WFCC ICCC-12 Conference 2010
WORLD FEDERATION FOR CULTURE COLLECTIONS
Biological Resource Centers: gateway to biodiversity and services for innovation in biotechnology

BIOTECHNOLOGICAL INNOVATION AND THE DEVELOPMENT OF BIO-BASED ECONOMIES

Session 2 - Innovation and intellectual property in the bio-economy age

WFCC ICCC-12 Conference 2010
World Federation for Culture Collections
Biological Resource Centers: gateway to biodiversity and services for innovation in biotechnology

Biotechnologies revolutionizing healthcare

Carlos M. Morel
Director
Center for Technological Development in Health (CDTS)
Oswaldo Cruz Foundation (Fiocruz)

Ministério da Saúde

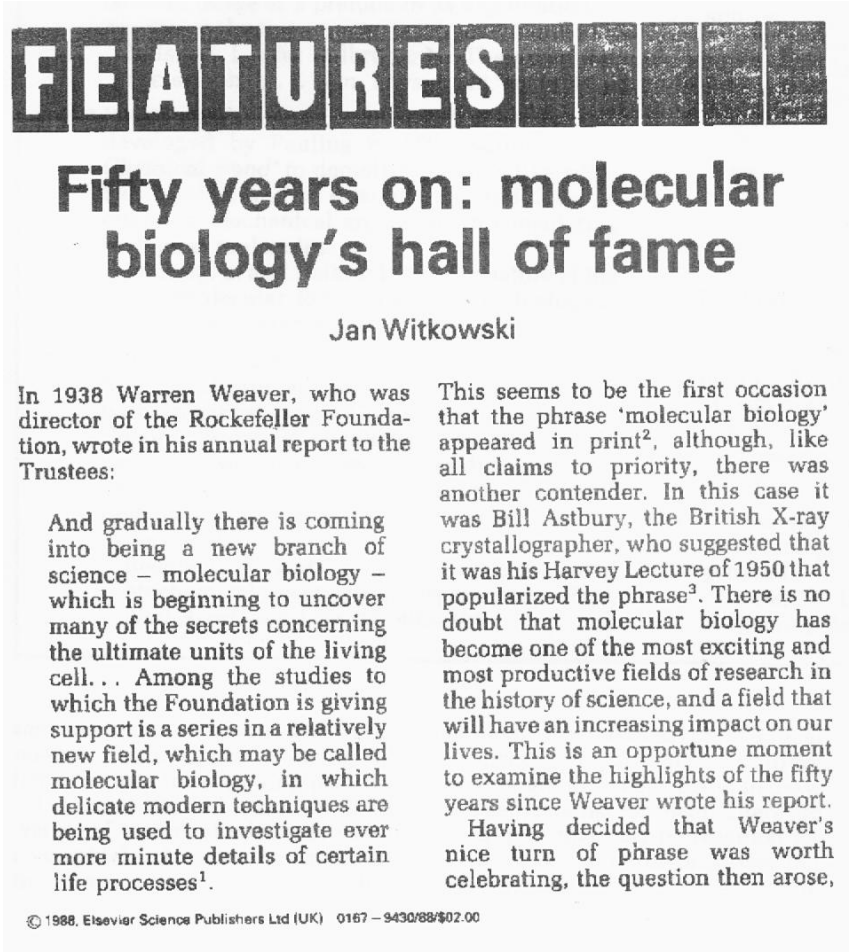
FIOCRUZ
Fundação Oswaldo Cruz

inct-idn
national institute of science and technology of innovation in neglected diseases

Molecular biology, networks, barriers

THE NEW SCIENCE AND THE NEW BIOTECHNOLOGY

Molecular biology: the basis of modern biotechnology



FEATURES

Fifty years on: molecular biology's hall of fame

Jan Witkowski

In 1938 Warren Weaver, who was director of the Rockefeller Foundation, wrote in his annual report to the Trustees:

> And gradually there is coming into being a new branch of science – molecular biology – which is beginning to uncover many of the secrets concerning the ultimate units of the living cell... Among the studies to which the Foundation is giving support is a series in a relatively new field, which may be called molecular biology, in which delicate modern techniques are being used to investigate ever more minute details of certain life processes[1].

This seems to be the first occasion that the phrase 'molecular biology' appeared in print[2], although, like all claims to priority, there was another contender. In this case it was Bill Astbury, the British X-ray crystallographer, who suggested that it was his Harvey Lecture of 1950 that popularized the phrase[3]. There is no doubt that molecular biology has become one of the most exciting and most productive fields of research in the history of science, and a field that will have an increasing impact on our lives. This is an opportune moment to examine the highlights of the fifty years since Weaver wrote his report.

Having decided that Weaver's nice turn of phrase was worth celebrating, the question then arose,

- 1938: the first occasion that the phrase '*molecular biology*' appeared in print

Witkowski J (1988) Fifty years on: molecular biology's hall of fame. *Trends in Biotechnology* 6:234-243

The new science of Molecular Biology

- Key advances, 1938-1988

  1938: The term "*molecular biology*" is used for the first time (Warren Weaver, Rockefeller Foundation)

  1944: Transformation of *Pneumococcus* by DNA (Avery)

  1953: DNA as a double helix (Watson & Crick)

  1961: Theory of the operon (Jacob & Monod)

  1972: Recombinant DNA (Paul Berg)

  1975: Monoclonal antibodies (Kohler & Milstein)

  1977: DNA sequencing (Gilbert; Sanger)

  1985: Polymerase Chain Reaction (PCR; Kary Mullis)

  … …

Witkowski J (1988) Fifty years on: molecular biology's hall of fame. *Trends in Biotechnology* 6:234-243

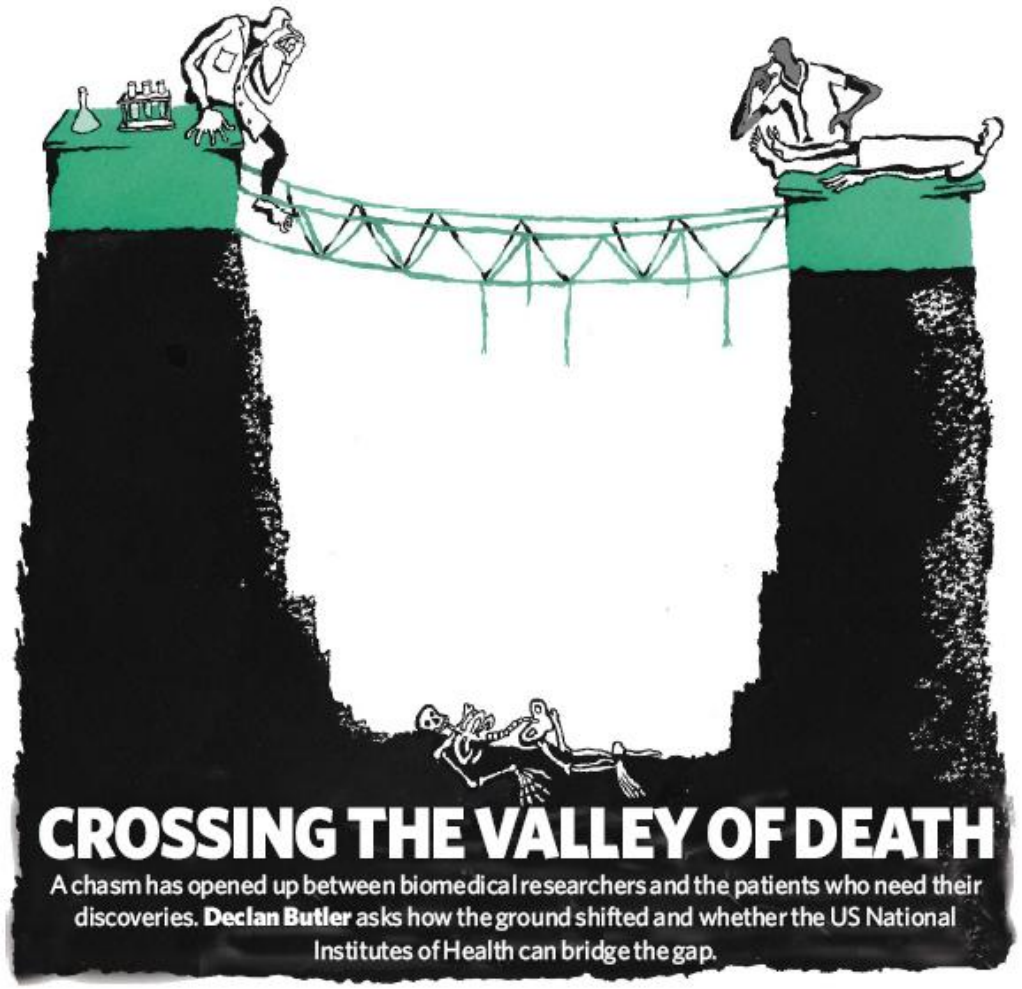
Evolution of the scientific enterprise (Barabási AL (2005) *Science* 308:639-641)

Evolution of the scientific enterprise. (**Left**) For centuries, creative individuals were embedded in an invisible college, that is, a community of scholars whose exchange of ideas represented the basis for scientific advances. Although intellectuals built on each other's work and communicated with each other, they published alone. Most great ideas were attributed to a few influential thinkers: Galileo, Newton, Darwin, and Einstein. Thus, the traditional scientific enterprise is best described by many isolated nodes (blue circles). (**Middle**) In the 20th century, science became an increasingly collaborative enterprise, resulting in such iconic pairs as the physicist Crick and the biologist Watson (left), who were responsible for unraveling DNA's structure. The joint publications documenting these collaborations shed light on the invisible college, replacing the hidden links with published coauthorships. (**Right**) Although it is unlikely that large collaborations—such as the D0 team in particle physics or the International Human Genome Sequencing Consortium pictured here—will come to dominate science, most fields need such collaborations. Indeed, the size of collaborative teams is increasing, turning the scientific enterprise into a densely interconnected network whose evolution is driven by simple universal laws.

