



DNDi

Drugs for Neglected Diseases *initiative*

Investing in the Development & Conservation of New Antibiotic Treatments: DNDi's Engagement

Origins of DNDi

1999

- First meeting to describe the lack of R&D for neglected diseases
- MSF commits the Nobel Peace Prize money to the DND Working Group
- JAMA article: 'Access to essential drugs in poor countries - A Lost Battle?'

July 2003

- Creation of DNDi
- Founding partners:
 - *Institut Pasteur, France*
 - *Indian Council of Medical Research, India*
 - *Kenya Medical research Institute, Kenya*
 - *Médecins Sans Frontières*
 - *Ministry of Health, Malaysia*
 - *Oswaldo Cruz Foundation/Fiocruz, Brazil*
 - *WHO –TDR (Special Programme for Research and Training in Tropical Diseases) as a permanent observer*



AMR = In turn, DNDi is ready for history to repeat itself based on what we have learned.



Address Immediate Patient Needs & Deliver Innovative Medicines: Short- and Long-term

*New chemical entities
(NCEs)*

*New formulations
New indications for
existing drugs*

*Completing
registration dossier
Geographical
extension*

**Long-
term projects**

**Medium-
term projects**

**Short-term
projects**



Research



Translation



Development



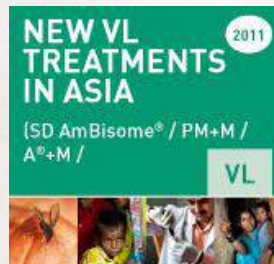
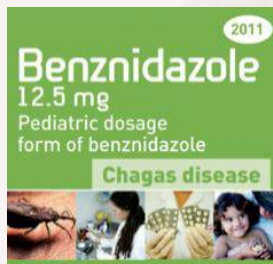
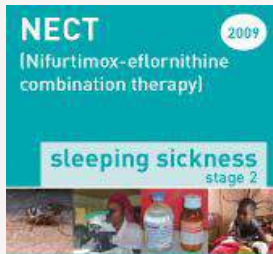
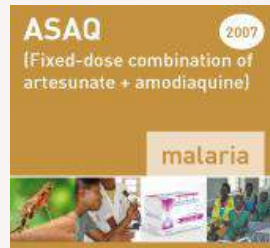
Implementation

**> 5
years**

**3-5
years**

**1-2
years**

In a decade of R&D, 6 new treatments delivered

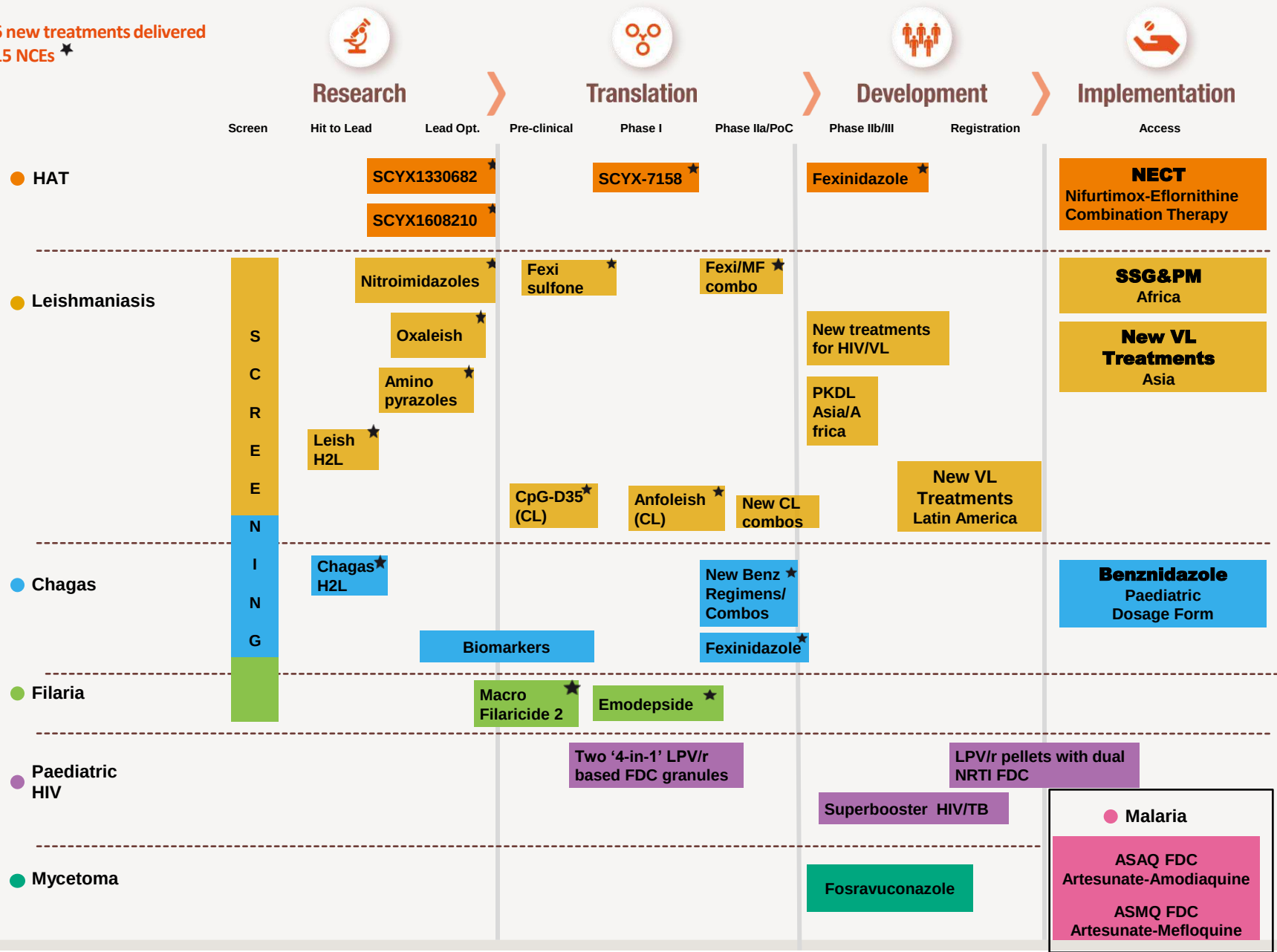


- ✓ Easy to use
- ✓ Affordable
- ✓ Field-adapted
- ✓ Non-patented

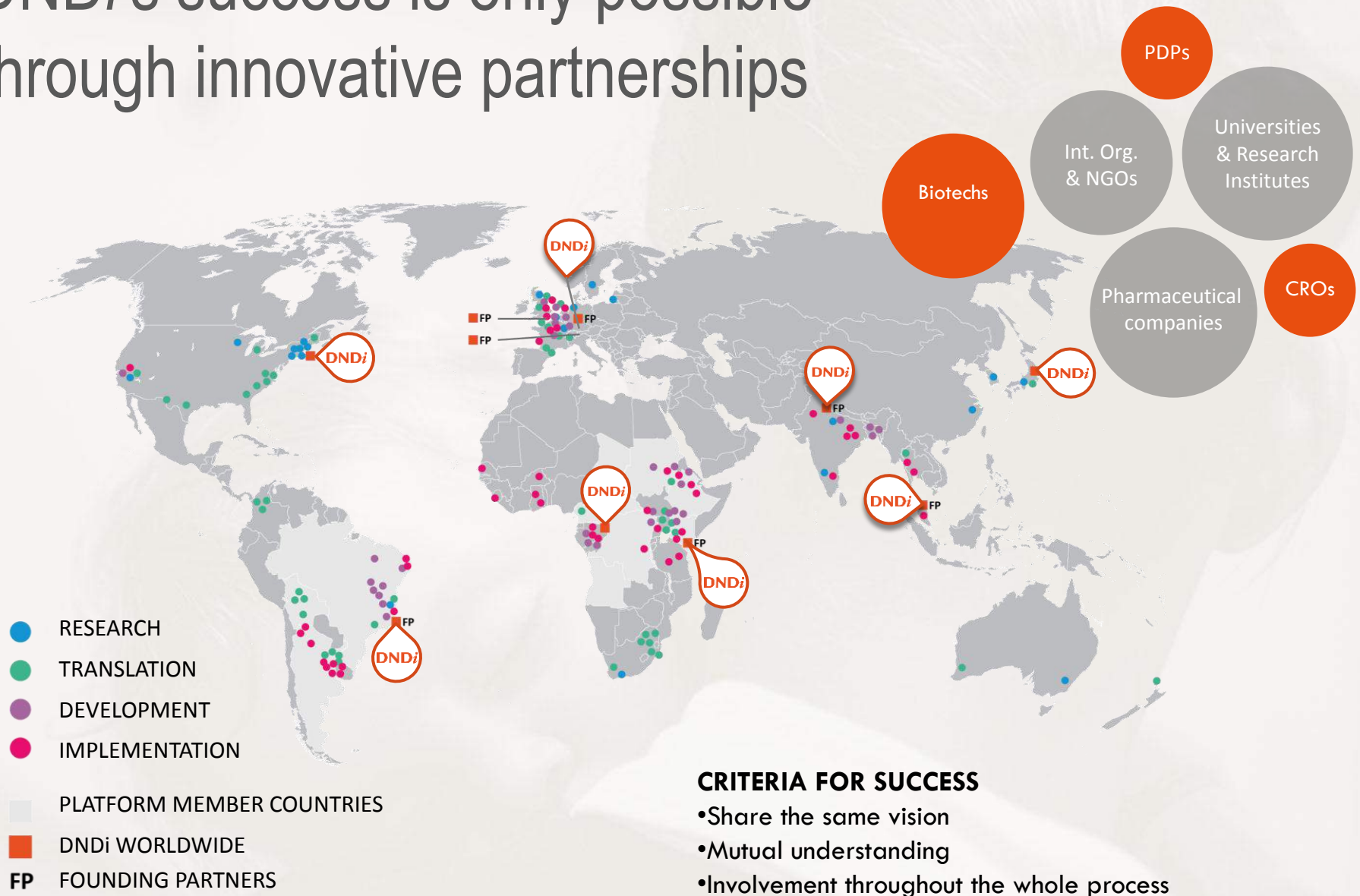
- **30 projects, 6 diseases areas**
- **15 entirely new chemical entities (NCEs)**
- **Over 130 partnerships**, most in endemic countries
- **150 staff**, half in endemic countries & 600 people working on DNDi projects
- **Over EUR 350 million** raised equally from public and private sources
- **3 regional disease-specific clinical trial platforms** and 2 technology transfers

DNDi Portfolio: A mix of existing drugs & NCEs

6 new treatments delivered
15 NCEs ★



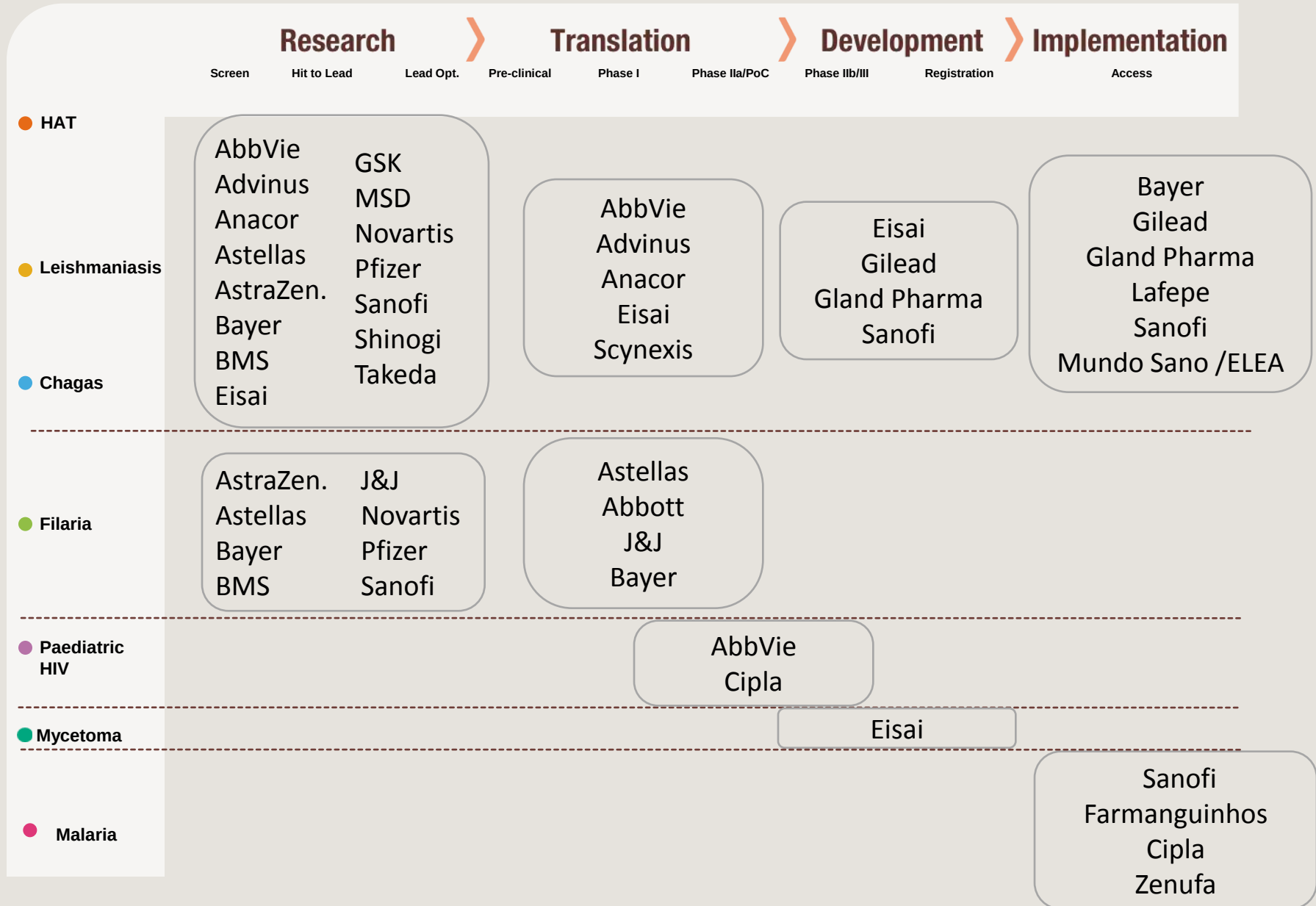
DNDi's success is only possible through innovative partnerships



CRITERIA FOR SUCCESS

- Share the same vision
- Mutual understanding
- Involvement throughout the whole process

Industrial Partnerships at All Stages of Development

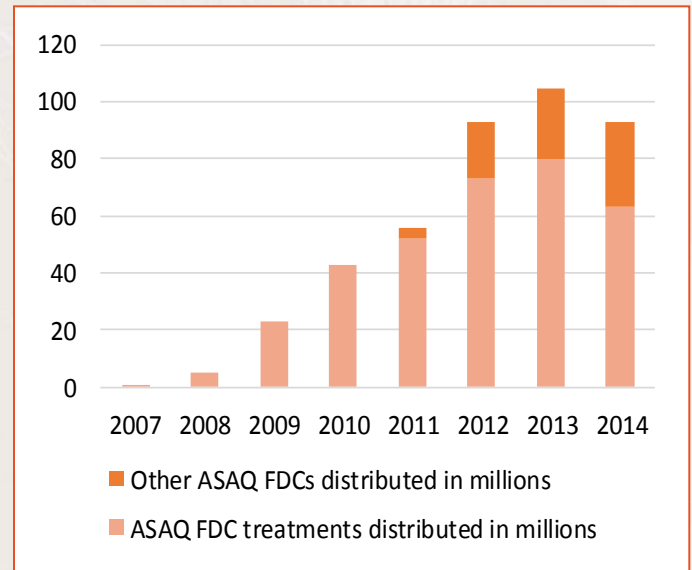


Combating malaria resistance: 2002 WHO recommendations

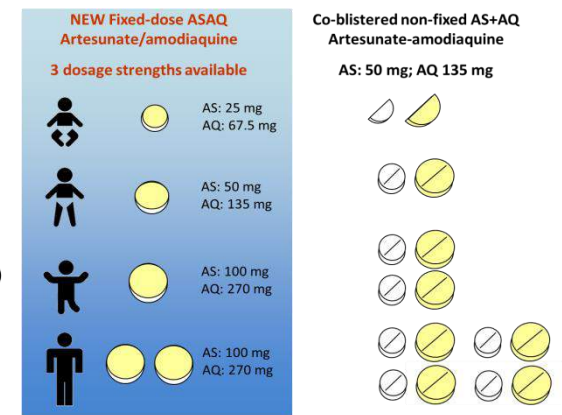
ASAQ FDC: > 400 Million Treatments Distributed

- Pre-qualified by WHO in 2008
- <1 USD for adults, < 0.5 cents for children
- Easy-to-use, non-patented
- Registered: 30 African countries, India, Ecuador, Colombia
- First Risk Management Plan with MMV and Sanofi
- Transfer of technology to Zenufa (Tanzania)

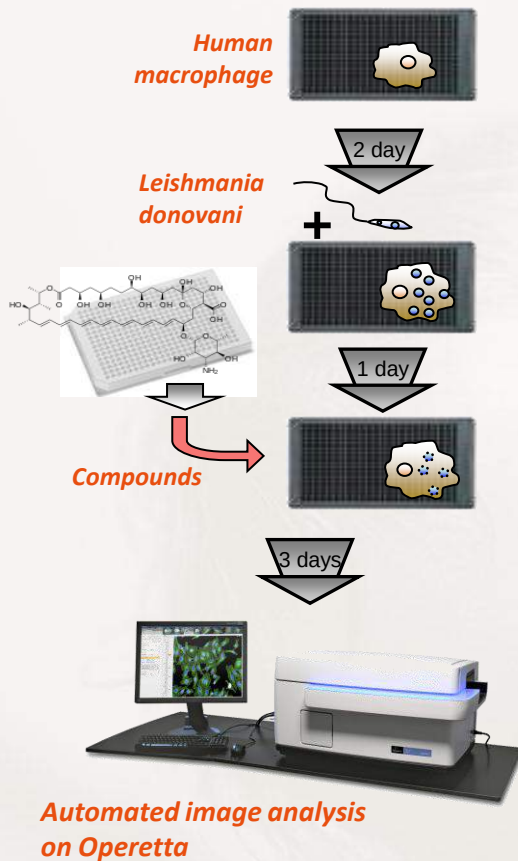
In partnership
with Sanofi



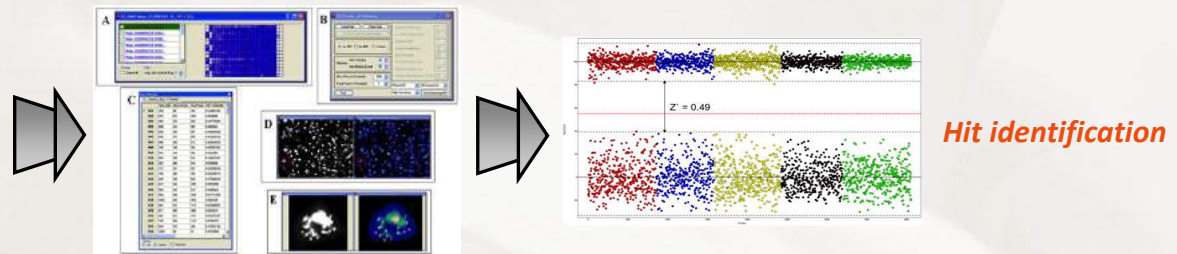
Simplified 3-Day Dose Regimen of ASAQ



Creating large-volume drug screening capacity: Institut Pasteur Korea



- Access to screening capacity (HCS technology) for VL and Chagas since 2008
- > 1.5 Mio compounds screened to date in collaboration with multiple Pharma partnerships
- e.g. for VL and Chagas: **20,000 compounds/month**
- Pasteur expertise in infectious diseases
- Technology developed as a public good



Exploring more open, collaborative drug discovery models

- A shift from bilateral to **multilateral collaboration**
- Companies working together on a **shared project**
- Ownership and intellectual property rules agreed in advance
- Three year countdown to launch in April 20015
- Project now underway and new companies ready to join



Partnering and research capacity building with MoHs and National Control Programmes

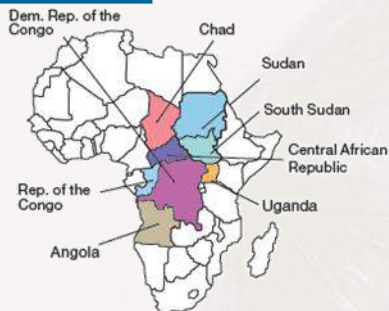
VL



Major Role of Regional Disease Platforms:

- Strengthening local capacities
- Conducting clinical trials (Phase II/III studies)
- Facilitating registration
- Accelerating implementation of new treatments (Phase IV & pharmacovigilance studies)
- **Defining patients' needs and target product profile (TPP)**

HAT



CHAGAS



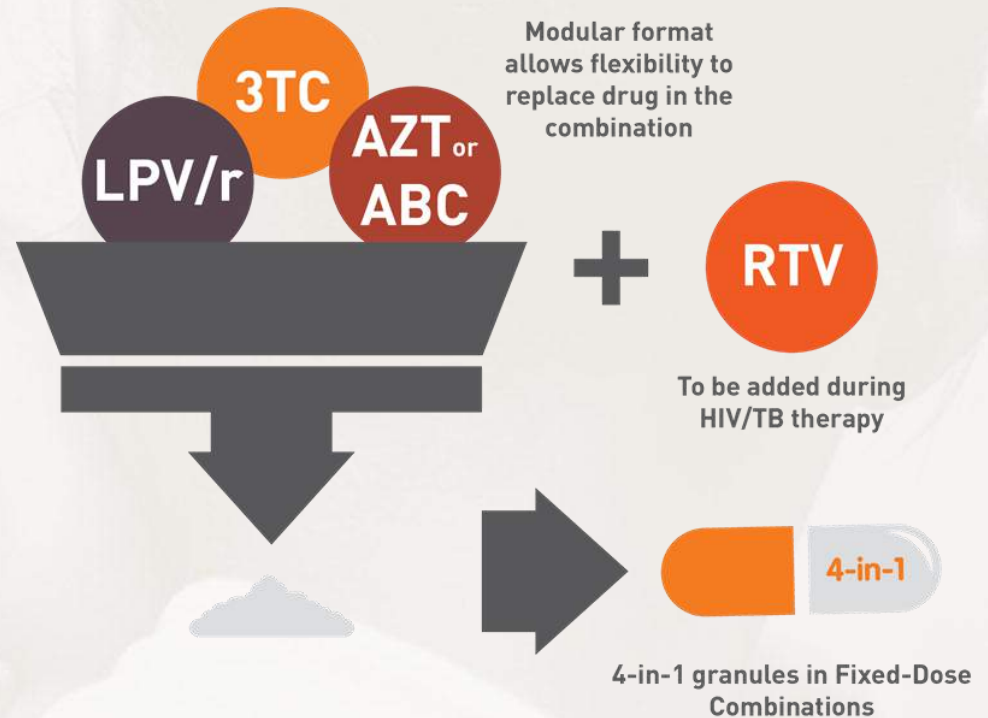
Countries highlighted on the map represent Chagas disease-endemic Latin American countries with platform members. Many other CCRRP members not shown on this map but are listed below.

