventions further is possible. The Innovative Developing Countries (IDCs) are heralding a new wave of change, displaying potential to address some of the challenges with new paradigms of health innovation and systems delivery.

"We're living in a time of tremendous growth, tremendous change, tremendous dynamism in global health and we have an opportunity to shape it in a way that will be much better than it is"

The remaining challenges relate to coverage of treatment, which still misses a huge portion of the poor (particularly the rural poor), sustainability, misalignment of funding to need and a dearth of emphasis on prevention.

The session emphasised the need to build developing countries' health systems to improve integration of health interventions.

3.1 Free Market Strategy in Healthcare: Key to achieving Product Availability and Access: Dr Stephen Malinga, Minister of Health, Uganda

In Uganda, the field of Maternal & Infant Health, which is seen as one of the primary indicators of a country's development, experiences a shortage of trained staff due to brain-drain, an absence of effective referral and community support and a lack of

confidence in modern medicine²⁷. Recognising the challenges its health system faces, Uganda is developing a strategy to bridge the gap between needs and access, aiming to encourage innovation through a free market approach. Its tiered system of referral aims to make more effective use of scarce health service resources at the district and regional levels.

Participant recommendations for areas of health research, policy & investment

- Behaviour change research
- Development of health education systems
- Knowledge transfer about best practices in prevention programmes
- Innovations in prevention and systems development
- Horizontal, systems-orientated rather than vertical, disease-specific interventions
- Development and scale-up of traditional medicines
- Analysis of health care systems to enable cost reduction at every stage

The Ugandan healthcare system aims to work with the private sector in extending healthcare through the “Health Strategic Plan Part Two”, and is developing a National Health Insurance Scheme and beginning to develop public-private partnerships (PPPs). Attempting to integrate new health workers into the community, from NGOs or other groups, has proven challenging not least because traditional healers are still the preferred source of healthcare. Behavioural research is needed to address problems of integrating modern medicine into rural communities. The problem is complex: for instance, where young women have been trained as birth attendants and health centre administrators there is often a mutual disrespect between them and the communities they serve²⁸.

²⁷ The vast majority of patients prefer to use traditional medicine over modern medicine.

²⁸ Often the position of the birth assistant is held by older women in society and these young women may be seen to be imposing on a community and breaking social norms and hierarchies in doing so. There are also suggestions that these women are not seen as treating their female patients with due respect and have in some cases been viewed as

Problems with access stem in part from intransigence in the health system to encourage technology transfer. The system suffers from a lack of policy frameworks to enable technology transfer and an ongoing need for human resource and institutional capacity building which could utilise and encourage collaborative research to bridge knowledge gaps.

“We need to use the money now to improve the healthcare services and strengthen them and not to focus on specific diseases”

3.2 New Solutions for Global Health Challenges: Ms. Patricia Atkinson, Bill & Melinda Gates Foundation, USA

For BMGF, the key principle of all investments and product development is to ensure global access to healthcare, through product development and ensuring cost-effective interventions; sufficient supply; effective delivery strategies and optimal product use. To understand and improve delivery of health products, the Foundation is focusing on product readiness, systems readiness and their symbiosis.

The HIV Vaccine Enterprise and the Malaria Vaccine Technology Roadmap are examples of the Foundation’s investments in product development. Other areas of focus include clinical trials capacity development²⁹ and strategies for product implementation and integrated delivery³⁰.

“Donors should be conscious of the degree to which their funding strategies distort local health solutions”

Product development partnerships (PDPs), created in the 1990s to tackle neglected diseases, have been by their very nature, innovative and have seen much success in creating exciting product pipelines focused on the needs of the poorest. They enable industry expertise to support development of public goods by independent not-for-profit entities which

seeking profit from their activities rather than serving the public good.

²⁹ e.g. the Malaria Clinical Trials Alliance.

³⁰ e.g. impacts of delivering one class of therapies in conjunction with other neglected tropical disease treatments, and scaling these for impact.

work to assure affordable and appropriate end-products for poor populations. The project management practices associated with PDPs, in which milestones and deliverables drive progress, have brought a new approach to global health product development (not previously utilised by the traditional public sector).

The PDPs' success has led to shrinking development pipelines. Consequently, efforts to sustain research into improved product profiles are still required to ensure focus in the "discovery engine". This will help to bring about "product readiness", alongside consideration of other important issues, such as the infrastructure and context of introducing a new product. Manufacturing innovation and development is also needed, and investment is going in to technologies such as plant-based solutions with the potential to facilitate technology transfer and lower cost manufacturing models which should lead to more affordable pricing models.

Participant discussion: Continued development of synergies is essential

- Initiatives need to be consolidated to avoid duplication
- Continued sharing of industry expertise is essential
- A horizontal approach (addressing health systems) will yield more than focusing on disease-specific product development alone
- PDPs will need to extend their partnerships to local health systems

Decision-making and prioritisation among many different products are challenging issues for developing country public health leaders. The Foundation's focus on "systems readiness" aims to facilitate policy-making and to ensure that health systems are ready to absorb the multiplicity of products available at affordable prices. It falls into a number of areas, including accurate market assessment, viewed as a critical success factor to ensure products are targeted to end-users. Catalytic investment to develop regulatory capacity and improved manufacturing strategies in developing countries is essential, along with innovative solutions to financing,

procurement and supply chain management. The PDPs have a critical role in supporting both product and systems readiness.

From a grant-making perspective, new models of smaller accelerated grants will be targeted to enable development of higher risk projects, particularly in the early-stage discovery phase which PDPs are often not able to support. BMGF recognises the need to work in close partnership with developing country stakeholders to reflect and support local priorities.

Participant recommendations to encourage sustainability of investments into neglected diseases

- Integrated support systems such as 'Village Reach' in Mozambique, which tie in vertical programmes at the district level (and below) need to be developed and piloted
- Ongoing donor support for PDPs is essential and will drive the continued involvement of industry in this field
- Government investment is likely to be the largest source of uncertainty, as governments are restricted by funding cycles and budgetary restrictions
- Policy makers should implement the recommendations of the Commission for Macroeconomics and Health (CMH)³¹

The Foundation is adopting a multi-disciplinary approach to address inter-related development issues, such as the reduction of diarrhoea which is reliant on good water systems and sanitation, healthcare financing, novel interventions, health insurance and possibly microfinance.

3.3 Innovation, Access and Public Health: Dr. Harold Jaffe, University of Oxford, UK

Providing HIV Therapy to the approximately 40 million people living with

³¹ THE CMH recommendations included vastly increased public sector commitment to R&D for diseases of the poor.

HIV/AIDS presents many challenges to developing country health systems. The current emphasis on treatment is not sustainable with so many new incidents of disease and increasing disease resistance to medicines, calling for a never-ending supply of both existing and new products. Consequently, in addition to supply chain sustainability of anti-retroviral (ARV) programmes and the need to increase the number of trained personnel, there is a need to focus on prevention. The increasing strain exerted on fragile health systems by the growing influx of ARVs in Africa (due to price reductions and funding subsidies) affects quality of delivery in other parts of those systems. The possible effects of funding plateaus in future should be factored in to current policy thinking, to assure populations are not left without treatment if priorities change.

In December 2006, UNAIDS estimated that only around twenty-eight percent of the approximately seven million persons needing treatment in low- and middle-income countries receive it, with most of these unmet needs being in Africa. The increase in generic drug manufacturing of highly active anti-retroviral therapy (HART)³² and the significant efforts of organisations such as the Clinton Foundation have enabled dramatic reductions in the price of HART, increasing the affordability of the treatment to developing countries³³ and leading to the a number of major international programmes engaged in supporting global access to and supply of HIV therapy to developing countries³⁴.

The increased supply of HART raises many challenges, including the need to deal with a widespread lack of knowledge of HIV status and the need for new models of health care. In order to address the lack of knowledge that many have around HIV infection status it is important to invest in clinical diagnosis and equipment for laboratory testing, the development of data

³² This has a dramatic impact on decreasing the mortality of HIV infected persons.

³³ The HART drug regimen in the US, initially costing around \$39 per day, is now available at around 1/100th of this cost.

³⁴ This includes the Global Fund, the World Bank Multi-Country AIDS Programme, and the US President's Emergency Plan for AIDS Relief (PEPFAR), which has budgeted USD \$15 billion over five years.

management systems and the need for a reliable and secure supply chain. It will not be possible to infinitely expand treatment programmes for a disease that is able to develop drug resistance.

"We will not be able to treat our way out of this epidemic"³⁵

Developing world health systems face a shortage of health clinics and trained personnel³⁶ and often cannot absorb the additional work-load that the distribution, administration and monitoring that is required for new products. There is an urgent need for additional human capital investment in this area.

The longer term challenges of increased supply relate to sustainability of funding and the inevitable conflicts between funding allocations and focus on both treatment/care and disease prevention. It is also critical to be mindful of the impacts the release of a particular product onto an over-burdened health system can cause and to avoid exhausting the minimum capacity. The recent focus on treatments for HIV/AIDS faces some criticism for crowding out other programmes and diverting staff from working on other health programmes designed to treat problems which affect poor populations.

While the total global resources devoted to HIV/AIDS have risen rapidly to over USD \$4 billion per year, funding is susceptible to shifting international priorities, and will peak, plateau, or perhaps even fall. HIV therapy is not curative if treatment is stopped, and raises the question of how countries can be responsible for their infected populations in a sustainable manner.

"The basic issue is going to be prevention. If we can't decrease the number of new infections globally, we will never keep up. So it seems [...] inevitable that we will reach a point where this is not a sustainable solution, and when that happens it's going to be a disaster"

³⁵ Kevin De Cock, World Health Organisation, personal communication.

³⁶ For instance, in Mozambique, there are about two doctors and twenty nurses per hundred thousand population.

3.4 Challenges to Vaccine Financing and Systems Support: Rebecca Affolder, GAVI Alliance, Switzerland

Through partnership, GAVI has accelerated access to vaccines and has provided a forum in which innovative ideas on development, finance and programming can be tested. New financing mechanisms that deliver sustainable immunisation have been successful, in particular an un-earmarked fund that produced fifteen million childhood immunisations. The replicability of this model for research and development (R&D) was explored.

Three core challenges which impact the wider usage of vaccines are as follows:

- 1. Insufficient and unpredictable funding at country level limits the ability of both governments and industry to plan on a multi-year basis.** Countries are unable to signal demand for products effectively
- 2. Insufficient commercial incentives** for vaccine producers to dedicate investment into R&D specific to the needs of the developing world
- 3. Weak and underfinanced basic health systems** across the public and private sectors are increasingly fragmented and undermined by inappropriate and/or uncoordinated development strategies

“Health systems represent the most significant challenge faced by the global health community [...] and financing healthy systems is going to take a lot of political leadership”

The third challenge reflects GAVI’s first strategic goal, which is to contribute to strengthening the capacity of health systems to deliver immunisations and other health services in a sustainable manner. GAVI achieved success in its first phase of work through giving countries un-earmarked immunisation services support which enabled countries to exercise their own strategies in developing training, management and infrastructure rehabilitation, among other areas³⁷. GAVI’s work has demonstrated that adequate financing of health systems is key to ensuring access to immunisation.

³⁷ The strengthening of immunisation services directly led to the increase in global Diphtheria Tetanus and Polio (DTP) coverage from 63% in 1999 to 71% in 2005.

Participant discussion: Creating new financing mechanisms is complex

- Establishing new financing mechanisms has heavy transaction costs
- There is a lack of responsibility for creating a funding mechanism at a global level
- There are challenges of reconciling a global “helicopter” ideological view with the practice at the ground level
- There is a lack of alignment over the best ways to front-load the cost of R&D and to send appropriate and fair signals out to industry
- It is important to carefully explore institutional rights and the part that they play in allowing financing mechanisms to function effectively

GAVI is able to create incentives for commercial organisations through collaboration. It builds industry confidence in the durability of future markets by giving certainty of demand for products through credible forecasting and provides an ethical investment for investors wishing to add this type of investment to their portfolio. This has enabled GAVI to establish innovative mechanisms for increasing the predictability of financing and thereby increase commercial incentives for R&D. One such mechanism is the International Finance Facility for Immunisation (IFFIm), launched in 2006 with an initial USD \$1 billion bond issuance that enabled governments to make long-term plans based on a predictable flow of funds. Through the purchase of vaccines and strengthening of health systems, the anticipated IFFIm investment of USD \$4 billion is expected to prevent five million child deaths between 2006 and 2015 and more than five million future adult deaths from hepatitis B-related liver disease.

A second innovative financing mechanism is the Advanced Market Commitment (AMC), which was described by one participant as being like a mortgage for R&D. It subsidises the future purchase (up to a pre-agreed price) of a specific number of doses if an appropriate vaccine is developed, providing a guarantee that the demand exists when the vaccine is finally

produced. By pledging that the funds will be available to purchase vaccines once they are developed and tested, the AMC mimics a secure vaccine market and removes the risk that countries will not be able to afford the high priority vaccine. The final price is much more affordable after the initial donor investment. A pilot AMC for pneumococcal vaccine was launched in February 2007 with a USD \$1.5 billion initial pledge by Italy, the UK, Canada, Norway, Russia and the Bill and Melinda Gates Foundation.

Working in partnership across different sectors, being accountable both individually and collectively to developing countries, and enforcing commitments which are mutually beneficial are all essential to continuing to make significant progress.

Participant recommendations for financing of developing country health systems

- Continued external support to poor governments for sustaining the development of fragile health systems is widely supported
- Cautious policy making is needed to avoid skewing the priorities of national governments towards diseases of priority to donors (HIV/ TB/Malaria) and away from areas of local priority
- Direct support to government rather than through NGOs would reduce fragmentation and complexity, which strains government coordination of health systems
- Increased dialogue and studying “success stories” could be very helpful

3.5 The Intergovernmental Working Group: Dr. Howard Zucker, WHO, Switzerland

The background, processes and future objectives of the WHO’s Intergovernmental Working Group on intellectual property rights, innovation and public health (IGWG) were described.

In 2004, the WHO tasked an independent commission³⁸ to analyse the relationship

³⁸ WHO’s Commission on Intellectual Property Rights (IPRs), Innovation and Public Health (CIPIH)
<http://www.who.int/intellectualproperty/en/>

between Intellectual Property Rights (IPRs), innovation and public health. The commission analysed various effects of intellectual property rights; upstream research leading to the subsequent development of medical products, both in the developing and the developed world and issues of access particularly in the developing countries. It also considered the impact of other funding incentive mechanisms and how to foster innovative capacity in developing countries.

The commission’s report was published in 2006 and increased global awareness of the problems around innovation and access to health products for the developing world. One of its conclusions was that intellectual property rights are important incentives for the development of new medicines and medical technologies but are an ineffective incentive mechanism for patient populations that are small or poor. The commission made about sixty recommendations to foster innovation and improve access, although concerns were recognised that those sixty mechanisms may be too costly to implement.

In May 2006, the 59th World Health Assembly (WHA) adopted a resolution (59.42), open to all interested member states, to provide a medium-term framework on the recommendations of the WHO commission report. The IGWG has developed a global strategy and plan of action which, among other objectives, is to look at the basis for needs-driven essential health R&D relevant to diseases which affect developing world populations³⁹.

The IGWG report prioritised several key areas:

- Promotion of R&D
- Building and improving innovative capacity in developing nations
- Improving delivery and access
- Ensuring sustainable financing mechanisms
- Establishing reporting processes
- Technology transfer, and Management of intellectual property rights.

³⁹ The final report was submitted in May 2008 to the 61st World Health Assembly.

**3.6 Who is Listening to Those in Need?:
Prof. Peter Ndumbe, University of Buea,
Cameroon**

Policy makers in developed and developing countries need to listen to those in developing countries who lack access to medicines. Health innovation, if properly nurtured, can improve health, drive evidence-based change in the health system and increase economic prosperity. Institutions which bridge the public and private sectors and build developing country R&D capacity in are needed.

Governments in developing countries have a responsibility for the health of their people, which can be fulfilled only by the provision of adequate health and social measures, informed opinion, and active cooperation on the part of the public. Due to resource limitations, governments are forced to prioritise around certain interventions.

Research is central to innovation and researchers, academics, entrepreneurs and venture capitalists, non profit organisations, policy makers and politicians need to engage with the public and communities to drive an appropriate, needs-driven agenda, based on expressed demand.

Linkage of the scientific, entrepreneurial and health delivery sectors is essential to enable research to be translated into accessible products. The Tropical Diseases Research programme (TDR) of the WHO has, over the last several decades, built an innovation pipeline which serves this function, and develops new tools and improved strategies for intervention to lead to more effective health impacts with a focus on capacity-building in knowledge management.

“Research is a raw resource that fuels the health economy and is the engine of change in the health system. Research and innovation must not only be an integral part of any plan for health care reform, it must be the centrepiece”

Government responsibility is critical to setting appropriate agendas, ensuring markets exist and ensuring adequate regulatory frameworks to encourage industry to operate. Public ‘safety nets’ are also needed to ensure that access to health can be normal and sustained.

Questions around accountability for addressing access were raised, including the roles and relationships between external actors and local governments and the challenges of scaling up community participation.

Participant recommendations for an integrated approach by government and policy makers in developing nations

- Develop a 'systems' approach which actively integrates health systems, communities and infrastructure with product development
- Adopt the role of system coordinator
- Focus on success stories from many different communities in order to engage effectively with heterogeneous communities
- Integrate anthropological analyses of local perceptions about health interventions to assist with reaching a wider audience and assessing whether a government is trusted
- Improve overall legitimacy through improved transparency and delivery
- Build strong regulatory institutions to enforce quality control to sustain industry and donor commitment
- Study how developing countries have closed the gap on OECD countries
- Build institutions and create enabling conditions for competitive markets to flourish

4. Strategies for Securing Product Availability and Access

Gill Samuels (Global Forum for Health Research) and Dianna Derhak (DNA International Consultancy) explored a range of private sector and partnership initiatives working to improve access to medicines and the development of indigenous capacity to support near-term product supply and future innovation.

Pharmaceutical industry case studies demonstrated the role of industry and described initiatives to work with developing countries in a number of partnership formats. Industry approaches including clinical trials and scientific research capacity building, tiered pricing, IP licensing and donation programmes among others were presented and discussed. Better reporting of adverse reactions, more trust and harmonisation at multiple levels (including regulatory requirements) and common goals for different agencies are among industry's priorities. More consolidation, demand and centralisation of procurement would improve the ease and efficiency of supply.

PDPs are making the impossible possible and making risk manageable. As products begin to come through to registration stages, concerted efforts are being made by PDPs to address downstream access issues, particularly in relation to securing supply chains for safe delivery of medicines and vaccines. However, different cultural perceptions and mistrust skew many of the activities that firms and PDPs are attempting, including clinical trials. A policy environment that provides proper incentives for firms and non-profits to fill the needs in the healthcare sector is needed.

The question of how the public sector can help to invest in the right places in the 'frontline' so that industry can play its optimum role in helping to create products for neglected diseases was raised. Further work is needed to shed light on what other competencies industry might be able to share with the non-profit sector, particularly around embedding or integrating new medicines. Additionally, as chronic diseases are becoming the biggest sources of mortality in the developing world, and since products available in the West are likely to be too

expensive or not compatible with existing healthcare systems in the developing world, incentives for industry to help create access to cheaper and less technologically demanding solutions need to be developed with urgency.