The new industry of Biotechnology

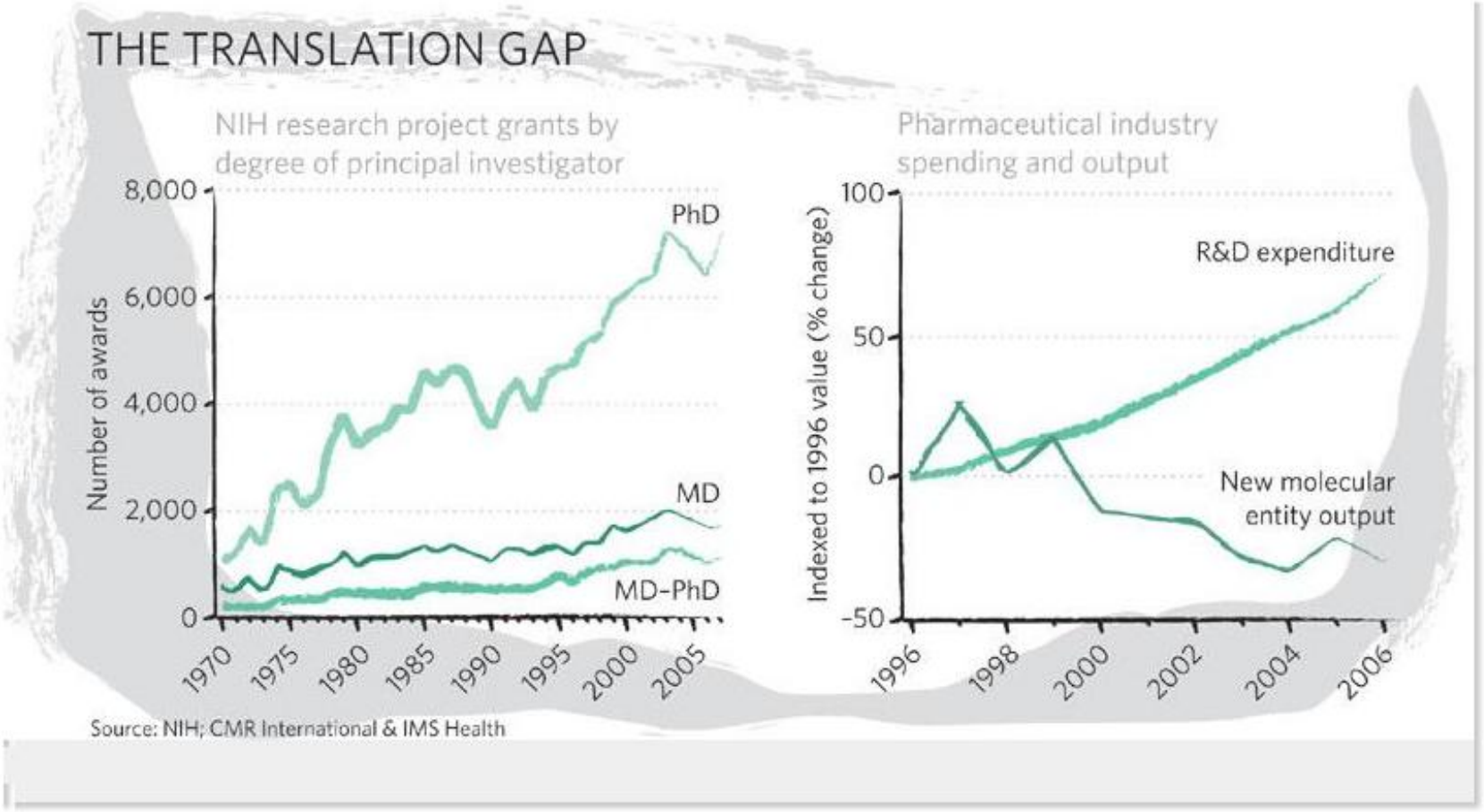
- 1978: Genentech and Eli Lilly produce ***insulin***
- 1980: Biogen produces ***interferon***
- 1988: five proteins from genetically engineered cells approved as drugs by the Food and Drug Administration (FDA)
  - Synthetic insulin, human growth hormone, hepatitis B vaccine, alpha-interferon, tissue plasminogen activator
- End of 1990s': > 125 genetically engineered drugs approved

From bench to bed:
Crossing the Valley of Death

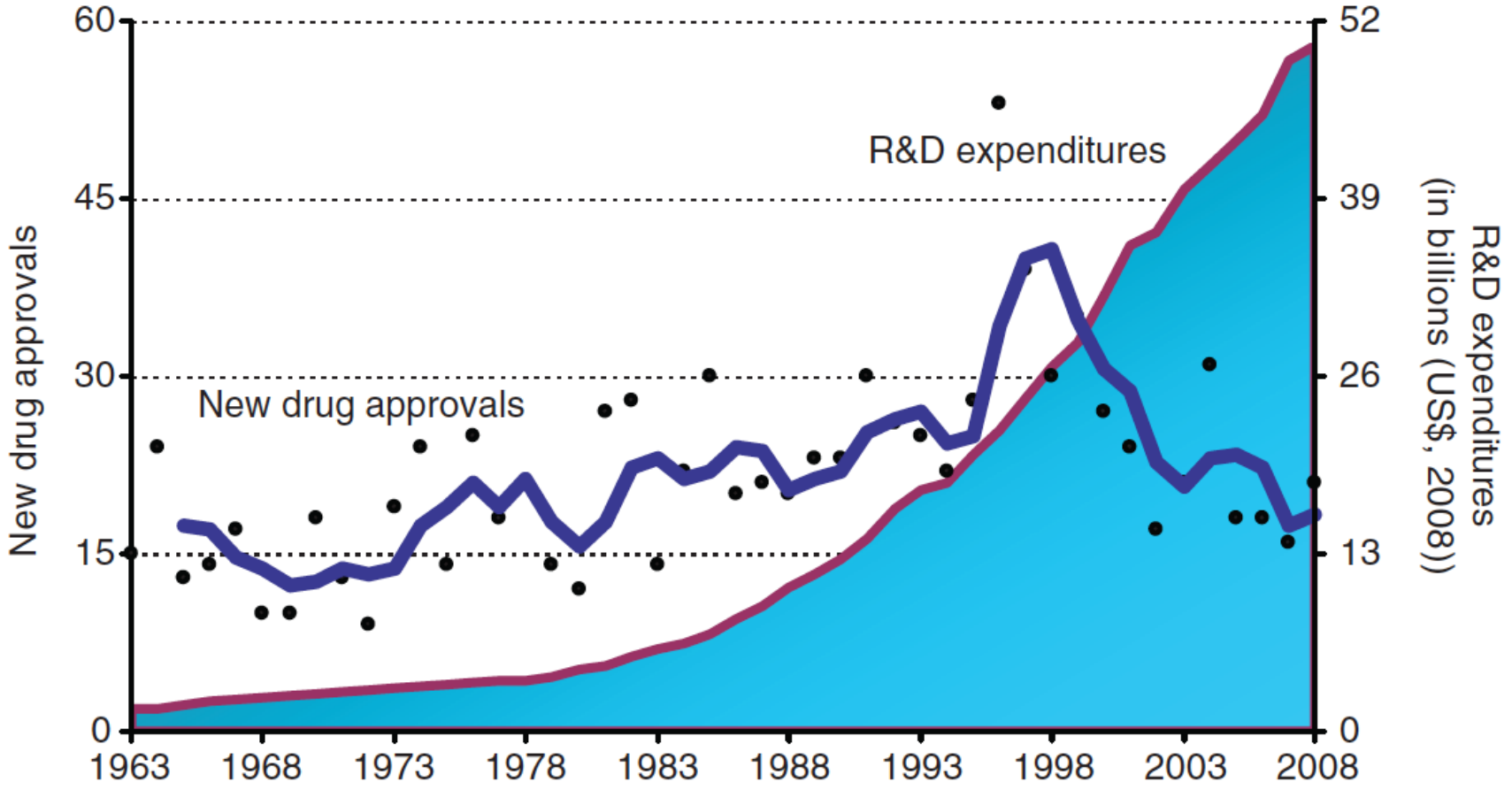


Butler D (2008) Translational research: crossing the valley of death. *Nature* **453**: 840-842

From bench to bed:
Crossing the Valley of Death



Big Pharma and the Valley of Death



Clinical Pharmacology & Therapeutics

Development

Clinical Pharmacology & Therapeutics (2010); doi:10.1038/clpt.2009.293

Deconstructing the Drug Development Process: The New Face of Innovation

K I Kaitin[1]

[1]Tufts Center for the Study of Drug Development, Tufts University, Boston, Massachusetts, USA

Correspondence: KI Kaitin, (kenneth.kaitin@tufts.edu)

Received 17 November 2009; Accepted 5 December 2009; Published online 3 February 2010.

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Abstract

Forged in the early 1960s, the paradigm for pharmaceutical innovation has remained virtually unchanged for nearly 50 years. During a period when most other research-based industries have made frequent and often sweeping modifications to their R&D processes, the pharmaceutical sector continues to utilize a drug development process that is slow, inefficient, risky, and expensive. Few who work in or follow the activities of the pharmaceutical industry question whether change is coming. They know that the pharmaceutical sector, as currently structured, is unable to deliver enough new products to market to generate revenues sufficient to sustain its own growth. Nearly all major drug developers are critically examining current R&D practices and, in some cases, considering a radical overhaul of their R&D models. But key questions remain. What will the landscape for pharmaceutical innovation look like in the future? And, who will develop tomorrow's medicines?

Deconstructing the Drug Development Process: The New Face of Innovation

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- Few who work in or follow the activities of the pharmaceutical industry question whether change is coming. They know that the pharmaceutical sector, as currently structured, is unable to deliver enough new products to market to generate revenues sufficient to sustain its own growth. Nearly all major drug developers are critically examining current R&D practices and, in some cases, considering a radical overhaul of their R&D models. But key questions remain. **What will the landscape for pharmaceutical innovation look like in the future? And, who will develop tomorrow's medicines?**

Deconstructing the Drug Development Process: The New Face of Innovation

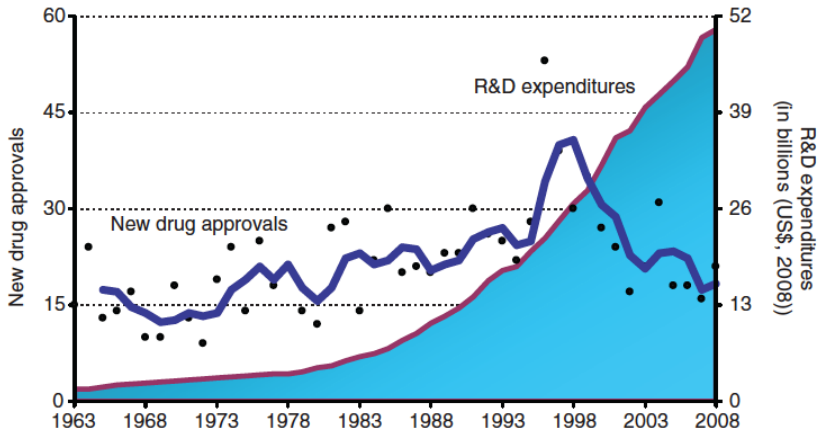


Figure 2 New drug approvals (dots), represented on the left vertical axis, and pharmaceutical R&D expenditures (shaded area), represented on the right vertical axis, in the United States from 1963 to 2008. R&D expenditures are presented in terms of constant 2008 dollar value. The trend line is a 3-year moving average. The source of drug approval data is the Tufts Center for the Study of Drug Development (CSDD). The source of R&D expenditure data is the Pharmaceutical Research and Manufacturers of America; Industry Profile 2009; conversion of actual expenses to constant dollars was performed by Tufts CSDD.

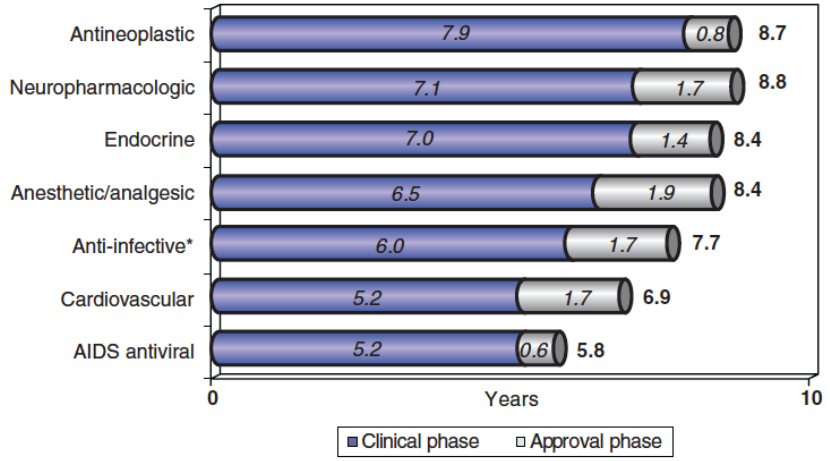


Figure 1 Clinical development times (from IND filing to NDA submission) and regulatory approval times (from NDA submission to approval) for new molecular entities approved by the US Food and Drug Administration during the 5-year period 2003–2007, grouped by therapeutic area. Analysis by the Tufts Center for the Study of Drug Development, based on data included in its approved products database. *Note that the anti-infectives category excludes AIDS antiviral agents. IND, investigational new drug application; NDA, new drug application.