For each disease, a Target Product Profile to guide all decisions (example of paediatric HIV)

IDEAL CHARACTERISTICS (TPP)

- 4 ARVs in one
- Simple to open and use with water, milk, food
- Good taste
- No fridge needed
- Suitable for infants (<2 months - 3 years)
- TB-treatment compatible
- Affordable for governments

PROCESS



Our new Business Plan 2015-2023:

A dynamic approach to address patient needs

Pipeline focus can quickly be adapted to:

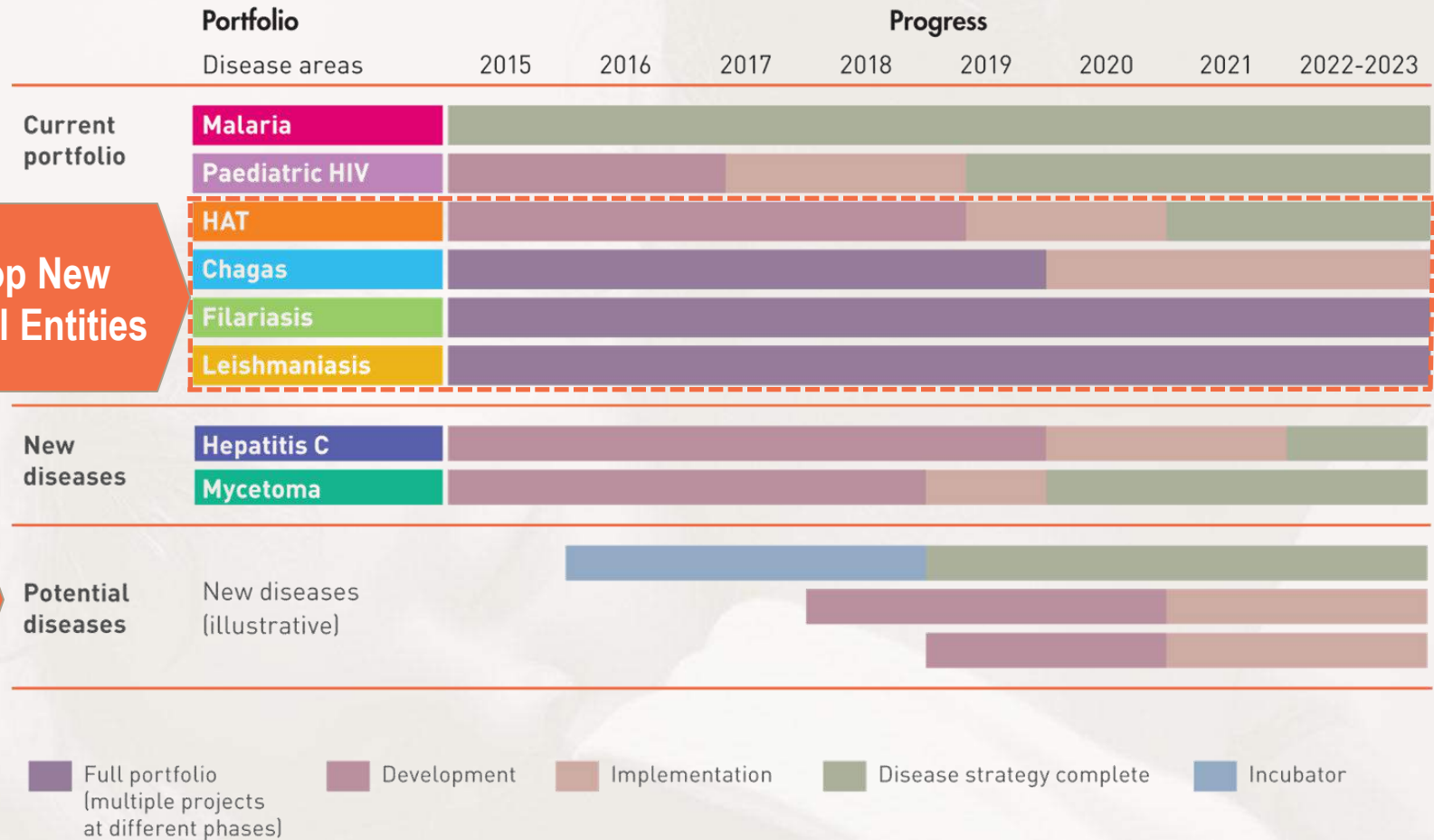
- stay aligned with changes in the environment
- rapidly respond to urgent patient needs
- address specific regional needs

*New
Opportunities*

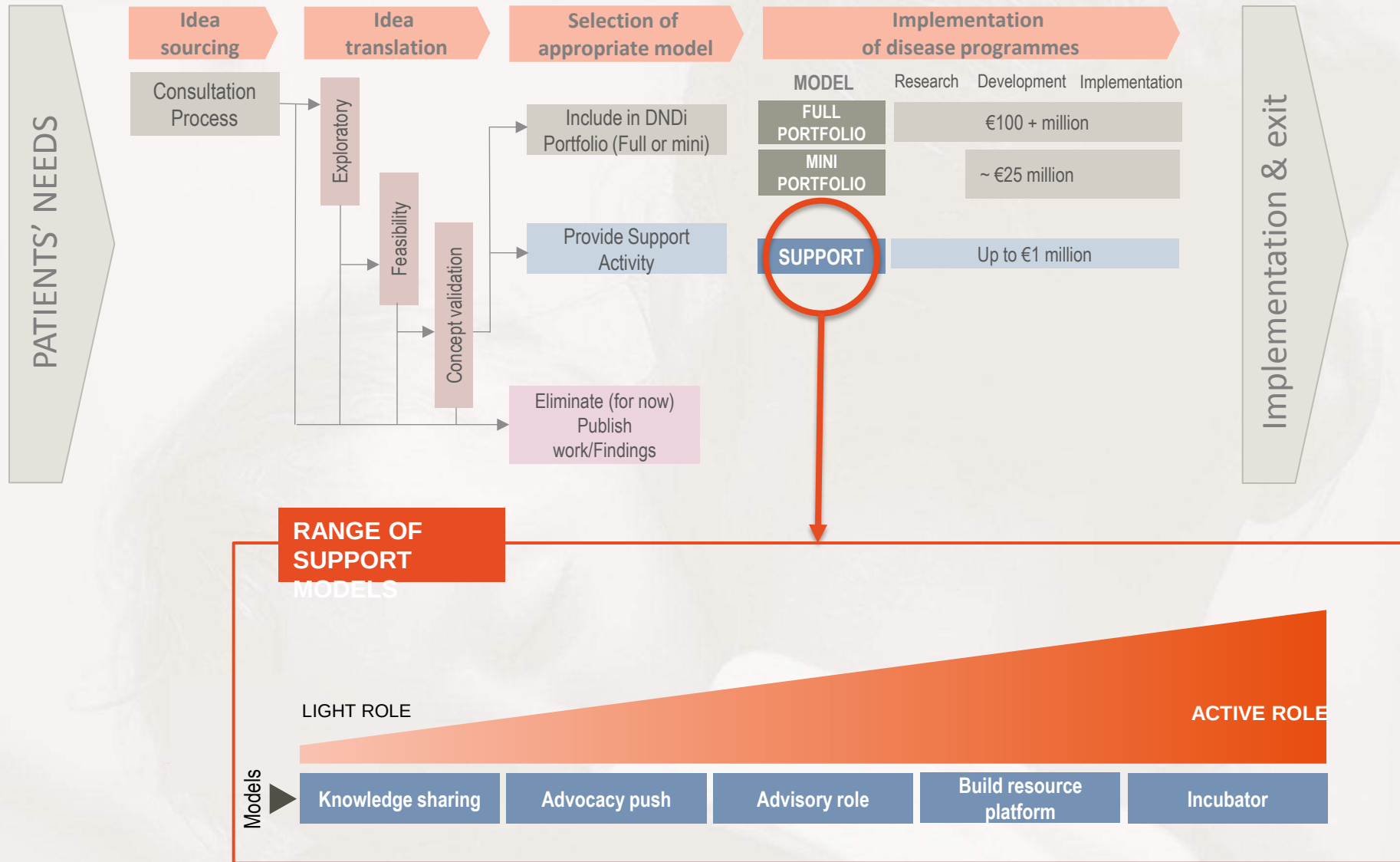
Disease Portfolio

*Completion
& exit*

Most neglected diseases remain at the core, with new diseases taken on progressively



How we will do it... operationally



Next steps for DNDi to incubate the facility

- Board decision in December 2015: go/no go
- Need for securing political support and stakeholder input
- We are **prepared to incubate** the Facility, in the same way MSF incubated DNDi, and WHO/TDR incubated FIND and MMV

THANK YOU!



Investing in the Development & Conservation of New Antibiotic Treatments



Global Antibiotic Research & Development Facility

Vision and Strategy

Vision

In cooperation with the public and private sectors:

- develop new antibiotic treatments addressing AMR
- promote their responsible use for optimal conservation
- while ensuring equitable access for all

by setting up a not-for-profit product development partnership that will focus on global health needs, while ensuring any new product is adapted to resource-limited settings.

The context

- Lack of sufficient **investment and incentives** for the development of antibiotic treatments
- WHA GAP requests WHO Secretariat to work on the creation of **new partnership(s) to address R&D gap**
- Many initiatives have been launched, but overall remain insufficient: **complementarity is key**
- Market-driven approaches are not structured to address **responsible use** and some of the unmet needs

The Role of WHO

- Take part in the set-up of the new partnership
- **Report on the antibiotic pipeline** to feed into the Global Health R&D Observatory
- Provide input on **priority setting**, target product profiles and overall direction
- Facilitate coordination with other initiatives, e.g. G7 global network meeting of researchers and experts in 2016/17
- Develop and pilot conservation approaches
- Develop options for a global framework for development and conservation (WHA68.7)



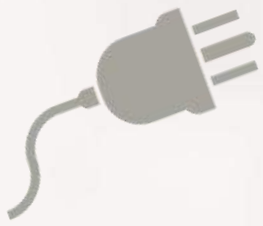
Existing & upcoming AMR R&D initiatives

	WHO-DNDi proposal	Innovative Medicines Initiative (IMI)	Proposals by Jim O’ Neill Review on AMR:		EU Joint Programming AMR	US Biomedical Advanced R&D Authority	EU FP 7 & HORIZON 2020
			Innovation Fund	Market entry rewards			
Task	Developer	Developer/ Funder	Funder	Funder	Funder	Funder	Funder
Main Focus	Product develop.	AMR basic research Prod. Develop.	Early stage research & early stages of product develop.	Product development (market entry rewards)	AMR Basic & preclinical research product develop.	Product develop.	AMR Basic research Product develop.
Specific public health needs	Global health needs & suitability for resource poor settings	Based on WHO’s priority medicines report	Yes	Rewards linked with unmet global needs	JPI AMR Strategic Research Agenda	Unmet medical need in US	Medical needs in Europe & globally, incl. LMIC
Products submitted to conservation strategies?	Yes	No	--	Yes, rewards linked with stewardship	No	Possible for ‘pull incentives’	--
Target product profiles?	Yes	No	No	Yes	No	Yes	No
Possibility to link with other initiatives?	Yes	Yes	Yes	Yes	Yes	Yes	If eligible under EU programme



Guiding Principles

- 1 Antibiotic development should be financed partly through a **global funding mechanism** and should experiment new models for conservation and access
- 2 Sustainable **investment** should be coordinated at country and international levels
- 3 R&D should focus on the **significant bacterial infections** with an emphasis on global needs
- 4 **Scientific relevance** shall guide choices
- 5 New antibiotics must be **affordable** for all and subject to a **global conservation** agenda



Three-Pronged Approach



1 Research and Development

- Conduct antibacterial research both with academia and the private sector, including paradigm-shifting approaches for antibiotic treatments.
- Support rapid and (near) point-of-care diagnostics as an essential component of the product development strategy.

2 Conservation

- Implement and test new incentive models, including de-linkage of R&D cost from price of product, to support responsible use initiatives.

3 Access

- Promote equitable, responsible access: ensuring access to all in need, while minimizing unnecessary use.



Short-Term Goals

- 1 Identify needs, gaps, top priorities for development of new antibiotics/antibiotic regimes unaddressed by other actors, ensure complementarity
- 2 Establish partnerships with existing R&D networks
- 3 Launch short-term projects to deliver needed therapeutic solutions (e.g. appropriate paediatric formulations or improved regimens of existing antibiotics)
- 4 In doing so, immediately test existing conservation and access proposals applied to short-term projects.



Long-Term Goals

- 1 Build, with partners, a solid **antibiotic R&D portfolio** to respond to longer-term needs to address AMR
- 2 Support the framework for the effective **conservation** (stewardship) of antibiotics, with WHO and countries
- 3 **Secure funding sources** to sustain continuous pipeline replenishment and test incentive mechanisms

Deliverables and Timelines

Five-Year Plan



Years 1-2

- Set up a core team and working network of public and private partners
- Finalize a business plan and establish budget for a minimum of five years
- Engage additional founding partners and funders for long-term support
- Establish **priority target product profiles** (TPPs)

Years 1-2 continued

- Establish governance, including scientific advisory board and international network of scientific experts
- Set up a independent legal entity
- Identify short- and long-term research projects
- Initiate 1-3 short term projects, for example:
 - improved paediatric formulations (form, dosage, shelf-life)
 - new formulations of existing drugs (appropriate dosage, administration route)
 - combinations of existing drugs to address AMR
 - establish feasibility of innovative projects (e.g. adjuvants', anti-virulence, dormancy breakers)

Years 3-5

- Continue initiated short-term projects and implement new projects
- Implement the business plan, including funding of innovative R&D proposals and of pilot conservation projects
- Secure long-term funding
- Launch long-term projects, for example:
 - combination screening platforms
 - platform for improved formulations;
 - support disruptive scientific approaches (e.g. anti-virulence)

Start-up and launch: no time to waste

Seed funding of 3+ million USD is required for:



- 4-6 FTEs for core team (DNDi to provide 1 FTE and infrastructure)
- raise further funding for new projects
- Set up initial projects

What commitments are needed today?

- Financial and political support – steering role
- Contribution of expertise – working groups
- Partnerships with your ongoing initiatives – complementarity!

Thank you!

Review of possible funding/incentive mechanisms and opportunities

TECHNICAL CONSULTATION JOINTLY HOSTED BY THE
WORLD HEALTH ORGANIZATION AND THE DRUGS FOR
NEGLECTED DISEASES *INITIATIVE*

November 13, 2015

John-Arne Røttingen
Norwegian Institute of Public Health
University of Oslo
Harvard T.H. Chan School of Public Health

Our understanding of the Partnership's Proposed Scope

- Address global public health and specific needs of developing countries, **targeting products that industry will not undertake due to lack of profitability**, for example:
 - Pediatric formulations
 - Combination therapies for Typhoid fever
 - New chemical entity for melioidosis
 - New chemical entity for gonorrhea (for HIV-positive)
- Ensure that **new antibiotics are affordable to all and are subject to a global conservation agenda**
- **NOT** novel antibiotics targeted for high income markets

Recent Challenges

FINANCIAL TIMES

Valeant and other riders of pharma must
belt are

Jonathan Ford

September 24,

Pharm

Andrew War

Share

Outcry o
opinion

There is a role for
global public goods,
especially for
incremental innovation

drugs...If

prescribed separately, the two drugs together would cost no more than \$20 or \$40 a month. By contrast...[the new combination pill]...costs about \$1,500 a month."

Focus on antibiotic innovation



To produce analysis of the global problems of antimicrobial resistance (AMR), and to propose concrete actions to tackle these internationally

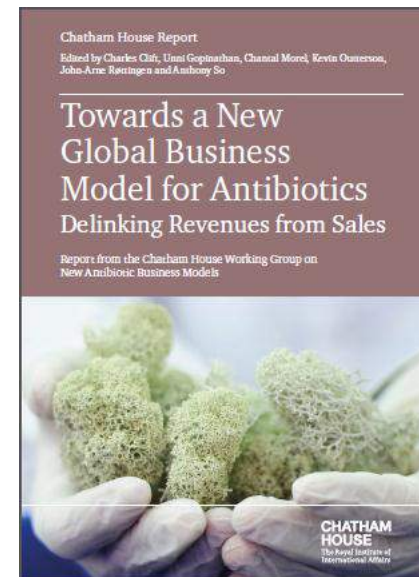


To explore novel economic strategies and reward models both to promote the development of new antibiotics and to bolster appropriate consumption of existing antibiotics

Convergence of principles



- Need for both “push” and “pull” mechanisms
- Delinkage (i.e., revenues delinked from volumes sold) built in
- Access and responsible use are integral considerations for all mechanisms
- Global collaboration and financing necessary



R&D allocation mechanisms

Discovery

Preclinical

Phase I

Phase II

Phase III

Licensure

Push mechanisms

Pull mechanisms

E
X
A
M
P
L
E
S

- Grants
- Milestone prizes
- Subsidies
- Tax breaks
- Open knowledge innovation

- Public-Private Partnerships
- Advance Market Commitment (AMC)
- Milestone and end prizes
- Volume guarantees

Trends in antibiotic consumption

“Two trends are contributing to a global scale-up in antibiotic consumption. First, **rising incomes are increasing access to antibiotics**. That is saving lives but also increasing use—both appropriate and inappropriate—which in turn is driving resistance. Second, the **increased demand for animal protein** and resulting intensification of food animal production is leading to greater use of antibiotics in agriculture, again driving resistance.”

CDDEP's The State of the World's Antibiotics Report, 2015

New paradigm in financing

- Existing health R&D financing mechanisms are either:
 - Financed through development aid
 - Focus on stimulating national/regional research with no agreed priority-setting and no linkages to responsible use and access
- Yet for this model:
 - Greatest need in middle-income countries
 - Advantages for all countries regardless of economic status (e.g., combination therapies, pediatric formulations, etc.)
 - Advantages across diseases (e.g., diagnostics for fever)

Current financing environment

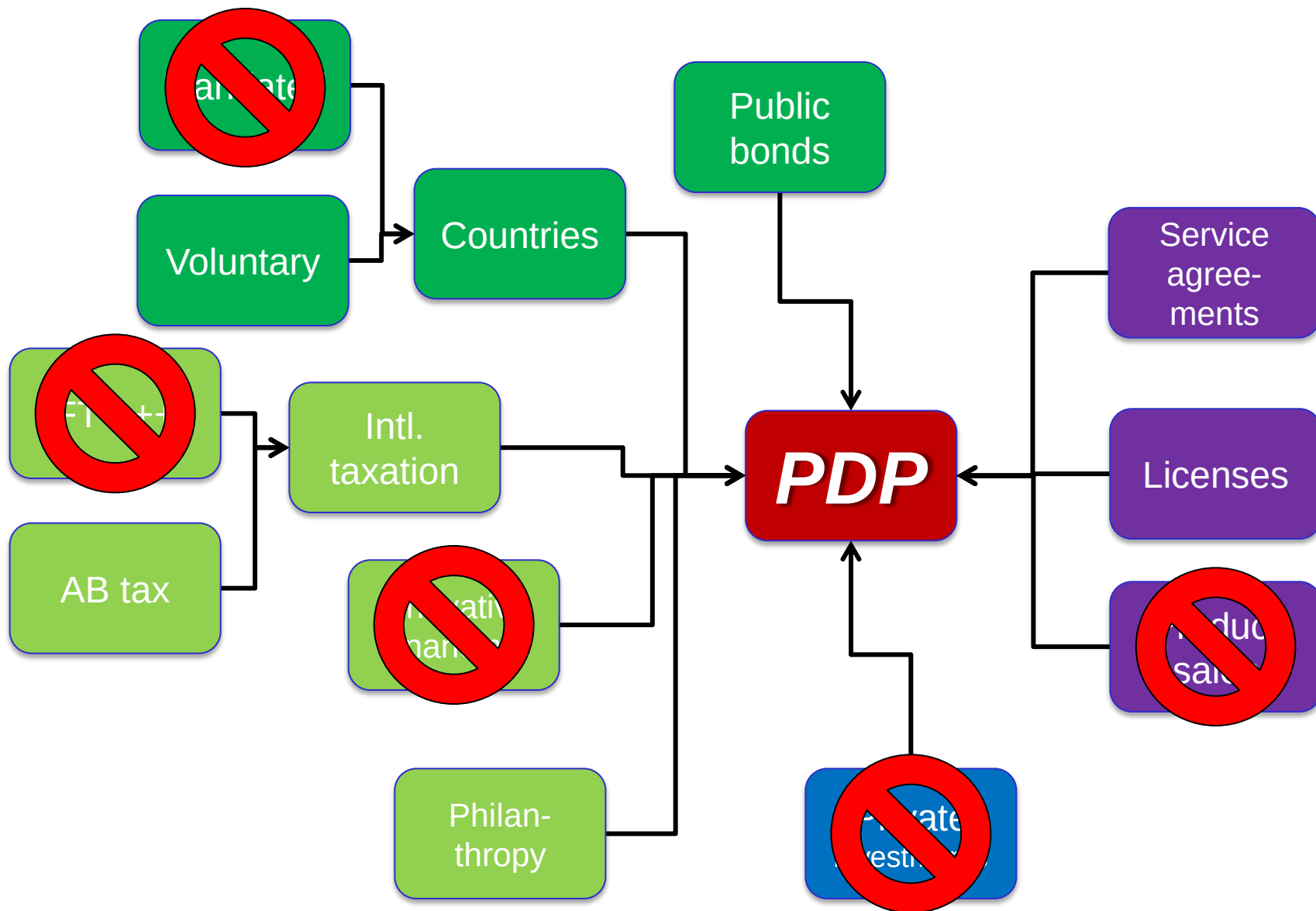
- Need to build on existing mechanisms and organizations
- DNDi has 10+ years experience developing drugs for neglected diseases.
- Landscape already contains BARDA, JPIAMR, IMI, UK-China Fund, Wellcome Trust
- None focus specifically on the needs of LMICs, where resistance is growing fastest.

Financing – raising funds



Potential financing

Payer	Mandatory	Voluntary
Individuals	Tax • Direct • Indirect – Sales taxes, “Sin taxes”, Antibiotic consumption, Airline tax	Gifts, donations, voluntary levies on tickets, phone bills etc.
Companies	Corporate tax Financial transaction tax	• Investment based upon expected ROI • Corporate social responsibility
Countries	Legally binding agreements Membership fees	Political allocation



Potential financing sources

Base financing:

- Voluntary governmental and/or foundation financed

Investor-based financing:

- Social impact bonds based upon revenues from patented technology contracts in high and middle income countries
- Licensing revenues from private companies (with stipulations regarding responsible use and access)
- Loans from EIB's IDFF

Grant-based research funding:

- Apply for funds from BARDA, JPIAMR, IMI, UK-China Fund, UNITAID, Wellcome Trust



Investing in the development of new antibiotics and their conservation: **A proposal for a global antibiotic research and development facility**

Dr Manica Balasegaram, Executive Director
MSF Access Campaign, November 2015

MSF and AMR

MSF can no longer safely assume the efficacy of simple antibiotics

- Bacterial infections one of the most common presentations in MSF projects
 - Including lethal invasive bacteria infections (IBI) such as bacteremia, meningitis, pneumonia and dysentery
- Risk of ineffective initial antibiotic treatment higher in MSF set-ups
 - Patients present later, with advanced disease, fewer safety nets for those inappropriately managed
- Antibiotic resistance (ABR) has emerged in most contexts where MSF works
- ABR is growing in severity; all regions of the world are affected to varying extents
 - High, middle and low IC countries affected
 - Many of the gaps in ABR surveillance exist where MSF operates
 - This in turn makes it difficult to understand true needs and gaps



Key problems

- Field surveillance
- Diagnostics
 - Especially to promote rationale use
- Drugs
 - Better formulations, combinations, regimes and new treatments/protocols where there is resistance



Key problems: diagnostic tools

In the field settings MSF cannot diagnoses bacterial infections with a high degree of sensitivity or specificity



Not enough national data exists to guide empirical choices

Lack of tools to distinguish bacterial infections from mycobacteria and non bacterial pathogens (eg viruses, parasites)

Cannot distinguish infections caused by sensitive / ABR bacteria

Microbiological capacity very limited in most MSF contexts (eg gram stain or blood culture not available)

Key problems: drugs

Marked increased in broad-spectrum antibiotics use:

- 3rd generation cephalosporins: ceftriaxone
- Fluroquinolones: ciprofloxacin
- β -Lactam/ β -lactamase inhibitors:
amoxicillin-clavulanate

This strategy has major costs:

- May drive further ABR
 - Most children leaving MSF ITFC are colonized with ESBL-producing gram negative bacteria (Niger, 2011)
- Unsustainable “arms race”
 - Bacteria evolve new resistance mechanisms
 - Highly ABR strains emerging in L&MICs eg Enterobacteriaceae strains expressing NDM-1
 - Few antibiotics in the development pipeline



However, improving access & patient care is our priority!