4.1 The Development of Paromomycin IM for Visceral Leishmaniasis: Ms. Katherine Woo, Institute for One World Health, USA

IOWH is paying increased attention to delivery and supply chain issues and has signed supply agreements with a local manufacturing company to deliver Paromomycin to treat Visceral Leishmaniasis (VL). The programme has also built partnerships with governments, NGOs, social enterprises, and companies both for-profit or non-profit in manufacturing and supply chain leadership to ensure that there will be local uptake and to facilitate long-term commitment both by local and federal government.

Paromomycin, used for the treatment of Visceral Leishmania (VL), is an old drug that was approved for broad antimicrobial use in the early 1950s and has a large safety database⁴⁰. With a large body of knowledge behind it, IOWH obtained funding from the Bill and Melinda Gates Foundation to conduct a Phase Three pivotal trial, which ran between 2003 and 2006. To deliver this product, IOWH has worked very closely with the Indian government, ICMR, and four key, principal investigators in India.

IOWH is currently focused on the implementation stage now that the drug has been approved in India. It created a Phase Four programme, which includes a scalable 'access' pilot, including:

- monitoring
- evaluation
- operational optimisation
- measurement of impact, and
- supply chain security and testing.

Several notable points were highlighted through the IOWH approach, including the need for behavioural research to provide the baseline for training and the need for a

⁴⁰ It is a twenty-one day daily injection, requiring a delivery system that ensures that the use of this drug is in compliance with its intended use.

basis for evaluating the economic impact of providing this treatment to communities. A tiered approach to health systems has been developed: a group of referral centres have been established, which will be staffed by community health workers who will diagnose the disease and refer patients to treatment centres.

Further points in response to discussion

- For PDPs, the importance of having a reliable partner in-country and the risk of having too many licensing partners in terms of quality control, are significant issues
- Government engagement is essential. Recommendations should be tied into wider parts of the political agenda⁴¹, creating the potential for political wins

4.2 On-the-horizon Developments in Biotech and Nanotechnology: Ms. Dianna Derhak, DNA International Consultancy, Ukraine

The Bio Ventures for Global Health (BVGH) partnering meeting (at the Biotechnology Industry Organisation annual conference) is a means to institutionalise a marketplace for neglected disease drug development. It is a means to build networks and new connections, essential to drug development.

4.3 Pharmaceutical Industry initiatives: Dr Richard Barker, Association of the British Pharmaceutical Industry, UK

The pharmaceuticals industry is committed to working with developing countries to influence improvements in healthcare delivery. The session provided insights into industry's activities with regards to access and what its opportunities and constraints are in this area.

Traditionally, industry has had a very important role in global health as probably the only proven nursery of innovation, but there is potential for industry to take this further. This is dependent on the crucially

⁴¹ That is, how an action to improve access to medicines also improves another aspect of the social structure and ties into other programmes that will represent a win for politicians.

important symbiosis between the research outputs of the public sector and what is done in the private sector.

Industry is willing to offer to partnerships a range of facilities and expertise such as off-the-shelf compound libraries for screening, drug donations and a range of technical expertise in research and development (R&D). On the management side, it has skills in portfolio management and in managing risks and understanding of markets. In order for these to be provided, industry needs to have a certain kind of facilitating environment in which to work. It is able to contribute more when public-private partnerships are strengthened, when there is a strong IP regime to protect its intellectual property and robust regulatory processes, standards and ethical approval processes in the country that it is trying to work in.

Industry activities in this area include partnering with the PDPs, donating medicines, building facilities, and being involved in programmes committing around \$5 billion since 2000. Industry is also engaged in focused R&D investment for previously neglected diseases.

To date industry initiatives have been on an individual company basis, but collective action is being contemplated in the following areas:

- 1. Discovery** – R&D for the truly neglected diseases, and some mechanisms that for malaria, TB and HIV have not been properly investigated. Industry is working on concepts such as sharing compound libraries
- 2. Development** – work with donors on a ‘global funders forum’ to give insight into developing an equitable, objective way of deciding which projects should move forward
- 3. Delivery** - work to build economic, sustainable, and secure pharmaceutical supply chains in developing countries (particularly rural areas, but also some of the urban areas) which are in many cases not functional. Industry is focusing on DFID’s MeTA initiative in Africa and looking to build partnerships to address supply chain challenges
- 4. Skills development** - better, more focused training programmes; knowledge transfer (the transfer of ideas

and expertise) in the form of exchanges and fellowships; building warehouses; and setting up and running clinical trials.

Good and sustainable local leadership, combined with sound economics behind the initiatives is critical to success

Private-Sector Case Studies

4.4. The Case of Merck: Dr. Diana Lanchoney, Merck, USA

Merck is engaged in a number of projects to improve access to medicines, which have revealed the need for enhanced collaboration. Tension exists for firms in deciding between institution-building projects versus results-focused projects. Approaches such as tiered-pricing have been integrated into Merck’s strategy for tackling access to medicines.

Merck’s focus is to deliver innovative products that are relevant to developing world health issues and in focusing on this accessibility has for example been eliminating all profit intent around novel vaccine products in GAVI eligible countries. The infrastructure and network of partnerships that Merck developed and the consideration of factors such as ability to pay, disease burden, and the developing world agenda have been key in enabling this progress. The approach is a result of researching the policies and practices of other companies and recognising the commitment of donors, governments and NGOs to make access happen.

“There is no other value or other sort of artificial construct that provides value to the industry more than IP. However, [...] there are multiple arrangements that can be taken to minimise intellectual property serving as a barrier to access”

Tiered pricing will now also be considered for early-stage products to amortise the risk for the public sector. The accuracy of demand forecasting is an important aspect of tiered pricing. Parallel trade also remains a concern and this impacts selection of partners and negotiations. An additional barrier to tiered pricing is where a product requires a diagnostic to be able to be effective as a second line treatment but the non-profit sector will not fund this,

placing too high a cost-burden on the private sector.

Collaboration and partnership with a wide range of stakeholders is essential. Examples of successful partnerships were illustrated with the cases of the Mectizan donation programme (targeted against Onchocerciasis); the African Comprehensive HIV/AIDS Partnerships (ACHAP), aimed at supply of free anti-retrovirals (ARVs) in Botswana; and the supply of the RotaTeq vaccine (against rotavirus) to Nicaragua for three years at no cost. Conversely, where donor support is not certain, and supply chains inadequate, implementation can be more challenging. For example, in the case of the Gardasil vaccine against human papilloma virus (HPV). Timeliness, trust and excellence are needed to frame an elevated level of partnership.

4.5 The Case of Ranbaxy and ARVs: Dr. Arun Purohit, Ranbaxy, India

The generics industry has a substantial network worldwide and is able to support delivery of medicines for all the major diseases. However it faces several challenges including rising costs of re-registering products in different national systems, fragmentation and unpredictability of demand. Centralisation of procurement may ameliorate these challenges.

The generics industry faces a number of challenges, including the current global deficit in funding for ARVs (around USD \$8 billion). Additional recent challenges include the WHO requirement to produce generic ARV drugs in combinations (Fixed Dose Combinations – or FDCs) and innovative forms, such as those suitable for children⁴². This requires expertise in bio equivalency and new manufacturing techniques and funds to adapt products to market needs, in order to speed up this process. There is also ongoing funding pressure for companies to produce the cheapest product possible within international safety and quality standards. Variations in regulatory requirements in

⁴² With the Clinton Foundation's focus on treatment of children, ARVs now also need to be prepared with paediatric requirements in mind, including the need for simpler treatment and more education for care givers.

different countries, however, cause delays to access, and WHO should play a major role in regulatory harmonisation. This could enable a tentative approval process to speed up access to a health product before it is approved by the usual process.

Larger batches of products are frequently required due to the increased funding and subsequent demand for ARVs. However, the demand side is not consolidated, which adds difficulty to the supply effort. Fragmentation needs to be reduced and procurement centralised, ideally to consolidate demand globally. A range of incentives for generics firms to remain in the neglected disease area might include grants to conduct bioequivalency and develop new manufacturing techniques, expanded market opportunities, advanced purchase agreements for bulk purchasing and a focus on regional purchasing.

Participant discussion: there are many potential challenges to sustained industry engagement

- Sustainability of donor funding in the long-term
- Variations in regulatory systems
- Counterfeit issues
- Trust and public perception of industry motives
- Trade-off between rapid access to treatment and exposure to lower levels of safety

4.6 The Case of Eli Lilly MDR: Dr. Gail Cassell⁴³, Eli Lilly, USA

Eli Lilly is involved in a variety of initiatives to address multi-drug resistant (MDR) Tuberculosis (TB). One initiative is based on a not-for-profit partnership in technology transfer with the Global Alliance for TB (GATB) for early-stage drug discovery and a partnership in Technology Transfer. The aim is to share specific and general manufacturing technologies to create self-sustaining centres of manufacturing excellence, which will support reliable producers and ensure an expanded supply of new drugs.

⁴³ Dr Gail Cassell was the listed speaker but could not attend the conference. Dr Gill Samuels presented Dr Cassell's slides.

The characteristics of these kinds of partnerships are:

- . technology transfer in countries with the highest disease burden*
- . drug supplies and concessionary prices*
- . training tools for healthcare professionals and*
- . training of trainers.*

Eli Lilly announced a partnership in June 2007 that will work to enhance the early stage discovery pipeline of the TB Alliance (GATB). This is a collaboration between a variety of partners, including National Institutes of Health (NIH) and National Institutes of Allergies and Infectious Diseases (NIAID), Medcam and Associated Technologies, academic and government sponsored researchers – with the goal of integrating scientific disciplines necessary for sustained discovery of new medicines. Lilly has made a financial contribution to the partners and is making over five hundred thousand compounds available for screening. It is providing access to computational tools, important for screening such a large number of compounds, to enable timely data analysis and molecular modelling. Lilly has also provided experienced drug discovery scientists representing some of the key disciplines involved in new drug discovery, medicinal chemistry, computational sciences and quantitative biology. They supplied discovery leadership in participation on the steering committee, providing experts who know how to manage not just projects, but also portfolios.

The Lilly TB Partnership in Technology Transfer will share specific and general manufacturing technologies to create self-sustaining centres of manufacturing excellence to support reliable producers to ensure expanded supply of new drugs. The partnership will negotiate a controlled price with manufacturing partners for WHO-sponsored purchases to assure supplies of affordable drugs and business sustainability. The partnership offers the technology to produce the medicines, training in good manufacturing practice (GMP) and good business practices to manufacturing firms in multi-drug resistant (MDR) TB hot-spots. It will second ten Lilly full-time staff for four years onsite. Facilities in China, South Africa, India and South Africa will receive technology to

support production of two major drugs. Communities and businesses engaged in prevention and treatment adherence have also partnered to strengthen health surveillance systems.

“The magnitude of challenge in this particular area of drug resistant TB is great. No single player has the resources and incentives to manage the entire process. And public private partnerships make the impossible possible”

Participant recommendations for technology transfer

- A holistic approach to technology transfer is needed, extending beyond *ad hoc* training or building and upgrading facilities in order to ensure sustainable impacts
- Technology and knowledge transfer should occur through collaboration and both parties should be learning in the process

4.7 The Case of Pfizer – Dr. Robert Mallett, USA

Pfizer’s focus is on building capacity in health systems. It was involved in the establishment of the International Trachoma Initiative, where it committed to supply one of its medicines free of charge for trachoma until the disease is eliminated. Its Global Health Fellows programme of secondments has helped develop infrastructure in government ministries. The building and continued funding of the Infectious Disease Institute (IDI) at Makerere University in Kampala, Uganda is providing training around a number of infectious diseases, particularly HIV, TB and Malaria.

The IDI Jump programme (which has attracted the support of Exxon Mobil and involves a partnership with Makerere University and the Ministry of Health) aims to train entire treatment teams at the health facility level, from medical personnel to a range of support personnel essential to the process. This model is designed to be scalable to other countries. Ghana, Senegal and Kenya have been chosen as the pilot sites model, under the counsel of FSG social impact advisors, particularly because the governments ‘had an appetite for action’.

A project with the WHO's Tropical Diseases Research (TDR) programme is underway regarding malaria management, with activities and collaboration in research, in development programmes ensuring quality manufacturing and in personnel exchange.

TDR has been granted access to Pfizer's compound library, which has over three million compounds. Pfizer has already targeted about fifteen compounds that have shown responsiveness to certain parasitic targets. Having identified some of the treatment gaps for malaria, the partnership has responded with a development component in malaria, using a FDC of Chloroquine and Zithromax in clinical trials in six countries in Africa, two in Asia, and two in South America. In Senegal, a 'malaria plan' has been developed, involving securing of the supply chain to reduce the potential harm of counterfeits.

In undertaking these programmes there are many challenges: human and physical clinical trials capacity; financial sustainability; weak regulatory systems; technical capacity for trials; public distrust of clinical trials processing; and a general distrust of the private sector. Funding shortages in Africa can translate into non-accredited laboratories using un-calibrated equipment and chemicals, leading to unreliable results. Obtaining patient consent and reliable participation in trials can be particularly challenging when there is a lack of education and understanding about western medicines.

4.8 Discussion

Clinical trials capacity in Africa

Despite Pfizer's findings of a dearth of clinical trials capacity, Mary Moran's group at the George Institute found a capable network in the malaria, rotavirus and - pneumococcal areas, including twenty three licensure standing sites in Africa capable of conducting malaria trials. Forward modelling on all malaria products that could be trialled in the next five years found that there is enough capacity for many thousands of adults and children to be enrolled through very good sites⁴⁴.

⁴⁴ Moran M, Guzman J, Ropars A, Jorgensen M, McDonald A, Potter S and Haile-Selassie H.

Sites like Manyisa in Mozambique that have trialled Rotavirus, Pneumococcal and malaria vaccines, had 2,500 infants enrolled in a GSK malaria vaccine trial, and produced competent dossiers to FDA standard.

In the HIV area, trials infrastructure is not as developed. Donors should be strengthening existing trials sites by giving core funding, rather than extending the network. To overcome some of these problems, it was recommended that greater support should be given to the ACRP (Association of Clinical Research Professionals) and that similar bodies that support local clinical trials and laboratories capacity development should be further supported to build up the competencies in clinical research and clinical research professionals in those countries. Policy needs to work through existing finance and physical structures rather than creating new systems from scratch, particularly in the arena of clinical trials.

Contract manufacturing in developing countries

All companies in the innovative sector are considering contract manufacturing under certain conditions:

- Exclusive licensing arrangements to prevent knowledge spillovers (to ensure that competitive advantage is not eroded) with low-cost manufacturers and governments that try to create access while ensuring control of the IP⁴⁵
- Contracting out to their own specifications, and
- Training of staff and development of facilities to assure quality - this requires intensive knowledge transfer partnership activity.

Exclusive licenses enable stronger relationships to be formed between the licensor and licensee which results in increased ease of knowledge and technology transfer and reduced transaction costs to enable high

The malaria product pipeline: planning for the future. The George Institute for International Health. London, United Kingdom, September 2007,

<http://www.thegeorgeinstitute.org/iih/media-and-publications/reports/2007.cfm>

⁴⁵ IP creates value and is central for the pharmaceuticals industry to remain a growing concern.

production standards. Especially with regard to vaccines, every licensing arrangement is a *“huge and ongoing investment that lasts over decades”*. Cost would therefore prohibit this type of investment occurring across multiple licensees. The issue of exclusive licensing is, however, contentious because open licenses enable price competition among generics firms and prevent high monopolistic pricing that prevents access to treatment.

In considering vaccine manufacturing capacity for the developing world, it was noted that the private sector is unable to invest adequately due to the high level of risk associated with vaccine production (that is, whereby the market is small⁴⁶ but a high number of doses is required⁴⁷). As such, to ensure that products reach the market five to ten years earlier than they currently do, the public sector should amortise the risk by making greater at-risk investment in manufacturing capacity. By investing an additional approximately USD \$20 million in each factory, should a specific product in development fail, it would enable adaptation to produce a range of products.

Public perceptions of shifting production and clinical trials to the developing world may provide a challenge to some of these activities. This is primarily due to developing country concerns about being used as guinea pigs, but also the potential economic impacts of losing ‘American jobs’ to other countries.

Risk

The issue of who will take the final responsibility if things go wrong years after product release as well as who will be the final insurer of the public good as well as other questions around risk bearing were discussed. These remain unanswered questions that need to be addressed by well-considered legislative instruments⁴⁸.

⁴⁶ The world market for vaccines is about twelve to fifteen billion dollars of which only five hundred million dollars comes from the developing world.

⁴⁷ Ten to a hundred times more doses are required in the developing world than in the developed world.

⁴⁸ On the issue of accountability with regards to products that are not yet in development, there was a recommendation to revisit the attempted BioShield legislation in the USA (2005) which

Society’s attitude to risk plays a substantial part in thinking about the issue of liability; a high level of risk aversion (which is becoming more predominant) can hinder the engine of innovation which drives new products on to the market. Public opinion – and consequently political authority, of which public opinion forms the basis - needs to be properly informed to better tolerate risk, through adequate communication efforts.

would provide government compensation for any action taken against bio terror related vaccine products and tried to cover vaccines for all neglected diseases in order to provide additional incentives to innovation.

5. The Interface of Science, Technology Transfer and Access

This session was chaired by Dr. Tony Bunn of the South Africa Medical Research Council and built on questions around how to establish and run partnerships, and the importance of trust and networks for innovation.

The biotechnology industry has awoken as a contributor to global health both due to realising its strategic responsibility and because of policy development considerations that will be critical to its success later. The industry is becoming interested in sharing its capabilities and knowledge, as well as products, where relevant. IP arrangements bring parties together and challenges related to IPRs can be overcome through “consideration for all parties and through transparent and equitable reward structures”.

There is a need for upfront transparency and fairness in negotiations for the development of successful, longer-term relationships. Governments need to better understand issues around bio prospecting and biodiversity, including the need to develop structured IP agreements that result in benefits going back to the countries of origin.

Access is increasingly dependent on innovative strategies around delivery systems. Delivery solutions need to be tailored to the communities they are directed at.

Counterfeiting raises the issue of non-compliance and undermines the effectiveness of therapies. Any solutions to these problems need to empower the consumer and to be transparent and sustainable

Donors need to respond to gaps in delivery and build on policy innovation. Their interventions should provide tools, confidence, empowerment and capacity and lead to change in developing country public health practice. With regards to ensuring positive outcomes, developing countries require financial independence as well as a national plan and strong leadership for health and access to medicines. A stronger educational system and technical capacity building will develop the role of developing countries in

product development and delivery partnerships as opposed to being merely repeat recipients of assistance.

Participant recommendations for capacity building

- Capacity building must be linked to community needs
- It is important to provide technical and grant-writing skills to researchers to enable them to become self-sufficient by securing local funding
- Trusting relationships are key to enabling fair IP ownership outcomes
- Capacity building must use and develop high and low-technology solutions to addressing community priorities

5.1 Biotechnology Companies and Innovation: James Geraghty, Genzyme Corp.

Emerging opportunities for the biotechnology industry in the global health field were presented with strategies for increasing engagement in the near future.