Deconstructing the Drug Development Process: The New Face of Innovation

Table 1 Patent expirations for 10 top-selling drugs each year

2009		2010		2011		2012	
Product	**2007 Sales ($MM)**	**Product**	**2007 Sales ($MM)**	**Product**	**2007 Sales ($MM)**	**Product**	**2007 Sales ($MM)**
Prevacid	3,962	Protonix	4,221	Lipitor	13,652	Diovan	5,012
Topamax	2,453	Cozaar/Hyzaar	3,350	Plavix	8,079	Singulair	4,266
Lamictal	2,194	Aricept	3,311	Advair	6,998	Lexapro	3,044
Valtrex	1,868	Levaquin	2,862	Zyprexa	4,661	Viagra	1,764
Cellcept	1,677	Effexor XR	2,657[a]	Actos	4,333	Avandia	1,754
Keppra	1,407	Taxotere	2,569	Seroquel	4,219	Symbicort	1,575
Flomax	1,399	Arimidex	1,730	Avapro	2,685	Zometa	1,297
Imitrex	1,370	Gemzar	1,592	Xalatan	1,604	Detrol	1,190
Adderall XR	1,031	Coreg	1,174	Avelox	1,013	Geodon	854
Suboxone	531[a]	NovoSeven	1,078	Xeloda	959	Provigil	852
Total	$17,892	Total	$24,544	Total	$48,203	Total	$21,608

[a]US sales only.

Data from Tufts center for the study of Drug Development, 2010; MedNews 27(7), 2008; http://www.drugs.com/top200.

Deconstructing the Drug Development Process: The New Face of Innovation

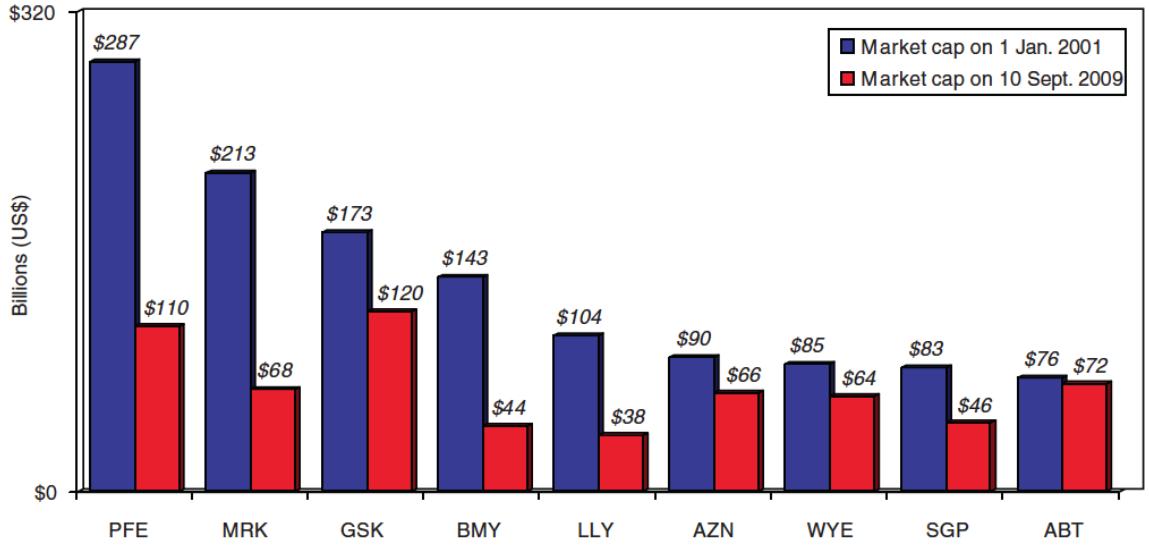
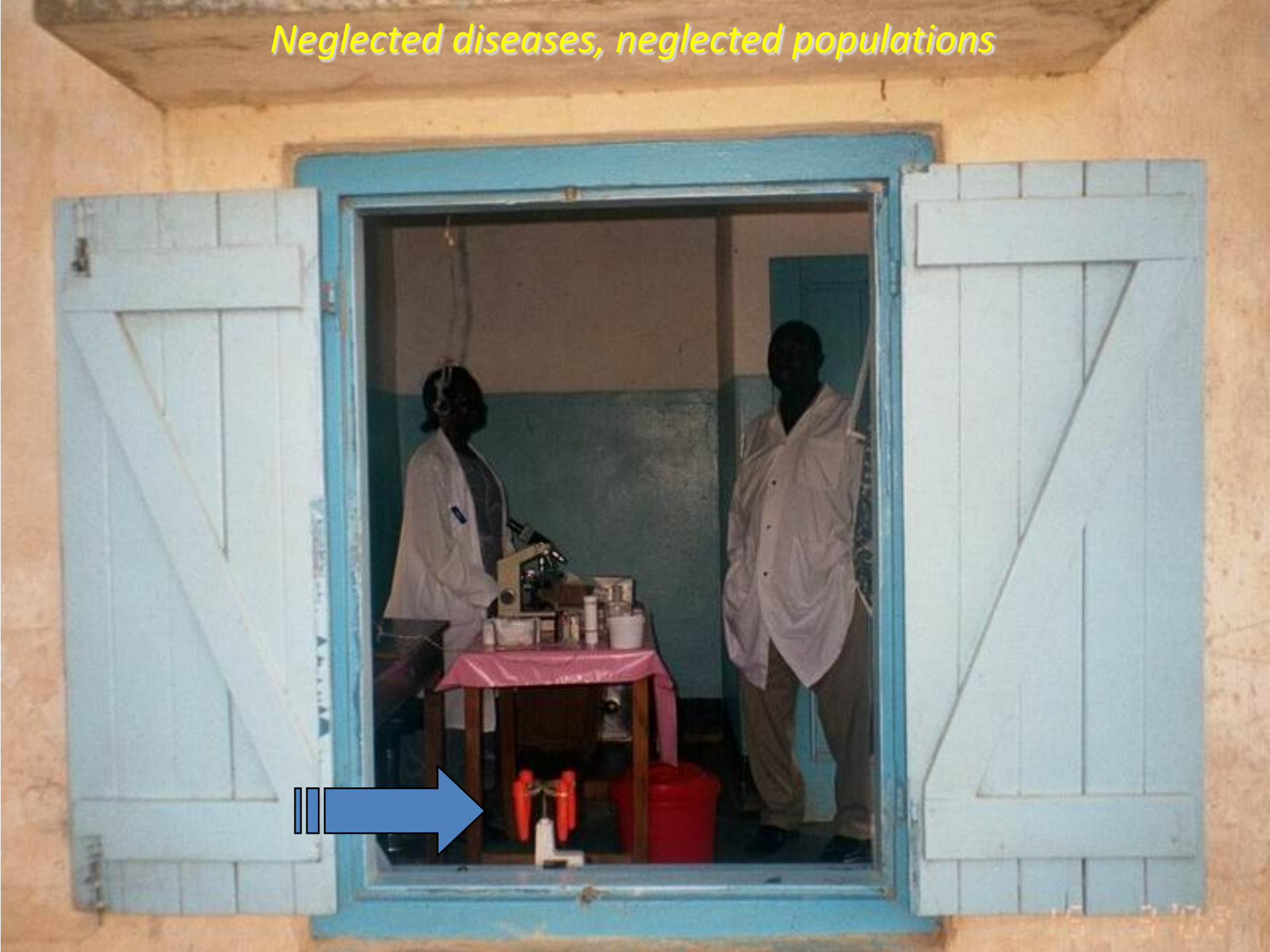


Figure 4 Market capitalization of top-tier pharmaceutical companies in January 2001 and September 2009. Cumulative loss in market capitalization for these companies over the period is $626 billion. Ticker symbols are as follows: ABT, Abbott; AZN, AstraZeneca; BMY, Bristol-Myers Squibb; GSK, GlaxoSmithKline; LLY, Lilly; MRK, Merck; PFE, Pfizer; SGP, Schering-Plough; WYE, Wyeth. Data from http://www.valueline.com; Tufts Center for the Study of Drug Development analysis.

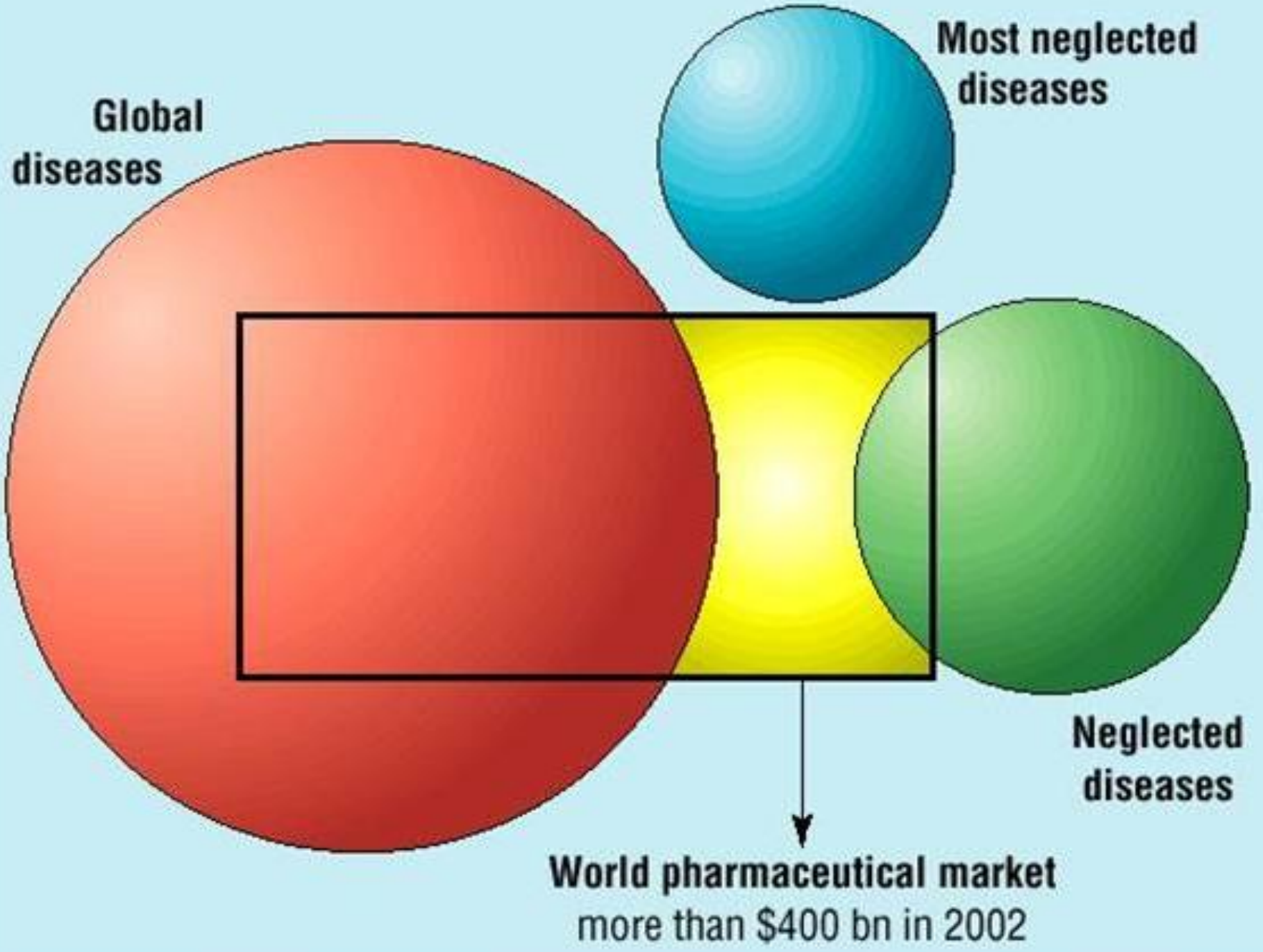
They desperately need new tools and interventions