Recent MSF field experience

CNS infection study, Mbarara, Uganda (2011)

- S pneumo with intermediate sensitivity to PCN, resistant to cotrimoxazole
- H influenzae resistant to amoxicillin, chloramphenicol
- ESBL E coli and Kleb pneumo
- Salmonella typhi resistant to cipro



Diarrhea, Niamey & Maradi, Niger (2009)

ESBL Salmonella documented
1/3 bacteria were resistant to all antibiotics available in Niger

What is needed?

- Strong global health perspective: defined priorities, TPPs etc
- Monitoring & surveillance
- Diagnostics (new tools, improved lab capacity)
- Updated guidelines and policies (international and national)
- Education and local capacity
- Regulation
- Rational use linked with access strategies
- Coordinated procurement and supply
- Appropriate uptake, compliance
- Clinical research capacity and platforms
- Alternative incentives to promote innovation and conservation



What is needed?

➤ Issues for the facility

- Strong global health perspective: defined priorities, TPPs etc
- Monitoring & surveillance
- Diagnostics (new tools, improved lab capacity)
- Updated guidelines and policies (international and national)
- Education and local capacity
- Regulation
- Rational use linked with access strategies
- Coordinated procurement and supply
- Appropriate uptake, compliance
- Clinical research capacity and platforms
- Alternative incentives to promote innovation and conservation



The facility: scientific added value

- R&D that will not be taken by other actors; improved formulations, combinations and updated dosing schedules – DNDi already has a track record
- Focus on specific diseases, especially where trials needed in LMIC context
- Potential focus on upstream ideas where risk taking can be encouraged
- PDPs (eg DNDi) have significant space to work on research, policy and early implementation in tandem with others including WHO and multilaterals (GF, UNITAID)



The facility: conservation and access

- Critical to have strong focus on LMIC and most vulnerable population access
- Diagnostics key in improving rationale use
 - improved integrated approach of fever management can significantly aid conservation
- Key role of essential medicines list (to ensure best policy) and WHO PQ (to promote uptake of best quality products)
- Facility could play similar role to The GDF for TB drugs (eg linking drug demand to supply and monitoring)
- Specific country level strategies need to be developed through further consultations
- Traditional incentive systems do not work: conservation & access promoted by different model based on de-linkage. Plenty of proposals that are ready for implementation!

The facility: set up

Real potential to develop a facility that will be global health focussed

Governance is key:

- Mandate and involvement of WHO but outside formal WHO structure (for flexibility)
- DNDi board/SAC serving as starting models (and allows time to develop the final governance structure)
- Governance not just a round table of donors
 - Independence must be ensured
 - Needs to ensure stays true to mission; takes and mitigates risks
 - Needs to provide required strategic technical and political input
 - Developing country presence is important
 - Technical expertise from a wide range of actors

Financing:

- Long term and sustainable
- Country commitments & contributions



Challenges for the facility

- Good understanding of needs and gaps for developing countries
 - Implementation of all aspects of GAP is therefore important to ultimately drive R&D agenda
- Political support and member state buy-in
 - Willingness of global health community and member states to implement something different to go beyond just talking about “alternative business models”
 - Sustainable, long term financing (including from developing countries)
- Identifying and implementing conservation strategies
 - Link with WHO critical
 - Important that WHO also has member state’s support to play a key role in AMR
- Creation of an open source and knowledge innovation model



www.msfacecess.org

Global Action Plan on Antimicrobial Resistance

Technical Consultation 13 November 2015

Global Antibiotic Research & Development Facility

Dr Marc Sprenger

Director Antimicrobial Resistance Secretariat



**World Health
Organization**

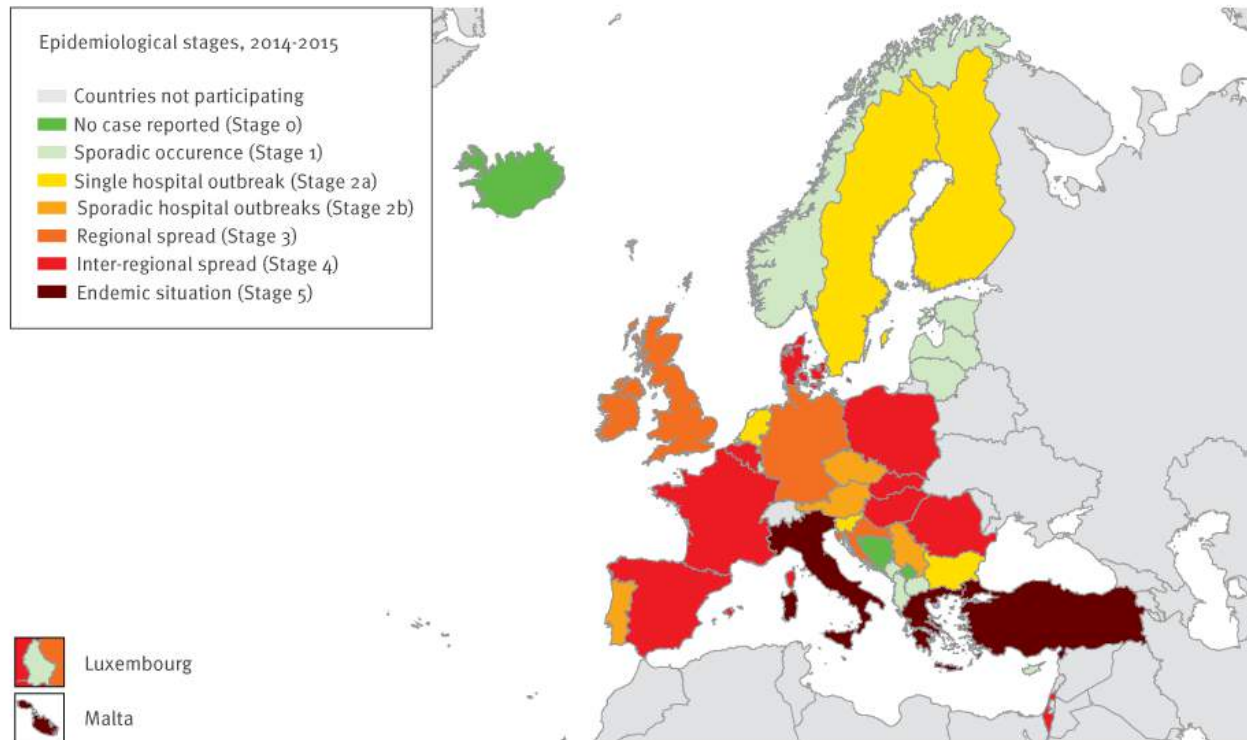
When are we entering the post-antibiotic era?

For some diseases we have already entered!

Fatal pneumonia because antibiotics are not working (*K. pneumoniae*)

Fatal infection with *Neisseria gonorrhoeae*

CPE in EU May 2015 (Albiger et al, Eurosurveillance 12Nov2015)
13/38 countries reported inter-regional spread of or an endemic situation for CPE



What is the cost of not taking action?

By 2050, AMR could lead to

- 10 million deaths every year
- reduction of 2%-3.5% in GDP globally

AMR Review

Between now and 2050, the world can expect to lose US\$ 600 to US\$ 100 trillion worth of economic output

Global Action Plan on Antimicrobial Resistance

One year in development

World Health Assembly, May 2014

Requests the Director General to develop a global plan

WHO leads development of the plan, May to Dec 2014

With advice from experts, Member States, forums and web consultations

WHO Executive Board, Jan 2015

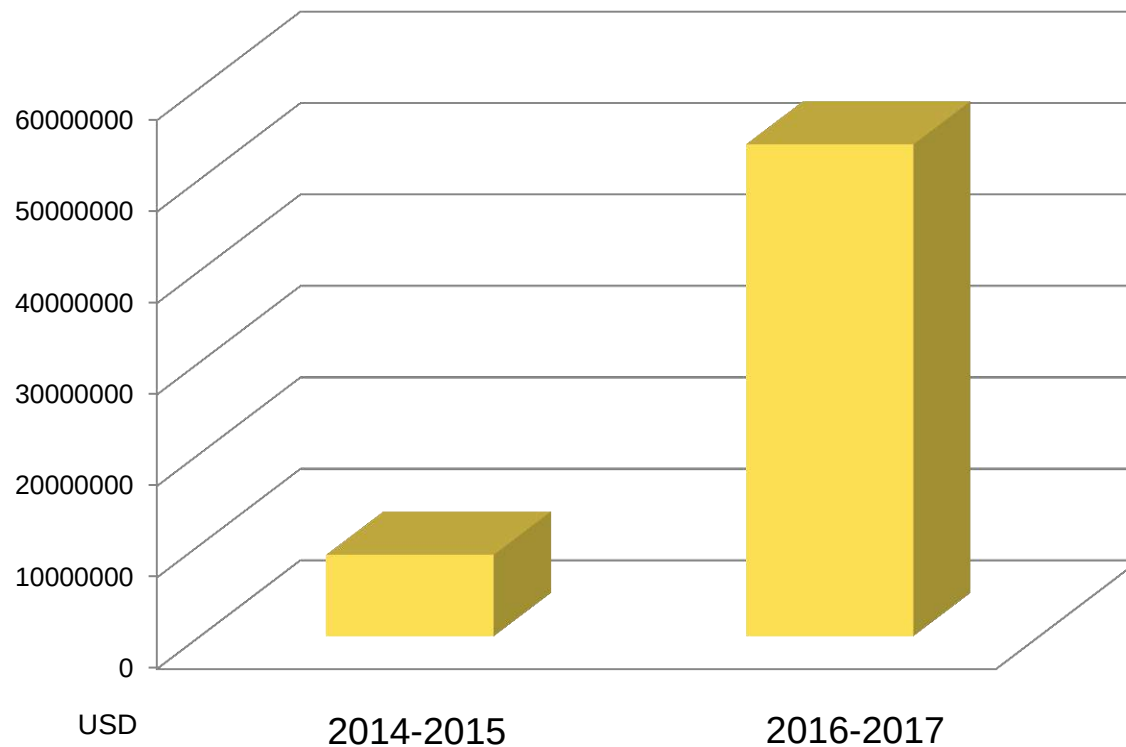
Expresses strong support to take plan to World Health Assembly

World Health Assembly, May 2015

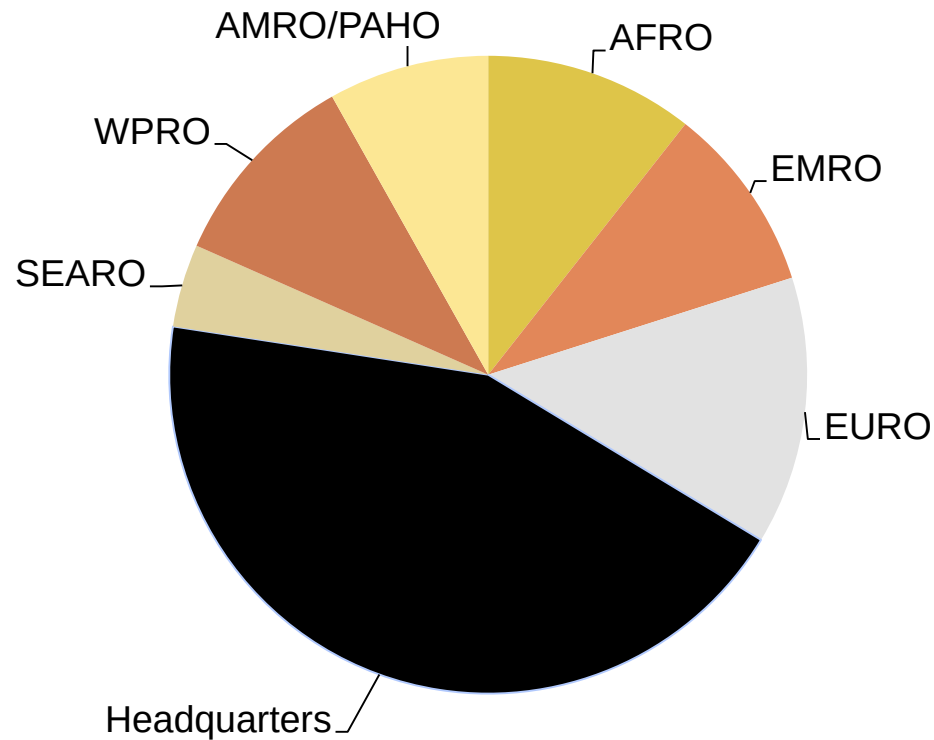
Adopts the Global Action Plan – over 50 supporting statements

Passes new resolution to support action – over 60 country sponsors

Increase in WHO organization-wide budget for AMR



Financial projections for 2016-2017: distribution by WHO Regional Office



Total: USD 53,792,873

Five strategic objectives:

1. Improve awareness and understanding (WAAW)
2. Strengthen knowledge through surveillance & research
3. Reduce the incidence of infection (IPC)
4. Optimize the use of antimicrobial medicines
5. Ensure sustainable investment (R&D)

National Action Plans

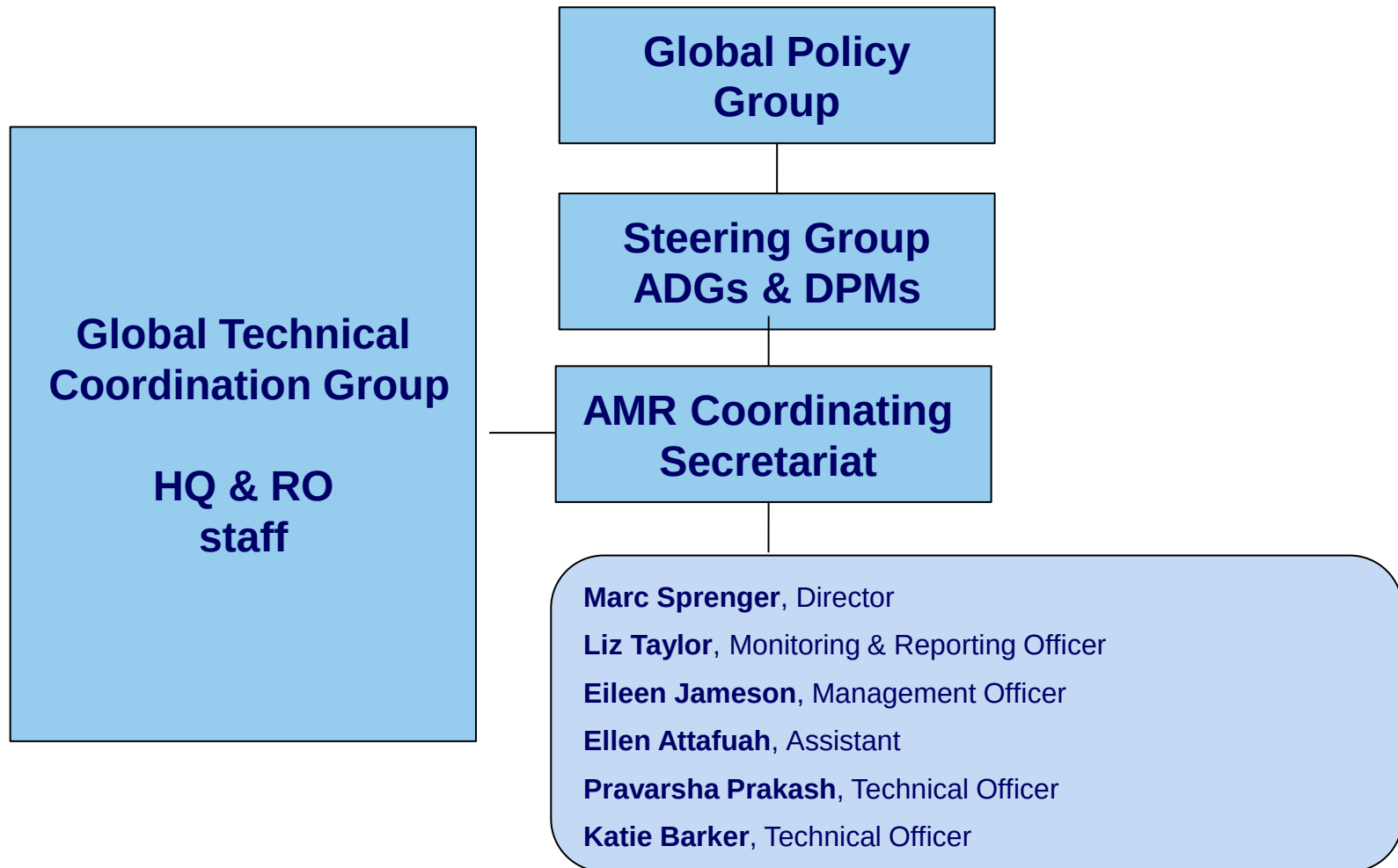
Implementation GAP: Guiding Principles

1. Realistic & achievable objectives
2. Take into account different capacities of Member States
3. Involve FAO and OIE, where appropriate
4. All-inclusive approach (HIV, TB and malaria)
5. Joint ownership between HQ and Regions
6. Communication!

Core value: together aligned
GAP is a big thing



GAP organizational structure



AMR secretariat



AMR Steering Group

1. Agree WHO work plan
2. Implementation plan proposal for donors & partners
3. Organization-wide resource mobilization strategy
4. Prioritize activities and **budget and funding allocation**

Meet quarterly

Implementation GAP: 10 work streams

1. Global communications campaign (Liv Lawe-Davies)
2. Support National Action Plans of MS (Carmem Pessoa)
3. Global Antimicrobial Resistance Surv System (Carmem Pessoa)
4. Support measures to improve IPC (Benedetta Allegranzi)
5. Monitor use & enhance stewardship of antibiotic use (Gilles Forte)

Implementation GAP: 10 work streams

6. Encourage R&D and explore new business models (Peter Beyer)
7. Improve point of care diagnostics (Francis Moussy)
8. Address the environmental drivers (Kate Medlicott)
9. Engage the United Nations General Assembly
10. Vaccines in order to prevent AMR (Martin Friede)

One Health liaison: Awa Aidara

Additional: HTM, STI, Maternal Health, etc

ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause. This is compromising our ability to treat infectious diseases and undermining many advances in medicine.

We must handle antibiotics with care so they remain effective for as long as possible.

WHAT YOU CAN DO



- 1 Only use antibiotics when prescribed by a certified health professional
- 2 Always take the full prescription, even if you feel better
- 3 Never use left over antibiotics
- 4 Never share antibiotics with others
- 5 Prevent infections by regularly washing your hands, avoiding close contact with sick people and keeping your vaccinations up to date

www.who.int/drugresistance

#AntibioticResistance



ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause. This is compromising our ability to treat infectious diseases and undermining many advances in medicine.

We must handle antibiotics with care so they remain effective for as long as possible.

WHAT HEALTH WORKERS CAN DO



- 1 **Prevent infections** by ensuring your hands, instruments and environment are clean
- 2 Keep your patients' **vaccinations** up to date
- 3 If you think a patient might need antibiotics, where possible, **test to confirm** and find out which one
- 4 Only prescribe and dispense antibiotics when they are **truly needed**
- 5 Prescribe and dispense the **right antibiotic at the right dose for the right duration**

www.who.int/drugresistance

#AntibioticResistance



ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause. This is compromising our ability to treat infectious diseases and undermining many advances in medicine.

We must handle antibiotics with care so they remain effective for as long as possible.

WHAT POLICY MAKERS CAN DO



- 1 Ensure you have a robust **national action plan** to tackle antibiotic resistance
- 2 Improve **surveillance** of antibiotic-resistant infections
- 3 Strengthen policies and **implementation** of infection prevention and control measures
- 4 **Regulate and promote** the appropriate use of quality medicines
- 5 Make information on the **impact** of antibiotic resistance available

www.who.int/drugresistance

#AntibioticResistance



CAUSES OF ANTIBIOTIC RESISTANCE

Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.



Over-prescribing of antibiotics



Patients not finishing their treatment



Over-use of antibiotics in livestock and fish farming



Poor infection control in hospitals and clinics



Lack of hygiene and poor sanitation



Lack of new antibiotics being developed

www.who.int/drugresistance

#AntibioticResistance

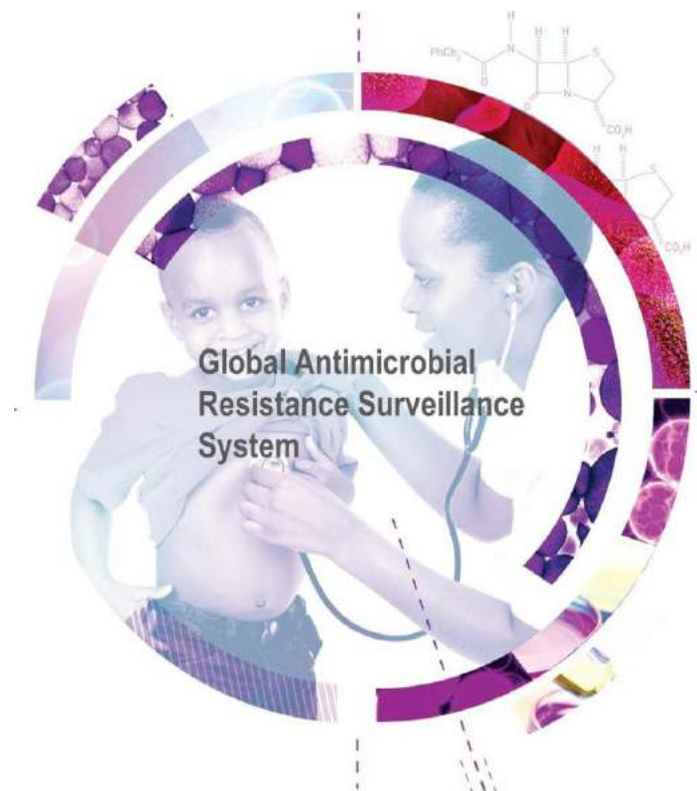


Global Antimicrobial Resistance Surveillance System (GLASS)

Lead: Carmem Pessoa

Goal

To achieve a monitoring capacity to capture essential information on the global situation of antimicrobial resistance and inform decision making.