The biotechnology industry has the potential to move new, interesting research possibilities through the drug development process to bring therapeutic innovations to the market. As demonstrated by the case studies given in the previous section, the pharmaceuticals industry is waking up to the need to conduct socially beneficial work so that they can influence areas of policy that affect how they conduct their own business. In comparison to the pharmaceuticals industry, there has until recently been relatively little involvement of the biotechnology industry in trying to address global health issues. For the biotechnology industry to be involved in this area is, however, a strategic responsibility as it will maximise the value of its assets and provide returns to shareholders. Engaging in global health serves industry’s interests in a number of ways, supporting, for example, efforts to maintain employee motivation and retention, to develop relationships with policy makers and governments and thought leaders in emerging markets, and potentially to develop capabilities.

“As this field moves forward and there is an explosion of activity, discoveries, and capabilities, the opportunities for the biotechnology industry to contribute more to global health is a great source of promise”

Biotechnology firms can increasingly contribute to development and delivery and act as useful partners to organisations and PDPs, through their scientific expertise abilities in the whole product and manufacture process, through management of IP and scientific collaborations.

Despite a widespread recognition of the capabilities and support that can be offered, the industry faces a series of perceived barriers to involvement and a widespread lack of awareness of the ways in which individuals and companies can contribute constructively. Firms in the biotechnology industry may assume that they do not have the relevant expertise to work in neglected diseases, for example, or that because firms are backed by investors or do not have large resources they are unable to divert precious capital. Perceived barriers in larger public companies make similar assumptions, but the constraint here is from the responsibility to the shareholders which may not permit resource diversions away from shorter-term profit making activities. There is also a great deal of caution and conservatism in the biotechnology industry around some of the adverse publicity that has been generated when biotechnology firms do become involved, which causes others to wish to remain inactive rather than expose themselves to risky publicity.

To address these barriers, partnership between industry and the global public health community is essential. As more and more people begin to get involved, the industry will come to realise that not to do it is more of a risk than to do it, so awareness-building and the sharing of models of IP in a collaborative process are essential. There is a need for industry to understand the principles that are important to the global public health community, whose primary concern is around providing mechanisms to maximise access through minimising costs and prices and making IP available (in terms of both patents and in the form of know-how

and skills needed to develop that IP) to enable this to happen.

Industry's needs are, in part, financial, and the costs of working in this field need to be as neutral as possible. As such, companies require pathways to offset the costs of doing work in this area. There is a need for a sustainable set of policies that allow the industry to continue to thrive and continue to attract investment to develop further innovation. Even though only a small number of biotechnology firms have enough products for them to have direct relevance for the developing world in terms of products, all biotechnology companies have capabilities that they can contribute, given an enabling policy environment. In particular, there is a gap that currently exists between taking interesting research possibilities and supporting them through the development process to actually bring innovative new therapies to the market; and this is the space in which the biotechnology industry has the greatest and perhaps the most unique capabilities to offer.

Participant recommendations for the involvement of industry

- Although governments have the over-arching responsibility for providing access where there is no commercial incentive for the private sector, the private sector could assume a role in addressing access through lending expertise on delivery and supply chain issues
- Infrastructure and distribution public-private partnerships should be considered as part of the solution to ensuring timely delivery of essential medicines
- Different models of capacity building will need to be in place for countries at different levels of development. In more developed countries (or Innovative Developing Countries, IDCs), where there is a relatively developed scientific and biomedical research capability, industry can engage with institutes directly, as in the developed countries⁴⁹
- For the least developed countries (LDCs), however, with less

⁴⁹ Demonstrated in the partnership between the Oswaldo Cruz Foundation in Brazil and Genzyme

advanced research and development capacity, a consortium approach with PDPs may be appropriate whereby industry can provide some guidance through broader collaboration

Industry can form new networks with leaders in areas such as neglected research to explore where capabilities could be most useful and are able to take advantage of experience and position themselves to form win-win IPR deals which strengthen and sustain relationships. Genzyme's experience with TDR in trypanosomiasis, MMV on malaria and FIOCRUZ on chagas disease demonstrates that IP relationships can be reasonably straightforward in reaching satisfactory outcomes for all parties. Its IP model typically stipulates that any discoveries will be made available on a royalty free, fully unrestricted, sub-licensable basis, to the non-profit group working in that field while Genzyme retains rights to potential applications that may occur for more commercially-relevant diseases.

“the perceived barriers are only perceived but they act as real barriers because people have not understood ways to overcome them. The perceptions reflect in many ways an obsolete environment. [...] The industry will come to realise that not to do it is more of a risk and more of a liability than to do it, so it's communication, it's awareness building, it's sharing models of IP. [...] It's a collaborative process.”

5.2 Improving Access to Existing Global Health Solutions: Dr Devi Sridhar, Global Economic Governance Programme, University of Oxford

Innovation in delivery systems, in the creation of appropriate policy space, and in approaches to funding is needed to address the growing gap between what technology can do and what is being delivered in poor communities.

Even where health technologies exist and may be relatively affordable, access is still poor, highlighting the need for innovation in delivery systems, beginning at the community level, where behavioural and

social research is essential. This may include addressing issues relating to gender balance and empowerment as much as educating users on the use of particular technologies.

Innovation is needed at the following levels:

Community - to determine what solutions are needed and the obstacles to delivery at that level;

National government - to provide an enabling environment by strengthening the health system. Sustainable institutions should be built to provide care, services and treatment which endure beyond the duration of external interventions; and

Global - by creating policy space for developing country governments to set their own priorities.

At the community level, the emphasis on a social cause and on listening to what communities actually want is crucial. For example, the Avahan initiative found that HIV-vulnerable populations did not want education at that point, they wanted protection. It is important to recognise non-economic factors such as family and community structure, as key elements which can hamper access and which require solutions that are not always technology led but which require solutions such as empowerment rights.

At the global level, despite rhetoric that horizontal, systems-building strategies should be adopted, predominantly vertical strategies are currently in place. Recipient countries often have to accept solutions that are usually tied to short term targets and measures and, as such, global policy priorities often skew national priority setting⁵⁰. Innovation is needed at this level to ensure that countries' national plans are strengthened through donor activity. Focus on one disease area (particularly HIV where there is enormous international attention) can hinder the evolution of all

⁵⁰ For example, in the Millennium Development Goals, there is nothing explicitly on Mental Health, so it is very difficult to get anything on mental health into the country development plan.

other health services, sending overall health indicators backwards⁵¹.

Participant discussion: advocacy and responsibility should be structured in a balanced way

- Shifting power to the 'bottom' is a welcome approach
- Incentives are needed for politicians in developing countries to delegate downwards, as opposed to taking credit for achievements themselves

In terms of global governance and the relationship between the most and least powerful nations, India provides a case of a country that has been successful in global negotiations. Its strength is based on the fact it has financial independence, and is therefore able to select which donors should be contributing; a national plan, which empowers it to decide which inputs to accept or refuse based on the fit with that plan; strong leadership of its public health agencies to ensure that donors receive challenge; and technical expertise to ensure that services can be delivered effectively and sustainably.

Ownership and accountability should be given to developing country governments, to align decision-making with accountability and ensure that decision-makers bear the risk if policies fail.

The following questions were raised for policy makers to consider:

- What are developing country national priorities, and are these the same as international priorities?
- What role do developing countries want global health institutions to play?
- What changes in the operation and structure of institutions of global health would be required to pursue these developing country priorities?⁵²

5.3 A Technology Driven Anti-counterfeiting Approach to Counterfeiting: Dr Prabuddha Ganguli and Dr Praful Naik of Bilcare, India

There is no consensus on the best approach to deal with the problem of

⁵¹ This happened in Haiti in 2002, when HIV infection rates were reduced, but all other health indicators were in decline.

⁵² e.g. structure of staffing, incentives and accountability.

counterfeiting, an industry which thrives on destabilising technological innovations. A technology driven anti-counterfeiting approach which empowers the consumer was presented.

Counterfeiting is a clandestine industry which is becoming a major barrier to genuine access and effective healthcare. It leads to non-compliance, resulting in the development of drug resistance and causes significant increases in healthcare management costs. There is no consensus on the approach to eliminating counterfeiting, although there is recognition that any solution should be policy driven to overcome the ongoing attempts of counterfeiters to beat technological interventions.

Technology-based solutions such as holograms that are tracked and traced using radio-frequency identification (RFID) are ineffective and any technology-based solution must enable the consumer participate in the whole process of health management. They must be commercially sustainable and also must be simple for the consumer to use⁵³.

Participant discussion: there are key necessary characteristics of policies to deal with counterfeit medicines

- Policies must acknowledge the rapid advances that counterfeiters are able to make (which undermine the effectiveness of technological solutions)
- Policies must not place an additional burden of cost onto the consumer
- Policies need to be more responsive to economic measures, such as lowering prices, than technology in reducing incentives to make or sell fake medicines⁵⁴
- Policies should create robust regulatory processes and international harmonisation of regulatory standards to enhance the safety of drugs on the market

⁵³ The particular device that Bilcare advocates integrates a variety of technologies into a comprehensive healthcare knowledge management system which interacts with all the stakeholders in the healthcare system.

⁵⁴ Note that lowering prices is an issue of contention for firms who claim that reputational issues relating to perceptions of product quality might be at stake if prices are lowered.

- It is important to invest in development of the integrity and security of supply chains
- It is necessary to build international collaboration with governmental agencies, international global bodies and firms taking proactive steps together to move forward

5.4 The Power of Networks for Innovation: Dr. Rafael Rangel-Aldao, Simon Bolivar University

Networks are critical for Innovation. Biological networks are in many ways similar to networks that we use for social communication and interaction. It is possible to use these networks for knowledge and technology transfer. The more connections, the more powerful the network and the greater the potential value extraction.

Biological networks work in a similar way to the networks that we use for social interaction and information e.g. the internet. Biological information is organised in small-world and scale-free networks where a few nodes become hubs dominating the entire network. The topology or architecture of such biological networks could be useful to predict and prevent major causes of morbidity worldwide. This knowledge from systems biology could also be transferred and translated to better health care of less developed countries.

A new health insurance model was given as an example, based on a university based consortium of healthcare, science and lifestyle that involves research translation from system biology to a health system using internal capacity to transfer technology. These are self-organising systems: autonomous networks that are interlinked and bring together science and medicine.

5.5 New Initiatives in Japan: Prof. Katsuya Tamai, University of Tokyo

Universities in Japan have embarked on several new initiatives aimed to develop IP rights and technology transfer. These initiatives have had a number of successful outcomes but are faced by notable structural and policy-related challenges because the system is not yet

mature and has only ambiguous targets and evaluation metrics.

In April 2004, Japanese universities became independent from the Ministry of Education, allowing universities to own their IP rights for the first time. As public sector support for universities reduced, they began to focus on managing intellectual assets to generate revenue. Many programmes were established dedicated to fostering university-industry collaboration but the specific impacts of these programmes were not measured properly and so are little understood. Despite this, some research was effectively developed in response to market needs⁵⁵; for regional development⁵⁶; and as public goods⁵⁷.

University employees in Japan are not legally permitted to assume executive roles in private firms, with the specific exception of start-up companies based on their own research outputs. In addition, the private sector in Japan is output-focused and hesitant to invest in university technologies where the potential return on investment is not easily identifiable. Consequently, it is far easier to generate funds from the public sector, which is less rigorous in examining outputs. Universities sometimes fabricate commercial partnerships or planned activities to secure more government funding. In the rural areas, universities are forming strong, genuine relationships with private companies in order to secure funds, although do not approach these collaborations with long-term partnership aspirations.

The system faces additional challenges such as the fact that IP strategy is not adequately linked to university management and individual researchers generally do not have good internal

⁵⁵ e.g. a start up company based on the technology of Kyushu University which is planning a Phase Three clinical study in the United States, and City University which is planning a Phase One clinical study in the United States.

⁵⁶ e.g. 'silicone sea belt' plan based on Kyushu University's activities.

⁵⁷ That is, where there is a high social need but a small financial market e.g. At Osaka University, Phase Two clinical trials for a malaria vaccine are being conducted in Indonesia, Uganda and Myanmar.

management support systems to enable the development of technologies.

5.6 ICBG Program and its Impact in Academia, Conservation and Drug Discovery in Latin America: Prof. Barbara Timmermann, University of Kansas

The International Cooperative Biodiversity Group (ICBG) focuses on building capacity in drug discovery from biodiversity for chronic and neglected diseases. It works through public-private collaborations which enable scientific training of developing country researchers in the US and the import of new technologies into developing world research laboratories.

The 1992 Biodiversity Convention signed in Rio aimed to give value to biodiversity and provided incentives to developing countries to conserve it. It changed the paradigm of R&D locally, calling for commitment by foreign researchers to its principals when working with host countries in the areas of drug discovery. The Convention prompted the US government to call for proposals to create multidisciplinary and international teams to promote the conservation of biological resources in host countries. One such proposal was the International Cooperative Biodiversity Group (the ICBG)⁵⁸.

The ICBG works in several research areas, including infectious diseases, cancer chemotherapy, cardiovascular, the central nervous system and women's health. It involves ethno-botanists, chemists, pharmacologists, and conservationists. Biological samples and initial chemistry come from the host countries to the laboratory for work to isolate natural products, using a bio-assay guided approach^{59,60}.

⁵⁸ Funded by the National Institutes of Health (NIH), the National Science Foundation (NSF), and the US Department of Agriculture (USDA)

⁵⁹ The assays are high throughput and cellular- and receptor-based.

⁶⁰ The ICBG has several lead components now in development which are undergoing Phase One trials and is also investigating the medicinal chemistry part of some of the lead compounds. The programme has three very good candidates at the moment for pure compounds, and in the area of essential medicines about ten are being pursued.

One of the conditions of the ICBG programme is to work on diseases of concern to developing countries. To fulfil this, it conducts work on drug discovery leads from anti-TB agents, in partnership with the University of Illinois in Chicago, specifically with the Institute of Tuberculosis Research.

The ICBG encompasses over twenty institutions⁶¹ all of which work with local peoples to create trust and contribute to conservation and economic goals. ICBG has also established laboratories in Latin America for chemical and microbiological work. It often takes considerable time to finalise negotiations and build this trust. One advantage of such partnerships for host countries is the potential for capacity building, for example alongside the modern research in chemistry conducted in the labs, there is also a focus on training and building new technical skills. Technology transfer has taken place in informatics, through workshops and on site training, also facilitating training of people across Latin America. This has built skills among the local research community, enabling it to generate further funding from local sources, often governmental.

Many scientists are also trained in the US university system, enabling transfer of knowledge across north/south America and within Latin America. Consequently, the number of PhDs and Masters graduates has also increased, enabling people to go on to work in further research, in government and in local non-profit organisations. There has resulted in an increasing number of publications in global peer reviewed journals authored by local scientists, demonstrating an increase in technical capacity and global linkages. Local education on conservation-related issues also forms a part of the workscope.

Because the ICBG program follows the Biodiversity Convention, all participating parties must respect IP rights and all members of the ICBG respect international agreements to ensure protection of local biodiversity. The IP issue has evolved very much on the basis of trial and error,

⁶¹ This includes institutions in Madagascar, Panama, the Philippines, Costa Rica, Fiji, and, until recently, a programme in Isuka in Nigeria.

as this kind of collaboration had not been done before. ICGB's license agreements specifically include benefits for the originating country, community and/or researchers of the plant or bacteria, as defined by US patent law, whereby fifty percent of the conservation assets are returned to the host country specifically for conservation projects. The advantage of the model is that it allows for developing countries to work with industrialised countries, with one sector contributing the technical know-how, and technology, and the other sector providing the biodiversity⁶².

Participant recommendations for IP negotiation and ownership issues that emerge from capacity-building technology transfer partnerships

- Good IP agreements are essential
- Expectation management is necessary because developing countries and universities may expect excessive returns for their inputs because they have an unrealistic understanding of what their contribution is worth
- Information asymmetry can be managed through the concept of 'principled negotiation' – that is, ensuring all parties are working from the same set of information, through an open and honest sharing of information, including an explanation of the profit margin calculation
- This will also require improved education and understanding the benefits of biodiversity conservation

5.7 Implementation of Biomedical and Information Technologies in Developing Countries: Prof. Eva Harris, University of California

The Sustainable Sciences Institute (SSI) follows a grassroots approach to capacity building for biomedical research, based on

⁶² Another example of directing benefits back to the host country was exhibited by the National Cancer Institute (NCI) which integrated a statement into its agreements to that effect. The amendment meant that NCI would license a compound to a company, requiring that the company would flow the benefit back to the originating country.

small scale, bottom-up projects which become self-sustaining.

SSI was established to help biomedical scientists and communities access education, training, funding information and equipment, mostly around infectious diseases and always with a public health impact objective. The focus of SSI has been on strengthening local scientific and healthcare capacity. It strives to create a culture of research that discourages brain drain and provides for a stability that is resistant to political and bureaucratic changes.

The on-site programme began with training in laboratory techniques, grant writing skills, manuscript writing, bioethics, and information technologies and bioinformatics. Small grants of around USD \$10,000 were allocated to support implementation of research to produce initial results that would enable students to attract further funding. Material aid is provided to address people's needs, and support is given for network-building and both north-south and south-south partnerships. Institutions with high levels of commitment receive increasing levels of support and become centres of excellence, sometimes with subsidiary offices. One collaboration between SSI and electrical engineers at Brooklyn developed low cost diagnostics⁶³. This led to UC Berkeley developing a well-regarded socially responsible licensing programme, which is now in place for all their patents.

The programme is based on south-south transfers in Latin America, using a train-the-trainer approach in the region. The impact of these programmes can be seen through: articles published; presentations delivered; grant proposals funded and ongoing scientific collaborations. A major indicator of success is the public health products developed in partnership with local institutions, which governments then utilise in their public health programmes.

Capacity building has to be long term and ongoing, to ensure support is not constrained to workshops, but ongoing through phone calls and emails.

⁶³ An immunodiagnostic sensor for infectious disease diagnosis.

The programme has a multiplier effect: by teaching grant writing skills, the programme participants can raise further funding to enable self sufficiency and the SSI can gradually withdraw its involvement. There have been a number of cases where this has happened and the research groups have then entered new research areas and taught their skills to other groups in the region. One case of success was the transfer of new barcode technologies to individuals running the Paediatric Dengue Vaccine Institute (PDVI) cohort study which enabled upgrading of local systems and improved access to information. It demonstrates how countries can use technologies to leap-frog and advance skills while also developing improved information management systems, in this case useful for clinical trials. This has been integrated in to the Ministry of Health to enable access to immunisation data within two months. Barcodes have also been implemented for use on vaccination cards, linked to monitoring of prenatal care.

Capacity itself acts as a pull mechanism and attracts funding and support. The need remains to engage donors to fund small-scale projects that enable large developments, areas not traditionally of interest to donors. Challenges in quality control and compliance still exist, but the primary challenge is how to scale up while still maintaining collaborative and personalised efforts.

5.8 Discussion

Biogenerics

Biogenerics may be a solution for developing countries, but policies have to strike a balance between providing low cost substitutes for proprietary products in a timely manner against maintaining sufficient incentives to continue to encourage and attract investment innovation. The first generation of biotechnology products are not patented in most of the developing world and there are generic versions in countries such as India. As patent protection develops in India, it will be important to bring in biogeneric legislation to provide sufficient time to reward innovation, in combination with a policy to allow a lower cost substitution at an appropriate time.