THE CHALLENGE OF NEGLECTED DISEASES

Neglected diseases, neglected populations

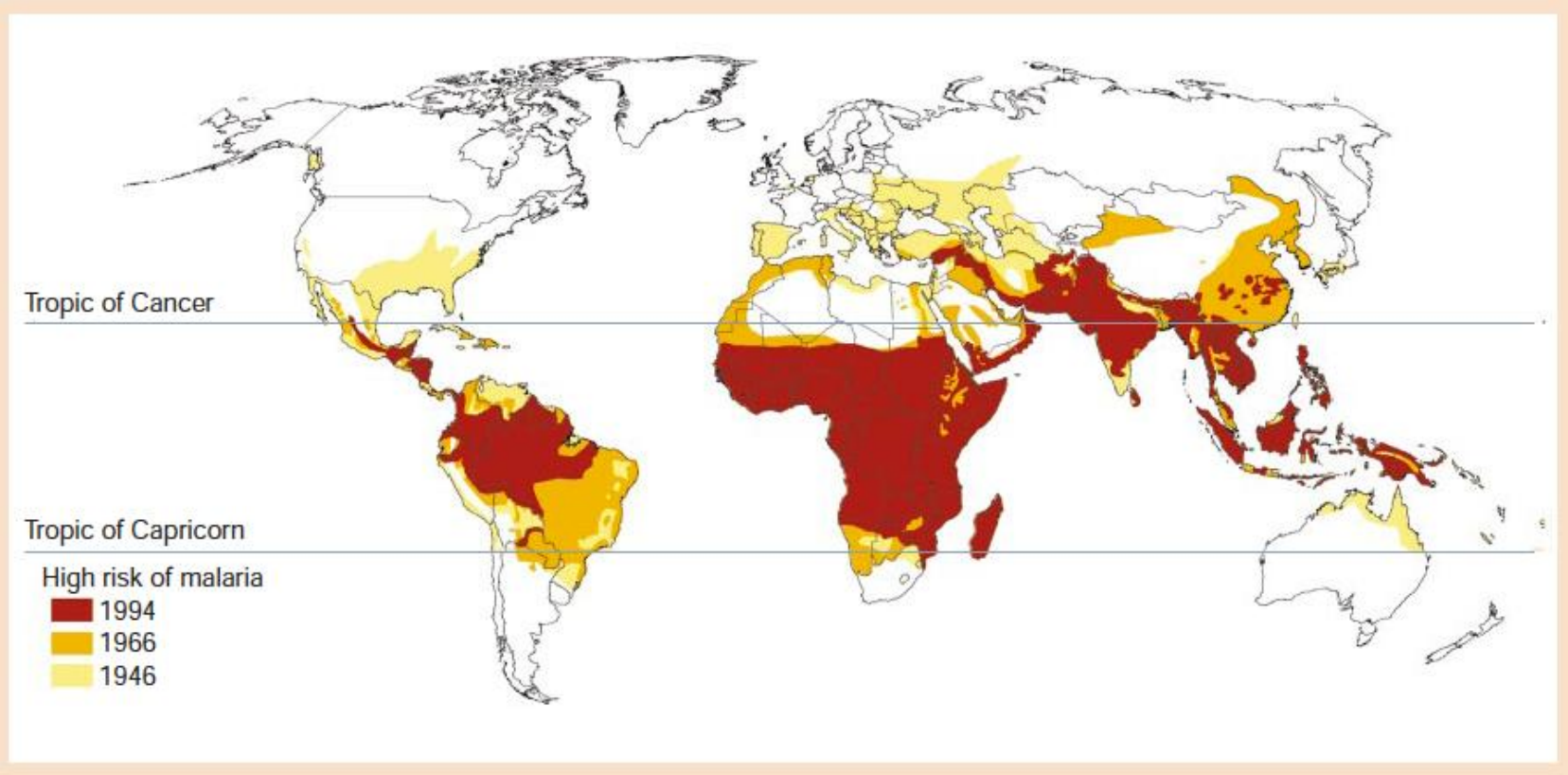


Kimalel Health Centre, Ministry of Health of Kenya, a KEMRI-DNDi partnership
http://picasaweb.google.com/cmmorel/20090620To25Kenya#


Most neglected diseases
Global diseases
Neglected diseases
World pharmaceutical market
more than $400 bn in 2002

Malaria: the challenge

- People at risk of malaria: > 2 billion
- Malaria cases each year: 500 million
- Malaria deaths each year: 1 million



Human Vaccines 6:1, 90-96; January 2010; © 2010 Landes Bioscience

From the circumsporozoite protein to the RTS, S/AS candidate vaccine

Joe Cohen,[1,*] Victor Nussenzweig,[2] Ruth Nussenzweig,[2] Johan Vekemans[1] and Amanda Leach[1]

[1]GlaxoSmithKline Biologicals; Belgium; [2]Department of Pathology; Langone New York University Medical Center; NY USA

Key words: malaria, vaccines, RTS,S, adjuvant systems, *Plasmodium falciparum*, circumsporozoite protein







MALARIA VACCINE TECHNOLOGY ROADMAP

mvi PATH
MALARIA VACCINE INITIATIVE

gsk

Critical scientific breakthroughs of the 1960s-70s

1967

Nature, 216:160-162, 1967

letters to nature

Nature **216**, 160 - 162 (14 October 1967); doi:10.1038/216160a0

Protective Immunity produced by the Injection of X-irradiated Sporozoites of *Plasmodium berghei*

R. S. NUSSENZWEIG, J. VANDERBERG, H. MOST & C. ORTON

Department of Preventive Medicine and Department of Radiology, New York University School of Medicine.

STUDIES with avian malaria have shown that killed sporozoites as well as sporozoites inactivated with ultraviolet light can produce a partial immunity after injection into birds[1,2]. On the other hand, attempts to use the erythrocytic stages of the parasite as the source of antigen have met with only limited success with avian[3], rodent[4] and monkey malaria[5,6]. Previous attempts to use killed sporozoites of the rodent malarial parasite, *Plasmodium berghei*, to immunize rodents have been unsuccessful. We therefore sought to determine whether protective immunity to this parasite could be achieved by partial inactivation of the injected sporozoites as opposed to injection of dead parasites. X-irradiation was chosen as the inactivating agent, because of the partial immunity obtained by vaccination with irradiated blood forms of malaria parasites[7–9]. This communication reports preliminary results on the production of protective immunity in mice by vaccination with X-irradiated sporozoites of *P. berghei*.

Immunization of man against sporozite-induced falciparum malaria

1973

DAVID F. CLYDE
HARRY MOST
VINCENT C. McCARTHY
JEROME P. VANDERBERG

American Journal of the Medical Sciences, 266:169-177, 1973

Scientific breakthroughs – 1980s’

1983

Identification and chemical synthesis of a tandemly repeated immunogenic region of *Plasmodium knowlesi* circumsporozoite protein

G. N. Godson*, J. Ellis*, P. Svec*, D. H. Schlesinger† & V. Nussenzweig‡

* Department of Biochemistry, † Department of Medicine and Cell Biology, ‡ Department of Pathology, New York University Medical Center, 550 First Avenue, New York, New York 10016, USA

1989

ADVANCES IN IMMUNOLOGY, VOL. 45

Rationale for the Development of an Engineered Sporozoite Malaria Vaccine

VICTOR NUSSENZWEIG* and RUTH S. NUSSENZWEIG†

*Department of Pathology and Kaplan Cancer Center, and
†Department of Medical and Molecular Parasitology,
New York University Medical Center,
New York, New York 10016

Technological developments

- 1984: GlaxoSmithKline (GSK) and the Walter Reed Army Institute of Research (WRAIR) entered into a *Collaborative R&D Agreement* to produce a malaria vaccine using genetic engineering techniques and expression systems developed at GSK
  - End of 80s, early 90s: widespread disappointment
  - Early 80s: GSK Hepatitis B recombinant vaccine produced in yeast

Technological breakthrough: RTS,S malaria vaccine candidate

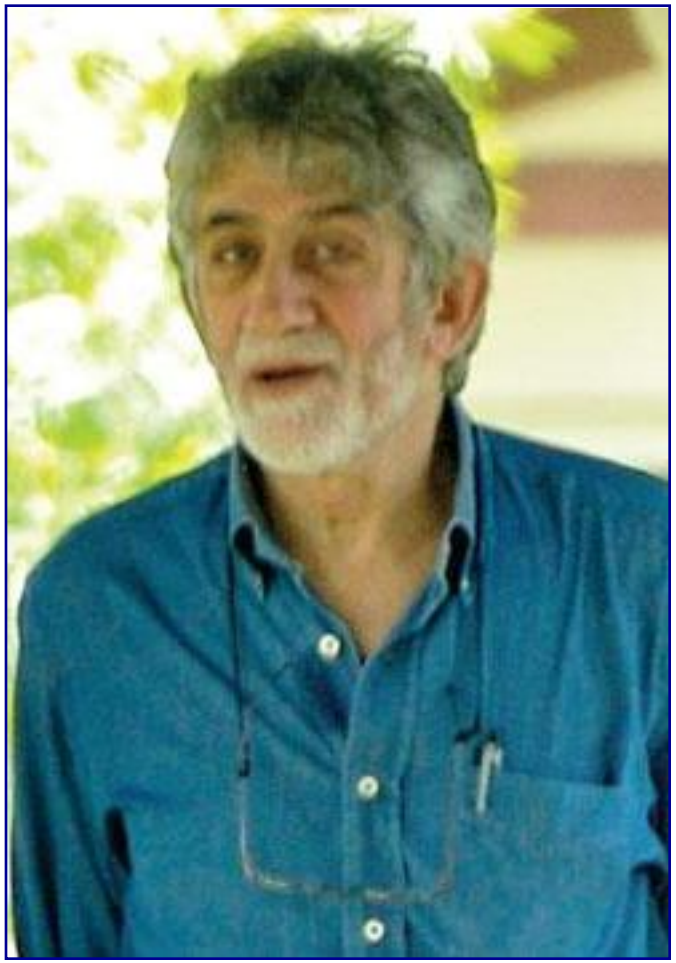
1988

HEPATITIS B SURFACE ANTIGEN AS CARRIER MATRIX FOR THE REPETITIVE EPITOPE OF THE CIRCUMSPOROZOITE PROTEIN OF *PLASMODIUM FALCIPARUM.*

Tineke Rutgers, Daniel Gordon[2], Anne Marie Gathoye, Michael Hollingdale[3], Wayne Hockmeyer[2], Martin Rosenberg[1] and Michel De Wilde.