Global Antimicrobial Resistance Surveillance System (GLASS)

Lead: Carmem Pessoa



GLASS future directions

Integrated foodborne AMR surveillance

- Food-animals
- Food
- Humans

Monitoring of antimicrobial use or consumption

**Surveillance of
bacterial resistance in
humans**

Environmental AMR surveillance

... other types of AMR surveillance

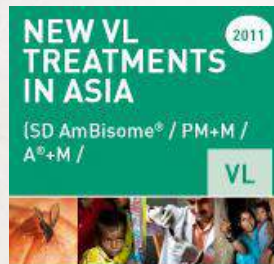
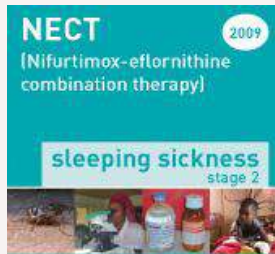
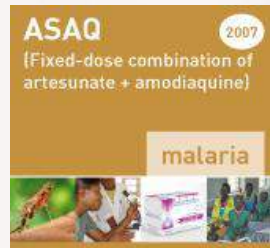
R&D and explore new business models

Lead: Peter Beyer

Global Antibiotic Research and Development Facility



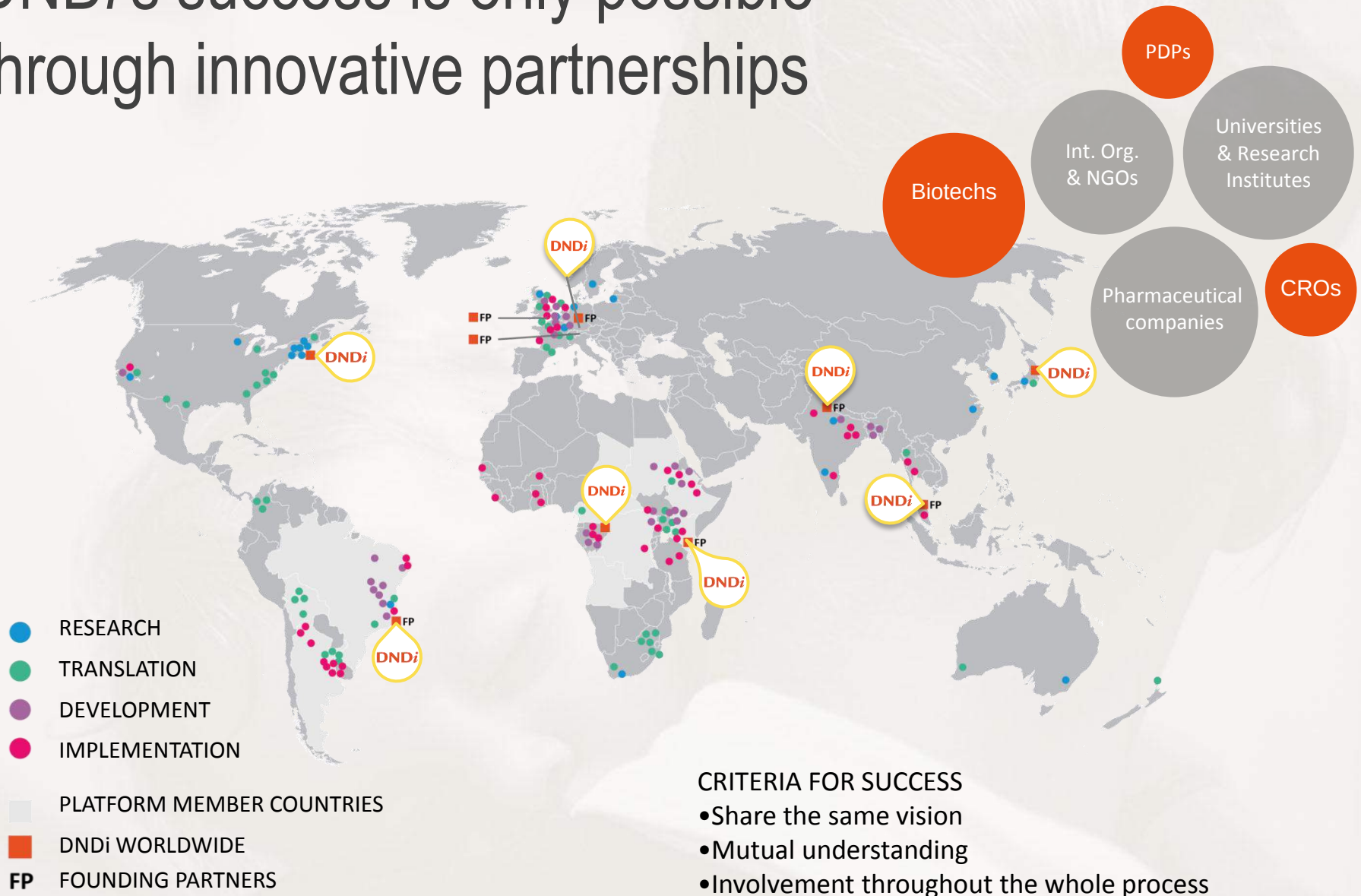
In a decade of R&D, 6 new treatments developed



- ✓ Easy to use
- ✓ Affordable
- ✓ Field-adapted
- ✓ Non-patented

- 30 projects, 6 diseases areas
- 15 entirely new chemical entities (NCEs)
- Over 130 partnerships, most in endemic countries
- 150 staff, half in endemic countries & 600 people working on DNDi projects
- Over EUR 350 million raised equally from public and private sources
- 3 regional disease-specific clinical trial platforms and 2 technology transfers

DNDi's success is only possible through innovative partnerships



Improve point of care diagnostics

Lead: Francis Moussy

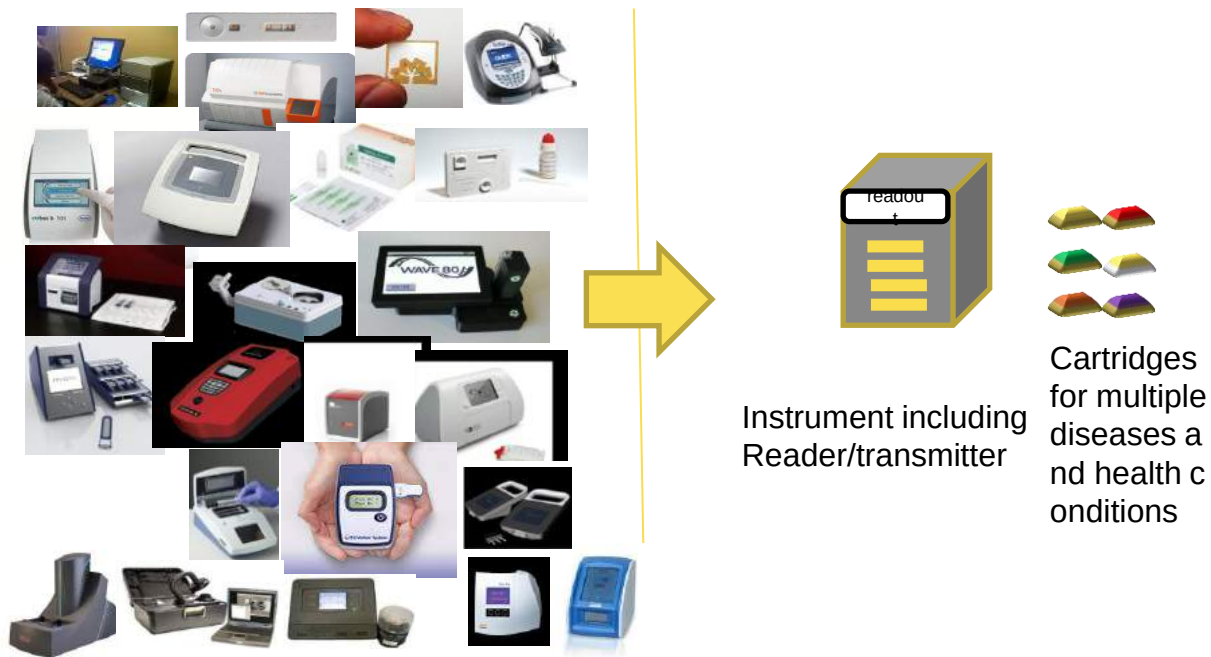
Point-of-Care Dx for LMICs for treatment, surveillance

Many areas with no elec, no refrige, no trained medical staff...

New PoC Dx suitable for LMICs need to be developed

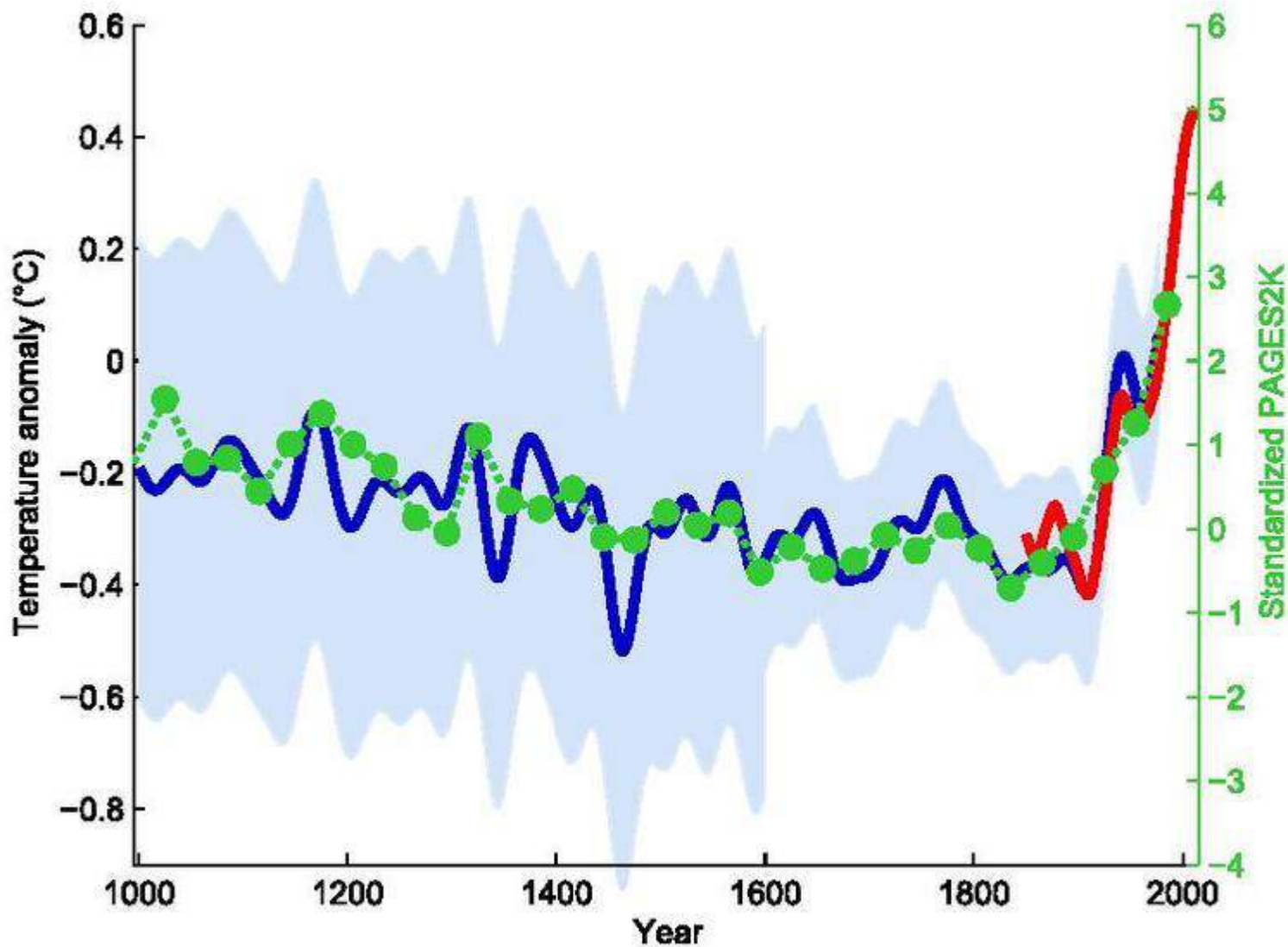


Low-cost, robust and open PoC diagnostics platforms

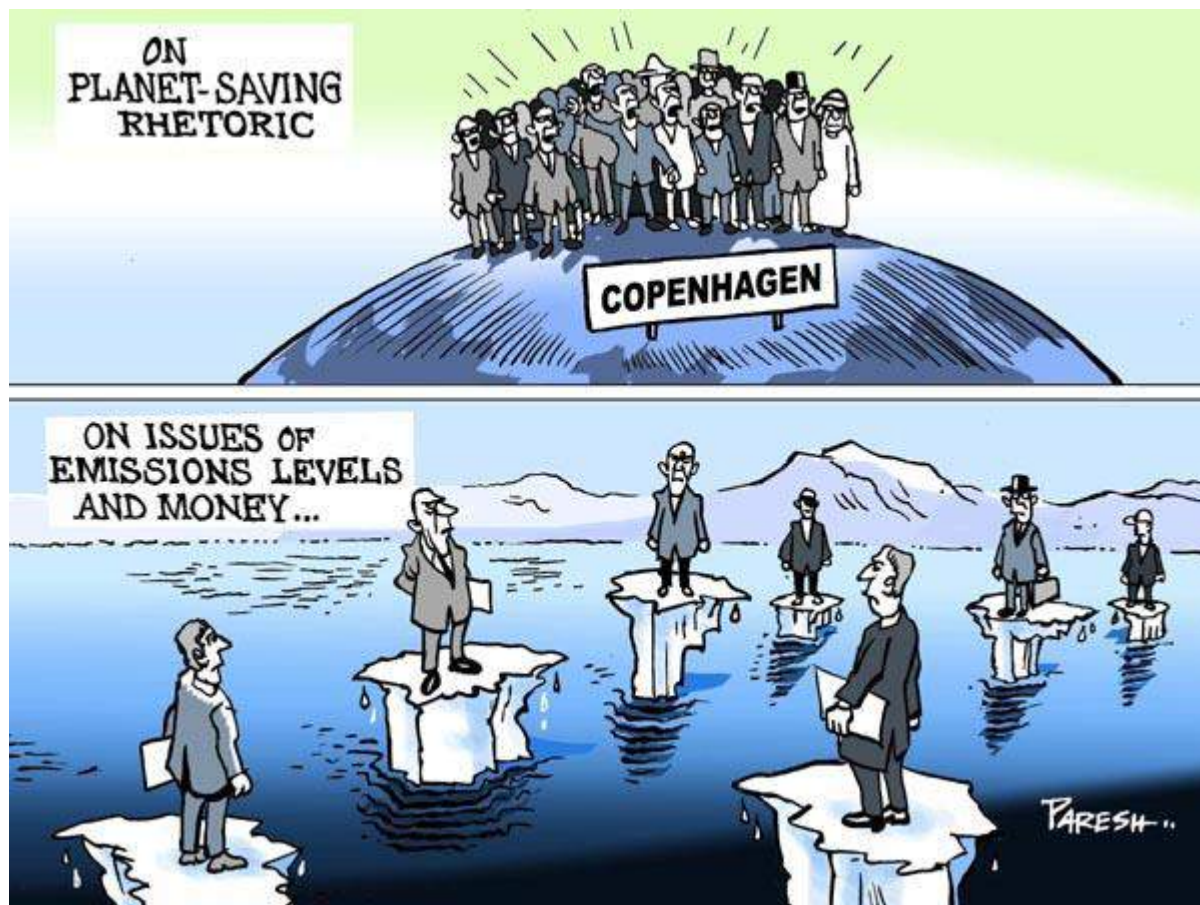


Engage United Nations General Assembly





Shift Words into Action



Shift Words into Action



Shift Words into Action: UN General Assembly 2016



One Health, liaison FAO / OIE

Lead: Awa Aidara



ANTIBIOTIC RESISTANCE



Antibiotic resistance happens when bacteria change and become resistant to the antibiotics used to treat the infections they cause.

The over-use and misuse of antibiotics in livestock, aquaculture and crops is contributing to antibiotic resistance and its spread into the environment, food chain and humans. This is compromising our ability to treat infectious diseases and undermining many advances in medicine.

We must handle antibiotics with care so they remain effective for as long as possible.

WHAT THE AGRICULTURE SECTOR CAN DO



- 1 Ensure that antibiotics given to animals—including food-producing and companion animals—are **only used to treat** infectious diseases and under veterinary supervision
- 2 **Vaccinate** animals to reduce the need for antibiotics and **develop alternatives** to the use of antibiotics in plants
- 3 Promote and apply **good practices** at all steps of production and processing of foods from animal and plant sources
- 4 Adopt **sustainable systems** with improved hygiene, biosecurity and stress-free handling of animals
- 5 Implement **international standards** for the responsible use of antibiotics, set out by OIE, FAO and WHO

www.who.int/drugresistance
www.oie.int/antimicrobial-resistance
www.fao.org/antimicrobial-resistance/en/

#AntibioticResistance



WORLD ORGANISATION FOR ANIMAL HEALTH
Protecting animals, preserving our future



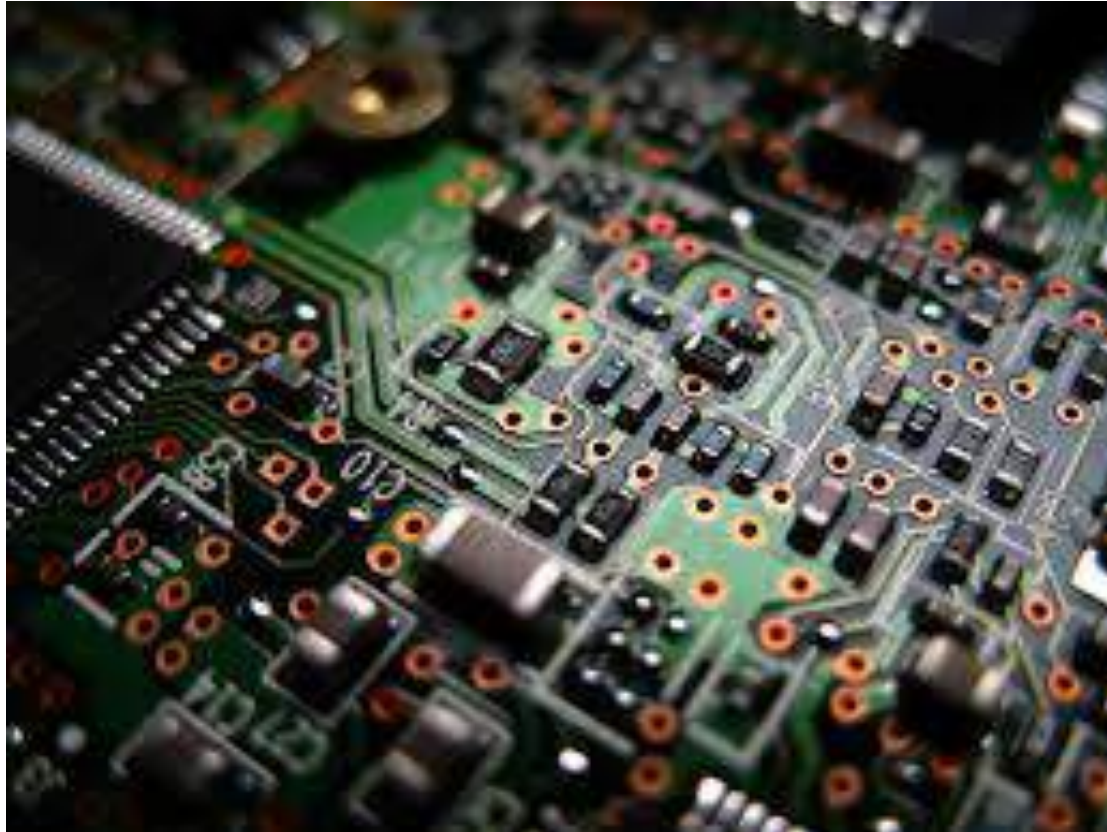
World Health Organization



International context

1. Global Health Security Agenda
2. G7
3. TATFAR
4. AMR review
5. Joint Programming Initiative AMR
6. Etc
7. Etc

International Initiatives: align



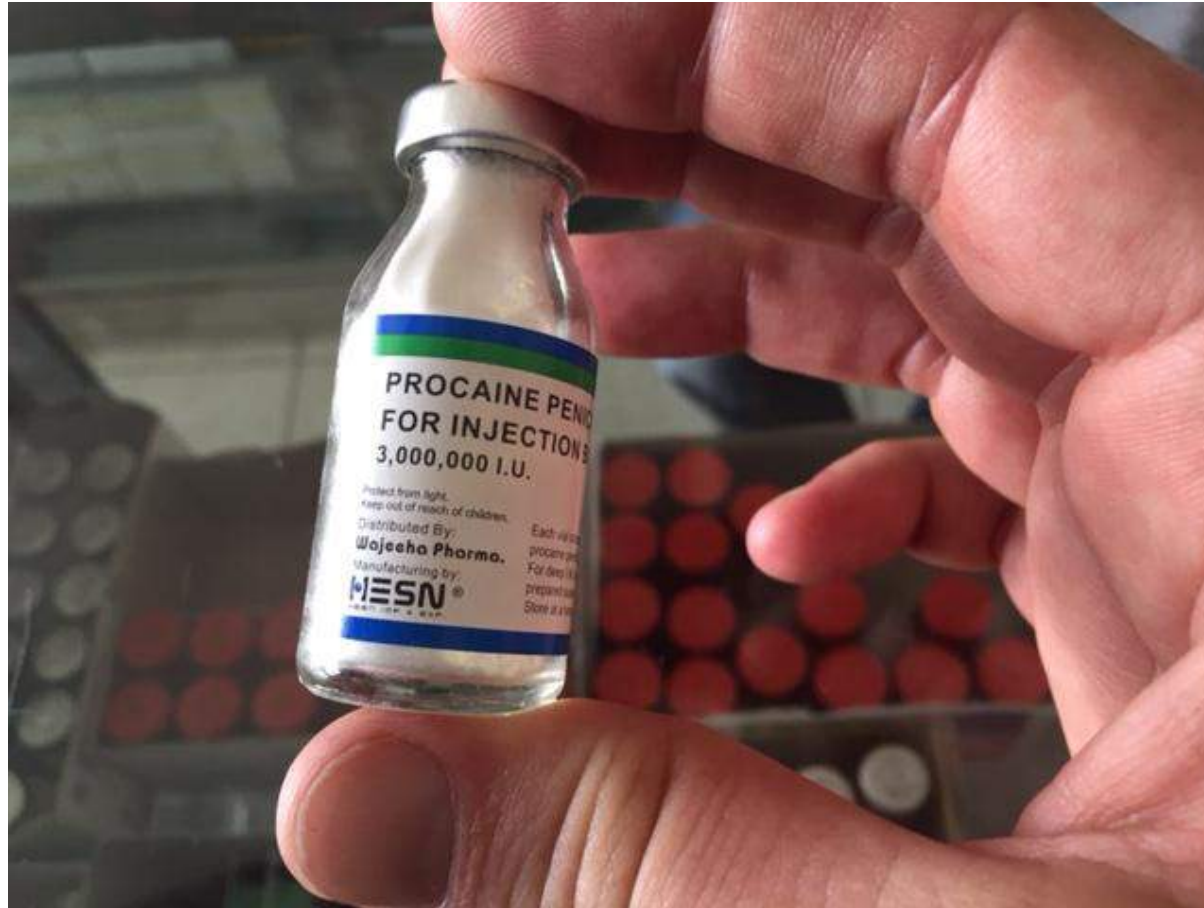
After 20h flight: reality check



No prescription needed, just take 2



No knowledge, no instruction



After 10h flight: reality check



Courtesy: FAO, HJ Ormel DVM

After 10h flight: reality check



Courtesy: FAO, HJ Ormel DVM

What did they tell me...

No medical microbiology lab in main hospital
No infection and prevention control in hospital
No drug regulation
No knowledge, no awareness
No money for GP

But committed local people and Country Office WHO

She is the champion!



No comment....