Orphan Drug Act and Neglected Diseases Drug Act

There are two primary ways in which the Orphan Drugs model could be useful in the area of neglected diseases. One is that the developed world, which pioneered orphan drug legislation, could create 'neglected disease' legislation that could provide the same kind of incentives that the Orphan Drug legislation provided, such as tax credits and relief from certain kinds of filing fees that enable early research in orphan diseases. There is some interest in trying to develop legislation like that in the US and Western Europe. One example of the price differential that is possible through this kind of legislation is visible in a product that MMV is developing, which is an IV Artesunate product that will be registered with the FDA under orphan drug legislation. The price differential between the public good that MMV will be responsible for in Africa and the use of this product by the US Department of Defence is about ten thousand to one.

Mary Moran's research into this in the EU showed, however, that the legislation has not overall been very effective for neglected diseases because the orphan drug monopoly term of ten years is actually less than the patent term plus the patent term retracting, meaning that firms obtain better protection simply by patenting normally.

Orphan Drug legislation:

- Has worked best for non-patentable areas
- Has encouraged the re-registration of many existing products for a neglected disease use, failing to encourage radical innovation in neglected disease areas
- Currently encourages non-novel product development for lower value markets, and
- Could be effective for neglected diseases either if its monopoly term is longer than the patent term and/or it is of use in a high-value market.

Orphan Disease legislation in a country like India⁶⁴ is potentially a more promising area of legislation, as developing countries

⁶⁴ India has large health problems and an emerging industry which might respond to stimulus for innovation in areas that are locally important.

do have very active drug markets that are available to developing country firms.

6. Partnerships in Promoting Innovation and Managing Risk

Dr K Satyanarayana (ICMR) and Andrew Farlow (Oxford University) chaired sessions which addressed partnerships for the development of products and the challenges related to product development and, increasingly, access and delivery.

The sessions explored:

- The need for policy and funding to be adapted to reflect the changing nature of research and development (R&D) for neglected diseases
- The different approaches used by product development public-private partnerships (PDPs) to bring low value products to the market by reducing and mitigating market risk
- The PDPs' approaches to access
- Government approaches to healthcare access through community led surveillance, planning and financing and private sector partnerships in Indonesia (Desa Siaga)
- Community based participatory research approaches to improving access (Spirit of E.A.G.L.E.S, USA)
- Advances in and challenges to developing country R&D and technology transfer partnerships (Chile).

A series of **case studies** presented by different product-development PDPs explored the different approaches to the “*eternal triangle of balancing time, risk and resources*”:

The tension between the importance of considering issues around access as early as possible in the product development process and the difficulties in predicting and managing access for products in early stages of development was discussed in this session.

It is useful to consider ‘access’ as a process in much the same way that R&D is a process and to unpack the various components down the value chain - from the initial decision to produce; through product development, manufacturing and scale-up; through product introduction and then to full scale distribution.

This session revealed that access improves if:

- Products are recognised as a public good
- It has been identified when and where products are best needed, there is as little asymmetry of information as possible
- Demand and supply gaps are reduced through community led surveillance, planning and financing (as in the case of Desa Siaga)
- Cultural integration tools such as community based participatory research (CBPR) are used.

Partnerships work best when:

- The partners are diverse
- They represent a range of disciplines
- They operate on mutual trust
- They work towards a common goal and when
- They include innovators, producers and end users in the partnerships.

With regards to fostering innovation, the session highlighted many deterrents to engaging in this area, particularly for academia and small start-ups in developed and developing countries.

Deterrents to innovation in developing countries include:

- Procedural and policy deterrents
- A lack of special tax incentives to form enterprise
- The fact that the majority of patents are transferred before they are granted

Models are needed which share the benefits of product innovation and provide access to markets to enable product innovation.

6.1 Strategies for Product Innovation: the PDPs: Dr. Mary Moran, The George Institute

The costs or risks are not uniform in the area of health product innovation and vary along the pathway by disease and stakeholder. It is important to consider the development process as a modular

process and recognise the need for different incentives through the process. PDPs are presenting smart and flexible ways of dealing with these.

Current policy thinking tends to be based on an old model, which is “big, Western, classical and past”. Policies are typically designed around the monolithic development model, for big pharmaceutical companies with exclusive or monopolistic skills in integration or in regulatory economies of scale. The second factor determining the model is that given very high costs and risks very high returns on investment are required. There is also a focus on the market as the key to stimulating innovation. As the current health innovation model is currently highly modular⁶⁵ and not concentrated in large firms, different incentives are needed for different stakeholders.

The main modules in modern drug and vaccine development are as follows.

1. **Discovery & innovation:** Ideas – or blue skies thinking - usually generated by academics and sometimes early spinouts. There is very high scientific risk at this stage, but the business risk and costs are low, which is partly why pharmaceutical companies’ neglected disease work is focused here.
2. **Commercial application:** Start-up companies with a platform technology or delivery mechanism to translate ideas into prototypes or products.
3. **Large scale clinical development:** This has traditionally been the purview of large pharmaceutical companies but increasingly CROs are doing this work, especially for PDPs but also for small firms and developing country firms⁶⁶. The scientific risk is quite low and by Phase Three the failure and

⁶⁵ For instance in the area of clinical development, a third of drugs in Phase Three trials are currently unlicensed, two thirds are outsourced, some to Contract Research Organisations (CROs). Manufacturing is very often outsourced to developing country (DC) companies, either producing generic drugs for sale under an originated name or producing regional brand products through voluntary licensing (e.g. Aspen in South Africa).

⁶⁶ For example, Dr Reddy’s of India holds many patents and a solid background from generic production.

attrition rates massively decline. However, the cost of running large scale clinical trials is high, as is the business risk from trial liability (particularly if a product has been trialled in pregnant women or children, and especially in developing countries).

4. Large scale manufacture and distribution for mass markets:

Traditionally the domain of large Western companies but developing country firms now have significant capability in this area⁶⁷ and are prominent in the first generation vaccine market⁶⁸. These firms are now entering into second generation vaccines and recombinant technologies, and conjugation technologies⁶⁹.

PDPs help to manage these costs and risks for the industry partner.

A further misconception within the old policy model is that it assumes that risk is uniform. The market risk varies by disease, however. When discussing neglected diseases and policy, this should be separated from the issue of the science: just like for the common cold, it is the science that is hindering vaccine development for diseases like malaria and AIDS, not the size of the market.

Risks also vary between stakeholders:

- For **developing country firms**, neglected disease R&D is an opportunity for technology transfer, not an opportunity cost.
- **Small companies** have a low cost, low return model and are satisfied to work with small markets, and lack the capacity for large markets. For many smaller firms today, a market of \$500m is exciting, while large firms would not see that as a sufficient incentive to become involved.
- With smaller biotechnology companies, there is also variability: **'Soft' biotechnology companies** do

bespoke R&D, contract research or specific development work for a PDP; **'Hard' biotechnology companies** do speculative product development, working from an idea, and requiring venture capital to develop it. These face much more risk than the soft company strategy which is very low or no risk.

- **Developing country firms** favour developing country markets, including public tender markets, because they appeal to their high volume, low margin model that evolved during years of experience as generic manufacturers.

The third principle that has been guiding policy development in the past is the notion that there is a single large market. However, there are actually many interim markets, 'mini-markets' for all the different groups of stakeholders. For instance:

- **Academics** want publications, long term research funding, and development of discoveries.
- **'Soft' companies** want contract research, proof of concept opportunities, low risk growth opportunities.
- **Small start-ups** need cash flow, proof of concept, collaborations with academics to get fresh ideas for their platform and an exit strategy.
- **Established firms** may want the end market but often not the commercial neglected disease market because it's not commercial for them.
- **Developing country firms** generally want the product market but they may want other things, including technology transfer, funding and access to new markets.

Rather than donors providing lump funding solutions for a diseases area, a modular incentives structure targeted at different actors should be developed, depending on what each stakeholder's 'market' is. A variety of incentives are listed by stakeholder in Table 1.

Current policy focuses on a one-winner approach, encourages high-risk development strategies based on a large monopoly prize. In practice, companies should focus on their area of comparative advantage and partner for the rest.

⁶⁷ For example, Ranbaxy, Cipla and Dr Reddy's are able to do cheap manufacturing and large scale developing country distribution,

⁶⁸ For instance, 80% of vaccinated children in the world have had a vaccine from The Serum Institute of India (SII),

⁶⁹ For example, the meningitis A conjugate vaccine has been developed by a developing country firm.

Table 1: Incentives by stakeholder

| Academics: |
|--|
| . Training should be given to enable start-ups to survive ⁷⁰ |
| . Funding should be allocated to nurture start ups before they are spun out |
| . Open source frameworks should be developed to let academics share ideas in areas such as x-ray crystallography or genomics |
| Hard and soft start-ups: |
| . 100% R&D funding ⁷¹ |
| . Support for incubators or means to feed ideas from academia to small companies |
| . IP management and protection to ensure they can protect their share of the market in developed world markets - Neglected disease ⁷² IP, by definition, doesn't have a high value, and is therefore relatively non-contentious. To avoid leakage of precious IP into other areas, firms need assurance that their IP can be ringfenced |
| . PDPs giving interim advance market commitments for things with proof of concept Phase Two |
| . Clinical development skills - through partnership to identify trial site networks, create regulatory dossiers |
| Industry: |
| . Industry platform initiatives ⁷³ |
| . Initiatives to lower time to market ⁷⁴ |
| . Outsourcing to CROs for R&D |
| . Using developing country firms for manufacture |
| . Using developing country CROs. |

⁷⁰ e.g. The Wellcome Trust Seeding Drug Discovery scheme fosters skills needed by academics in areas such as project management and medicinal chemistry, to ensure start up survival.

⁷¹ e.g. US SBRI grants give 100% cross coverage for small companies lacking the funds to invest in non-commercial areas.

⁷² e.g. malaria, sleeping sickness, chagas disease, the Helminths products, dengue.

⁷³ For example, the EC is already has one with large companies for surrogate markers so instead of doing a two year follow up you have a market that lets you terminate your trial after six months.

⁷⁴ For example, developing predictive models, animal models, and fast tracking.

Participant recommendations: development for PDPs

- It would be worthwhile investing in examining the facilitation of PDPs gauge lessons from progress
- This investment could also act as an incubator to identify and nurture areas of pre-competitive space
- Further, a mechanism such as this would reduce duplication and increase efficiency through knowledge transfer.

Public-Private Partnership Case Studies

6.2 The Aeras Foundation: Achieving Access: Dr. Jerald Sadoff, Aeras Global TB Vaccine Foundation

Aeras operates as a not-for-profit pharmaceutical company, conducting research, development and manufacturing activities. It has a number of partnering strategies all based on the notion that control of IP enables better ultimate control of price and distribution.

Aeras aims to develop vaccines that ensure access, aiming to develop a fully accessible vaccine against tuberculosis (TB) within the next 7 to 9 years. It operates like a biotechnology firm, focused on product development, clinical trials and production rather than operating as a virtual PDP model.

A PDP's sustained investment in high risk projects may balance a firm's opportunity costs. There is a clear market and, as there is a clear development path with developed field sites and early approval of principle studies, there is reduced financial risk. These factors provide incentives for private sector partners.

Market and product profiling is central to the Aeras model (and other PDPs) because "*the way you develop something is the way you end up selling it*". As with the other PDPs, Aeras partners with industry, academic groups, philanthropy and governments.

To ensure access for vaccines, Aeras requires guarantees (legally obtained early in the development) that profit-making enterprises will provide availability and affordable pricing. Sufficient quantities of vaccine to meet the uptake curve are

essential and this is based on understanding the predicted uptake curve. This informs predictions which have to be taken at risk to size the manufacturing component. Plants have to be built before a vaccine's efficacy is known and, in the developing world particularly, a huge investment is needed to build plants that can meet the approximately three hundred million doses needed a year for a three dose vaccine.

The vaccine also has to be affordable and funds are needed to procure it. Vaccines are very sensitive to economies of scale because the majority of the cost involved is in testing and validation. The equipment and labour costs are fairly low in comparison. The difficulty lies in trying to predict what is affordable and this depends on what people are willing to pay, which varies among social groups.

There are variations in access issues faced by PDPs involved in vaccines and therapeutics and particularly where treatments are very novel and where people are not aware of the disease or the medical approach to them. For a number of technical, supply-related and socio-psychological reasons, vaccines often pose a greater challenge than therapeutics

To achieve availability and affordable pricing, which are dependent on manufacturing, Aeras outlined a number of options for PDPs in terms of development arrangements and partnership models. Working with the classical pharmaceutical companies reduces risk and reduces the complexity of the process. A mix of old and newer models is ideal. *"If you want to reduce risk you work with what's worked in the past and you work with what might work in the future."*

Its models are as follows:

1. The Developer: PDP manufacturing and distributes with or without developing world partners.

This requires invention or licensure of all the IP. It requires having a manufacturing facility, or outsourcing to a contract manufacturing group (although the pitfalls of this are reliance on the clinical research outsourcing (CROs) schedule and interests which may shift, leading to

broken contracts and delays). An advantage of this model is its financial sustainability as it relies on selling in the developed world to enable use of the profits to sustain the sales at a loss in the developing world. The burden of risk on one party and reliance on a funder to support the high costs and risk upfront are a disadvantage of the model. A barrier has been the high returns that universities expect on their technologies.

2. Industrial partner manufacturing and distribution: with or without cost plus purchase by the PDP for developing world markets.

A PDP has flexibility to pick the best technologies and to bear risk well, to diversify manufacturing and to ensure regional manufacturing and distribution and to hold a lower cost of manufacturing. However, and through working with development partners the cost advantage of large scale production can be lost. Regulatory standards can also be difficult to meet and technology transfer can be disruptive and difficult to manage. However, Aeras has been a successful in managing this and recently engaged in technology transfer with a Chinese manufacturer.

3. Manufacture by developing country partner:

In this case there needs to be an experienced manufacturing partner willing to participate. Aeras partnered with Crucell in this way, Crucell shared IP and expertise in delivery and manufacturing in exchange for Aeras' knowledge and experience.

IP and knowledge transfer advantages can be difficult to manage. In particular when there is more than one partner involved in this kind of model, it becomes a great challenge to mix IP from different sources. There are high opportunity costs for industrial partners that have to be compensated somehow, such as via sales in the whole market in the developed world, or royalties. Development is more expensive because there is a loss of control over manufacturing, cost and distribution. While low cost manufacturing for vaccines is not as critical for a company as time to market⁷⁵, the

⁷⁵ If it takes an extra year for a firm to reduce manufacturing costs from USD \$2 to fifty cents

difference between \$2 and fifty cents can be absolutely critical in relation to supply for the developing world. The potential returns from this model may not enable PDP sustainability into second generation entities, limiting further improvements.

“It’s hard enough to transfer between one department and another when we’re all working together, let alone transfer to a different country”

There are incentives for industrial partners to invest in capacity for the developing world at sustainable and affordable prices, with improved estimates of market size, the management of IP and sustained investment into such projects from PDPs and donors. However a mixed model is needed to really enable progress. To ensure affordable pricing and access Aeras requires all of these strategies to come into practice to some extent. It is important to consider every viewpoint and every incentive – whether it is the “old” market focussed innovation or using different approaches to manage risk.

6.3 Potential New Approaches to Scientific and Financial Innovation in PDPs - the example of AIDS Vaccines: Mr. Labeeb M. Abboud, IAVI

IAVI is a fully integrated organisation with an active R&D programme, also engaged in policy and advocacy work and community preparedness. In partnership with industry, it uses IP arrangements to ensure future access to a vaccine, with a combination of IP management, license rights and technology transfer. It tries to introduce novel IP and licensing terms to ensure access.

To improve the product development pipeline IAVI developed a vaccine development partnership model with industry and academia to absorb some of the early stage risk in vaccine development and to accelerate technologies with funding, scientific, clinical, and regulatory expertise⁷⁶. It

they will lose between USD \$500 million and \$1 billion, which can never be made up on the marginal cost of manufacturing.

⁷⁶ IAVI helped develop the first AIDS vaccine designed for Africa, sponsored the first AIDS vaccine trials in a number of countries, including Kenya and Zambia and Rwanda and

works in partnership with developing country scientists, community and political leaders. IAVI has had more than forty partnerships with industry and ten vaccine candidates, six of which have gone into trials.

IAVI is working to address several of the major scientific obstacles that need to be resolved for there to be a fully preventive AIDS vaccine, such as questions around how to identify neutralising antibodies, how to design safe vaccines that mimic the mechanism of protection that are found in live attenuated vaccines, and vector design. It is also engaged in strengthening clinical testing infrastructure and clinical laboratory infrastructure in developing countries⁷⁷. Support for an immunology lab at London University’s Imperial College is working to support and develop local capacity within the laboratory infrastructure in some of these networks (providing construction, equipment, training, support and standardisation).

IAVI’s advocacy efforts work to secure and sustain global commitment to the HIV vaccine research enterprise both in terms of political and financial support. It aims to advance the policy environment and engages developing countries as partners using an in-country model that builds capacity and political and public support for work at the site and community levels, regionally and nationally. Part of its work aims to strengthen education and awareness and to build capacity around research studies and trials and to encourage the acceptance of future vaccines.

IAVI is moving forward with small screening ‘test of concept’ trials to find preliminary indications of potential efficacy to help guide product development, with the aim of prioritising resources to accelerate time lines by several years. It has begun working with support from the Bill and Melinda Gates Foundation to

India and helped enlarge the pipeline of candidates (today there are about thirty vaccine candidates in trials). IAVI works in parallel with various strategies, trying to move fast and terminate programmes when they fail to meet milestones.

⁷⁷ It supports twelve sites in Africa in partnership with local universities, institutes and NGOs.

contrast, compare and try to prioritise novel, high risk replicating vectors. It is also working with regulators to try and anticipate their concerns and address them early on in order to open the pathway if a development is worth pursuing.

The PDP works to strengthen partnerships with industry, including IP arrangements to ensure future access to a vaccine, with a combination of IP management, license rights and technology transfer. It tries to insert novel IP and licensing terms to ensure access.

In addition to these activities, IAVI is promoting innovative financing and alternative push and pull mechanisms to stimulate investment in R&D. As part of this stream, it has launched an innovation fund co-funded by the Bill and Melinda Gates Foundation working to augment existing approaches and to search outside of the mainstream HIV vaccine work currently ongoing for new, innovative ideas and technologies that may offer promise to the field.

6.4 PDVI – What is the End Game?: Dr. Harold Margolis, PDVI

The Paediatric Dengue Vaccine Initiative (PDVI)'s mission involves accelerating vaccine evaluation as well as introduction of vaccines. Vaccine discovery has not been part of the PDVI mission. PDVI's programmes on access involve working with a developing country vaccine regulators network; developing a series of dengue prevention boards for Asia and the Americas; and developing a public health network (engaged in activities such as surveillance and diagnostics). Its measure of success will be to introduce dengue vaccines into the national immunisation programmes of at least one developing country in each dengue endemic region.

The dengue vaccine is transitioning from discovery into Phase Three trials. The process is highly complex as the product needs to protect against four viruses with a tetravalent vaccine, most of which are live attenuated vaccines. There are potential safety issues including the concern that the vaccine could put patients at risk for more severe dengue if they have had previous infection.