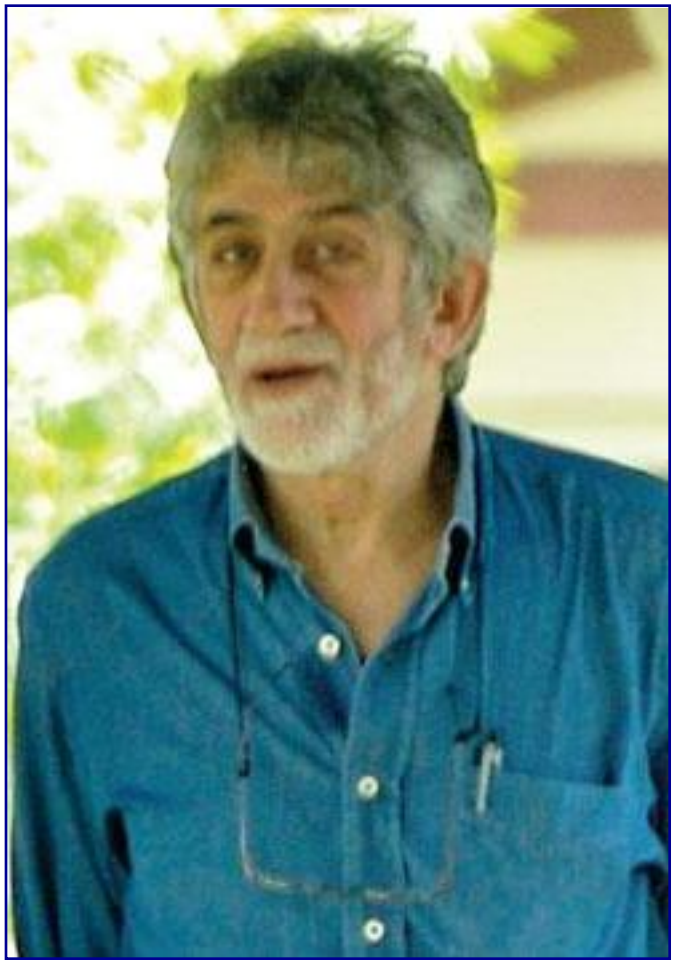
Department of Molecular Genetics, Smith Kline—RIT, 89 rue de l'Institut, B-1330 Rixensart, Belgium. [1]Smith Kline and French Laboratories, 1500 Spring Garden street, Philadelphia, PA 19101. [2]Department of Immunology, Walter Reed Army Institute of Research, Washington DC 20307. [3]Biomedical Research Institute, Rockville, Maryland 20852. *Present address: Praxis Biologics, Inc., Rochester, New York 14623.

Technological breakthrough: RTS,S malaria vaccine candidate



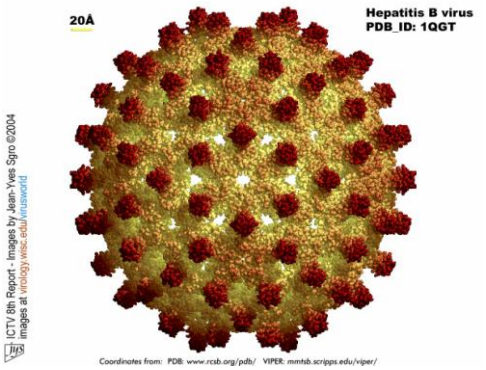
- Faced with turning the repeating fragment from the protein into a real vaccine, Cohen decided to use lessons that the company had learned from its successful development of a recombinant **hepatitis B vaccine**, Engerix-B
- That vaccine consisted of a surface antigen protein from hepatitis grown in yeast; at high enough concentrations that protein spontaneously forms **virus-like particles** that have a greater effect on the antibody-making parts of the immune system than loose proteins could
- Fusing the repeat region from the CSP to the hepatitis surface antigen protein, Cohen hoped, would make **similar particles festooned with the CSP fragments** and thus able to provoke the production of antibodies targeted at the sporozoites.

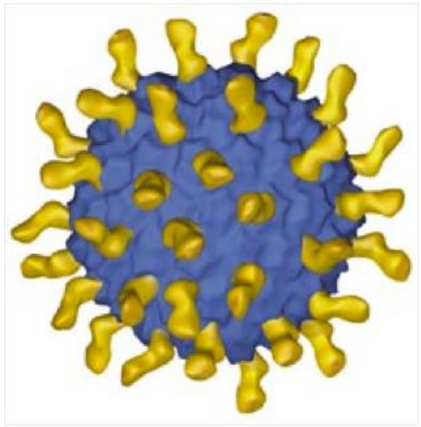
Technological breakthrough: RTS,S malaria vaccine candidate



- Given a widespread suspicion that ***antibodies*** wouldn't be enough to elicit immunity, Cohen went on to add a fragment from the tail end of the CSP that was thought likely to interest the other arm of the immune system — the arm that prompts ***T cells*** to attack infected cells
- The resultant "double whammy", as Cohen calls it, was a gene for a protein containing the antibody-inducing ***repeat*** **(R)**, the portion recognized by ***T cell*** white blood cells **(T)** and the hepatitis B ***surface*** antigen **(S)**.
- With all these additions, though, the surface antigen protein lost its knack for self assembly. Through a lot of fine tuning, Cohen finally hit on a way to regain it:
  <u>one part RTS</u> to <u>four parts plain old S</u>
- **RTS,S was born**

Technological breakthrough: RTS,S malaria vaccine candidate





Model: Cytos Biotechnology

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- **RTS,S was born**

A critical development: a new adjuvant system

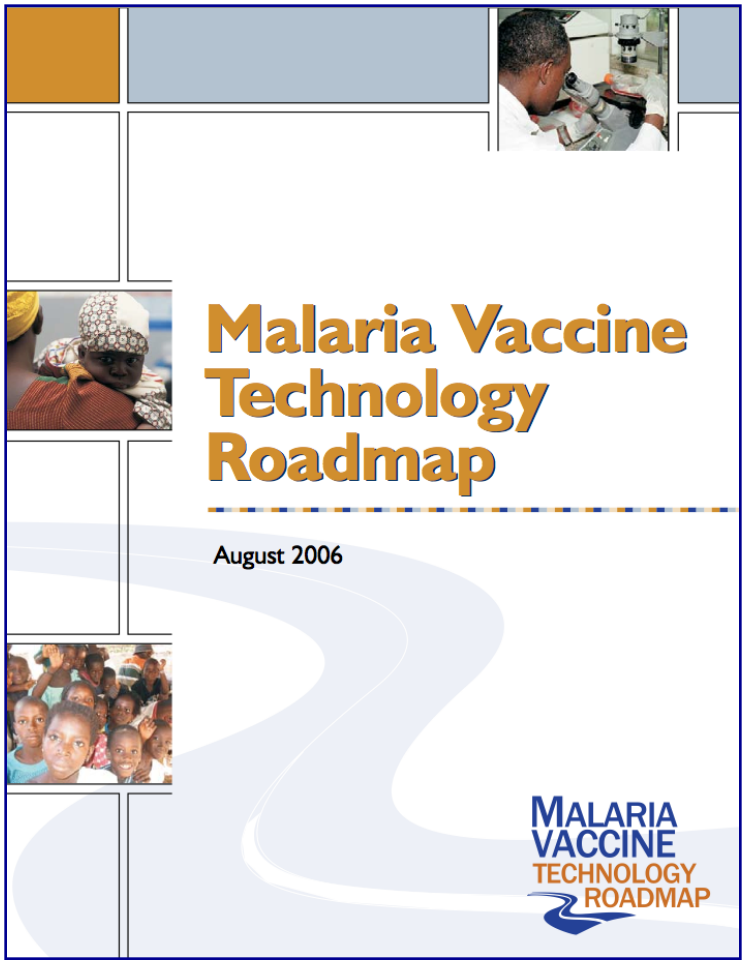
Development of RTS,S/AS02: a purified subunit-based malaria vaccine candidate formulated with a novel adjuvant

Nathalie Garçon†, D Gray Heppner and Joe Cohen

During the past decade, tremendous progress has been made in process development allowing for the production of large quantities of recombinant antigens, as well as in the understanding of the immune mechanisms underlying protection. Parallel to this, various and numerous adjuvant systems have been developed and tested in animal models and in clinical trials but have rarely induced protection. This review will discuss the development of a new adjuvant system (AS02) in combination with a malaria vaccine antigen candidate. To date, this vaccine is the only one to demonstrate protection in man in artificial challenge as well as in natural field trials. It has been established that this adjuvant system is capable of eliciting high antibody titers along with strong cell-mediated immunity which both contribute to the efficacy of the vaccine.

Expert Rev. Vaccines 2(2), 231–238 (2003)

2006: Malaria Vaccine Technology Roadmap launched



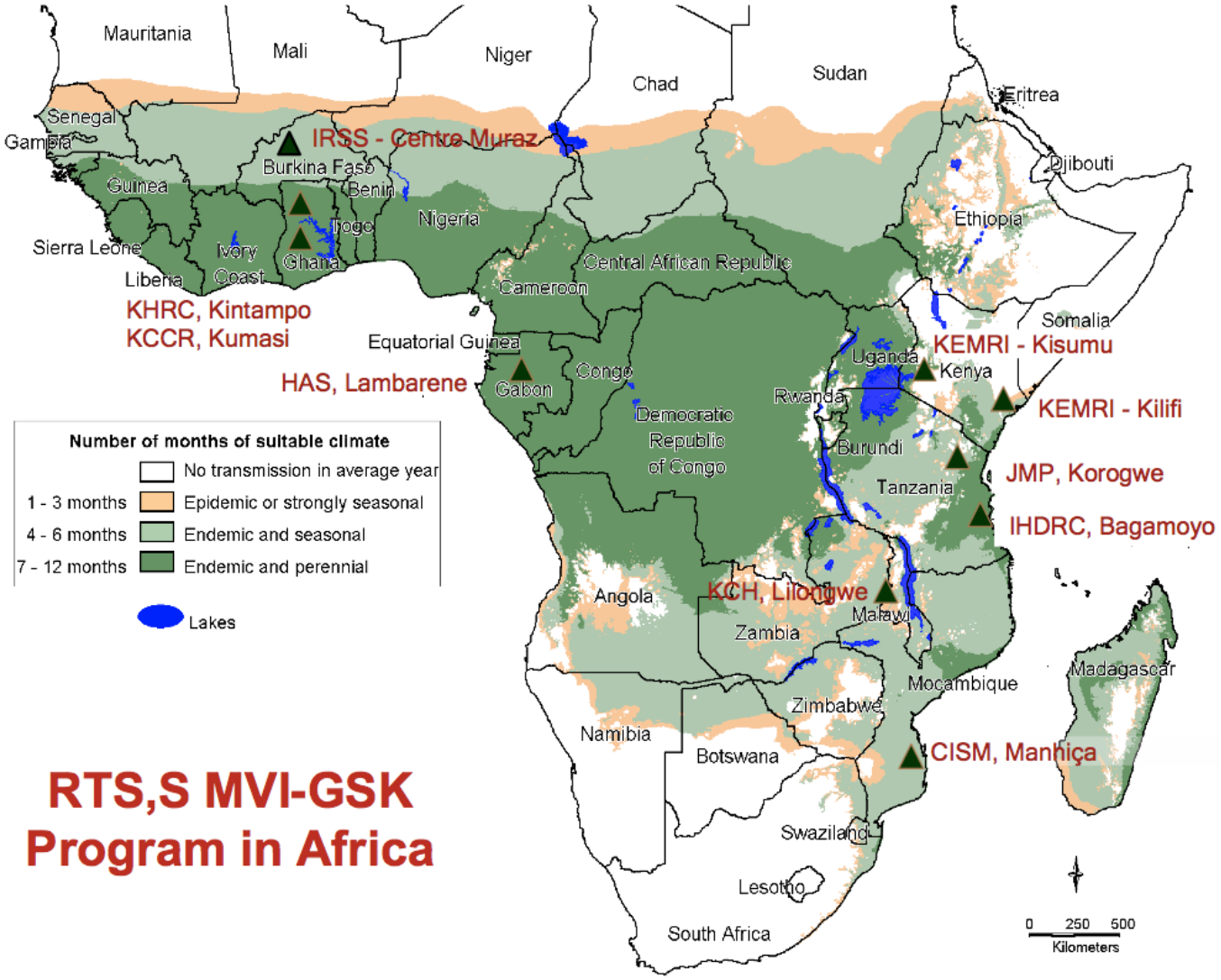
- The World Health Organization, PATH MVI, the Bill & Melinda Gates Foundation and the Wellcome Trust, together with representatives of the European and Developing Countries Clinical Trials Partnership (EDCTP), the European Malaria Vaccine Initiative (EMVI), the European Commission (Directorate General for Research), the United States National Institute for Allergy and Infectious Diseases (NIAID), and the United States Agency for International Development (USAID) form part of a **malaria vaccine funders' group**, with the WHO Initiative for Vaccine Research as its focal point. The group's participation and support was critical to the Roadmap process.