Miracle...after 1 day

Global Antibiotic R&D Facility



Conclusion

1. Global Action Plan AMR is ambitious
2. Global Action Plan AMR: joint responsibility

Thank you

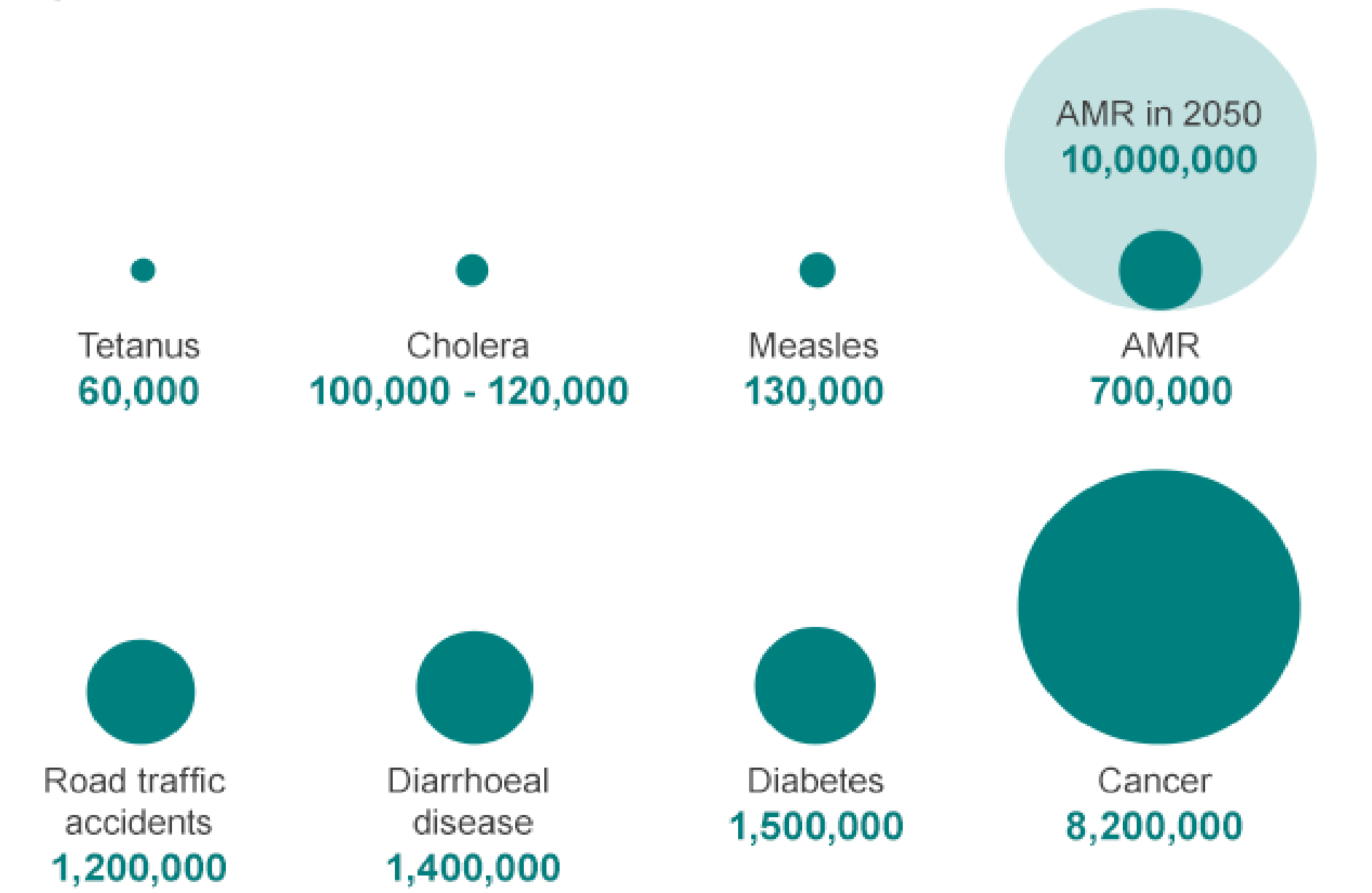


Antimicrobial Resistance in Developing Countries

Prof. Nirmal Kumar Ganguly
Visiting Professor of Eminence
Policy Center for Biomedical Research
THSTI, Faridabad, India
Former DG ICMR, India

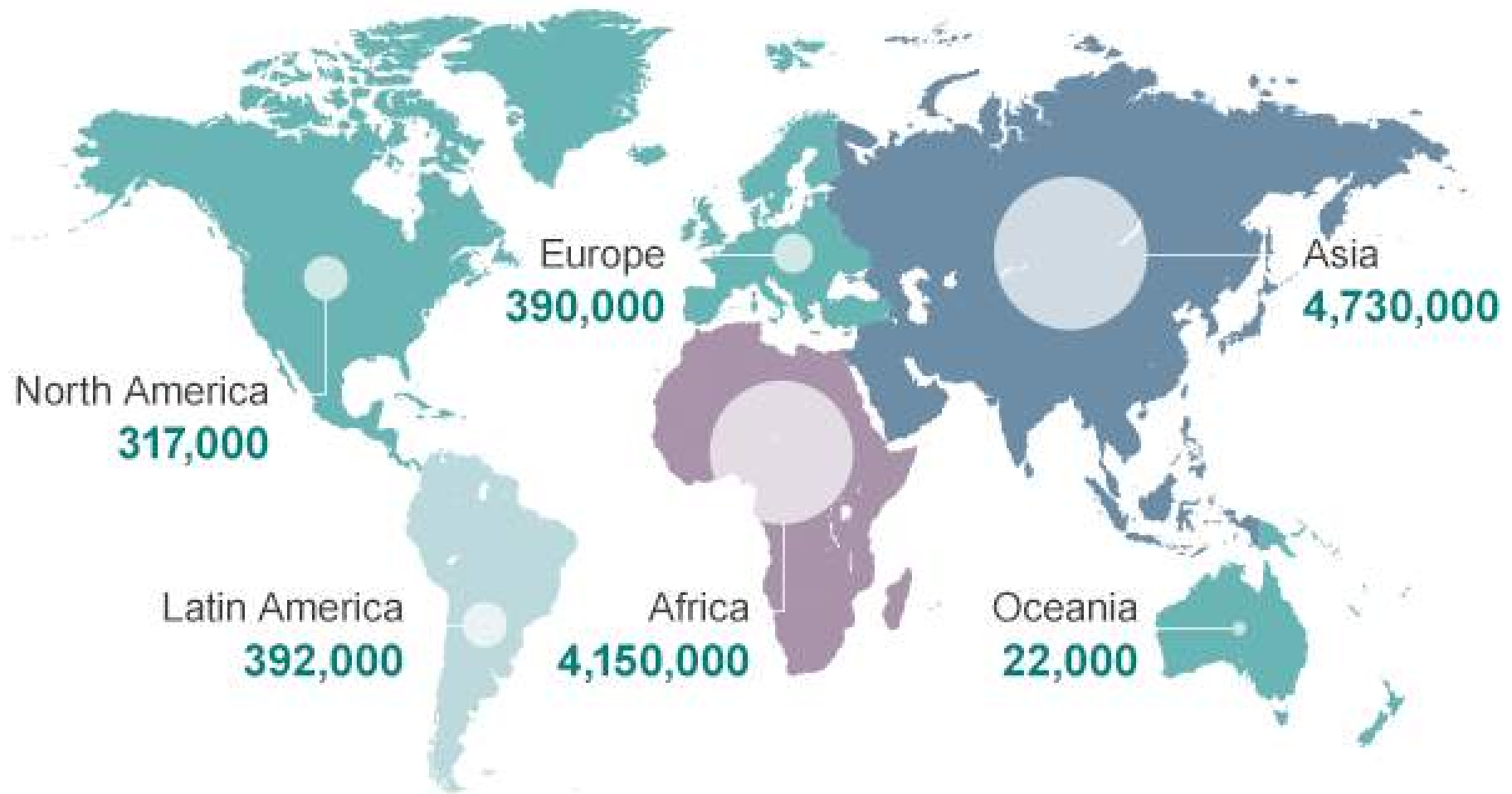
Global Trends

Deaths attributable to antimicrobial resistance every year compared to other major causes of death



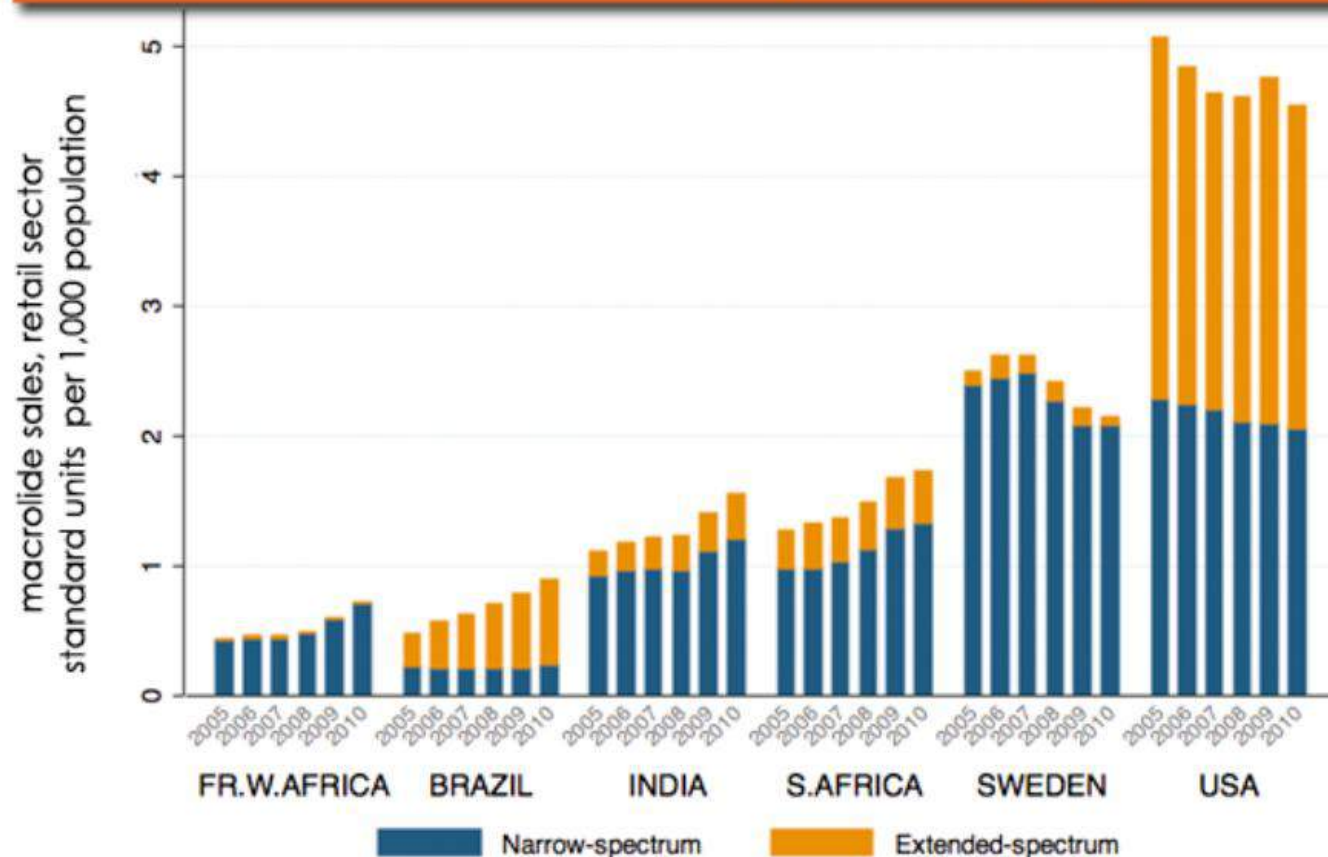
Source: Review on Antimicrobial Resistance 2014

Deaths attributable to antimicrobial resistance every year by 2050



Source: Review on Antimicrobial Resistance 2014

Extended-spectrum macrolide use is highly prevalent in the United States, and increasing in developing countries



Data source: Based on data obtained under license from IMS Health MIDAS™ (January 2005–December 2010); IMS Health Incorporated. All rights reserved.

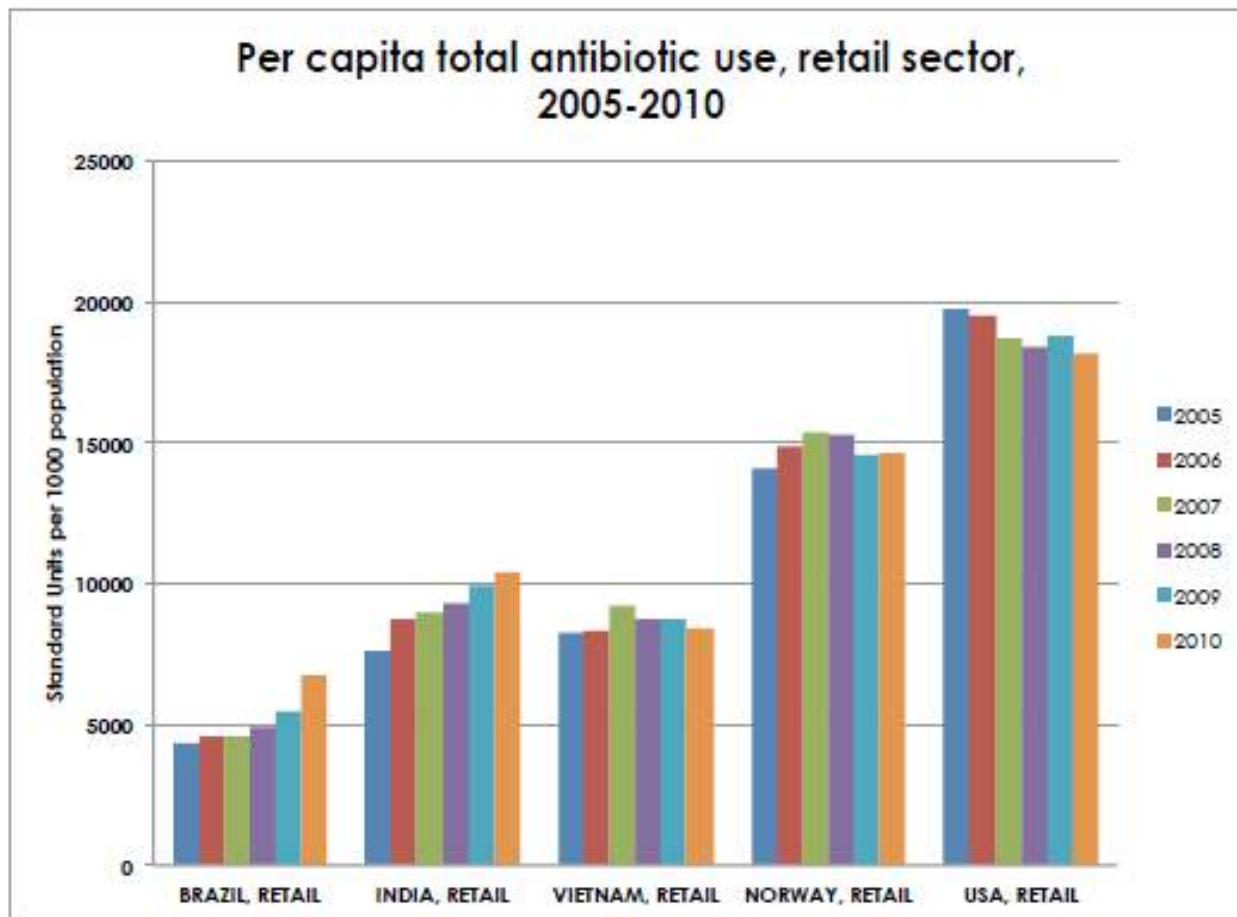


CDDEP

THE CENTER FOR
Disease Dynamics,
Economics & Policy

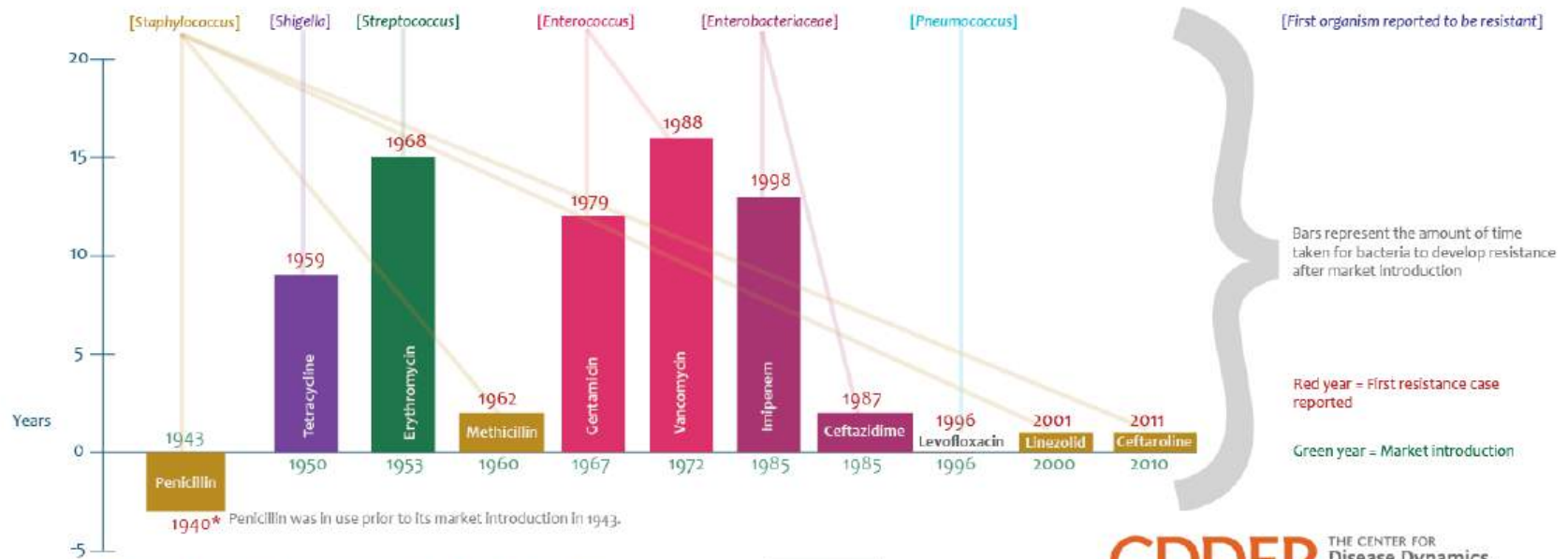
WASHINGTON DC • NEW DELHI

Antibiotic consumption is increasing in developing countries...



Source: Based on data obtained under license from IMS Health MIDAS™ (January 2005-December 2010); IMS Health Incorporated. All Rights Reserved.

Once an antibiotic is introduced, resistance is not far behind...



Data source: Antibiotic Resistance Threats in the United States, 2013.
US Centers for Disease Control and Prevention (CDC).



CDDEP THE CENTER FOR
Disease Dynamics,
Economics & Policy
WASHINGTON DC • NEW DELHI

Non-prescription use of antimicrobials

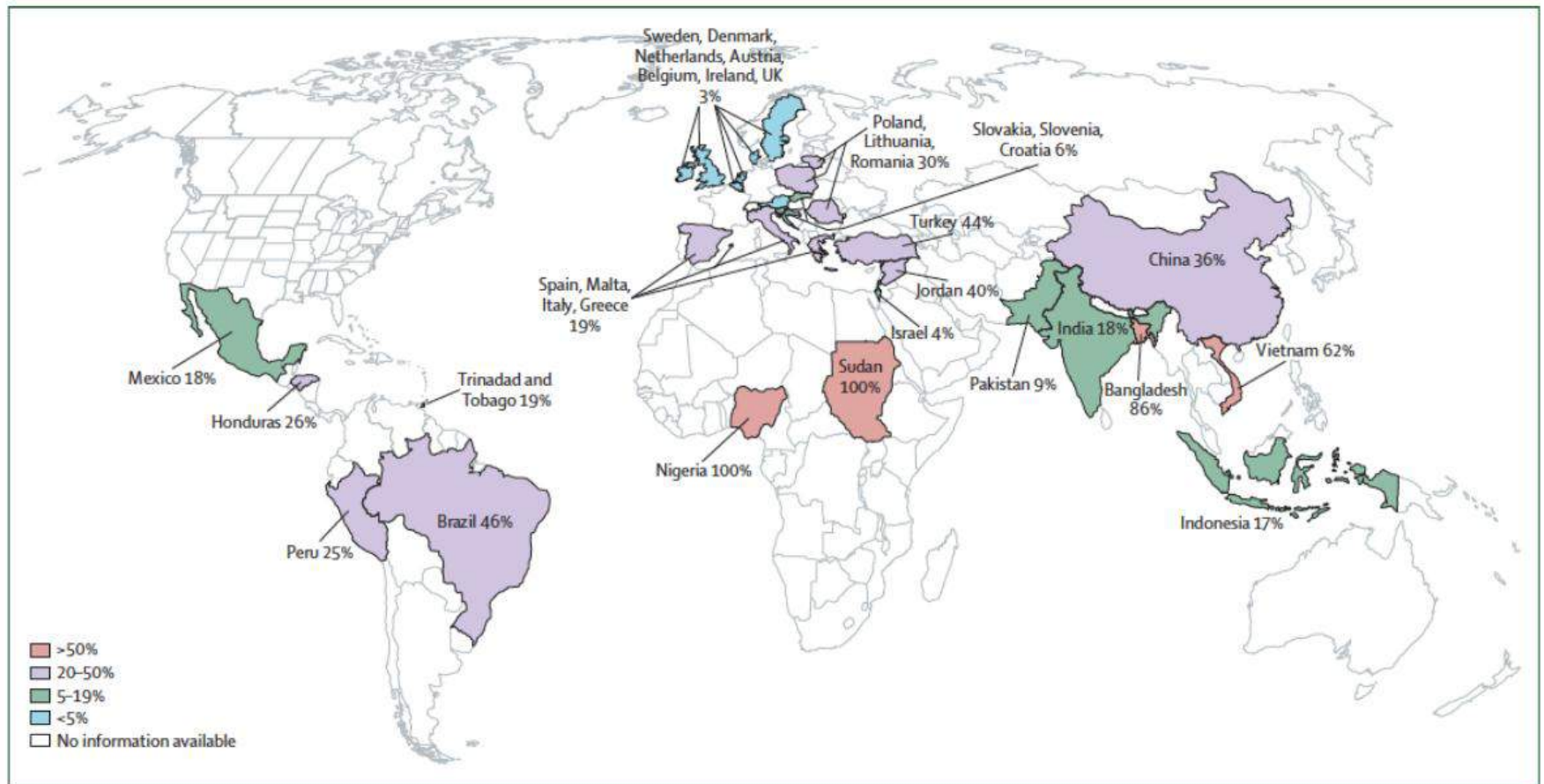
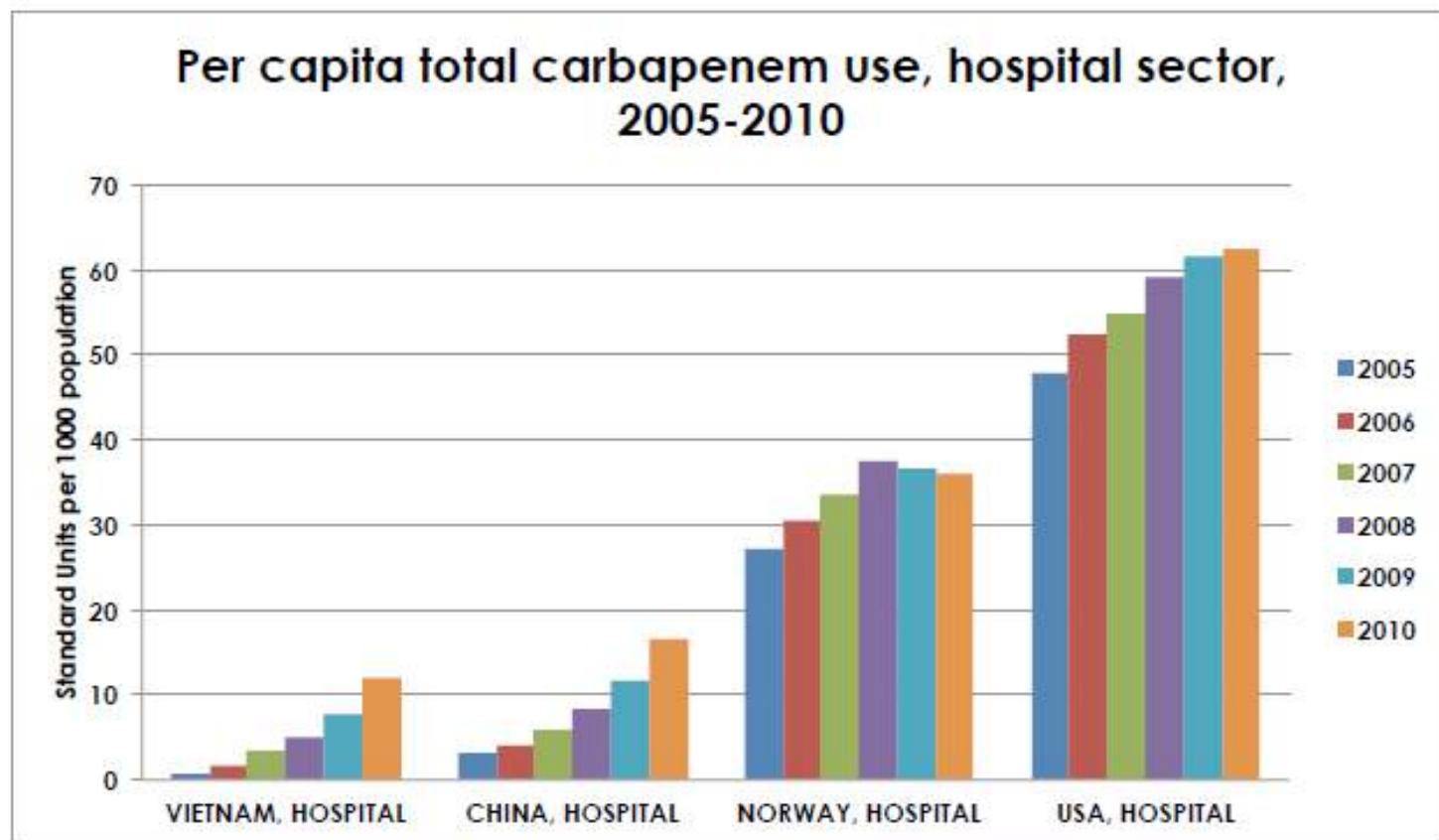