Unlike some of the other products being developed by PDPs, the market for dengue is almost exclusively a developing country market. While this vaccine is likely to be introduced as an Expanded Programme on Immunisation (EPI) vaccine probably in the second year of life, in order to fully stop dengue transmission, catch-up immunisation is needed, meaning that older children or adolescents will also need to be immunised. This number will be quite variable depending on country epidemiology, and will pose a challenge in terms of introduction and production.

As with the other PDPs, a portfolio approach has been taken for a number of reasons including the fact that there is no assurance of success as there are many unknowns on the technical side. Affordability is a critical outcome, and healthy product competition leads to best pricing and greater choice. Finally, the portfolio approach addresses the need to ensure sustained supply and production. PDVI has strategic partnerships with vaccine and diagnostics developers and manufacturers, conducting supportive R&D focused on diagnostic issues and looking for better assays.

6.5 The PATH Strategy: Dr. Michael Free, PATH

The Program for Appropriate Technology in Health (PATH) has had over a hundred partnerships with commercial companies to advance over sixty technologies, many of them currently in use or in the pipeline.

PATH works in three areas of activity: innovation, introduction and integration, all of which overlap and require early thinking and preparation as well as engagement of all the constituencies at every stage. Partnership harnesses innovation capacity and commercial capital.

The question of how to ensure that health innovations reach populations where this impact is really needed is critical. To meet this requirement it is important to understand the needs of vulnerable, at-risk populations; to create the right incentives and to support targeted public investment to engage the right organisations to develop appropriate, sustainable technologies; to build the evidence base for informed decisions; and to focus on

systems strengthening for distribution and delivery and use. This systems strengthening element is vital, unless efforts are made to focus on this area there is likely to be a pile-up of products coming through the pipeline without appropriate strategies for delivery.

PATH works to build the evidence base for informed decision-making by different stakeholders – users or patients, policy makers and international agencies and donors - all of whom require a different value proposition and consequently different sets of evidence. At the innovation stage, users or patients are engaged as co-designers; at the introduction stage, the target country decision-makers are engaged as co-evaluators; and at the integration stage international agencies are engaged as co-promoters. In this way there is broad ownership of the solutions that are being brought forward across the whole process. With different groups' interests engaged, the motivation for developing the process further to create a sustainable solution is strong.

A number of cases were given to highlight PATH's approach:

- 1. The new second generation women's condom** is at a late stage of innovation and will be highly acceptable in four countries. It is ready for its final clinical trials, but commercial companies are reluctant to get involved in an early stage because they have concerns about the viability of the markets. As a consequence, a large amount of public sector investment is required to reduce both the technical risks and some of the market risks as well.
- 2. Oxytosine Uniject is meant for post-partum haemorrhage control for births in the home.** The intent is that it will be used by community health workers and so this needs to be demonstrated. The product also needs to demonstrate that it provides marginal benefit over alternative approaches. Country-led decision making is critical and must align with international policy to ensure that policies are aligned with this essentially new best practice. This in turn will improve the environment for

commercial companies to mobilise more commercial capital and resources to develop new technologies.

- 3. The vaccine vial monitor, a heat label, measures heat exposure** and has effectively transformed the way vaccines are managed around the world. Ensuring policy alignment to get the product in wide use is essential. Additionally, bringing companies on board can be challenging as this may be a disruptive technology for them.

It is clear that successful product development alone will not drive the integration of innovations. To achieve the high impact for the populations at risk it is necessary that investments be made to achieve sustained use on a large scale.

6.6. The South African Malaria Initiative: Jane Morris, African Centre for Gene Technologies

The South African Malaria Initiative (SAMI) is a nascent PDP, currently seeking business partnerships and evolving its processes. It has an IP framework agreement in place. A priority is to involve Africa in the R&D and partnership process and to build skills and the tools for the future in laboratory testing and validation as well as a high throughput screening platform.

SAMI is one of the few PDPs whose secretariat is located in the developing world. It focuses initially on the discovery pipeline with a number of drug leads feeding into it. It is exploring novel biomarkers and diagnostics technology, and will narrow its pipeline down as fast as reasonably possible. Core expertise groups are engaged to bring modern technologies to bear, developing IP and building global networks.

SAMI benefits from a strong base of cutting-edge research and facilities, with much drawn from its network. It is consequently able to invest in people and activities, rather than the "bricks and mortar". It also benefits from having unique holdings of live mosquito cultures in South Africa as well as access to field sites and collaborations in many African countries.

With regards to intellectual property, SAMI has developed innovative and novel IP policies with a strong consortium agreement to enable very structured collaboration. However, SAMI faces a number of challenges: it does not possess the regulatory capacity to compile a regulatory dossier that will take a product through the necessary regulatory hurdles. Additionally, although there is capacity for production of generics in Africa, there is only limited capacity for production of new compounds. Like many other PDPs, it will need to rely on partners to undertake some of these activities.

To-date SAMI has achieved the following:

- A drug delivery system to reverse chloroquine resistance
- provisional patent covering the anti-malarial activity of another drug that has been previously registered for other uses
- A novel rapid diagnostic test ready for field screening by mid-2009
- A novel *in vitro* high throughput screening assay validated against a new target, and
- Target accepted for *in silico* virtual screening in an international programme called 'Wisdom', based in France, to generate a range of new leads for that particular target.

6.7 MMV - Moving to Access: Dr. Chris Hentschel, Medicines for Malaria Venture

The Medicines for Malaria Venture (MMV) conducts R&D, collects and analyses drug information, builds awareness, and generates support particularly for MMV products. MMV's attention is turning towards ensuring access to the products it develops and is increasingly becoming involved in Phase Three trials (which is the market feedback phase), registration and what is termed in the private sector 'commercialisation'.

MMV's original mission was to register new products, but has now changed its strategy, to become involved in access. In the absence of a specific body which accepted innovation and integrated new products into the ultimate goal of reducing morbidity and mortality, so that products in late development stages or even in the registration process could be used

optimally, MMV has adopted delivery into its model.

By incorporating the downstream into MMV's remit, MMV is able to use its expertise and experience gained from its involvement in product development to inform on pricing and placing products – providing the necessary information to ensure an effective public good as a result. As such, MMV will be engaging in the market feedback phase of drug development which is essential to developers, creating a virtuous circle that enables effective portfolio management. As Jerry Sadoff noted earlier in his presentation on Aeras, passing products on to a third party for distribution can be problematic if that party's priorities change.

Through taking full ownership of the product and being the authority on all benefits and also limitations of the product, the PDP is able to take product forward like nascent pharmaceutical companies, taking on the role of ensuring access, which is termed 'commercialisation' in the private sector. However, there are different views on the roles and functions of PDPs particularly in relation to access and delivery and some deliberately separate delivery from development.

"Nobody feels more passionate about products than the people who have been involved in developing them, nobody understands them better and nobody is able to actually discuss the merits as well as the problems of products than those involved in developing them"

Like PATH and IAVI, MMV will continue to collect and analyse information, build awareness and advocate support for its products. Where poor-quality products already exist in the marketplace, there is need for transferring the installed user base away from substitutes⁷⁸ to higher-quality products, which can be a difficult process.

⁷⁸ This is a significant problem: in Nigeria alone there are more than 700 products registered as anti-malarials with the local Nigerian authority, yet only one of those (Coartem) meets any kind of international standard.

With regards to pricing, Orphan Drug legislation has had a positive impact on lowering the price of MMV's products: the differential between the public good that MMV will be responsible for and the use of this product in the US is very significant, with the Department of Defence paying around ten thousand times more than customers in Africa will pay.

Participant recommendations: in considering access, it is important for PDPs to...

- Incorporate thinking on access from as early as possible in a development process
- Be aware of the tension faced by PDPs in accomplishing product development as fast as possible and strengthening and building capacity in developing countries to enable them to engage more fully in the product development process
- Conceptualise a product profile suitable for use in developing countries – i.e. affordable, durable, at the right quality, which can get to the right patient at the right time
- Use IP arrangements that allow flexible pricing and manufacturing strategies
- Invest in demand forecasting
- Mobilise financial resources
- Invest in marketing and positioning of a product, and distribution of the product through public and private social marketing channels
- Form partnerships with existing supply mechanisms, including PEPFAR, JSI and others
- Consider capacity building programmes. Some hold the view that deliberate capacity building efforts should be initiated by PDPs, while others believe that capacity will be automatically developed through partnerships within a framework of common goals

There will need to be a major transformation of the PDPs, to go from very lean, effective product development organisations to those that move downstream, undertaking manufacture, marketing and delivery

The challenges of coordinating large-scale international clinical trials (including ethical and behavioural issues that vary between countries, which pose challenges for trials coordinators) require alignment of motivation between all the different partners and high levels of sustained investment to ensure success.

MMV's management philosophy is to under-promise and over-deliver in order to defeat sceptical views on what PDPs can and cannot deliver:

“public-private partnerships can revolutionise discovery, development and delivery if they have management, motivation and money, and money is terribly important”

6.8 IPM Case Study: Dr. Zeda Rosenberg, International Partnership for Microbicides (IPM)

The International Partnership for Microbicides (IPM) works to reduce time to licensure to get anti-HIV microbicide products onto the market as quickly as possible. Where products have been previously dismissed by the pharmaceuticals industry for not having good oral biological availability, IPM seeks non-exclusive, royalty-free licenses or material transfer agreements (MTA's) to explore topical bio availability and ultimately to develop, manufacture and distribute antiviral compounds as microbicides. Using licensed products from industry enables risk and cost reduction because of the investment that has already been made. In addition to the licenses, IPM receives ongoing technical support from some companies⁷⁹. Community preparedness to ensure participation in clinical trials is an essential component of its work.

IPM's mission is to accelerate the development and availability of microbicides for use by women in developing countries, for prevention of HIV transmission. IPM's goal was to expand the microbicides pipeline to hasten product development, to increase public and private sector collaboration and to provide

⁷⁹ For example synthetic chemists from industry have been working with IPM's for drug synthesis.

resources to the field. A microbicides field existed before IPM and there are currently several Phase Three trials of products that were developed in an earlier generation of product development. IPM was created to discover new products and also to help those who are already in the field, by supporting external and internal research and development and increasing the awareness of microbicides, which was low when the PDP was created.

IPM's goal is to look at highly active antiretroviral drugs that have been developed or are in research for indication for therapy for HIV, and adapt them for prevention. It takes drugs that are in oral form as pills or as injectables, and formulates them in topical formulations such as gels, creams, and intra-vaginal rings to use for prevention. To do this, IPM has developed innovative agreements with large pharmaceutical firms to be able to develop their antiretroviral drugs as topical formulations.

IPM acts as a "bridge" between companies who may have technologies that could contribute to combination microbicides for the developing world. To date, IPM's partnerships with industry have been based on non-exclusive, royalty-free licenses to develop, manufacture and distribute antiviral compounds as microbicides in developing countries. In general, grant-back license of chemical modifications to the compound is typically required by the company. This means that any improvements to a molecule are owned by the company. The grant-back licenses of products or formulations are subject to future negotiation as the end-state of the product is not known at the time of the negotiation. Additionally, IPM's licenses enable any combination for the purpose of a microbicide for the developing world.

In addition to the licenses, from some companies technical support is provided to support creation of the API, or active pharmaceutical ingredient, which is very difficult to make for some of these products. Site evaluation tools for Africa are also developed in partnership with firms, particularly where they are exploring treatments for other diseases.

Territory and access are controversial issues for companies considering markets

in countries such as Brazil, China, India and Russia which may be profitable. Tibotec gave a favourable arrangement concerning territorial rights and this has served as a template for use with other companies. Others have also given worldwide rights. The compound is still proprietary and distribution is always on an affordable basis.

Participant discussion: working across countries and partners for PDPs

- The framework for patenting is around incentivising future commercial partners, preventing blockage, and trying to control the use of a technology to ensure access
- Territory and access can be an issue in negotiations with many companies, particularly for those markets which are more developed, such as in China, Brazil, India and Russia

Elaborate investment in the clinical site capacity and clinical research is critical as microbicides require a very complex trial design. The building of site capacity is a multi-step process, involving working with communities, in-site development, and conducting site incident studies to assure that the trial sample size is appropriate. As many trials have been stopped because of lack of proper preparedness and engagement of the community (e.g. oral prophylaxis access studies); to reduce time to licensure substantial effort is put into engaging the community at multiple levels.

IPM is also researching a variety of delivery approaches as many women cannot, for a range of cultural reasons, negotiate topical microbicide use at the time of sex. They may, for instance, need long-acting sustained release formulations, at minimum of once a day so that a woman could use a gel at any time during the day and it would be active for twenty-four hours, or the intra-vaginal rings which have thirty to ninety days' supplies of ARVs. Additionally, as these are products that women will need to use when they feel well, rather than for a therapeutic indication, safety and acceptability studies are necessary.

Access typically requires investment in education, marketing or management, and this relies on local partnerships across a variety of stakeholders

For topical microbicides the greatest risk for failure is the lack of surrogate markers and consequently the inability to prioritise in advance which products will give the most likely chance of success. Without a successful Phase Three, validation of any of the pre-clinical or animal models is impossible, which means that product decision making is currently “*in a data-free zone*”. The selection is therefore quite arbitrary or random, and so the chances of failure are very high. Discussions are currently underway on adaptive design for clinical trials to assist IPM to calculate the numbers of sites needed to predict early which products are most likely to succeed.

6.9 The Evolution of PDPs: Best Practices: Dr Adrian Towse, Office for Health Economics⁸⁰

PDPs are a cost-effective intervention for health improvement. A recent study by FSG aims to support performance evaluation (based on a range of performance metrics) to enable donors to make investment decisions.

In principle, if donors put money into health research then the sort of payoffs that they will achieve (in terms of the DALYs averted and the dollars that they are investing) from PDPs are extremely promising. If there is uptake and use of PDPs’ new products, health spending will be displaced, meaning that the PDPs appear to represent very good value for money for the donor community.

Cost-effectiveness may not be the only reason for making a funding decision (political reasons and other priorities may also have a significant influence) and donors are often cognisant that if countries do not adopt a new technology despite proven cost-effectiveness, then their R&D funding will have been wasted.

The shift in the focus of PDPs towards access or ‘delivery’ preparedness⁸¹ is

⁸⁰ Presentation originally to be delivered by Kyle Peterson, FSG Social Impact Advisors.

likely to be appealing to donors. How well an organisation can deal with risk or the extent to which they are subject to political risk affects decisions to fund particular initiatives. This affects decisions to fund R&D in new products versus delivery and integration of existing products.

For donors to ensure they are investing appropriately, performance measurement is necessary.

A recent FSG report establishes four performance indicators for PDP, relating to:

- 1. Management** of the portfolio, from R&D to commercialisation, and conformity to timelines
- 2. The internal functioning** of the organisation
- 3. The access environment** (including policy and political environment and measures to ensure access once the product is developed)
- 4. The extent of health impact** from the final products

PDPs are well placed to manage a portfolio of products, which is important as it allows some ability to deal with product failure: “*diversification balances risk*”. The role of PDPs in building technical capacities in developing countries is an important activity, particularly where achieving health impacts may not be a near-term goal.

6.10 Desa Siaga – A Strategy for Health Investment: Siti Sundari, Ministry of Health, Indonesia

An Indonesian Ministry of Health village-level initiative, Desa Siaga, addresses access from a health systems perspective, particularly health development activities implemented at the grassroots level.

In Indonesia lack of access to health services and an unbalanced distribution of health personnel, including factors related to poverty and low social conditions, are all challenges to health equity. To overcome these problems the Ministry of Health has developed initiatives to focus on building self-sufficient and healthy

⁸¹ As compared to two years previously, where the emphasis had been on building R&D portfolios where failure is acceptable.

communities to improve the country's health.

The government only supports health services down to the sub-district and health centre level but has invested in the village health clinic to provide access to healthcare for the community. Desa Siaga is a village health clinic providing basic healthcare, with community surveillance for disease and treatment, mental health and promotion of healthy lifestyles. It also promotes safe community systems and donor community health insurance plans. The government invests by supporting provision of drugs and health facilities, competent health personnel, health resources guidelines and training.

The community strengthens its capital through active participation; planning and monitoring of health development; provision of transportation and emergency centre health services; and provision of funding. Stakeholder participation is critical to health development. This is complemented by corporate social responsibility programmes by the private sector through provision of funds for scholarship training; incentives for community health workers; and community support activities such as maternity wards or family activities.

Political will is essential to the success of this initiative. Local government provides seventy percent of funds allocated at the village level and instructs village officials to be more active in the monitoring and reporting of local health conditions. The government provides funds to support the poor, elderly and infirm. In return for these investments, Desa Siaga promises healthy, confident populations with improved social norms and social cohesion, and consequent economic benefits.

6.11 Universities-Private Sector Relationships in Developing Countries: Dr. Jose Miguel Flores, Flores & Asociados, Universidad de Concepción

Chilean innovation is hindered by a lack of adequate R&D investment both from the public and private sectors. Technology transfer is hindered by the reluctance of universities to set up internal technology transfer facilities, due to perceptions of high costs of investment as well as a lack

of experience among staff. Access to government funding for R&D is hampered by high levels of bureaucracy. Consequently private-sector research spending in Chile should be boosted to enable universities to shift from reliance on government funds to partnership with the private sector.

Small and medium sized enterprises (SMEs) in Chile have difficulty accessing government funding because of high bureaucratic hurdles which necessitate hiring in expensive specialist skills such as legal expertise. Poor communications between government offices such as the Patent Office and the National Institute of Health also hinders innovation in Chile, in addition to a high level of taxation which erodes potential returns.

Participant discussion: the role of universities in R&D and innovation

- It was agreed that universities everywhere, including those with their own technology transfer functions in developed countries, face immense challenges.
- These may stem from the fact that they are not involved in the product development phase of the innovation process, do not know the market players and have scientists who may wish to retain control over the direction of the research output
- To address these problem, universities should be involved in wider policy discussions of how knowledge gets used in the marketplace to ensure the public interest is represented

Trust and good communication channels, appropriate contractual policies and a clear understanding that most patents would be transferred before they were granted are central to the Chilean technology transfer approach.

Participant discussion: the impact of the Bayh-Dole Act and the role of patents

- Although the Bayh-Dole Act is often looked upon as a model that developing countries may wish to emulate, a large literature exists indicating that ability to commercialise university inventions is very heterogeneous and the technology transfer process can be slow and frustrating⁸²
- Bayh-Dole type models may also be responsible for skewing universities' attitudes towards technology transfer, creating confusion as to whether the university should be prioritising commercial returns or social returns
- Patenting cannot be a proxy for innovation as it is the ability to translate patents into products which generates value, rather than the ability to file and maintain patents
- To achieve returns, an invention must not only be novel but must be disruptive in the marketplace, meaning that it is an enormous challenge to enable truly successful innovations that generate substantial returns to come to fruition

6.12 From Recruitment to Implementation of Contemporary Research in Traditional Environments: Ms. Paulette Baukol, Mayo Clinic

The Mayo Clinic's recruitment, retention and delivery processes with regard to the HPV vaccine highlight that working with communities is key to advancing access. Community-based participatory research (CBPR) is a "collaborative approach to research that equitably involves all partners in the research process and recognises unique strengths that each brings". CBPR begins with a research topic of importance to the community and has the aim of combining knowledge with action in achieving social change" to improve health outcomes and eliminate health disparities. It can be adapted for

⁸² For instance, the abilities and motivations of the research scientists and the technology transfer officers vary, as do the quality of the relationships and understanding between them.

other culturally sensitive communities and has worked successfully for almost ten years, establishing trusting relationships and participation.