Public-Private Partnerships support large-scale clinical trials of RTS,S

- PATH (Program for Appropriate Technology in Health)Malaria Vaccine Initiative (MVI) and GlaxoSmithKline (GSK) Biologicals, in collaboration with Africa-based research institutions, have completed **Phase 2** clinical trials of GSK's candidate vaccine RTS,S in Mozambique, Tanzania, Gabon, Ghana, and Kenya
- A large-scale **Phase 3** trial—the last stage of development before the vaccine is submitted to regulatory authorities—was launched in May 2009. That trial includes additional sites in Burkina Faso, Kenya, and Malawi.

RTS,S Clinical Research Center Network

(*source: Christian Loucq, MD Director, PATH Malaria Vaccine Initiative*)



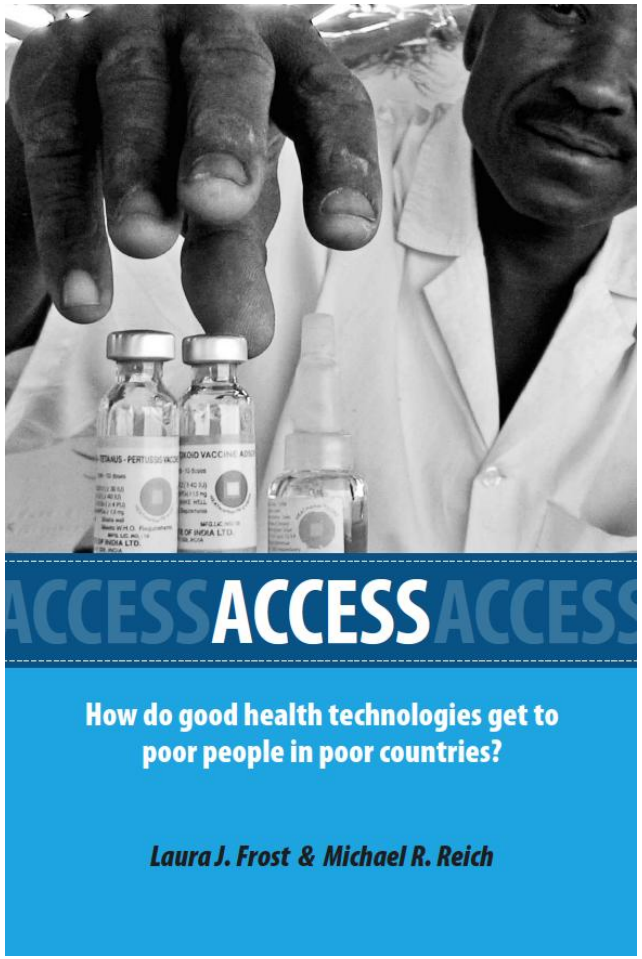
Hard work, collaboration and critical breakthroughs generated a robust candidate malaria vaccine

- *Scientific breakthroughs*
  - Research findings
  - New science of molecular biology
- *Technological breakthroughs*
  - Hepatitis B virus-like proteins & CSP protein
  - New adjuvants
- *Management and financial breakthroughs*
  - Partnerships for Product Development (PDPs)
  - Malaria vaccine funders' group (WHO/IVR)

Innovation, intellectual property rights, prices, and policies

ACCESS, ACCESS, ACCESS

What will be needed if a new drug or vaccine a comes through? Answer: **ACCESS**



http://www.accessbook.org

"We live in an extraordinary time in the history of public health: never before has the world had such powerful technologies to fight disease and improve lives. Yet medical breakthroughs mean little if they fail to reach those in greatest need. Today, millions of people in the poorest countries do not have access to effective vaccines, medicines, and other life-saving tools (…)

I am hopeful that in the coming years, the speed of improvements in global health will continue. With dedication and ingenuity, ***we can create a world in which all people have access to the tools they need to live healthy, productive lives****."*

Tadataka Yamada, M.D.
President, Global Health Program
Bill & Melinda Gates Foundation

A Global Strategy and a Plan of Action

SIXTY-FIRST WORLD HEALTH ASSEMBLY **WHA61.21**

Agenda item 11.6 **24 May 2008**

Global strategy and plan of action on public health, innovation and intellectual property

The Sixty-first World Health Assembly,

Having considered the report of the Intergovernmental Working Group on Public Health, Innovation and Intellectual Property;[1]

Recalling the establishment pursuant to resolution WHA59.24 of an intergovernmental working group to draw up a global strategy and plan of action in order to provide a medium-term framework based on the recommendations of the Commission on Intellectual Property, Innovation and Public Health, and to secure, inter alia, an enhanced and sustainable basis for needs-driven, essential health research and development relevant to diseases that disproportionately affect developing countries, proposing clear objectives and priorities for research and development, and estimating funding needs in this area;

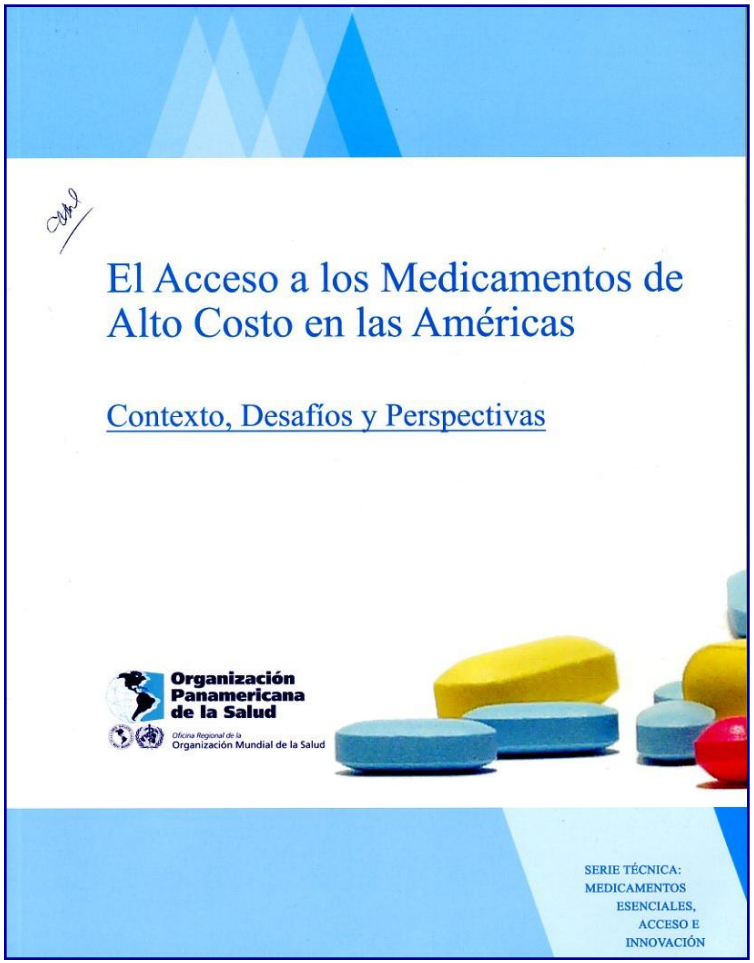
Recalling resolutions WHA49.14 and WHA52.19 on revised drug strategy, WHA53.14 and WHA54.10 and WHA57.14 on HIV/AIDS, WHA56.27 on intellectual property rights, innovation and public health, WHA58.34 on the Ministerial Summit on Health Research, WHA59.26 on international trade and health; and WHA60.30 on public health, innovation and intellectual property;

Welcoming the progress made by the Intergovernmental Working Group in elaborating the global strategy and the identification of the stakeholders in the plan of action,

1. ADOPTS the global strategy and the agreed parts of the plan of action[2] on public health, innovation and intellectual property, attached to this resolution;

Be coherent on access and delivery

*"…encourage and support the application and management of **intellectual property** in a manner that maximizes health-related innovation, especially to meet the R&D needs of developing countries, protects public health and promotes access to medicines for all, as well as explore and implement, where appropriate, possible incentive schemes for R&D"*



From TRIPS-Minus, to TRIPS, to TRIPS-Plus

- *"…during the past few years, a number of countries have adapted and incorporated more enhanced levels of IPR protection unwillingly as a result of pressures exerted on them by the industrialized countries, either under the WTO or under some bilateral free trade agreements. The latter trend was championed by* ***the United States and the European Union*** *in their latest free trade and association agreements…"*

El-Said M (2005) The Road from TRIPS-Minus, to TRIPS, to TRIPS-Plus. Implications of IPRs for the Arab World. *The Journal of World Intellectual Property* 8(1):53-65

Coherence

5. **Coherence**: The above-mentioned principles should apply to all EU policies which directly or indirectly affect health in the EU and non-EU countries. The main policies which will require special attention are development (of local capacity), mobility (mitigation of the effects of brain drain), trade (ensuring access to essential medicines for the poor) and research (equity of priorities on global health research and development of new medicines and measures).

Question 16: What are the keys to ensuring equitable access to medicine and how could the EU help to do more on this, including by supporting innovation and management of intellectual property rights?

Coherence?

5. **Coherence**: The above-mentioned principles should apply to all EU policies which directly or indirectly affect health in the EU and non-EU countries. The main policies which will require special attention are development (of local capacity), mobility (mitigation of the effects of brain drain), trade (ensuring access to essential medicines for the poor) and research (equity of priorities on global health research and development of new medicines and measures).

Intervention by Brazil at WTO General Council on seizure of 500 kilos of generic medicines by Dutch customs authorities

View | What links here

Submitted by thiru on 3. February 2009 - 14:08

Brazil WTO India The Netherlands Other country trade disputes

On this day, 3 February 2009, H.E. Ambassador Roberto AZEVÊDO, Permanent Representative of Brazil to the World Trade Organization (WTO) and other economic organizations in Geneva made the following intervention at the WTO General Council meeting on the seizure by Dutch authorities of a cargo of 500 kilos of losartan potassium en route from India to Brazil.

An informed source notes that India and 16 other members of WTO including Argentina, Bolivia, Burkina Faso, China, Costa Rica, Cuba, Ecuador, Egypt, Indonesia, Israel, Nigeria, Peru, Pakistan, South Africa, Thailand and Venezuela supported Brazil's intervention.