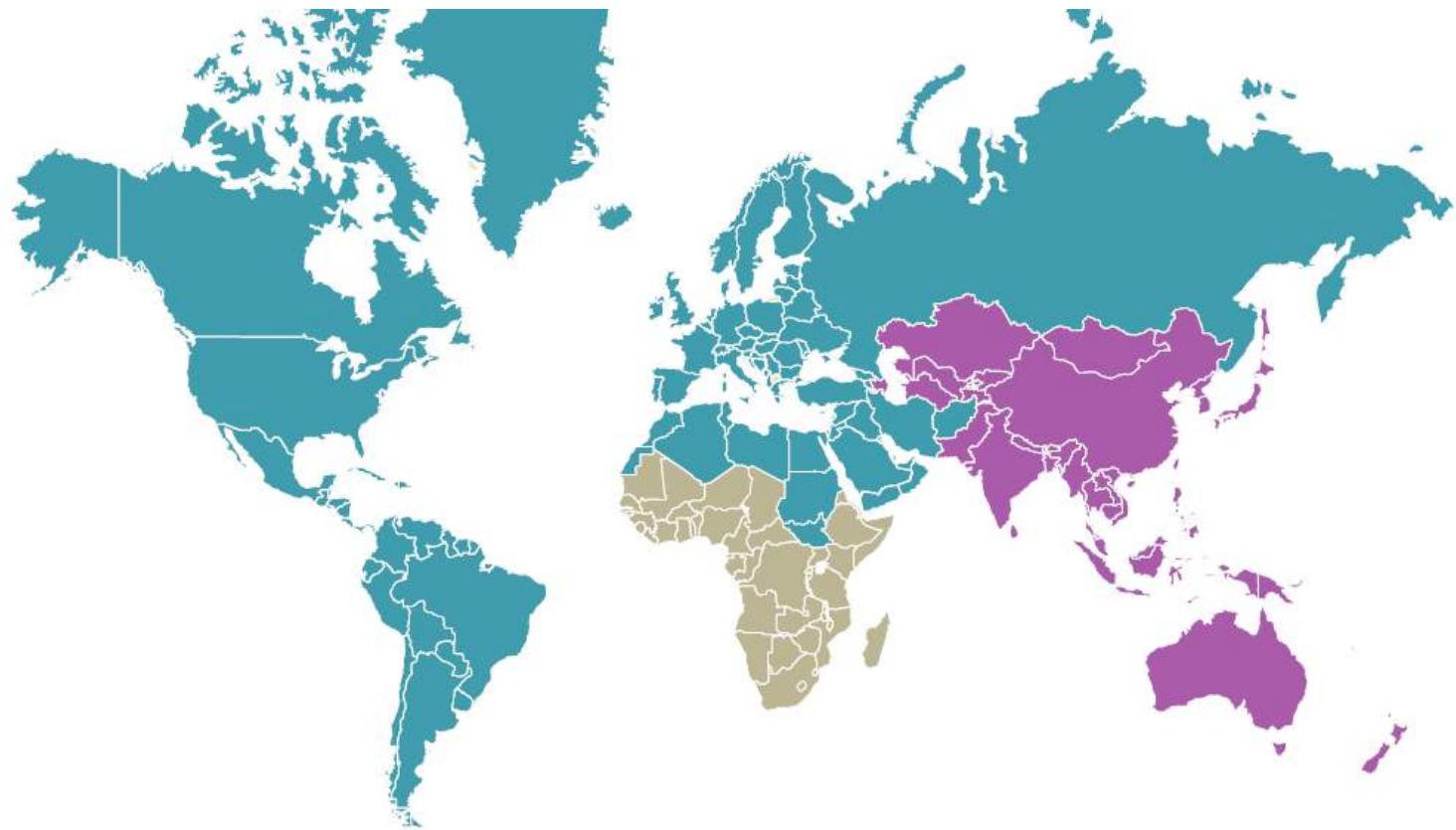
Figure 2: Frequency of non-prescription use of antimicrobials in the general population based on published works
In small areas, countries with similar frequency of non-prescription antimicrobial use have been grouped.

Hospital use of carbapenems is rapidly growing



Source: Based on data obtained under license from IMS Health MIDAS™ (January 1999-December 2010); IMS Health Incorporated. All Rights Reserved.

Potential loss of in GDP, % fall compared to baseline scenario in 2050



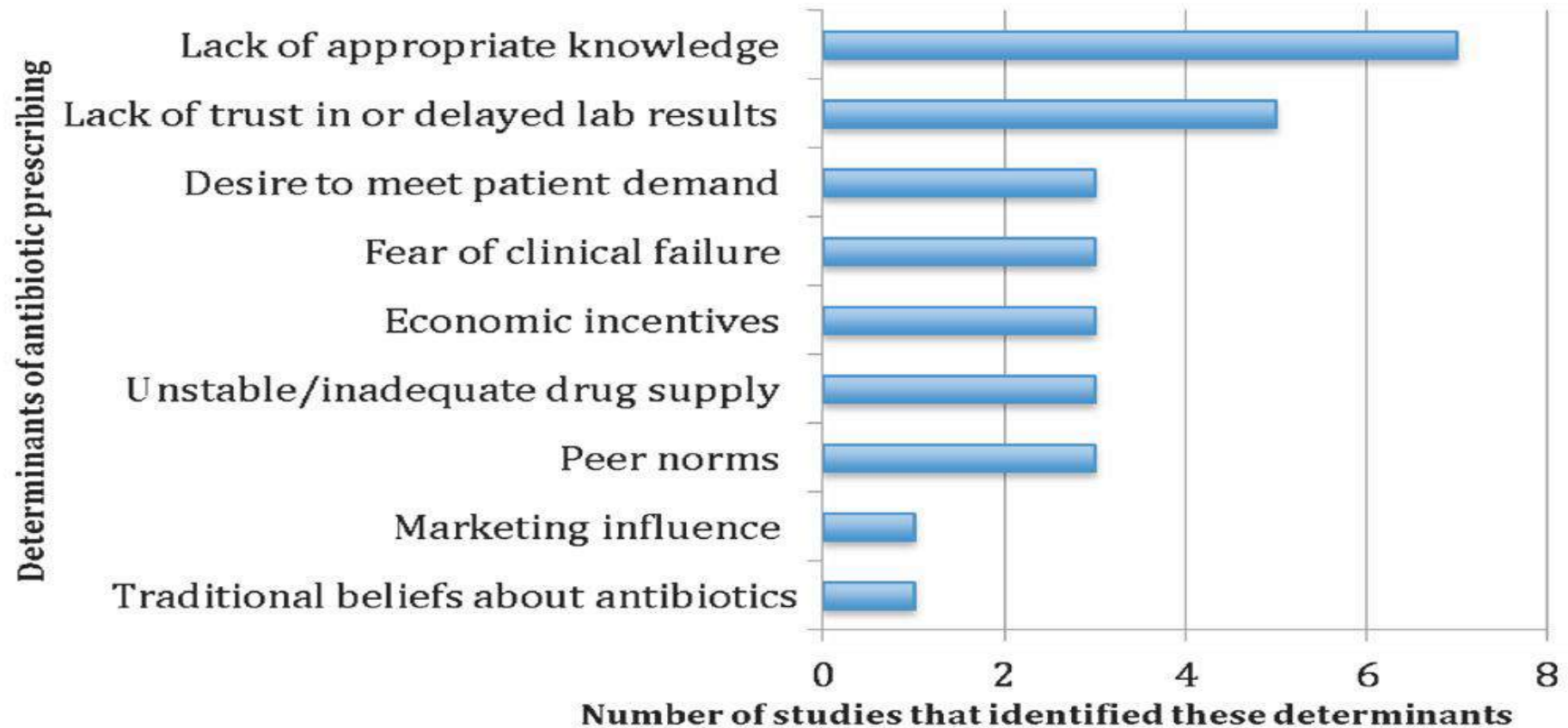
Key: ■ <5 ■ 5-10 ■ >10

Source: KMPG project

INDIA

Status Paper: Rationalizing antibiotic use to limit antibiotic resistance in India+

Global Antibiotic Resistance Partnership (GARP) - India Working Group



Action needed a global level to tackle emerging threats like NDM-1

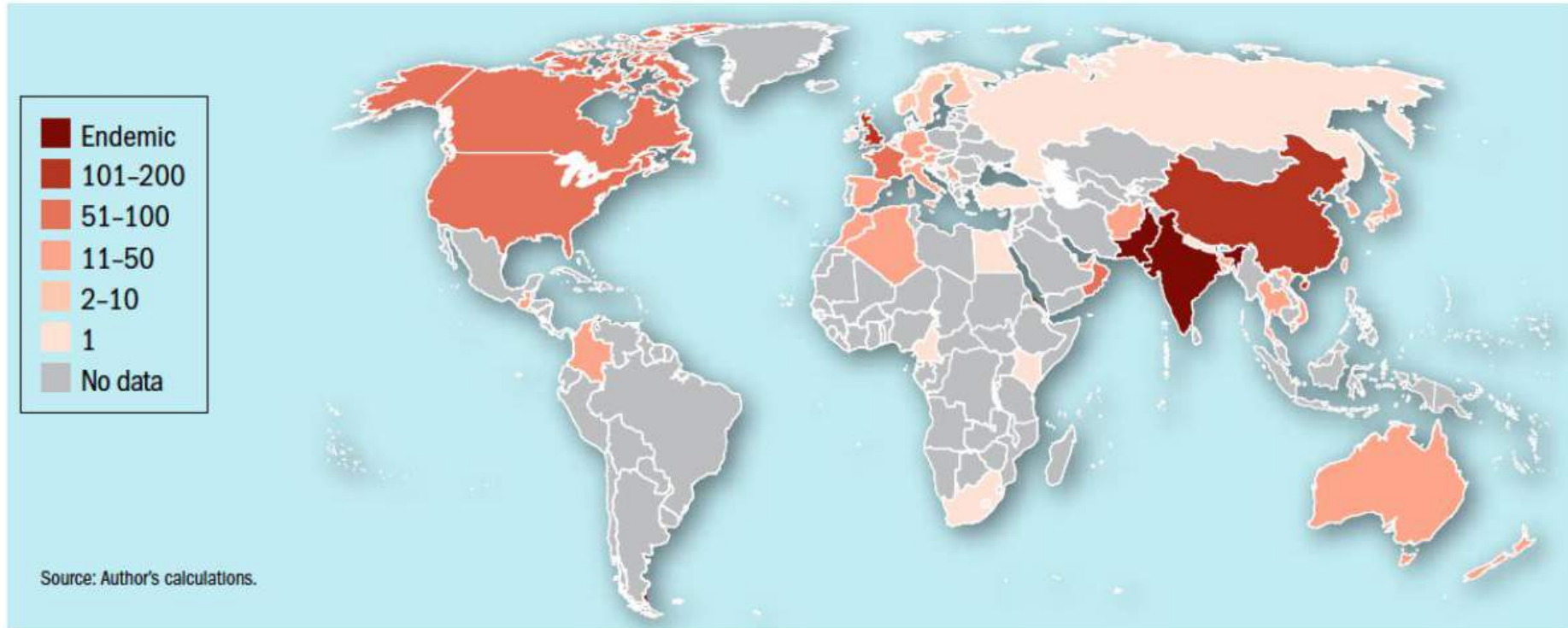


Table 2. Distribution of resistance determinants among Enterobacteriaceae isolates (2007–2011).

Isolate and resistance determinants	Total (%)	2007	2008	2009	2010	2011
		No. of strains				
<i>Escherichia coli</i>	27 (26)	4	9	2	4	8
<i>bla</i> _{SHV}	6 (26)	0	3	0	1	2
<i>bla</i> _{TEM}	16 (69)	0	7	1	3	5
<i>bla</i> _{OXA}	8 (35)	2	2	1	0	3
<i>bla</i> _{CTXM}	20 (87)	2	6	1	4	7
<i>bla</i> _{CMY}	5 (19)	0	2	1	0	2
<i>bla</i> _{NDM}	6 (22)	0	1	1	1	3
Negative for all determinants	4 (15)	2	2	0	0	0
<i>Klebsiella pneumoniae</i>	68 (65)	20	12	10	15	11
<i>bla</i> _{SHV}	40 (63)	14	2	10	10	4
<i>bla</i> _{TEM}	51 (80)	17	11	8	11	4
<i>bla</i> _{OXA}	30 (47)	11	6	3	5	5
<i>bla</i> _{CTXM}	58 (91)	17	9	8	14	10
<i>bla</i> _{NDM}	6 (9)	0	0	0	5	1
Negative for all determinants	4 (6)	2	1	0	0	1
<i>Enterobacter cloacae</i>	8 (7.6)	1	2	1	3	2
<i>bla</i> _{SHV}	1 (12)	0	0	0	1	0
<i>bla</i> _{TEM}	7 (87)	1	1	1	2	2
<i>bla</i> _{OXA}	6 (75)	1	1	1	2	1
<i>bla</i> _{CTXM}	8 (100)	1	1	1	3	2
<i>bla</i> _{ACT}	2 (25)	0	1	0	1	0
<i>bla</i> _{NDM}	3 (37)	0	0	0	1	2
Negative for all determinants	0 (0)	0	0	0	0	0

ICU
Jan ., 2008 - Dec., 2010 Blood Isolates
3 Yrs. (n = 1928)

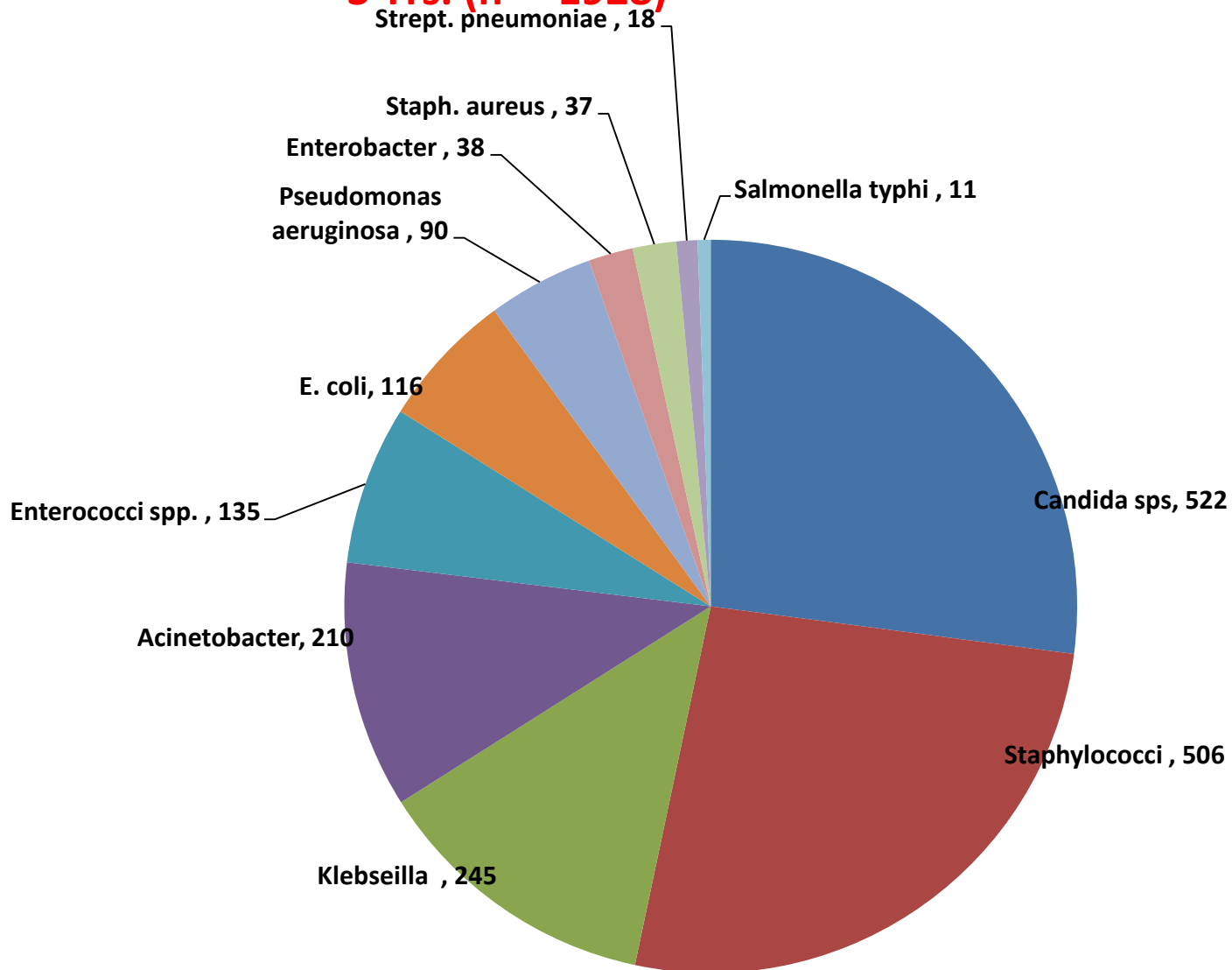


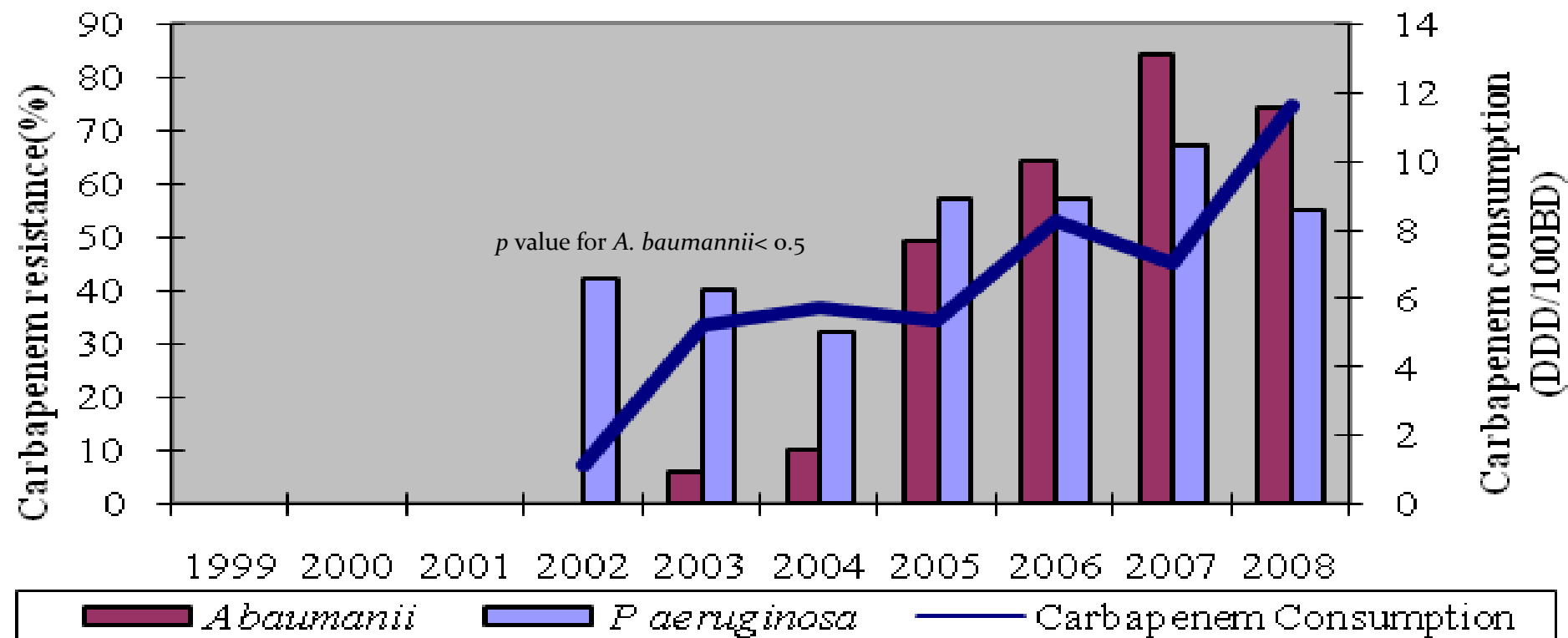
Table I: Trends of isolation rates, antimicrobial consumption and resistance *K.pneumoniae*

<i>K.pneumoniae</i> (% resistance)	Years										P value
	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	
Cefotaxime	75	80	94	89	81	89	98	95	95	97	0.008
Amikacin	70	70	76	90	77	77	89	76	59	45	0.17
Ciprofloxacin	64	80	64	83	82	66	81	86	64	84	0.411
Piperacillin+ Tazobactam			55	71	51	64	67	60	88	84	0.055
Carbapenems			2.4	1.7	0	0	7	3	47	52	0.039
ESBL			48	55	68	74	66	58	44	40	0.332
Amp C	—	—	—	—	—	—	—	—	—	8%	—
Carbapenemase producer	—	—	—	—	—	—	—	—	—	51%	—

Table I: Trends of isolation rates, antimicrobial consumption *E.coli*

(% resistance)	2000	2001	2002	2003	Years 2004	2005	2006	2007	2008	2009	p value
Amikacin	57	63	68	87	75	69	58	67	57	14	0.11 5
Ciprofloxacin	53	62	84	90	49	86	89	95	98	91	0.03 7
Piperacillin+ Tazobactam			53	67	47	37	30	27	10	42	0.08
Carbapenem			3	2	0	0	2	6	10	6	0.10 5
ESBL			40	45	58	60	75	78	61	61	0.05
Amp C	—	—	—	—	—	—	—	—	—	8%	—
Carbapenemase producer	—	—	—	—	—	—	—	—	—	15%	—

Association between carbapenem consumption and resistance in *P.aeruginosa* and *A. baumannii* (SGRH)



Chennai Declaration on AMR: India

- "The Chennai Declaration" named after the city where the meeting took place, is the consensus evolved out of the meeting and co-authored by representatives of various medical societies. The document is based on realistic goals and objectives, with a deep understanding of the background Indian scenario.