Cancer is becoming the leading cause of death among American Indians, with breast, colorectal and lung cancer the most common. In eight of the nine Indian Health Service areas, lung cancer linked to smoking is the most common type of cancer death and is the second leading cause of death among American Indians older than forty-five years of age. Although there are nine hundred thousand to 1.3 million American Indians in America, there is only one American Indian oncologist worldwide. There are also fewer than ninety doctors for every one hundred thousand Indians, compared to 229 per 100,000 nationally. As a result there is a severe lack of native researchers working to address diseases relevant to this population.

Through development of a network of companies, communities, researchers, sub-contractors, partners, and existing cancer programs the Mayo Clinic submitted a proposal to the National Cancer Institute to conduct research into this area. The network was named 'The Spirit of E.A.G.L.E.S.'⁸³.

The network had the specific aim, among others, of addressing research on cancer prevention, and controlled treatment and quality-of-life interventions in its first phase. In its second phase it began to address treatment and to improve access to and utilisation of culturally competent cancer interventions.

The network enables a number of important partnerships, which provide different contributions to addressing cancer in the community. For example, partnership with the Cancer Information Service created a programme called 'Cancer 101' which educates communities that are unfamiliar as well as interested in working with communities. Oregon Health

⁸³ The name 'The Spirit of E.A.G.L.E.S.' is based on an acronym standing for Education, Advocacy, Grants (community grants), Leadership (training tribal leaders and other leaders in Indian healthcare), Elders, and Scholarships (for students and American Indian physicians and community health representatives).

Sciences University put together the Native Researchers Cancer Control Training Programme, which provides training on how to conduct research regarding cancer and co-ordinates grant-writing training workshops. Native American Cancer Research put together clinical trials for community health representatives as well as for those doing research with American Indians, to explain what it is like to go in to these communities to do clinical trials. At the University of Wisconsin, Spirit of E.A.G.L.E.S is building capacity and teaching the American Indians how to build capacity.

In dealing with cancer and dissemination of the HPV vaccine, the Centres for Disease Control (CDC) worked with the Spirit of Eagles to develop culturally appropriate materials. This case demonstrates that a well-established network of individuals with similar backgrounds and interests can maximise resources and minimise duplication of effort and funding. It can help assure success of projects and partnerships. To assure access, communities need to be engaged from discovery to delivery and CBPR has been a successful model for the American Indian and Alaskan native community.

7. Managing Intellectual Property for Health and Agricultural Innovation

Linda Gonzales chaired this session on global IP policies, foreign direct investment and the relationship to health and agricultural innovation. Regarding the World Trade Organisation's TRIPS Agreement (the Trade Related Aspects of Intellectual Property Rights), the flexibilities that exist in setting policy and national standards were noted, as well as the effect of the agreement on raising the cost of access to technology. The MIHR-PIPRA "Intellectual Property Handbook in Health and Agricultural Innovation" provides a guiding reference for LDCs in development efforts to enable innovations in agriculture biotechnology to continue to provide products for improved health and well-being.

Participant discussion: the role of TRIPS in developing technology transfer and innovation

- To achieve economic wellbeing, countries must invest in and develop technology
- To develop technology, countries can either innovate domestically or import technologies
- Many developing countries have relatively weak innovative capacity domestically, so it is important to keep channels for imported technology as open as possible
- In the era of globalisation, there is competition for capital, and weak IPR standards or non-compliance with TRIPS may be a critical deterrent to firms, leading them to invest elsewhere
- It is therefore important to satisfy at least the minimum TRIPS criteria and standards for protection of intellectual property

7.1 The WTO TRIPS Agreement and Public Health: Ms. Jayashree Watal, World Trade Organisation

There has been a lack of definitional agreement of the scope and nature of the flexibility in TRIPS and also uncertainty around the extent to which TRIPS would be interpreted by all WTO members in the same pro-public health way. TRIPS is a

guide to good practice. Each country needs to take responsibility for flexibilities in IP law and to take decisions at a national level rather than through the international community. The system need not be used if capacity is produced locally and if there are voluntary licenses.

There has also been apprehension from developing countries regarding possible pressure from trading partners not to practice this flexibility. Recognising these issues, the Doha Declaration (in November 2001) resulted in improved guidance for interpretation of the TRIPS agreement. TRIPS stipulates that WTO members have the right to grant compulsory licenses and the freedom to determine the grounds for granting these licenses. WTO members also have the right to determine what constitutes a 'national emergency' or other circumstances of 'extreme urgency', which would then allow such flexibilities to be enacted. Certain provisions were made for LDCs, including the extension of the grace period (which grants exemption from TRIPS obligations for pharmaceutical products) to January 2016.

Following the amendments⁸⁴ it was agreed that, subject to certain conditions, Article 31(f), which stated that there should be no export of the predominant part of the production under a compulsory license, might be waived. This allowed exports to take place under compulsory license from a WTO member with manufacturing capacity in pharmaceuticals to another WTO member with insufficient capacity to produce its own medicines. There has been only one notification of the use of this amendment (Rwanda) and there has been some criticism from NGOs that the procedural timeline is too cumbersome for developing countries. However, both the importing and exporting country have only to notify the TRIPS Council, and these notifications are not subject to a specific timeframe limitation. The WTO believes that the existence of generic medicines outside the patent system can render the Article 31(f) amendment obsolete, as exports are not controlled by the provisions described in it. Furthermore, circumstances where there are compulsory licenses or situations where exports prove to be restrictive are rare.

⁸⁴ August 2003 and December 2005.

As the TRIPS agreement does not make any obligations on governments to take action⁸⁵, there are difficulties in ensuring enforcement of IP rights and quality control

7.2 TRIPS. Did the Sky Fall?: Prof. Keith Maskus, University of Colorado

The purpose of TRIPS was to improve prospects for innovation, to expand information flows into developing countries and to encourage technology transfer. There is an explicit obligation placed on developed countries to provide mechanisms under which their firms will transfer technologies to less developed countries (66(2)). Problems may emerge when intellectual property protection is increased (for instance, in terms of patent eligibility and compulsory licensing). However, the TRIPS Agreement provides substantial flexibility in terms of allowing countries to set standards, and IP reforms have improved prospects for collaborative intellectual property management across borders and for achieving effective contracts.

Problems related to unrestricted protection of IP may be as follows:

- Support of market power in the presence of weak competition, for example a monopolist with patents could use its position to restrict imitative competition and block innovation, particularly in a less developed country with less competition
- Restriction of fair-use access to educational, scientific and cultural materials
- Raised cost of inputs, medicines, agricultural technologies etc. and
- Permanent or quasi-permanent shift in the terms of trade for a country, through raising the cost of access to technology (which is still largely imported in most developing countries).

However, it is important to note that there are many factors related to technological

⁸⁵ This is with the exception of counterfeit and copyright issues.

change and innovation, and it is very difficult to isolate the effects of one aspect as a matter of statistical causation. It is too early as yet to analyse in a systematic sense the evidence on the impact of TRIPS, but researchers have shown that it is necessary to take country-specific circumstances into consideration, and that overall the ability of patent reformists to generate more domestic innovation in developing countries *per se* tends to be limited. In almost all cases the pressure to reform patent laws have come from international pressures rather than domestically (e.g. from international corporations that want to transfer technologies through the patent system to a country⁸⁶). What matters in terms of the effects of patent reform on licensing is that it reduces the cost of technology transfer transactions and provides incentives.

The intellectual property regime is more about extending markets than extending innovation *per se*

Whether patents end up raising the cost of medicines depends on whether domestic production of similar medicines disappears after patents are registered by international companies, the structure of competition, the existence of insurance markets and the degree to which infrastructure within a country is developed for delivery. Existing price studies typically fail to account for patent standards that may limit market power and, because they are static, can only speculate about induced research and development (R&D).

Analysis of the literature shows that IP reforms have improved prospects for collaborative intellectual property management across borders and for achieving effective contracts. However, progress on establishing real price differentiation in both pharmaceutical markets and technology licensing contracts outside of PDPs and in commercial markets has been frustratingly slow. This is not due directly to TRIPS but rather because of factors such as a backlash against TRIPS to protect IP, exports and technology transfer at the

⁸⁶ A study in the Quarterly Journal of Economics gives substantial evidence that across almost all manufacturing industries, US multinational enterprises are quite sensitive in a positive way to licensing technologies internationally after patent reforms.

same time in the pharmaceutical and agricultural industries.

Other policies in the international community can also have a significant effect. If the US continues to shift its focus towards enforcement and technology transfer rather than purely revolving around patent policies, this may also have an interesting impact on access to medicines in developing countries.

Participant discussion: the importance of context when considering IP markets

- A robust patent system in a country encourages inward investment and technology transfer, in particular
- However, the situation within a country, particularly relating to factors such as educational progress and infrastructure, are important variables in gauging impact

7.3 IP and Agricultural Innovation: Prof. Magdy Madkour, Biobliotheca Alexandria, Egypt

The Agricultural Genetic Engineering Research Institute (AGERI) aims to promote agricultural stability through biotechnology products through commercialising its research. It has established a technology transfer office to enable it to handle IP and technology transfer.

Agricultural innovation in Egypt is characterised by several challenges, including the limited arable land base⁸⁷, the exclusive source of water (the Nile) and large population growth. In response to the fact that modern technologies, and particularly biotechnology, can contribute to alleviating the difficulties in meeting the agricultural needs of the population, Egypt has established an institute within the Ministry of Agriculture called the Agricultural Genetic Engineering Research Institute (AGERI).

IP protection and increased awareness of IP law in scientific research and at a policy level are needed to encourage effective

⁸⁷ Only 5% of the geographical area of Egypt is cultivated.

capacity building in Egypt. The IP Law was revised in 2002, to cover plant varieties as well as normal aspects of IP (patents, geographical indications, trademarks and copyrights). An office for technology transfer has been established which trains scientists in IP, particularly relating to biotechnology. AGERI also set up a special services unit for technology transfer in order to generate funds and to ensure that scientists are rewarded for their work and see the benefits of partnership.

AGERI's collaborations have led to commercialisation and have yielded several patents – including AGERIN, an environmentally friendly insecticide which was a joint venture between private investors and AGERIN/GESU, and a collaboration with MONSANTO developing insect-resistant cotton. The benefits of these public-private partnerships are clear. There is increased efficiency at all levels and also higher quality products, through sharing expertise across the sectors, with the private sector supporting wide-scale production and speeding up the production process as well as supporting quality control. Other benefits from partnerships relate to progress in attitudes, for example in the acceptance of transgenic cotton in both Egypt and neighbouring African and Asian countries.

Participant recommendations for alternative approaches

- Plant-derived vaccines may offer opportunities for cost reductions
- However, there is often a reluctance to alter the standard methods of developing vaccines (i.e. inactive and recombinant vaccines)
- There is a perceived high opportunity cost in transferring knowledge and skills to a different area

7.4 IP, Pharmaceuticals and Foreign Direct Investment: Dr. Douglas Lippoldt, OECD

The TRIPS agreement was drafted with the intention of promoting technological innovation, transfer and dissemination of technology in a manner conducive to social and economic welfare. Research shows that there seems to be a positive

relationship between the ability of pharmaceutical firms to capitalise on their innovation and protect it using IP and their willingness to trade, invest or to transfer technology in to new markets and TRIPS-plus may increase the attractiveness of a country to investors, particularly in the pharmaceuticals sector.

There has been an increase in the index of patent rights⁸⁸ in both OECD and developing countries since TRIPS was signed, although there has been variation particularly across developing countries⁸⁹. There has been a significant uptake, even in OECD countries, in the stringency of intellectual property protection that is available, and the same pattern can be shown in the enforcement of IP rights. There is about a 1:1 relationship between increases in patent rights strength and increases in R&D expenditure; and also in non-resident patent applications.

IP protection can raise the cost of technology but it also makes it possible, in some cases, to access technologies⁹⁰

Global pharmaceutical production capacity provides a view of potential technology transfer flows, and this highlights the potential to match the development and technology transfer promise of TRIPS. The overall average share of R&D expenditure relative to production in the manufacturing sector is 2.6%, compared to the pharmaceutical sector for which it is 10.5%. R&D expenditure relative to the value added from R&D is 22% in the pharmaceutical sector compared to 7.2% in the manufacturing sector.

There has been an increase in flows of foreign direct investment (FDI), which nearly doubled between 1992-2002, and gross inflows nearly doubled again between 2002 and 2006, reaching \$1335bn in 2006⁹¹. However, these flows are still circulating primarily between OECD countries and there is a great deal

⁸⁸ This covers membership in international treaties, coverage, restrictions on rights, enforcement provisions and duration of protection.

⁸⁹ Lippoldt and Park, forthcoming.

⁹⁰ On the flip side, a lack of IP rights protection can deter potential investors from giving access to technologies.

⁹¹ Economist Intelligence Unit.

of variability within them. In trying to understand the relationship of FDI, imports, R&D, and the ratio of non-resident patent filings to an index of patent protection between 1990 and 2005, preliminary research results show that factors affecting FDI include IPR concerns, as well as other characteristics of the destination market⁹² and market scalability. Comparing these results to an older paper by the same authors (looking at the period 1990-2000) when the wave of patent reform was much less mature, the relationship between strengthening of patent rights and US outward-FDI in the pharmaceutical sector is much weaker, indicating that there may have been a lag in response to patent reform.

In conclusion, there seems to be a positive relationship between the ability of pharmaceutical firms to capitalise on their innovation and protect it using IP, and their willingness to trade, invest or to transfer technology in to new markets. TRIPS-plus may increase the attractiveness of a country to investors particularly in the pharmaceuticals sector. For example, Singapore has gone beyond the basic TRIPS recommendations and has done very well in attracting investment in the pharmaceutical sector,

Participant discussion: the impact of TRIPs in India

- There has been a notable change in attitudes in the Indian pharmaceutical industry, which is now investing in innovative R&D-based activities
- New partnerships are taking place with the international pharmaceutical industry, enabling two-way technology transfers and the development of capability and expertise

⁹² In the regression analysis it is necessary to account for many control variables: IPRs, especially patents, appear to be important but they are one factor among many.

7.5 Case study: ICMR: Dr. K. Satyanarayana, Indian Council for Medical Research

A case study on the Indian Council for Medical Research (ICMR) in the post-TRIPS era was presented, looking particularly at its approach to technology transfer and formation of public-private partnerships. A partnership with IAVI showed that strategic partnerships can beneficially harness innovation capacity. It also revealed the need for public-sector agencies to partner with industry and international agencies to share expertise in order to get products developed. The government needs to be sensitised on IP issues (as historically the Indian government believed that it should own everything). The need to develop best practices in IP management and the policy space for any mid-course changes was highlighted.

The long-term goals of ICMR are to strengthen existing capacity for R&D in neglected diseases, to set up and strengthen capability for regulation and ethical conduct of clinical trials, to secure the market for new medicines, to encourage industry to be more engaged in neglected diseases and to find innovative ways to share their resources, and to seek participation of donor agencies.

In the 1990s, the ICMR realised the importance of public-private partnerships. At that time the ICMR had very little experience with working with industry and understanding the concerns of the industry, which were focused around tangible outcomes and ownership in a different way to the public sector. It worked to identify means to overcome related challenges, including the absence of templates or models to use and a lack of understanding of the complex dynamics that shape successful technology partnering for public health outcomes.

At that time all IP was ultimately owned by the Indian government and no industry would have been happy to collaborate with ICMR under these conditions. It was therefore necessary to reformulate policies to ensure that the right mix of ownership, access and exclusivity was agreed so that project goals could be achieved.

Partnerships are very important. An example was given of the development

and evaluation of suitable HIV vaccines for use in India through partnership with IAVI. In this case, the short-term goals of the ICMR were to work in cooperation with pharmaceutical companies to provide access to an affordable HIV vaccine for India and other developing countries; to collaborate with the private sector to secure and access new vaccine technologies as India did not have access to ARVs; and to participate in the development of one or more projects for developing safe and effective AIDS vaccine(s) suitable for India. Through partnership, ICMR was involved in the development of a vaccine, the conduct of clinical trials, the establishment of partnerships to design, develop and evaluate candidate AIDS vaccines appropriate for use in India and the transfer of technology.

ICMR's strengths included technical know-how in developing and trialing a vaccine. IAVI was experienced in AIDS vaccine development and evaluation and in helping with the transfer of technology for manufacturing, the manufacturers and technology providers provided manufacturing expertise, and the Indian Government prioritised vaccines for HIV/AIDS. Each partner had a very specific role in capacity building and providing technical expertise and in committing to the management of IP.

Several agreements between the partners were needed to resolve IP issues, including how to handle existing IP, the new IP to be generated and how to balance public and private interests. It was agreed that the Government of India would have exclusive rights to use all patents and other IP in India and neighbouring SAARC countries, and IAVI would get a non-exclusive, worldwide, royalty free sub-licensable license to all new patents and other intellectual property. A joint Project Management Committee was set up with IAVI and ICMR to coordinate and monitor the periodic assessment, refinement and revision of R&D.

Product innovation and introduction must be complemented by policy and financial support for integration into health systems. Government engagement is essential for the clinical and ethical testing of new products; decisions about their

introductions and use; and in encouraging civil society participation. Finally, independent evaluation and monitoring is essential.

India may become a natural 'hub' for public health innovation because it is a very unique market⁹³ that will need to stimulate R&D and innovation to benefit poorer populations. Substantial inward FDI has increased R&D collaboration and resulted in a commitment to stronger IP in India.

7.6 IP, Innovation and Access – New Insights from the MIHR/PIPRA Handbook: Dr. Anatole Krattiger, Arizona State University

Dr Krattiger offered an overview of the relationship between IP management, innovation and access, particularly relating to PDPs. This was supported by an introduction to The MIHR/PIPRA IP Handbook, which provides tools and theory to support improved planning, negotiation and management of IPRs in health and agricultural innovation.

The principles of access and impact are conceptually very simple but from the beginning of the research stage it becomes an interactive and complex process. The overlap between research, development, production and delivery means that there is a great challenge in making IP deals upfront because they have many repercussions several years down the line. One of the challenges is to consider the whole process before knowing all the parameters that exist around access.

The MIHR/PIPRA IP Handbook focuses on IP and strategies for access and acts as a plan for charting the management of innovations and ownership. This is very important to optimise outputs. IP is one of the fundamental determinants of innovation and is a means of transferring value between partners. These sources of value differ between the corporate/industry model and the PDPs. PDPs have a different style of business to corporate deals and the way universities work, and

⁹³ A huge proportion (around two thirds) of the population of the country is poor and a third of the world's poor live in India. India also has one of the most privatised healthcare systems in the world.

there is still scope for people to learn and to recognise the differences. Although the tools are essentially the same, the criteria on how to make decisions are often very different. PDP values include rights to practice; degree of exclusivity; patent expenses; the right to sublicense; future improvements from licensors and licensees; infringement issues; quality control; and regulatory approval. Product liability should also be seen as a value.