SOCIETY - NETHERLANDS - NIGERIA

Dutch confiscation of HIV drugs for Nigeria threatening

Patent discord embarrasses EU and Clinton foundation

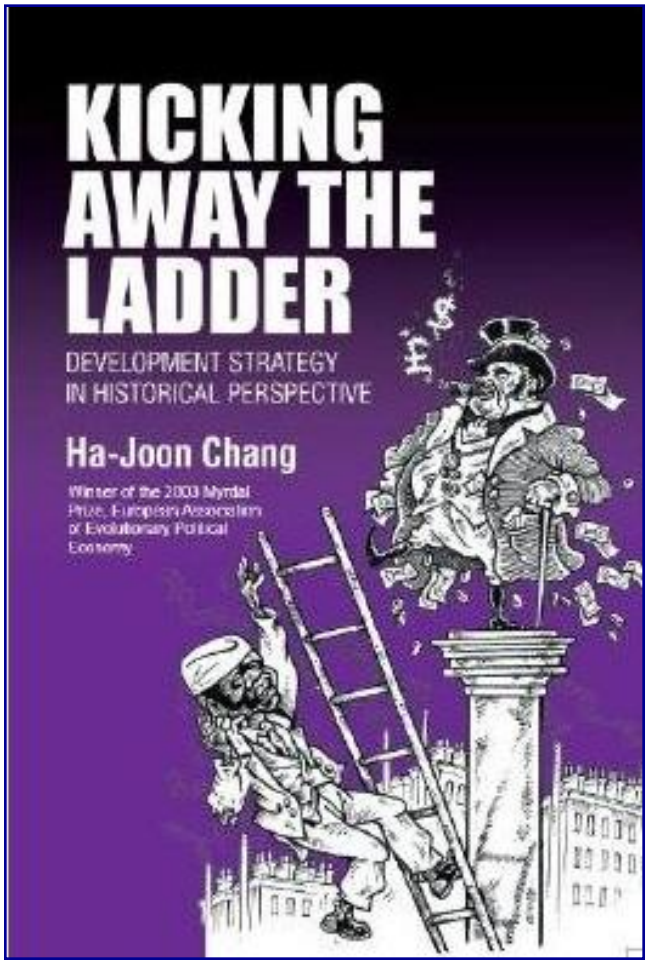
THURSDAY 5 MARCH 2009 / BY ANDREW JACK IN LONDON, FRANCES WILLIAMS IN GENEVA AND MICHAEL STEEN IN AMSTERDAM

Dozens of HIV patients have been placed at risk after the Dutch authorities seized consignments of Indian-made medicines shipped via Schipol airport for distribution to clinics in Nigeria, a multilateral agency on Wednesday said.

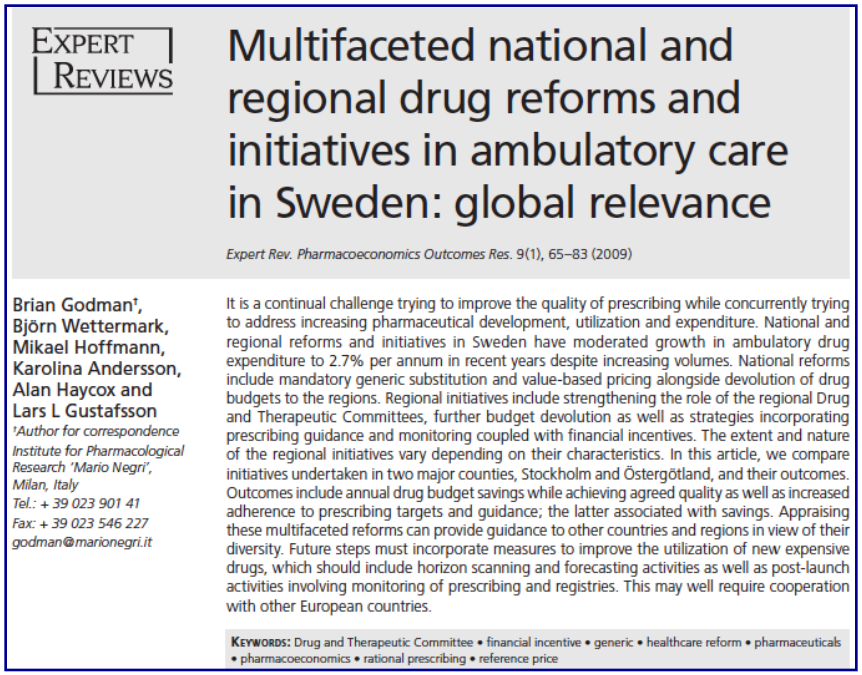
Officials claimed the drugs were counterfeits and violated patent rules but Unitaid, the Geneva-based agency which paid for the medicines, demanded their release and said the claims were "misleading".

The action - the latest seizure of drugs shipped via the Netherlands to developing countries - has highlighted tensions between European Union legislation and special patent rules on medicines agreed by the World Trade Organisation, which on Wednesday offered to intervene in the dispute.

Industrialized countries: Two options ahead



Drug reforms and ambulatory care initiatives in Sweden



EXPERT REVIEWS

Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance

Expert Rev. Pharmacoeconomics Outcomes Res. 9(1), 65–83 (2009)

Brian Godman†, Björn Wettermark, Mikael Hoffmann, Karolina Andersson, Alan Haycox and Lars L Gustafsson

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It is a continual challenge trying to improve the quality of prescribing while concurrently trying to address increasing pharmaceutical development, utilization and expenditure. National and regional reforms and initiatives in Sweden have moderated growth in ambulatory drug expenditure to 2.7% per annum in recent years despite increasing volumes. National reforms include mandatory generic substitution and value-based pricing alongside devolution of drug budgets to the regions. Regional initiatives include strengthening the role of the regional Drug and Therapeutic Committees, further budget devolution as well as strategies incorporating prescribing guidance and monitoring coupled with financial incentives. The extent and nature of the regional initiatives vary depending on their characteristics. In this article, we compare initiatives undertaken in two major counties, Stockholm and Östergötland, and their outcomes. Outcomes include annual drug budget savings while achieving agreed quality as well as increased adherence to prescribing targets and guidance; the latter associated with savings. Appraising these multifaceted reforms can provide guidance to other countries and regions in view of their diversity. Future steps must incorporate measures to improve the utilization of new expensive drugs, which should include horizon scanning and forecasting activities as well as post-launch activities involving monitoring of prescribing and registries. This may well require cooperation with other European countries.

KEYWORDS: Drug and Therapeutic Committee • financial incentive • generic • healthcare reform • pharmaceuticals • pharmacoeconomics • rational prescribing • reference price

Godman B et al (2009) Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. *Expert Review of Pharmacoeconomics & Outcomes Research 9*:65-83

- Three principles
  - Swedish residents should have equal access to high-quality care, irrespective of their status and income
  - Patients in greatest need take precedence
  - Treatment choices should consider both costs and outcomes

2002: Mandatory generic substitution

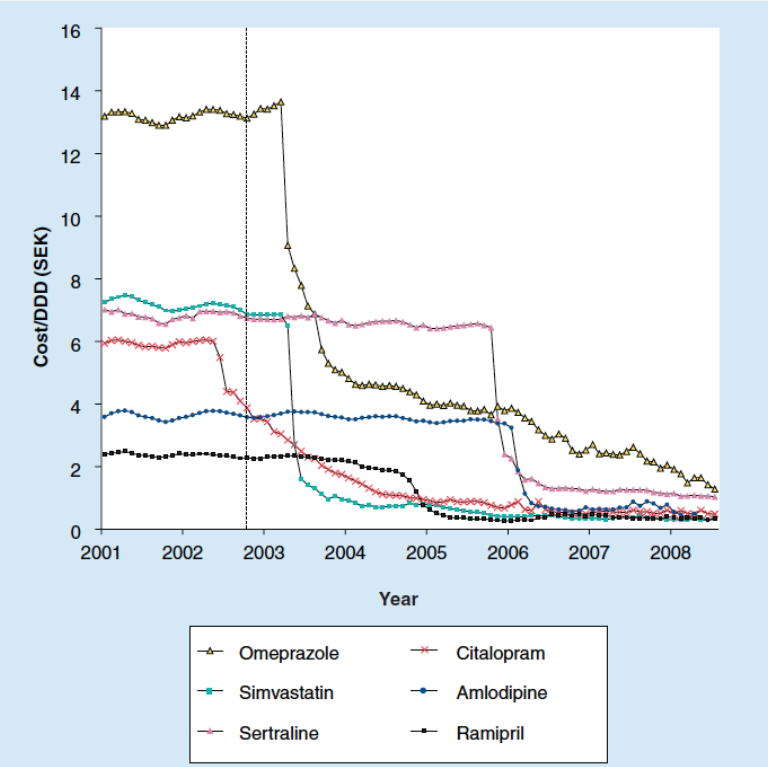
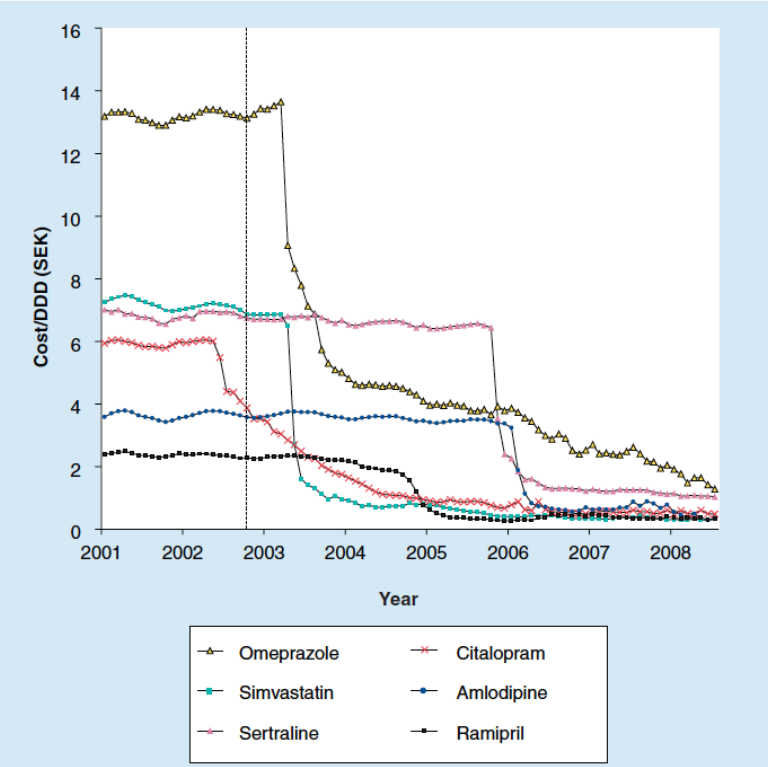


Figure 2. Cost/DDD for six products contained within the top 25 prescribed ambulatory care products in Sweden on a DDD basis where multiple copies became available just before or after 2002.
The dotted line denotes the instigation of mandatory generic substitution.
DDD: Defined daily dose.
Data from [108].

- Only the cheapest substitutable product available in the community pharmacy is reimbursed
- *Medical Products Agency* reviews and decides which products are substitutable

Godman B et al (2009) Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. *Expert Review of Pharmacoeconomics & Outcomes Research 9*:65-83

Limiting pharmaceutical company activity



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The dotted line denotes the instigation of mandatory generic substitution.
DDD: Defined daily dose.
Data from [108].