Antimicrobial Resistance Research and Surveillance network: India

Indian Council of Medical Research



Source; Dr. Kamini Walia ICMR



Antimicrobial Research and Surveillance Network at ICMR

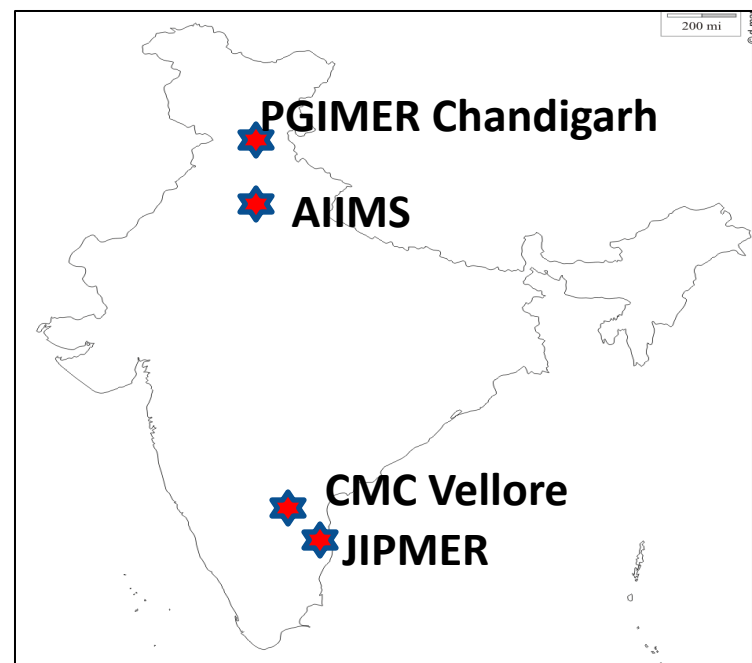
- Antimicrobial Resistance Research and Surveillance
- Antimicrobial Stewardship Program
 - Treatment guidelines
 - Infection control policy document
 - Prescription practices
 - Focus on infectious diseases



Antimicrobial Research and Surveillance Network at ICMR

- Nodal centres are focal points for six pathogenic groups:
 - *Enterobacteriaceae* / sepsis (PGIMER)
 - Fungal pathogens (PGIMER)
 - Gram negative non-fermenters (CMC)
 - Enteric fever organisms (AIIMS)
 - Diarrhoeagenic organisms (CMC)
 - MRSA, Enterococcus (JIPMER)
- 15 Regional Centres (RC) proposed

Nodal Centres



Major imperatives: Standardisation and uniformity



Antimicrobial Surveillance and Research network

Updates.....

- Data collection at nodal centers initiated on September 1, 2013
 - Almost 18,000 isolates tested
- SOPs (bacteriology and mycology) available at ICMR website
- Data managed by the Bioinformatics team at ICMR HQs

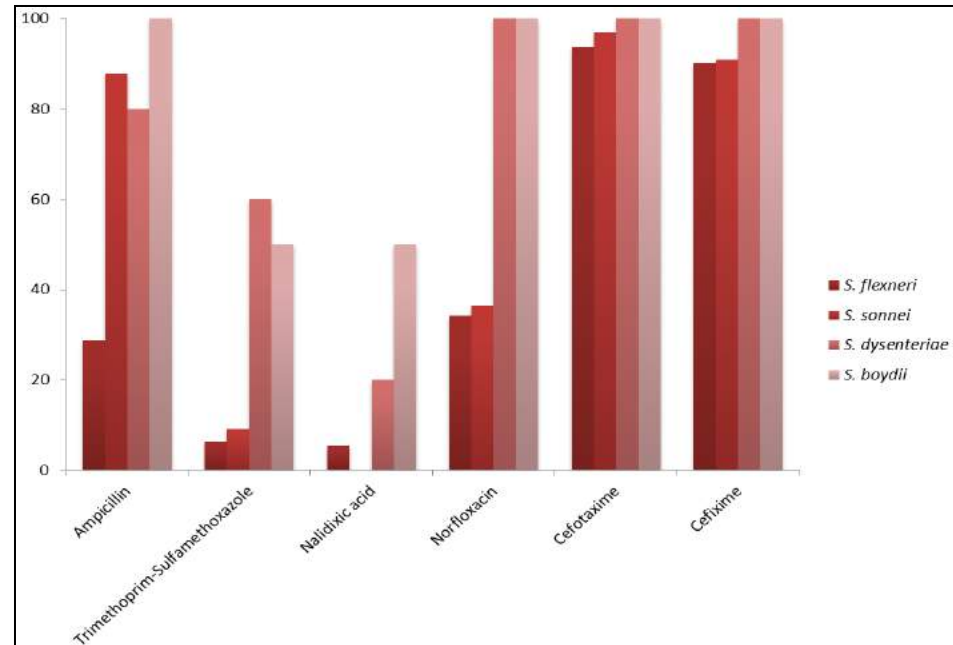




ICMR's Antimicrobial Surveillance and Research network

Shigella spp

- High resistance to nalidixic acid
- 50 % R to norfloxacin and ampicillin
- Association of ESBL genes with *qnr* genes – rare among Indian isolates
- *bla*_{CTX-M-15} occurrence in *Shigella* spp increases the threat for spread of cephalosporin resistance among Enterobacteriaceae

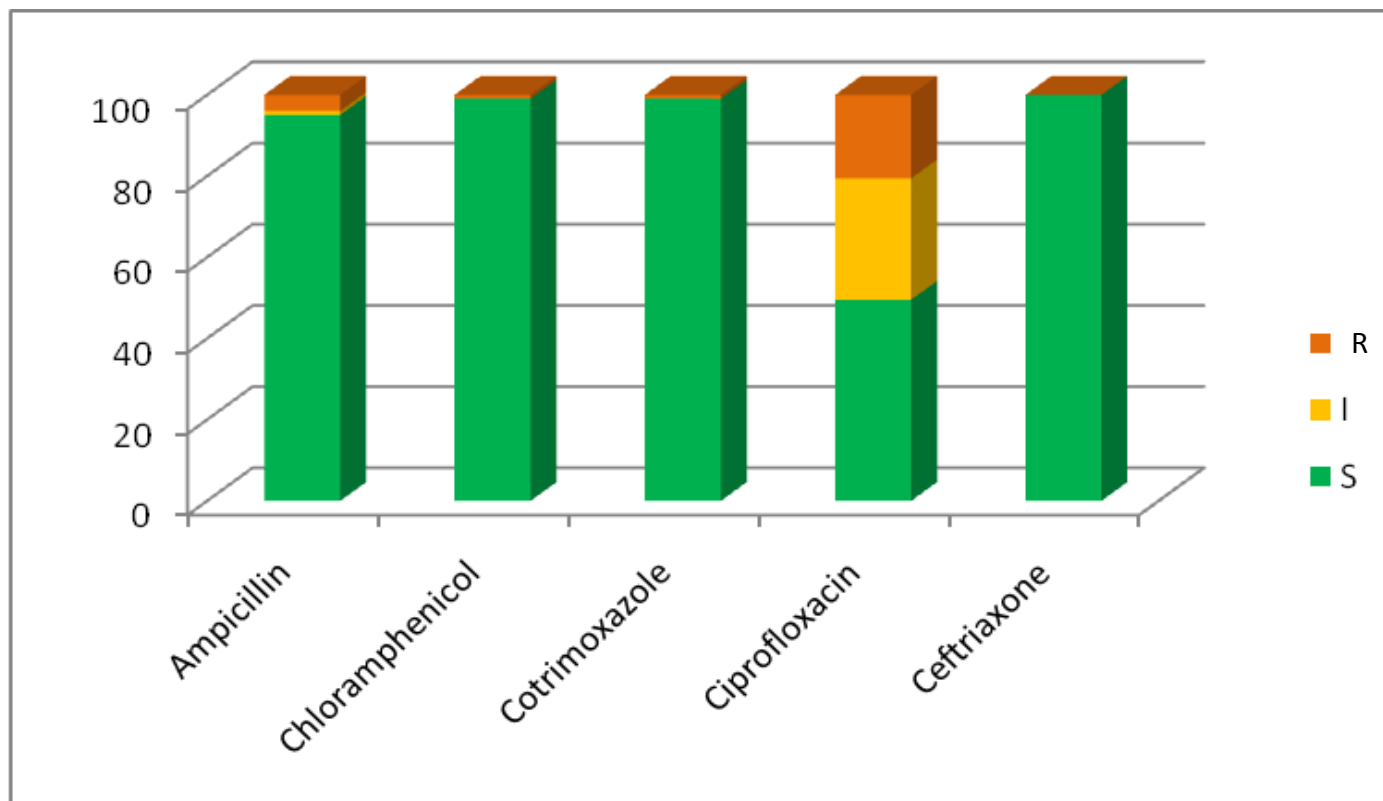


Organism (n = 31)	Genes for sulfonamide resistance		Genes for β – lactam resistance				Genes for quinolone resistance
	dhfr1a	Sul II	bla _{OXA}	bla _{TEM}	bla _{CTX-M-1}	AmpC	qnr A, B, S
<i>S. flexneri</i> (n = 22)	22	15	12	4	2	2	6
<i>S. sonnei</i> (n = 6)	6	5	-	-	1	-	1



ICMR's Antimicrobial Surveillance and Research network

Salmonella typhi

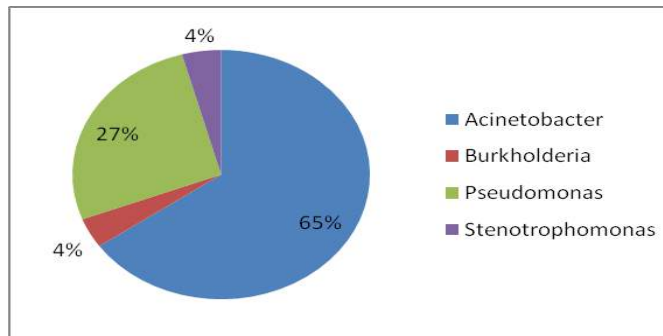
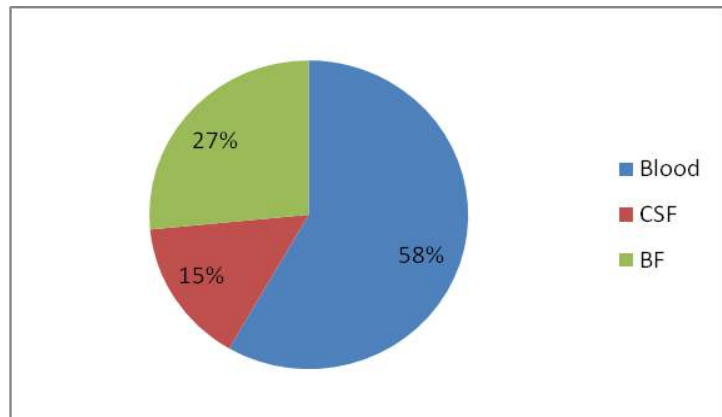


- *S. typhi* multidrug resistance (MDR) : ampicillin, chloramphenicol and trimethoprim – sulfamethoxazole - downward trend
- High resistance to FQ, cephalosporins in *S. typhi* is increasingly reported



Antimicrobial Surveillance and Research network

Non-fermenting gram negative bacilli (NFGNB)



- *Acinetobacter* species 60% isolates, *Pseudomonas* species 24%, *Strophomonas* species 4%, *Burkholderia* species 4%.
- All isolates of *P aeruginosa* were susceptible to colistin, followed by imipenem (85%), amikacin (80%), ciprofloxacin (80%), piperacillin-tazobactam (58%) and meropenem (50%)
- *A baumannii* isolates showed maximum susceptibility was to colistin (99%) followed by imipenem (53%) and meropenem (53%).



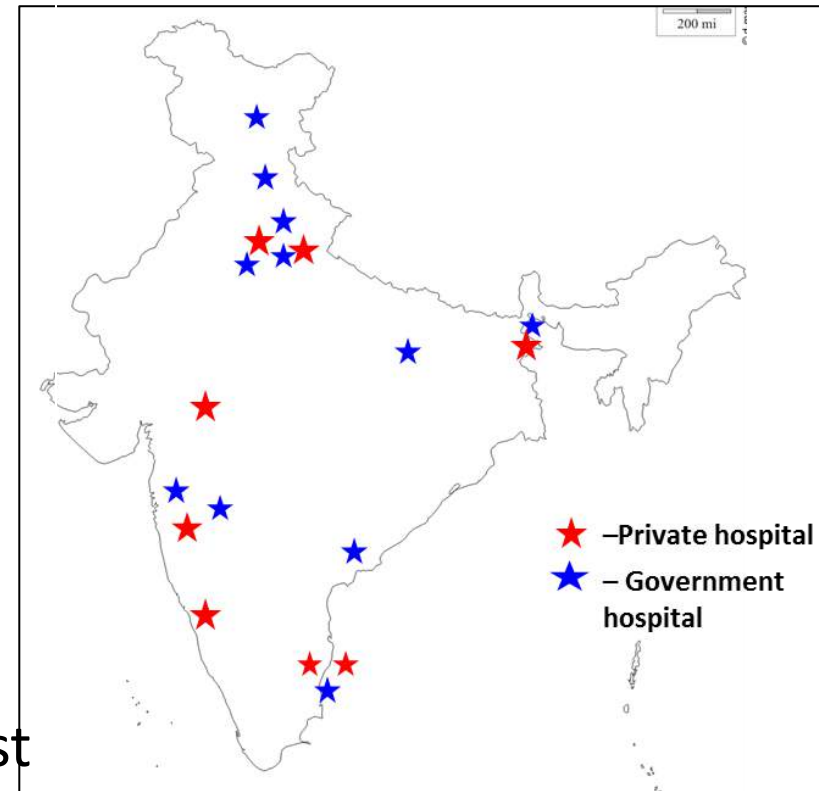
No. of genes identified in CRO multiplex PCR reaction

ORGANISM	NC	'n'	SPM	IMP	VIM	NDM	OXA-48 Like	KPC
P. aeruginosa	CMC	55	0	0	10	9	1	0
	AIIMS	9	0	0	4	0	0	0
	JIPMER	14	0	0	2	0	0	0
Acinetobacter sp.	CMC	30	0	0	0	4	0	0
	AIIMS	9	0	0	0	2	0	0
	JIPMER	30	0	0	1	3	0	0



ICMR Antimicrobial Stewardship Program: Survey of Practices, 2014

- 20 Hospitals: 13 public and 7 private
- AMSP documents in 4/20 hospitals
- Accreditations better in private hospitals
- Infection control document in 20/20
- Comprehensive treatment guidelines missing in most hospitals
 - Syndrome specific guidelines frequently available
- AMSP not linked with IT system in most hospitals
- Most hospitals do not have infectious disease physicians and clinical pharmacists





Antimicrobial Surveillance and Research network

E. coli from blood

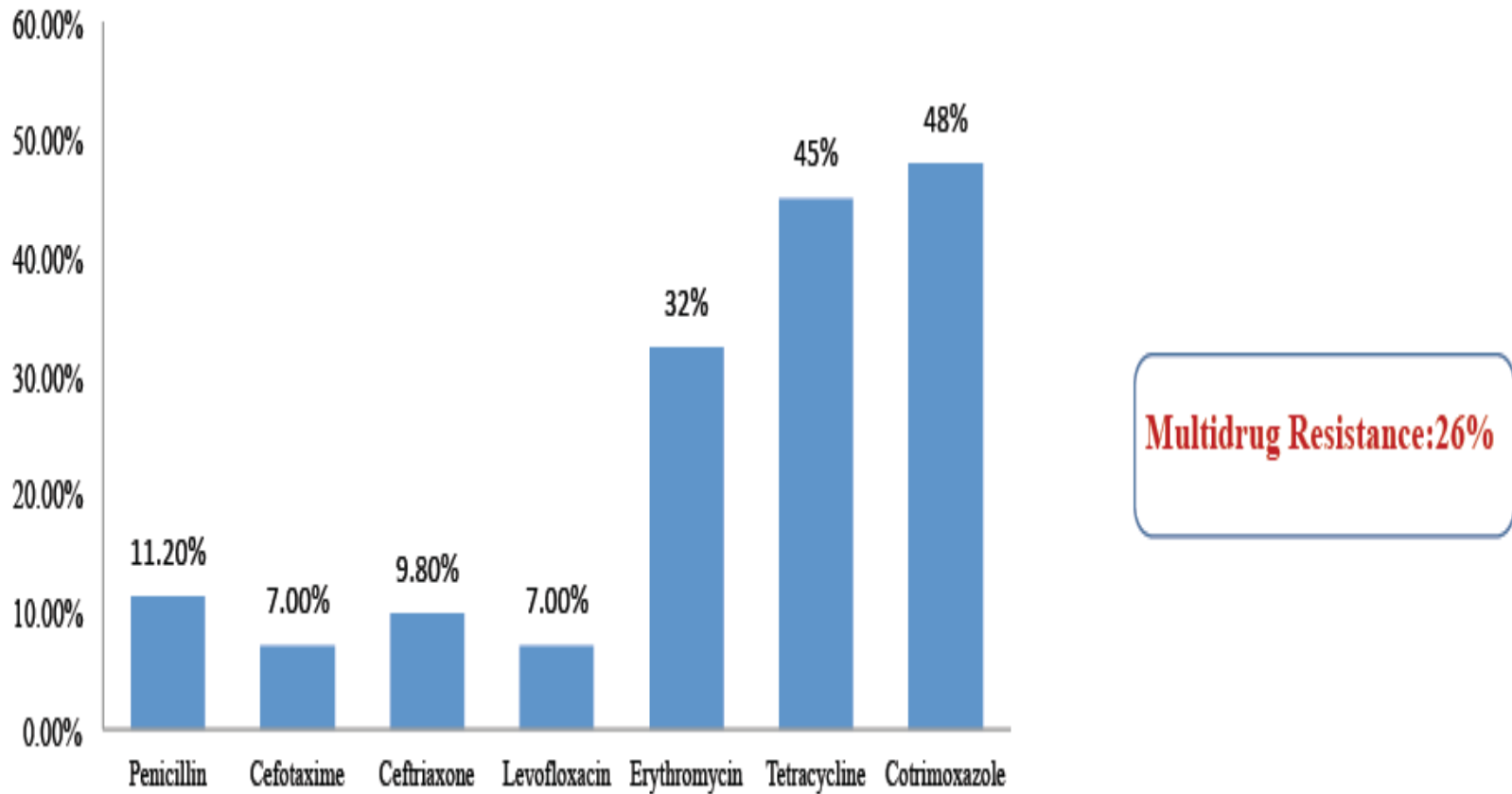
	PGIMER	CMC Vellore	JIPMER
	% sensitivity		
Cefotaxime	<10	30	19
Cef-sulbatam	50	80	80
Amikacin	78	>90	83
Ceftazidime	8	25	30

Klebsiella spp from blood

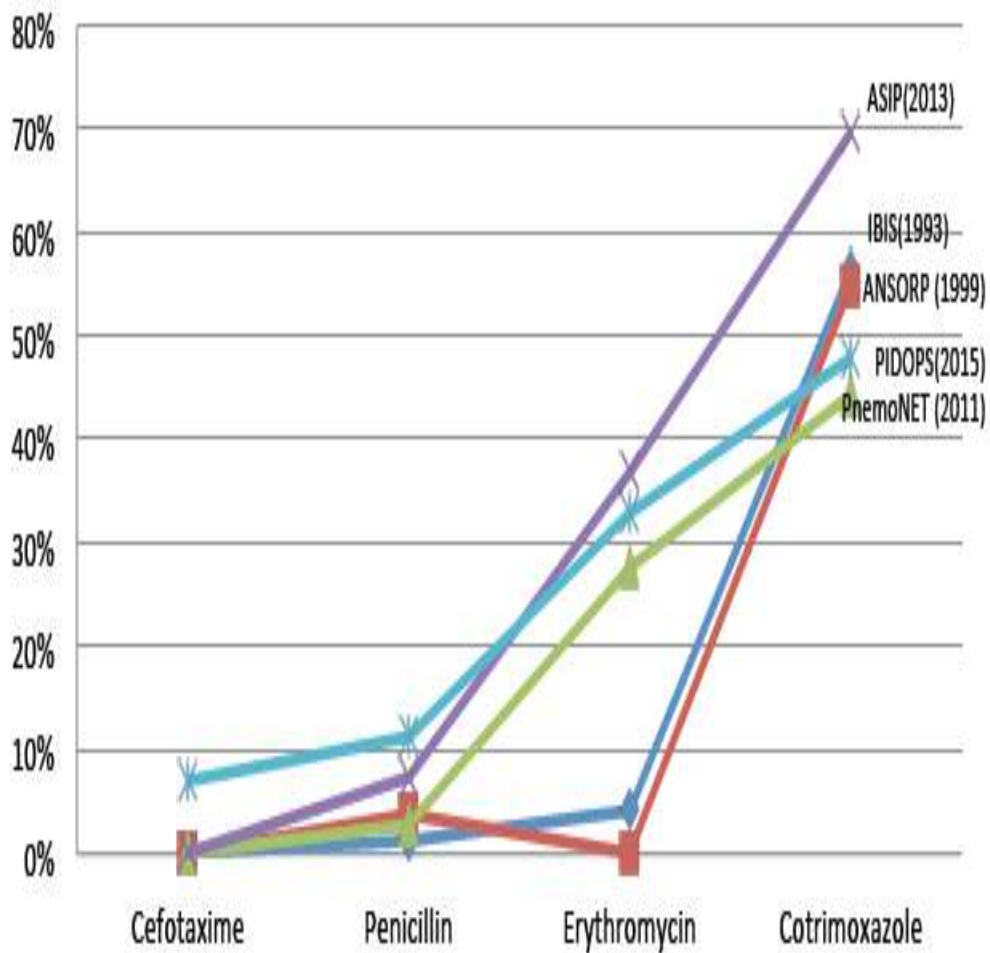
	PGIMER	CMC Vellore	JIPMER
	% sensitivity		
Cefotaxime	<10	40	6
Cef-sulbatam	20	60	32
Amikacin	<40	60	42
Ceftazidime	8	40	8
Pip-Tazo	30	45	****

Trends in Anti-microbiome

Pan Indian Distribution of Pneumococcal Serotypes



Trends in Anti-microbiome



PIDOPS study: Dr. K L Ravi

Foreign collaborations

- **National Institute of Allergy and Infectious Diseases, NIH, USA**
 - Systems biology
 - Epidemiology of neonatal sepsis
 - Clinical trials for new entities
- **Center for Disease Control, USA**
 - Strengthening infection control
- **Research Council Norway, Norway**
 - Methods for assessment of the burden of resistance
 - Integrated project surveillance systems for AMR and antibiotic use in humans and/or animals.
 - Ecological, evolutionary and molecular studies of AMR in clinical and non-clinical environments.