While, in principle, IP tools are the same (patents, trademarks, data protection), the deals also incorporate a number of issues including patenting strategy: out-licensing strategy; patent enforcement and infringement policy; pricing; and capturing added value. Writing patent applications to assure effective field-of-use licensing is another important issue.

Potential future issues should be considered by PDPs in advance to ensure they are prepared to deal with them, for example issues around branding of products and the need for trademarks to enable deals to be made both upstream and downstream.

7.7 Discussion

Pricing

With regards to pricing strategies, even when low-volume high pricing is combined with a high-volume low-price strategy, a “middle market” in developing countries may not be addressed adequately. This issue of middle market power and whether it has the necessary critical mass or the insurance infrastructure to support the demand was discussed. These issues give a strong indication that new pricing models and more infrastructural development in the insurance markets are needed.

The political, institutional and international pressures faced by companies to integrate prices may stem from price controls⁹⁴. In turn, this may encourage corporations to license manufacturing to a developing-country partner for distribution, in order to avoid some of the constraints associated with tiered pricing.

It is often not clear how much the patient actually pays compared to what the

company charges because taxes are levied on pharmaceutical products, and supply chain fragmentation distorts prices for end-users⁹⁵.

Good practice examples –Singapore

Certain countries are particularly good examples of making progress in encouraging strong IP and technology transfer. For instance, Singapore levered policy by providing matched funding for pharmaceutical companies who wanted to build laboratories or do clinical trials in Singapore. The country focused on increasing the number of people educated in science, and in particular women in science, and set up an initiative where officials were sent to universities to discover innovation that could be used entrepreneurially.

⁹⁴ e.g. reference pricing which is typically set across the whole of the EU and which can act as a barrier to innovation.

⁹⁵ The Medicines Transparency Alliance Initiative (MeTA) has been set up by the UK government’s Department for International Development to address these issues.

8. Financing for Innovation and Technology Transfer

This session was chaired by Jose Miguel Flores. It illustrated that the formation of companies is critical to effective technology transfer. The sustainability of new healthcare delivery systems is critical to success. Due consideration needs to be given to local involvement and buy-in, considering local needs and local contributions to sustaining the effort. Providing motivation to different stakeholders to invest is the key. Policy makers need to be more aware of the challenges associated with financing models and to deal with these upfront.

Different technologies in different disease areas will require different incentives

8.1 Who Really Pays?: Prof. Adrian Towse, Office of Health Economics

Push and pull mechanisms related to incentivising research and development (R&D), including accelerated development and introduction plans (ADIPs) to address market access issues, stimulate and encourage private-sector companies to undertake R&D in neglected disease areas. The Advanced Market Commitment mechanism (AMC) has recently gained momentum within the international community in addition to supply contracts (by the Global Fund, UNESCO, GAVI and others) to ensure that poor governments are not required to carry the full cost of purchasing new public health products.

PDPs, which create candidates coming through discovery and Phase One trials, and AMCs, which reduce company's risk in Phase Two and Three trials and guarantee a price, can play a role in combination to provide incentives. The PDP has a significant role in market preparedness (i.e. in trying to ensure that companies are able to get access to markets). Despite acknowledgement of this synergy, there is still a lack of clarity about the designation of roles and accountabilities between the market incentives (AMC) and PDPs.

Both incentives and risk are major issues in thinking about AMCs, affecting questions such as where the lowest cost of capital is, whether competition through an AMC is likely to produce higher product quality, who is likely to have the lowest costs, and what the impact is on being rewarded at the end of R&D timelines.

Participant discussion: AMCs

- It is important that the criteria for project selection for application of the AMC, should be made more transparent
- Factors such as the extent of competition, the market size and the net present value (NPV) are important
- There is scope for debate over whether the AMC is aimed only at early-stage products and how it will progress in practice

8.2 Axios Partnership in Tanzania: Dr. Anne Reeler, Axios International

The Axios model is based on pharmaceutical products that are made available to the poor either for free or at reduced prices. Axios supplies health institutions in almost a hundred countries. Axios engages in supply chain management and logistics⁹⁶ around chronic diseases because there has been so much involvement in acute disease management that the healthcare system is particularly challenged by chronic disease⁹⁷.

Through encouraging local communities to assess their own needs, the Axios approach emphasises creation of local ownership to enable sustainability of an initiative once the donor or foreign partner withdraws its funding support. It combines representatives of the Ministry of Health, regional and district health authorities, communities and sometimes patients. Axios provides technical support to enable local stakeholders to define action plans and it operates on a five-year timeline to ensure durability.

⁹⁶ This was done by Axios in seventeen States in Nigeria.

⁹⁷ Additionally, in Ethiopia it works to build capacity for breast cancer treatment, trying to build clinical diagrams, a system for diagnostics and a referral system.

The Axios approach involves capacity building and early plans to transfer to full management by local stakeholders, which are viewed as central to creating sustainable initiatives. Axios uses a phased approach to capacity building, where initially a high level of technical assistance is required until later phases when the partners' level of competence increases. The phases involve needs assessment; capacity building; raising competence levels; and transition to local management and sustainability. A change management approach to communication supports each phase of capacity building.

The transfer of costs to local stakeholders is also planned from initial phases, with a gradual absorption of costs into local budgets that is planned in and communicated early on. To ensure that the projects last, all activities should be incorporated into the supervisory schedules of various professional levels of the healthcare system.

The Axios experience shows that the best technical methods may be subsumed by the interests of particular social networks. Political factors regarding uptake of interventions need much more consideration when programmes and policies are being planned.

The major challenge to ensuring that capacity building activities are sustainable is getting the approaches adopted into national policy. To address this, scientists and technicians need to understand better how to influence policy in order get projects scaled up. Cultural integration and ensuring that programmes fit with the local government agenda is also important. Absorptive capacity is also essential and this is reliant on local government-building institutions and developing appropriate policy.

More work is needed on the best means of influencing policy and, to ensure sustainability, ensuring that programmes become integrated into the national agenda. Policymakers should be consulted to share examples of where programmes have failed and where they have succeeded in order to structure new policies appropriately.

"We need to use the amount of money that we have now to strengthen healthcare systems...it's about the quality of the healthcare"

8.3 The Chile Foundation, Mr. Marcos Kulka, Chile Foundation Case Study

The Chile Foundation (Fundacion Chile) is a private, not-for-profit institution which has been called the most entrepreneurial company in Chile. Different models of technology transfer and capacity building have been developed in a variety of technology areas, based on company formation which is dependent on networks.

In its thirty-one years the Chile Foundation has contributed more than \$2m to the Chilean economy and has become a competitor in global industries such as salmon farming. It was created by the Chilean government and the ITT Corporation (USA), and two years ago the world's largest mining firm, BHP Bilton, became a co-owner.

The company is a private-public alliance that is privately controlled but strives for social returns on investment through, for instance, economic growth and capacity building. It is a virtual incubator, with a current portfolio of twenty companies which accelerates Chile's key clusters, especially in natural resources, by bringing innovation to the market. It has created economic growth through the generation of more than seventy companies, and has contributed to the development of human capital. It has introduced the concept of innovation as a key critical element for Chile's competitive success and is currently almost self-financing. Its use of public-sector funds is limited to a maximum of 30-50% in any project to ensure that market demand is driving its efforts.

The company is organised by industrial sectors and technologies⁹⁸. It conducts and also outsources R&D. Its main product is company formation in partnership with the private sector. Its approach is to demonstrate to industry the potential or actual success of a new technology, which is scaled up to the

⁹⁸ It has projects in marine resources, agriculture, forestry and human capital.

formation of a new company.

Different forms of technology transfer are relevant in different places. These may include incubators, company start-ups or licenses

In addition to competitive grants and lateral funds, entrepreneurship is supported through a range of incentives and programmes that enable scientists and business people to collaborate. Proof-of-concept studies are supported through a \$1m 'failure fund', which enables risk-taking for early-stage projects. After five or six years, when companies reach a steady state, Fundacion Chile sells them to recoup funds for re-investment into new projects.

Fundacion Chile's network is its major asset for value creation, and accelerates development through connecting developers with suppliers⁹⁹. It utilises the following models:

1. **Transfer and adaptation** – start-up companies created, looking for examples of success elsewhere
2. **Transfer and internal/in-house R&D**
3. **R&D management in networks** – in biotechnology, it identifies different technologies and genes and creates a product through bringing the components together. Transaction costs are very high with this model¹⁰⁰.
4. **Package technologies** which are licensed to companies worldwide – e.g. license to Novartis for which it receives royalty for a salmon vaccine

⁹⁹ e.g. in renewable energy, biotechnology and the food value chain there are partnerships with many countries.

¹⁰⁰ e.g. a Genome consortium that is working in cost reduction and quality, good quality improvement, genetic transformation and cloning.

Participant discussion: the nurturing of entrepreneurship

- Governments should focus significant effort into developing environments conducive for stimulating innovation and supporting entrepreneurship
- Research institutes and universities should actively seek technologies from abroad

8.4 The Intersection of Economics and Access: Mr. Andrew Farlow, University of Oxford

The sustainability of infrastructure, human resources, vaccine programmes and global health funding were explored.

Human resources are severely affected by different priorities in global health. In the past, sub-Saharan Africa (compared with South Asia and East Asia) exhibited a big proportion of capital flight per worker, and even though this is in decline, so-called "brain drain" is on the rise. As health workers are in short supply, the sustainability of health systems is an issue¹⁰¹. Policy decisions about health services in developed countries that pull in health workers from poorer countries have an impact on health services in other countries. This should be considered more carefully during the decision making process.

In terms of the sustainability of vaccine programmes, twenty-seven million children still are not vaccinated with the basic package, DTP3. Between 2005-2015, it is estimated that GAVI will need US\$18 billion to support the delivery of existing vaccines, but the future funding needs – beyond 2015 - of such organisations, which will in many ways reflect what has been required to date, have not yet been addressed. This is another area which should receive more policy attention. Additionally, although there has been a push for self-sufficiency as the ultimate goal for developing countries, countries in the short term need to use efficiently both

¹⁰¹ There is a shortage of 4m health workers globally, with the US and UK sucking in workers from abroad to supplement shortages in their own systems (in particular there is a critical shortage of health worker providers and managers, doctors, nurses and midwives).

domestic and supplementary external resources to achieve target levels of immunisation.

Current incentive models focus on discovery and development and have not yet adequately focused on the delivery aspect which policymakers are advocating.

Participant recommendation: areas of importance for the policy agenda

- Policymakers must give attention to the delivery agenda, rather than placing the focus exclusively on discovery and development incentives
- This may include greater investment in infrastructure (e.g. roads, power and good ports) which brings significant economic returns and supports the delivery agenda
- The need for greater interaction between the users and producers of technology in addition to a wide range of technology user needs must be considered and invested in

The International Finance Facility for Immunisations (IFFIm) is a scaled down version of the USD \$75 billion per year IFF, promoted to frontload investment into developing countries to generate growth and, ultimately, to prevent the need for aid flows later. While the benefits of this model applied to immunisation are that it offers stable funding, sustainability for countries, greater stability of supply and lower prices, and has attracted some new sponsors that have not contributed to immunisation programs before, there are some concerns associated with it, namely that the flow into immunisation later will fall off as it is repaid and if those levels still need to be sustained a new generation of politicians will have to support a policy idea that they did not instigate.

Additionally, the transaction costs have proven to be higher than expected and, though they are not a 'problem' *per se*, need to be factored in. Recent experience in setting up new mechanisms tells us that all mechanisms, even if appearing deceptively simple, are usually more complicated in practice and involve transaction costs and delays in setting up.

Recent initiatives such as the PAHO revolving fund, independent vaccine initiatives, ARIVAS, and prize mechanisms (AMCs) were also described. Where investment is made early to support R&D, there are concerns that this investment may inadvertently act as an inefficient subsidy, be difficult to make genuinely credible, be open to the risk of on-the-ground infrastructure failures, and be inconsistent with the philosophy of some PDPs.

A key consideration with these funding mechanisms is ensuring public resources are spent wisely. The mechanisms need to generate investment into R&D for neglected diseases to create affordable products without providing unjustified subsidies. It is also important to ensure that the next phases of investment are secure.

8.5 Funding for Biotechnology in Africa: Prof. Diran Makinde, African BIO

The New Partnership for African Development (NEPAD) is an African-led, multi-national, pan-African organisation which is not state-centric, but is reliant on connections with government Ministers. NEPAD's structure, mission and recent position papers and reports were described, particularly in relation to the biosciences¹⁰². By working from the country level but pooling the approaches at a regional level, the relevance of NEPAD's policy making and activity is heightened.

The factors determining the future of technology in Africa were highlighted, including the need for coherent, appropriate policies on national systems of innovation. Policy should be encouraging public investment of 0.87% GDP to formal R&D and should be encouraging private firms to invest 1.8% of their revenue into R&D. A current lack of commitment to financing R&D in biotechnology exists in Africa generally, although South Africa has demonstrated more commitment to support for R&D and, more recently, Nigeria and Egypt have committed to do the same.

¹⁰² NEPAD focuses on four areas in the biosciences: mining, agriculture, health and environment.

Control of clinical trials and harmonisation of biosafety policies at the sub-regional level are issues that NEPAD considers to be of importance to ensure that African countries have an ability to assess technologies themselves and avoid duplication of effort between countries. There is a lack of alignment between what has been expressed in existing biosafety frameworks and regional technology development efforts, including NEPAD regional hubs.

Funding issues and sustainability questions are also hindering innovation. With regards to capacity building, an African needs-driven technology agenda is required, based on an African-centred network model in the biosciences, as well as support for universities and research institutions to focus on innovation and utilise the public-private partnerships (which may invest in developing their knowledge into new technologies). The focus of NEPAD's capacity-building programmes will also be on building in-country capacity rather than risking "brain drain" through outward exchanges. Greater awareness is needed on both IPR issues and public awareness and acceptance of biotechnology.

8.6 Discussion

Approaches to capacity building through organisations such as NEPAD

Tension exists between top-down and bottom-up capacity-building and policy approaches. NEPAD provides an example of a top-down approach which may not have adequate accountability. The counterargument to this is that the linkage to government ministers in a number of countries provides connectivity to different interest groups in these countries and in doing so tries to assure access to expertise. Additionally, NEPAD is able to disburse funds effectively across countries which need them. It is also able to exert appropriate pressure on countries to ensure that they commit to important science and technology commitments that assure economic growth.

In terms of benefits of NEPAD's approach, many international donors prefer to deal with NEPAD because of its political connectivity and as an organisation where they can see their money well spent. Its infrastructure is designed to prevent wastage and its outcomes should be

measurable. Further, in an attempt to reflect real needs of African populations, its policies are developed by nation states themselves. However, there is fear that it might not be effective because responsibility is removed from individual governments due to the fact that it is based on a group ministerial-level approach. There is also a concern that it focuses on fashionable areas like biotechnology (which is reliant on sophisticated and costly inputs and is therefore expensive to set up) when more basic needs in less fashionable areas might be neglected (e.g. devices) where infrastructures already exist.

Innovation & IP Policies in Developing Countries

A great deal of innovation goes on in every country, which may not be easily recognisable as a saleable commodity. Drawing these out to generate economic and social gains is a challenge which needs to be addressed by all countries¹⁰³.

It is difficult to engineer success in one sector without taking into account some of the broader framework conditions such as those that permit market mechanisms to function and provide enterprises incentives. It is difficult for governments to engineer solutions across the board, especially because countries that are under-developed tend to have weak government capacity.

¹⁰³ In the UK, a report titled 'Getting Innovation' discusses identifying and bringing out hidden innovations in the UK economy.

9. Closing Discussion

The final session was devoted to discussion of some of the broad themes which ran through the conference including networks, sustainability and driving greater activity in addressing access through the establishment of performance metrics and monitoring of health impacts.

Networks

Networks are critical to addressing both the innovation and delivery components of access, not just for sharing ideas but 'as the birthplace of partnerships'. The importance of interdisciplinary interactions and mutual trust in developing a flow of information across partnerships should not be underestimated in achieving development in global health.

A Rockefeller Foundation study of global research and development (R&D) networks in health revealed that the most highly connected hub in the public sector was the University of Oxford while the most connected in the private sector was GlaxoSmithKline (GSK). The reason for the latter was because independent economic studies of GSK's partnerships and focus areas revealed that it could not afford to discontinue work in the neglected disease areas because costs incurred later would be too high and therefore it was important to keep those areas of the portfolio a priority. This illustrates the importance of networks for addressing critical issues.

The conference highlighted the need to leverage the power of networking and partnership development to promote innovation. As illustrated by examples including the presentation on Fundacion Chile, countries that have learnt how to build up extensive networks have seen entrepreneurship and strong partnerships enabling technology and information transfer. Synergies that improve efficiency should be identified, including collaboration on data management systems and processes to avoid duplication. Multi-sectoral stakeholders should be brought together to drive political connectivity. Internal and local developing-country human capital resources should be mobilised.

The discussion raised the following questions for further exploration:

- How do you establish networks?
- How do you manage them in developed and developing countries?
- How do you monitor them?
- How do you evaluate them?
- Have PDP networks developed?
- What do healthcare and supply-based NGO networks tell us?

Partnerships

Building on the extensive discussion around the value of networks, the importance of well structured and well balanced partnership was also discussed in detail. In the context of the policy space and in relations with donors, developing countries need to have some financial independence from donors in order to dictate terms of agreement. Further, it is important to further develop technical capacity and experience in issues such as management of IP so that the skills and expertise are there to enable genuine negotiation and for developing countries to play a bigger role in partnerships rather than just being recipients of assistance.

Looking particularly at how PDPs, industry and governments can focus on access, it was agreed that it is important to engage with all players. However, resources need to be made available so that capacity building in the long term can take place. Industry requires a facilitating environment to operate well. Academia also needs this facilitating environment and to be proactive in seeking partnerships with industry, in order to see more efficient development and innovative processes. Governments need help to invest in the right places so that industry and groups can play their optimum role. It is also important to be aware of the different incentives as the extent to which different groups can be at a comparative advantage in engaging at different stages of the market and development process. These incentives must be managed in an efficient and timely manner. It is necessary for there to be a level of transparency and trust in building partnerships.

Throughout the conference there was extensive discussion about who should take responsibility for a process or a partnership. As global health can be

considered a global public good, one particular question would be who is to be the final insurer of each product as part of the global public good and who will take responsibility if somewhere during the development process and partnership there are failures. There was a strong argument that governments need to take responsibility to ensure that initiatives and collaborations are sustainable after for example initial donor involvement.

Sustainability

There was general agreement of the need to ensure sustainability by considering access, human resources, and infrastructure, including a focus on upgrading existing biomedical infrastructure. Efforts to ensure initiatives are sustainable should focus on the involvement of communities in capacity building, on developing collaborations based on mutual trust and interest and in engaging with policy.

There was, however, tension around the word “sustainability”, particularly with regards to donor funding for PDPs and supply of health interventions. Some participants felt that the word might indicate never-ending, sustained support for initiatives. A lack of consideration of timing and feasibility could skew priorities towards ensuring “sustainability” in a sense that might limit resources that could be directed towards other issues in the interim. In general, participants agreed that it was beneficial to strive towards sustainability in the sense that countries could support themselves. However, sustainability should be interpreted in relation to milestones achieved rather than ‘for ever’: milestones have changed in recognition of the need for this. For example, rather than focusing purely on finishing Phase Three clinical trials as the main aim and milestone for PDPs, the international health community now recognises that the major milestone is public health impact. As such, access programmes and PDPs in particular need to define what their milestones are and how they are going to achieve them with resources that would be given to them. A conference such as this can be a way of debating those milestones.