- National agreements signed between *Swedish Association of Pharmaceutical Industries* and the *Swedish Medical Association* limiting contact with physicians and healthcare professionals
- Funding for attending congresses changed with funding for travel and accommodation divided between councils and companies

Godman B et al (2009) Multifaceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. *Expert Review of Pharmacoeconomics & Outcomes Research 9*:65-83

Factors influencing pharmaceutical expenditure (Godman et al, 2009)

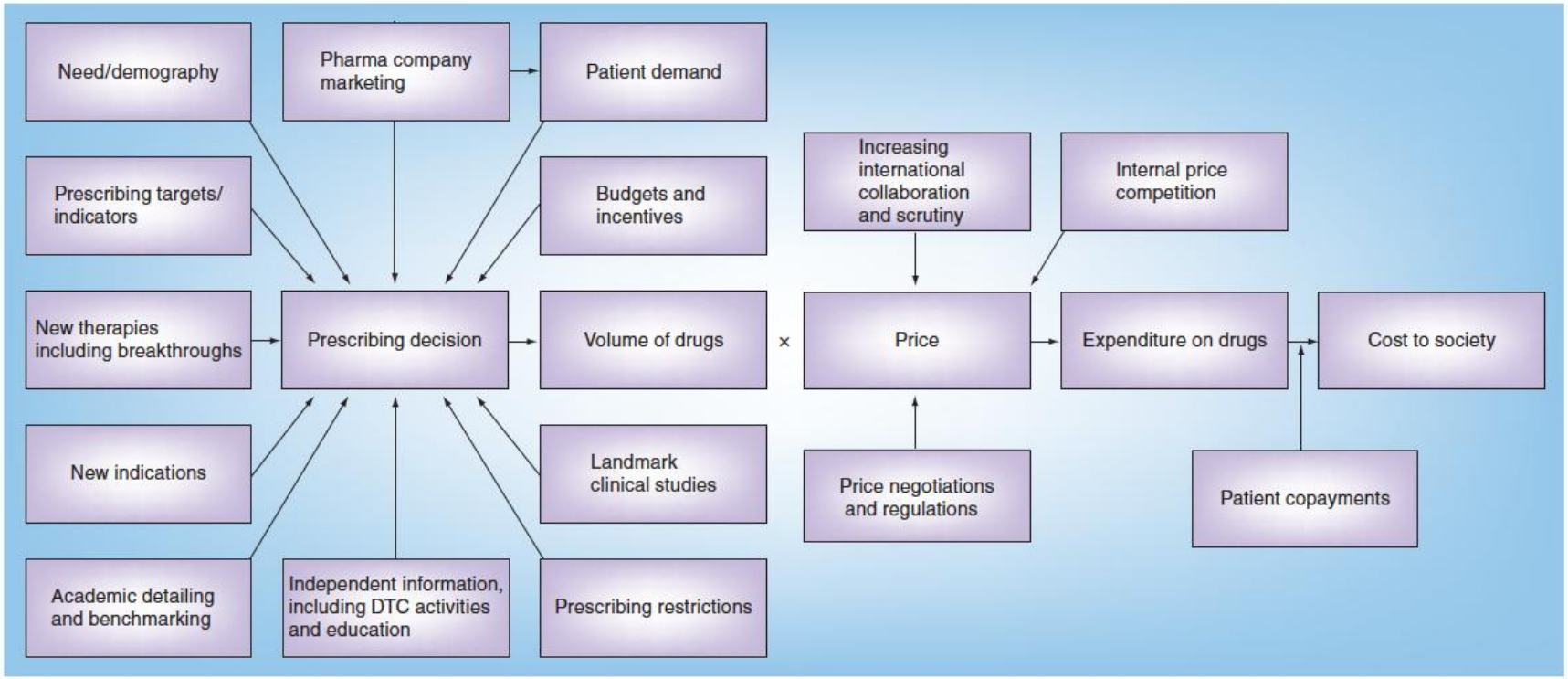

Figure 1. Factors influencing pharmaceutical expenditure.
Data from [21].

Godman B, Wettermark B, Hoffmann M, Andersson K, Haycox A, Gustafsson LL (2009) Multi-faceted national and regional drug reforms and initiatives in ambulatory care in Sweden: global relevance. *Expert Review of Pharmacoeconomics & Outcomes Research,* **2009***, 9*, 65-83

Intellectual property rights and innovation in developing countries

IP highly protected

IP not protected

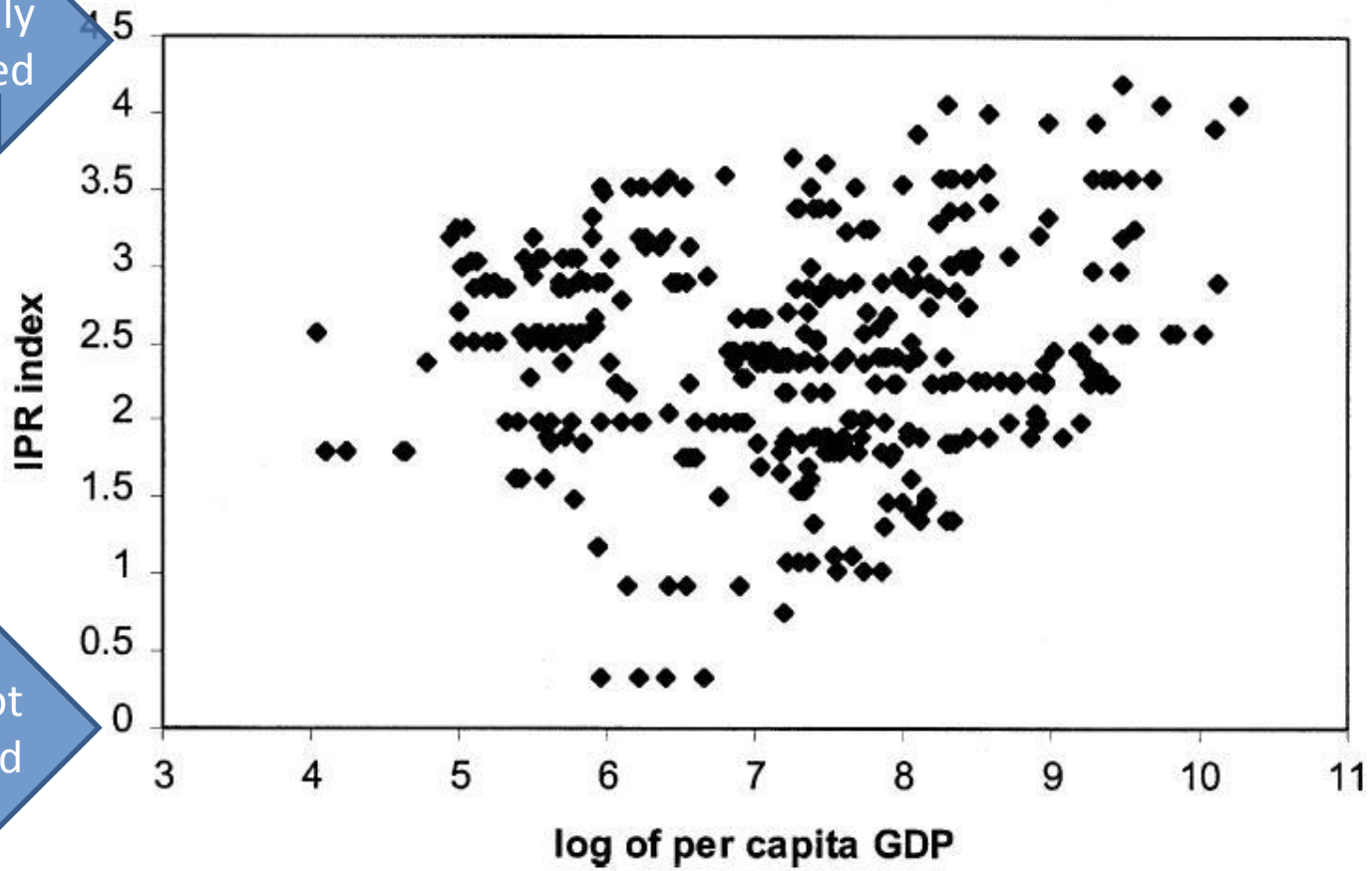

Fig. 2. A scatter plot of the relationship between IPRs and per capita GDP.

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

Intellectual property rights and innovation in developing countries

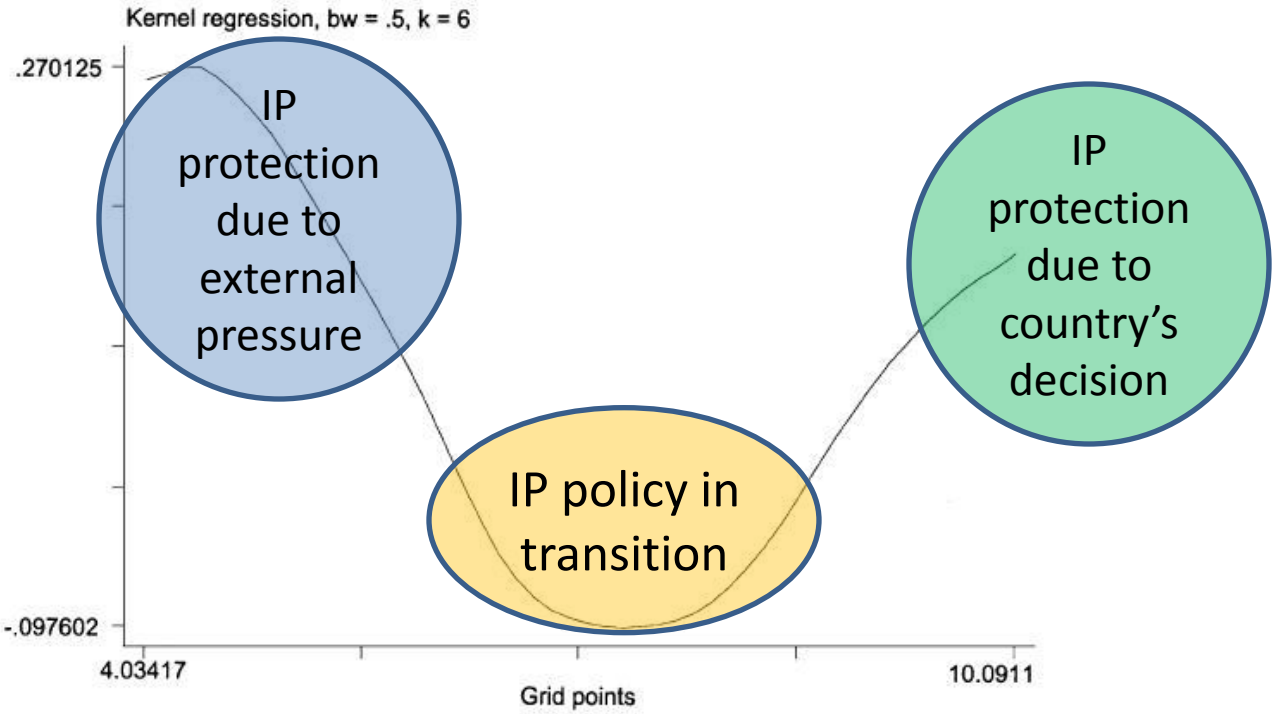

Fig. 3. Semiparametric estimates of the effect of GDP per capita on IPRs.

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

Brazil's policy on intellectual property: opinion of a multinational CEO

Mônica Scaramuzzo, de São Paulo

Novartis define fábrica de US$ 500 mi

Companhia suíça produzirá vacinas em PE, primeira unidade na América Latina. O presidente da Novartis no Brasil, Alexander Triebnigg, disse que a estratégia é oferecer um completo portfólio

Source: *Valor Econômico*, August 26, 2010

- "A decisão de investir no Brasil reflete a estabilidade e previsibilidade política e jurídica do país, ***a existência de forte lei de propriedade intelectual***, sólidas políticas de saúde na área de prevenção de doenças com um programa de imunização reconhecido como um dos melhores do mundo, além de uma agência reguladora pré-qualificada pela Organização Mundial de Saúde (OMS) para suporte a planos de exportação"
- *"The decision to invest in Brazil reflects the stability and the legal and political predictability of the country, **the existence of a strong law protecting intellectual property**, solid health policies on disease prevention based on an immunization program recognized as one of the best in the world, in addition to a WHO pre-qualified regulatory agency to support export plans"*

http://www.cdtsfiocruz-english.blogspot.com

Thank you

Muito obrigado

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Ministério da Saúde

FIOCRUZ

Fundação Oswaldo Cruz

inct-idn

national institute of science and technology of innovation in neglected diseases