Sustainability can also be considered in terms of affordability. This also requires the definition of an end-point, or various

milestones along the way to focus on and to drive lower costs. In order for an initiative to be sustainable it requires low costs in the long term. It is important to look at costs not only in production, allocation but in the structures that exist in health systems. At each stage of valuing a product there may be further costs – it is important to be aware of this and to reduce these costs, making processes more efficient overall.

Driving Progress in Access and Delivery

This conference was successful in bringing together people from extensively diverse backgrounds in order to discuss and debate challenges and possible strategies for bringing the gap in global health innovation. The need for policy-makers, product development partnerships and initiatives engaged in capacity building to focus on access as early as possible was one key theme that was referred to again during this closing discussion. The need for the creation of enabling environments to facilitate efficient product delivery and to encourage innovation and technology transfer was also referred to, with participants discussing success stories from countries such as India. There has been significant progress in India as the recognition of the importance of suitable licensing arrangements has changed the way that companies operate across different sectors, now including the biotechnology sector. It is now standard to consider and incorporate IP rights into arrangements, which has encouraged two-way technology transfer.

As discussed throughout the conference, there are many difficulties that arise when dealing with access and delivery. It is important to learn from successful initiatives and to focus on training, research and other ways of developing capacity within countries. With this critical mass of engaged people at a grassroots level it is possible for capacity to act like a pull mechanism, attracting resources to develop programmes further. However there was a great deal of discussion around the difficulties in scaling up programmes that are successful at a local level, as complications such as political engagement can limit this. Changing policy and managerial behaviours towards an access orientation may rely on

performance measurement. As such, metrics to evaluate performance and effective public health impact should continue to be developed, using benchmarking tools to promote accountability and improved governance.

Appendix A: Agenda for The Oxford Conference on Innovation and Technology Transfer for Global Health

***Bridging the Gap in Global Health Innovation – From Needs to Access
University of Oxford, 9 -13 September 2007***

**The Conference is Dedicated to the Memory of the late Prof. Sanjaya Lall
Green College, University of Oxford**

Monday, September 10

Plenary Lecture

Health Innovation: the neglected capacity of developing countries to address neglected diseases.

Dr. Carlos Morel, Scientific Director, Center for Technological Development in Health, Oswaldo Cruz Foundation (FIOCRUZ), Rio de Janeiro, Brazil

Dimensions of the challenges

Session Chair – John Kilama, Global Bioscience Development Institute

Free Market strategy in Healthcare: Key to achieving Product Availability and Access: Dr. Stephen Malinga*¹⁰⁴, Minister of Health, Uganda

New Solutions for Global Health Challenges: Ms. Patricia Atkinson, Bill & Melinda Gates Foundation

Innovation, Access and Public Health: Dr. Harold Jaffe, University of Oxford

Who is Listening to Those in Need?: Prof. Peter Ndumbe*, University of Buea

Challenges to Vaccine Financing and Systems Support: Rebecca Affolder, GAVI Alliance

The Intergovernmental Working Group: Dr. Howard Zucker, WHO

Strategies for Securing Product Availability and Access

Session Co-Chairs – Dr. Gill Samuels, Global Forum for Health Research, Ms. Dianna Derhak, DNA International Consultancy

The Development of Paromomycin IM for Visceral Leishmaniasis: Ms. Katherine Woo, Institute for One World Health

On-the-horizon Developments in Biotech and Nanotechnology: Ms. Dianna Derhak, DNA International Consultancy

The Case of Merck: Dr. Diana Lanchoney, Merck

The Case of Ranbaxy and ARVs: Dr. Arun Purohit, Ranbaxy

¹⁰⁴ All speakers marked with an asterisk are Sanjaya Lall Fellows

The Case of Eli Lilly MDDR: Dr. Gail Cassell, Eli Lilly [Dr Gill Samuels]

The Case of Pfizer: Dr. Robert Mallett

Panel with discussion of all session papers

Tuesday, September 11

The Interface of Science, Technology Transfer and Access

Session Chair – Dr. Tony Bunn*, South Africa Medical Research Council

Biotechnology Companies and Innovation: James Geraghty, Genzyme Corp.

Improving Access to Existing Global Health Solutions: Dr Devi Sridhar, Global Economic Governance Programme, University of Oxford

Designing of Anti-counterfeiting Solutions in a Comprehensive Patient Centric Healthcare System: Dr. P. Ganguli*, CEO, VISION-IPR, Mumbai

The Power of Networks for Innovation: Dr. Rafael Rangel-Aldao*, Simon Bolivar University

New Initiatives in Japan: Prof. Katsuya Tamai, University of Tokyo

ICBG Program and its Impact in Academia, Conservation and Drug Discovery in Latin America: Prof. Barbara Timmermann, University of Kansas

Implementation of Biomedical and Information Technologies in Developing Countries: Prof. Eva Harris, Ministry of Health, Nicaragua and University of California

Panel with discussion of all session papers

Partnerships in Promoting Innovation and Managing Risk

Session Chair – Dr. K. Satyanarayana*, Indian Council for Medical Research

Strategies for product innovation: the PDPs: Dr. Mary Moran, The George Institute

The Aeras Foundation: Achieving Access: Dr. Jerald Sadoff, Aeras Global TB Vaccine Foundation

Potential new approaches to scientific and financial innovation in PDPs - the example of AIDS vaccines: Mr. Labeeb M. Abboud, IAVI

PDVI – what is the end game?: Dr. Harold Margolis, PDVI

The PATH Strategy: Dr. Michael Free, PATH

The South African Malaria Initiative- a case study: Prof. Jane Morris*, African Centre for Gene Technologies

Wednesday, September 12

Partnerships in Promoting Innovation and Managing Risk (continued)

Session Chair – Mr. Andrew Farlow, University of Oxford

MMV - Moving to Access: Dr. Chris Hentschel, Medicines for Malaria Venture

IPM Case Study: Dr. Zeda Rosenberg, International Partnership for Microbicides (IPM)

The Evolution of PDPs: Best Practices: Prof Adrian Towse, Office of Health Economics

From Recruitment to Implementation of Contemporary Research in Traditional environments: Ms. Paulette Baukol, Mayo Clinic

Universities-Private Sector relationships in Developing Countries: Dr. Jose Miguel Flores*, Flores & Asociados, Universidad de Concepción

Desa Siaga - A Strategy for Health Investment: Siti Sundari*, Center for Health Systems and Policy R&D, Indonesia

Managing Intellectual Property for Health and Agricultural Innovation

Session Chair - Prof. Linda Gonzales, University of Western Kentucky

The WTO TRIPS Agreement and Public Health: Ms. Jayashree Watal, World Trade Organization

TRIPS. Did the Sky Fall?: Prof. Keith Maskus, University of Colorado

IP and Agricultural Innovation: Prof. Magdy Madkour*, Egypt

IP, Pharmaceuticals and Foreign Direct Investment: Mr. Douglas Lippoldt, OECD

Case study: ICMR: Dr. K. Satyanarayana*, Indian Council for Medical Research

IP, Innovation and Access – New Insights from the MIHR/PIpra Handbook: Dr. Anatole Krattiger, Arizona State University

Thursday, September 13

Financing for Innovation and Technology Transfer

Session Chair – Dr. Jose Miguel Flores*, Flores & Asociados, Universidad de Concepción, Santiago, Chile

Who Really Pays? Three Donor Investment Choices: Prof Adrian Towse, Office of Health Economics

Axios Partnership in Tanzania: Dr. Anne Reeler*, Axios International

The Chile Foundation, Mr. Marcos Kulka*, Chile Foundation Case Study

The Intersection of Economics and Access: Mr. Andrew Farlow, University of Oxford

Funding for Biotechnology in Africa: Prof. Diran Makinde*, NEPAD Biosciences, West Africa Biosciences Network, Dakar, Senegal

Closing Session

Session Co-Chairs: Ms. Lita Nelsen, MIT and Dr. Peter Ndumbe*, University of Buea

Discussion

Planning for 2009

Adjourn

Appendix B: Delegates List

| First name | Last name | Organisation |
|------------------|--------------|---|
| Labeeb M. | Abboud | International AIDS Vaccine Initiative, USA |
| Rebecca | Affolder | GAVI Alliance, Switzerland |
| Sahar | Aly | Center for Special Studies and Programs, Academic and Cultural Sector, Bibliotheca Alexandrina, Egypt |
| Patricia | Atkinson | Bill & Melinda Gates Foundation, USA |
| Richard | Barker | Association of British Pharmaceutical Industries (ABPI), UK |
| Rajaie | Batniji | Global Economic Governance Programme, UK |
| Paulette | Baukol | Mayo Clinic, USA |
| Senthuran | Bhuvanendra | University of Oxford, UK |
| Catherine | Boyle | The Business |
| Tony | Bunn | SA Medical Research Council, South Africa |
| Joel | Calmet | sanofi Pasteur, France |
| Cathryn | Campbell | Needle & Rosenberg P.C., USA |
| Junko | Chapman | MIHR, UK |
| Dianna | Derhak | DNA International Consultancy, Ukraine |
| Don | Douglas | Pediatric Dengue Vaccine Initiative (PDVI), Korea |
| Andrew | Farlow | University of Oxford, UK |
| Jose Miguel | Flores Acuna | Flores & Asociados, Universidad de Concepcion, Chile |
| Michael | Free | PATH, USA |
| Prabuddha (Ramu) | Ganguli | VISION-IPR, India |
| James | Geraghty | Genzyme Corporation, USA |
| Ciara | Goldstein | Global Alliance for TB Drug Development, Belgium |
| Linda | Gonzales | Western Kentucky University, USA |
| Eva | Harris | UC Berkeley, USA |
| Rachelle | Harris | MIHR, UK |
| Maria | Hassard | NHS Innovations SW, UK |
| Philip | Hedger | Pfizer Inc., USA |
| Chris | Hentschel | Medicines for Malaria Venture, Switzerland |
| Paul | Herrling | Novartis International AG, Switzerland |
| Harold | Jaffe | Department of Public Health, University of Oxford, UK |
| Mohammed Abul | Kalam | Institute of Epidemiology, Disease Control & Research (IEDCR) |
| Rita | Khanna | Aeras Global TB Vaccine Foundation, USA |
| John | Kilama | Global Bioscience Development Institute, Inc., USA |
| Anatole | Krattiger | ASU, USA |
| Kulka | Marcos | Chile Foundation, Chile |

| | | |
|--------------------|--------------|---|
| Pranay | Lal | Centre for Sustainable Health and Development, India |
| Diana | Lanchoney | Merck & Co., Inc., USA |
| Craig | Landsberg | Acorn Technologies, South Africa |
| Douglas | Lippoldt | OECD / OCDE, France |
| Glaudina | Loots | Department of Science and Technology, South Africa |
| Milton | Lore | Bridgeworks Africa Limited, Kenya |
| Magdy | Madkour | Library of Alexandria, Egypt |
| Krisztian | Magori | OXITEC LIMITED, UK |
| Richard | Mahoney | Pediatric Dengue Vaccine Initiative, Korea |
| Diran | Makinde | NEPAD, West Africa Biosciences Network |
| Robert | Mallett | Pfizer Inc., USA |
| Stephen | Mallinga | Ministry of Health, Uganda |
| Michael F. | Maltese | Global Medical Knowledge, Inc. and Massachusetts Institute of Technology, USA |
| Saberi | Marais | Innovation Centre, Medical Research Council of South Africa, South Africa |
| Harold S. | Margolis | Pediatric Dengue Vaccine Initiative, Korea |
| Keith | Maskus | University of Colorado, USA |
| Lena | Mass | University of Oxford, UK |
| Kenneth Kamwi | Matengu | University of Namibia, Multidisciplinary Research Centre, Namibia |
| Stephen | Matlin | Global Forum for Health Research, Switzerland |
| Tom | Mclean | IVCC |
| Sarah | Miller | University of Oxford, UK |
| Mary | Moran | The George Institute, UK |
| Carlos | Morel | Oswaldo Cruz Foundation (FIOCRUZ), Brazil |
| Jane | Morris | African Centre for GeneTechnologies, South Africa |
| Praful | Naik | Bilcare Limited, India |
| Mary Grace Kyeyune | Nambatya | Ministry of Health, Uganda |
| Peter | Ndumbe | University of Buea, Cameroon |
| Anita | Nel | InnovUS, Stellenbosch University, South Africa |
| Daniel | Nelki | The Wellcome Trust, UK |
| Yukiko | Nishimura | University of Tokyo, Japan |
| Adelani | Ogunrinade | National University of Lesotho, Southern Africa |
| Kyle | Peterson | FSG - Social Impact Advisors, USA |
| Mike | Poltorak | University of Oxford,, UK |
| Arun | Purohit | Ranbaxy Laboratories Ltd, India |
| Rayapu | Ramesh Babu | BOSS & CIPCA (CBO), India |
| Matheo | Raphael | Tanzania Commission for Science & Technology, Tanzania |
| Rafael | Rangel-Aldao | Simon Bolivar University, Venezuela |
| Anne | Reeler | AXIOS INTERNATIONAL, France |

| | | |
|--------------|---------------|---|
| Wesley | Ronoh | Kenya Medical Research Institute, Kenya |
| Zeda | Rosenberg | International Partnership for Microbicides (IPM), USA |
| Jerald | Sadoff | Aeras Global TB Vaccine Foundation, USA |
| Gill | Samuels | Pfizer Inc., USA |
| K. | Satyanarayana | Indian Council of Medical Research, India |
| Pramilla | Senanayake | GFHR, Switzerland |
| Mohamed | Shams | Faculty of Pharmacy- Mansoura University, Egypt |
| Mclean | Sibanda | Innovation Fund South Africa, South Africa |
| Devi | Sridhar | Global Economic Governance Programme, University of Oxford, UK |
| Sadhana | Srivastava | Indian Council o Medical Research, India |
| Edward David | Sturrock | University of Cape Town, South Africa |
| Dana | Sumilo | University of Oxford, UK |
| Siti | Sundari | The Center for Health System and Policy Research and Development, MOH, Rep. Indonesia |
| Katsuya | Tamai | University of Tokyo, Japan |
| Mark Andrew | Taylor | NHS Institute of Innovation and Improvement, UK |
| Barbara | Timmermann | University of Kansas, USA |
| Sarah | Tomlin | Nature Magazine, UK |
| Adrian | Towse | Office of Health Economics, UK |
| Katherine | Underwood | Oxford University North American Office, UK |
| Frans | van den Boom | IAVI, USA |
| Saul | Walker | IPM, USA |
| Lauren | Walters | Partners in Health, USA |
| Jayashree | Watal | WTO, USA |
| Katherine | Woo | Institute for OneWorld Health, USA |
| David | Zapol | FSG - Social Impact Advisors, USA |
| Howard | Zucker | World Health Organization, Switzerland |

Appendix C: Sanjaya Lall Fellows

The Bill and Melinda Gates Foundation generously supported 30 delegates from developing and middle-income countries. These delegates were drawn from: Bangladesh; Cameroon; Chile; Egypt; India; Indonesia; Kenya; Lesotho; Namibia; Senegal; South Africa; Sri Lanka; Tanzania; Uganda; and Venezuela.

Dr. Sahar Aly
Mr. Rajaaie Batniji
Dr. Tony Bunn
Dr. Jose Miguel Flores Acuna
Prof. Prabuddha Ganguli
Dr. Mohammed Abul Kalam
Mr. Marcos Kulka
Mr. Pranay Lal
Mr. Craig Landsberg
Mr. Milton Lore
Prof. Magy Madkour
Prof. Diran Makinde
Dr. Stephen Mallinga
Mr. Saberi Marais
Dr. Kenneth Kamwi Matengu
Prof. Jane Morris
Dr. Mary Grace Nambatya Kyeyune
Prof. Peter Ndumbe
Mrs. Anita Nel
Prof. Adelani Ogunrinade
Dr. Rayapu Ramesh Babu
Dr. Matheo Raphael
Dr. Rafael Rangel-Aldao
Dr. Anne Reeler
Mr. Wesley Ronoh
Dr. K. Satyanarayana
Dr. Pramilla Senanayake
Dr. Mohamed El Houseny El Sebehy Shams
Mr. McLean Sibanda
Dr. Sadhana Srivastava
Prof. Edward David Sturrock
Dr. Siti Sundari

Appendix D: Glossary

| | |
|-------|--|
| ABPI | Association of the British Pharmaceutical Industry |
| ACHAP | The African Comprehensive HIV/AIDS Partnerships (ACHAP) |
| AGERI | The Agricultural Genetic Engineering Research Institute |
| AIDS | Acquired Immune Deficiency Syndrome |
| AMC | Advanced Market Commitment |
| ARV | Anti Retroviral |
| BMGF | The Bill and Melinda Gates Foundation |
| CBPR | Community Based Participatory Research |
| CDC | Center for Disease Control |
| CMH | Commission for Macroeconomics and Health |
| CRO | Clinical Research Outsourcing |
| DALY | Disability Adjusted Life Years |
| DUI | Dual Use and Interactive Knowledge |
| EPI | Expanded Program on Immunisation |
| FDA | Food and Drug Administration |
| FDC | Fixed Dose Combinations |
| GAVI | Global Alliance for Vaccines and Immunisation |
| GDP | Gross Domestic Product |
| GMP | Good Manufacturing Practice |
| GSK | Glaxo Smith Kline |
| HART | Highly Active Anti-retroviral Therapy |
| HIV | The Human Immunodeficiency Virus |
| IAVI | International AIDS Vaccine Initiative |
| ICGB | The International Cooperative Biodiversity Group |
| ICMR | Indian Council for Medical Research |
| IDC | Innovative Developing Country |
| IFF | International Finance Facility |
| IIFIm | International Finance Facility for Immunisation |
| IGWG | The Inter-governmental Working Group on Public Health, Innovation and Intellectual Property |
| IP | Intellectual Property |
| IPM | International Partnership for Microbicides |
| IPR | Intellectual Property Rights |
| IVI | International Vaccine Institute |
| LDC | Less Developed Country |
| MDR | Multi-Drug Resistant |
| MDG | Millennium Development Goals |
| MIHR | Centre for the Management of Intellectual Property in Health R&D |
| MMV | Medicines for Malaria Venture |
| OECD | Organisation for Economic Co-operation and Development |
| PATH | Program for Appropriate Technology in Health |
| PDVI | Paediatric Dengue Vaccine Initiative |
| PDP | Product Development Partnership |
| PPP | Public-Private Partnership |
| R&D | Research and Development |
| SAMI | South African Malaria Vaccines Initiative |
| SME | Small and Medium Sized Enterprises |
| SSI | The Sustainable Sciences Institute |
| STI | Science, Technology and Innovation |
| TB | Tuberculosis |
| TRIPS | Trade Related Aspects of Intellectual Property Rights |
| VL | Visceral Leishmaniasis |
| WHA | World Health Assembly |
| WHO | World Health Organisation |
| WTO | World Trade Organisation |