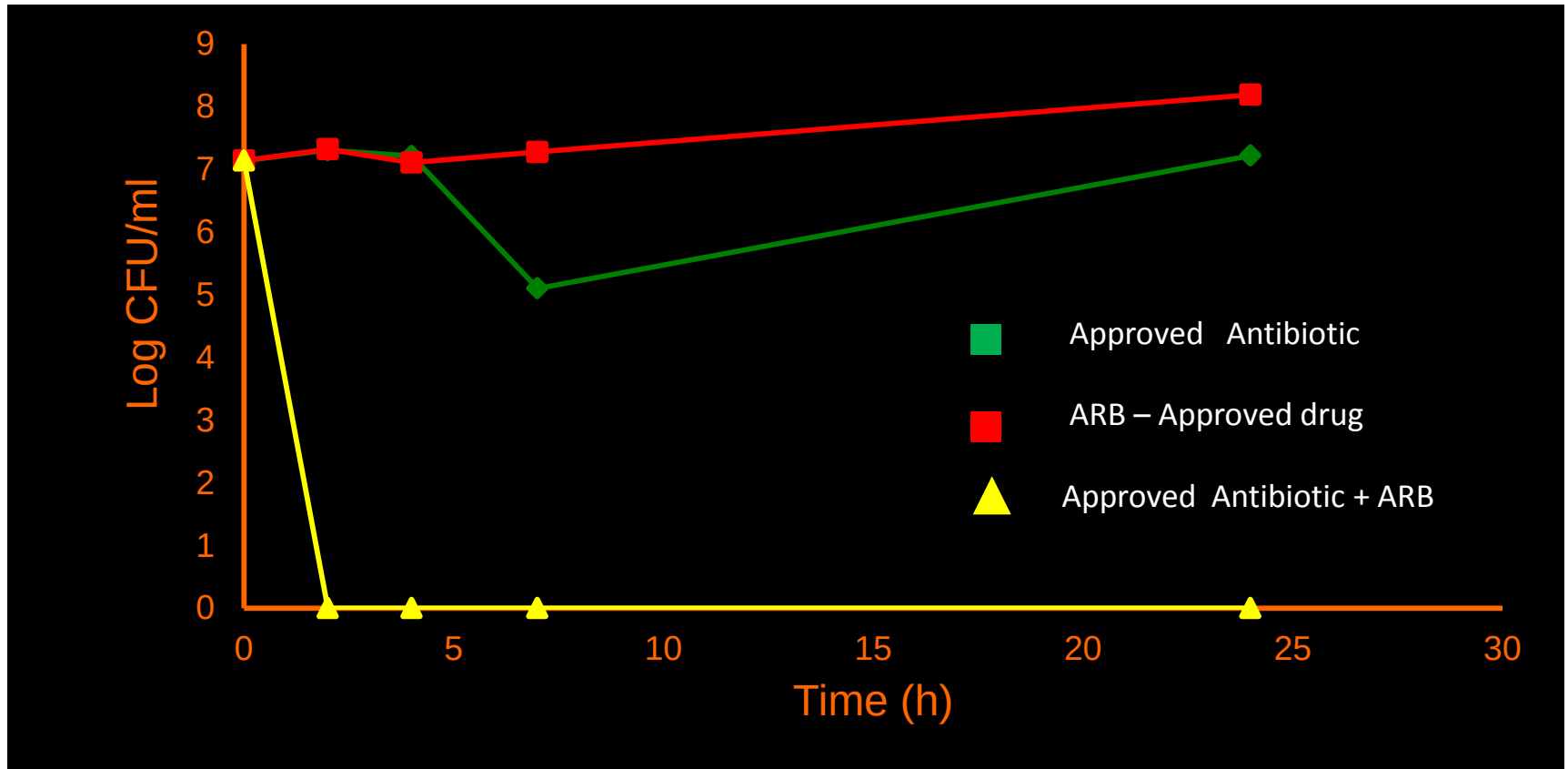


Antimicrobial Resistance – Cadila Approach

Collaborative effort with UK organization

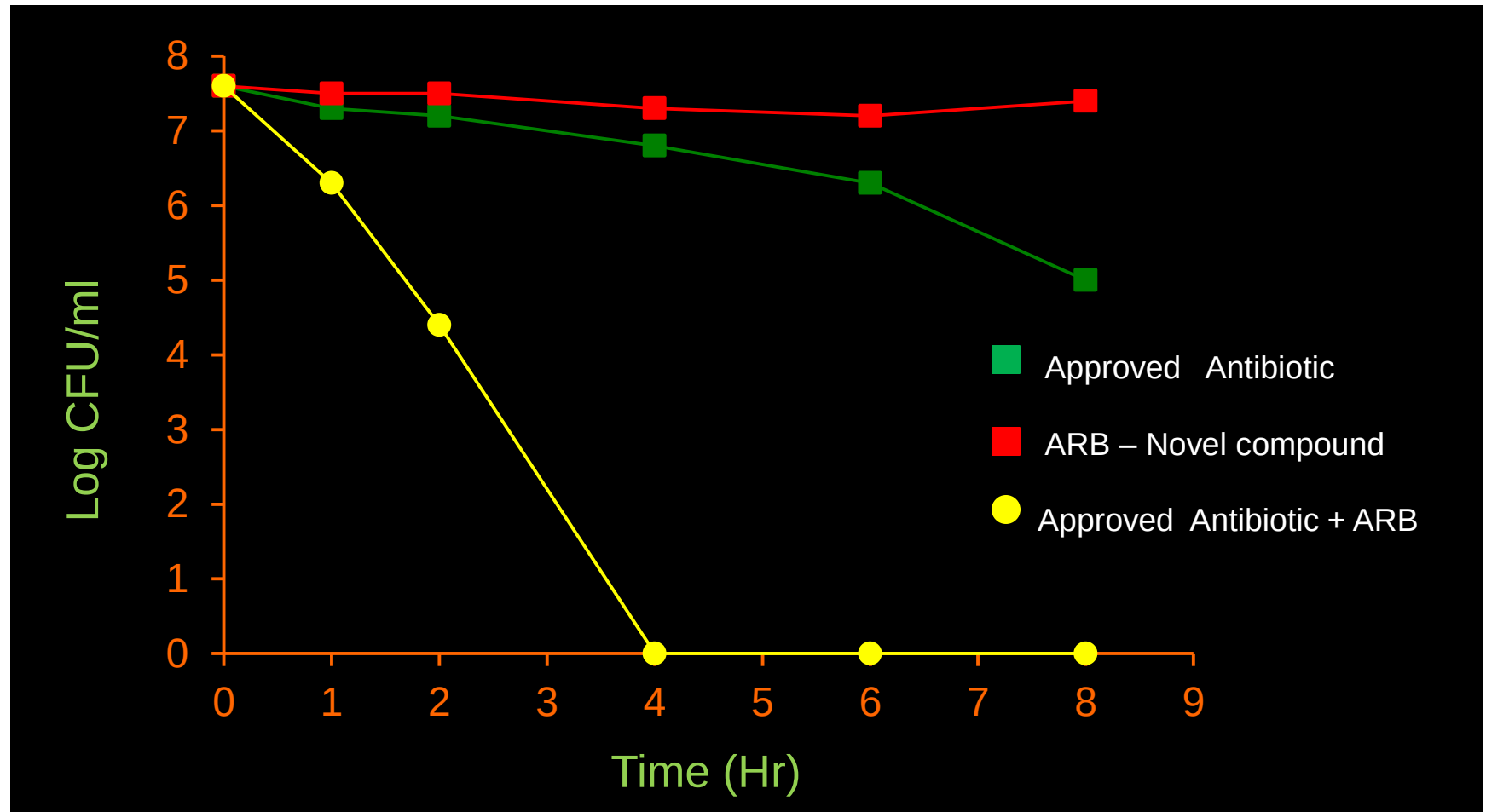
- Develop antibiotic resistance breakers (ARB) to rejuvenate known – approved antibiotics.
- Antibiotic Resistance Breakers
 - Improves efficacy of approved antibiotics
 - Effective against resistant organism
 - Faster killing
 - Least Chance of developing resistance
 - Effective against multiplying as well as non-multiplying organisms
 - Known compounds (approved drugs) as well as Novel compounds with no/minimal antibacterial activity

ARB and MDR Gram –ve organisms



Faster Killing of resistant organisms

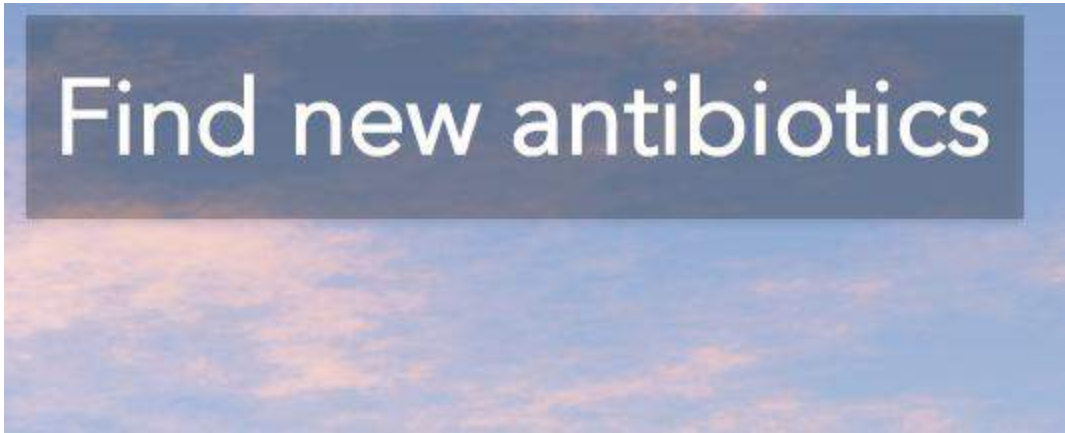
ARB and MRSA infection



Faster Killing of resistant organisms

Need for proactive actions to assist developing countries in strengthening systems to address AMR risks

- Strengthening national and international interdisciplinary cooperation and developing holistic strategies and action plans
- Improving regulatory frameworks based on internationally agreed principles and standards (Codex, OIE)
- Reducing the need for antimicrobials in animal husbandry, by improving animal health disease prevention and good practices along the chain
- Strengthening food and human surveillance systems for AMR and the quantities of all antimicrobials being used at the national level
- Raising awareness (among veterinarians, value chain actors including producers and the public) about AMR
- Developing appropriate policies/guidance on the prudent and responsible use of antimicrobials in animal husbandry
- Supporting research to generate data on the prevalence and trends in AMR, as well as supporting risk assessment, risk management and risk communication in the AMR area



Find new antibiotics

THANK YOU

Access Innovation and Conservation

The experience of ReAct

Otto Cars MD PhD
Professor Infectious Diseases
Uppsala University, Sweden
Founder and senior adviser ReAct



Antibiotic Resistance: A silent tsunami

Modern medicine

CANCER
TREATMENT

HIP
REPLACEMENTS

ORGAN
TRANSPLANTS

Child and
maternal health

GONORRHOEA

PRETERM
BABIES

COMPLICATED
DELIVERIES

Basic
medicine

WOUND
INFECTIONS

URINARY TRACT
INFECTIONS

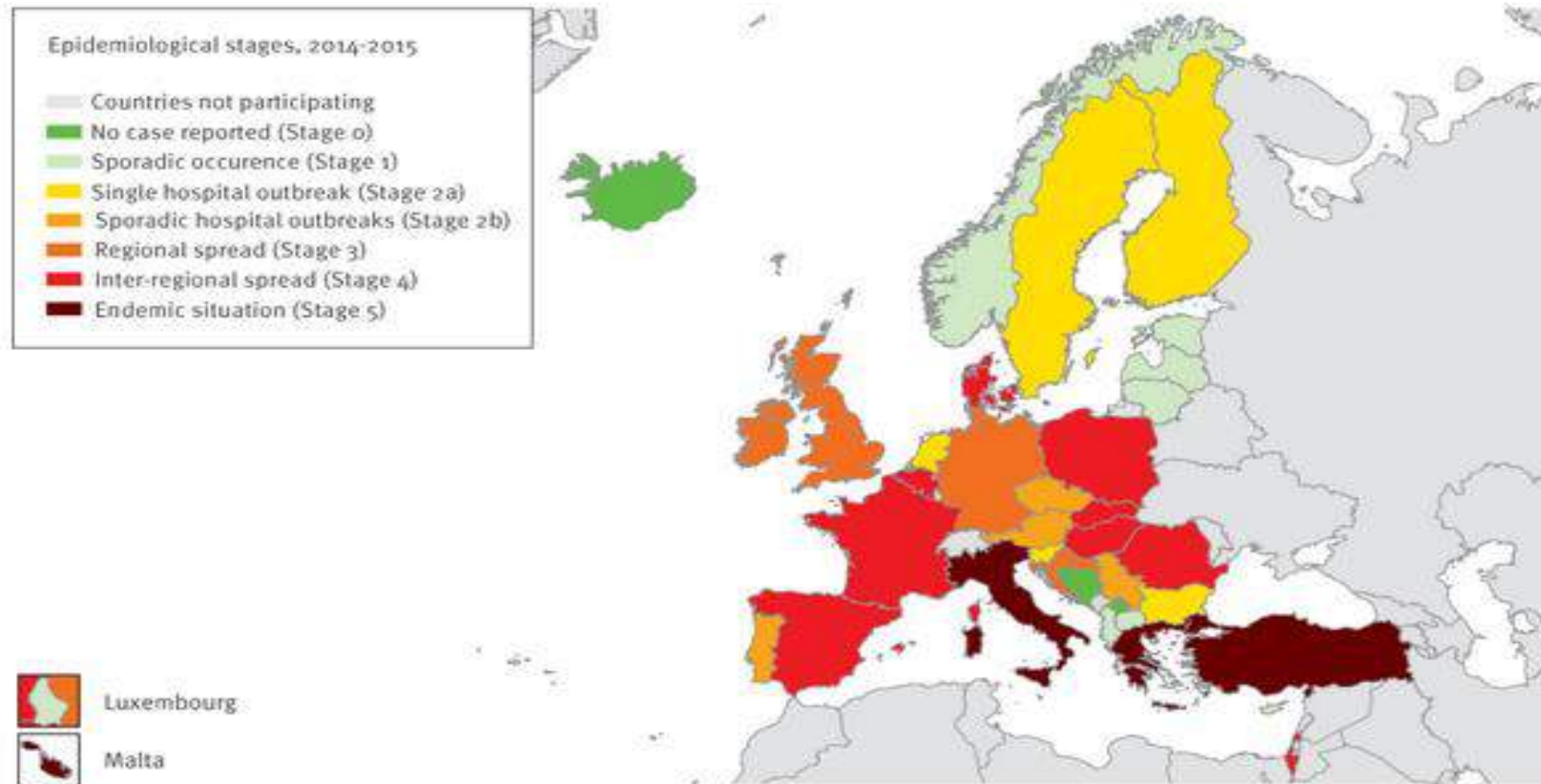
PNEUMONIA

BLOOD
INFECTIONS



Figure 1

Occurrence of carbapenemase-producing *Enterobacteriaceae* based on self-assessment by national experts, 38 European countries, May 2015





TECHNICAL REPORT

The bacterial challenge: time to react

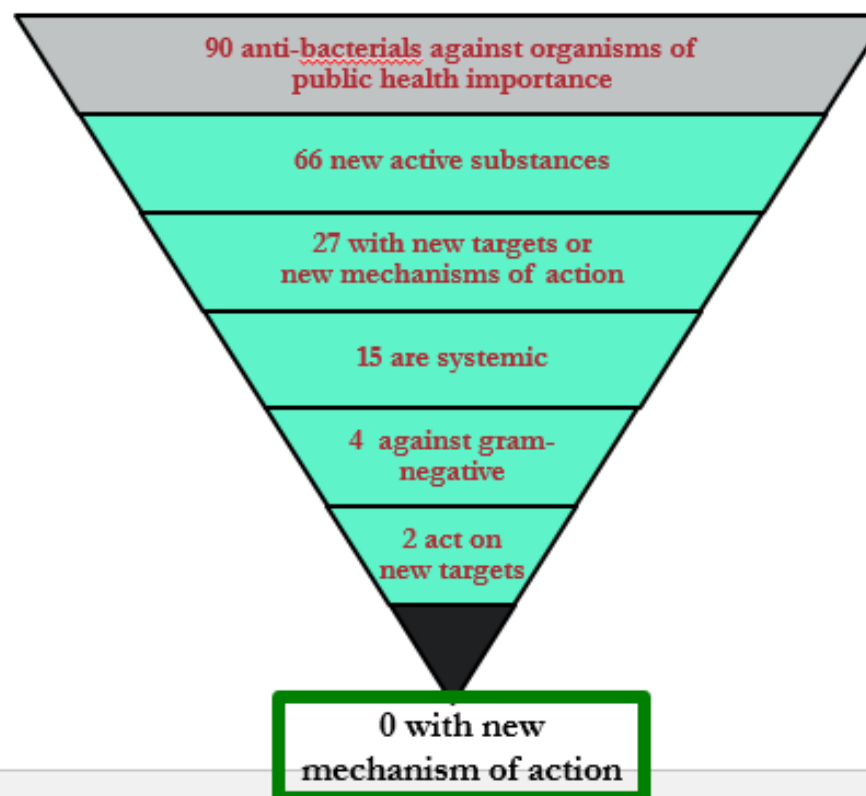
A call to narrow the gap between
multidrug-resistant bacteria in the EU and
the development of new antibacterial agents

www.ecdc.europa.eu
www.emea.europa.eu

The shortfall of the R&D pipeline

EMA-ECDC-ReAct pipeline analysis

Freire-Moran, et al. Critical shortage of new antibiotics in development
against multidrug-resistant *Drug Resistance Updates* 2011; 14: 118-124.



Antibiotic resistance—the need for global solutions



Ramanan Laxminarayan, Adriano Duse, Chand Wattal, Anita K M Zaidi, Heiman F L Wertheim, Nithima Sumpradit, Erika Vlieghe, Gabriel Levy Hara, Ian M Gould, Herman Goossens, Christina Greko, Anthony D So, Maryam Bigdeli, Göran Tomson, Will Woodhouse, Eva Ombaka, Arturo Quizhpe Peralta, Farah Naz Qamar, Fatima Mir, Sam Kariuki, Zulfiqar A Bhutta, Anthony Coates, Richard Bergstrom, Gerard D Wright, Eric D Brown, Otto Cars

“The infrastructure of antibiotic discovery both in academia and in industry is at a dangerously low level and needs to be rebuilt”



A leaking system



New antibiotics

Marketing

Volume sales

Misaligned financial incentives

Irrational use

“ Nobody likes to lose business. We give whatever they ask. Competition, location of shops, license issues...everything has become commercialized ”
- Urban pharmacist

“Even reputed companies offer complimentaries. If you prescribe more, they offer air conditioned car or free tickets.... Of late, we are forced to try new antibiotics ”
- Urban doctor

Typical Pharmaceutical Economic Model: Return is driven by sales volume



Investment

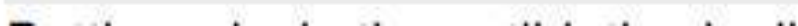
Preclinical and clinical
development.
Demonstration of
safety & efficacy

Return of Investment

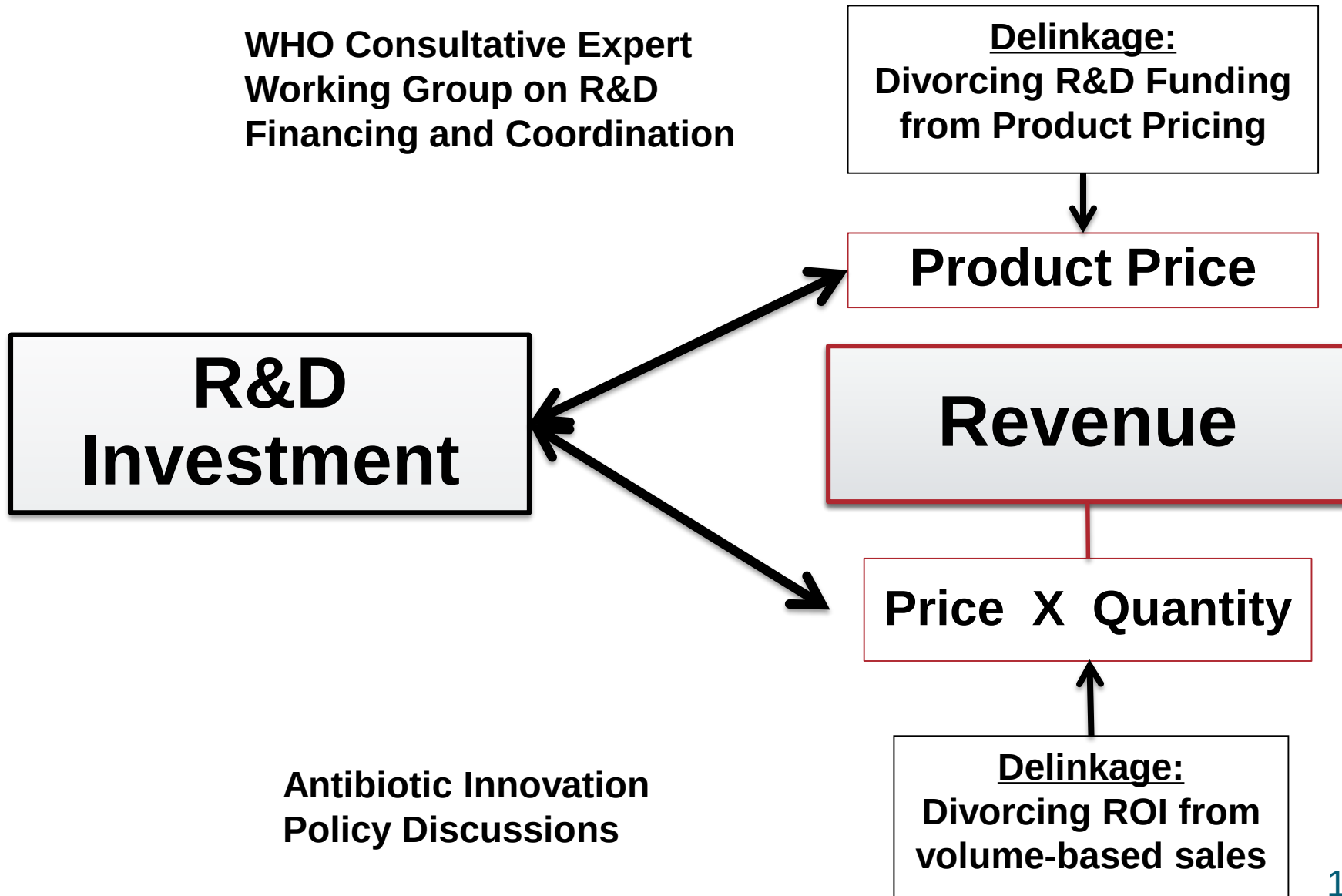
Price (somewhat) controlled by
authorities/payers

Volume (somewhat) driven by company and
competition

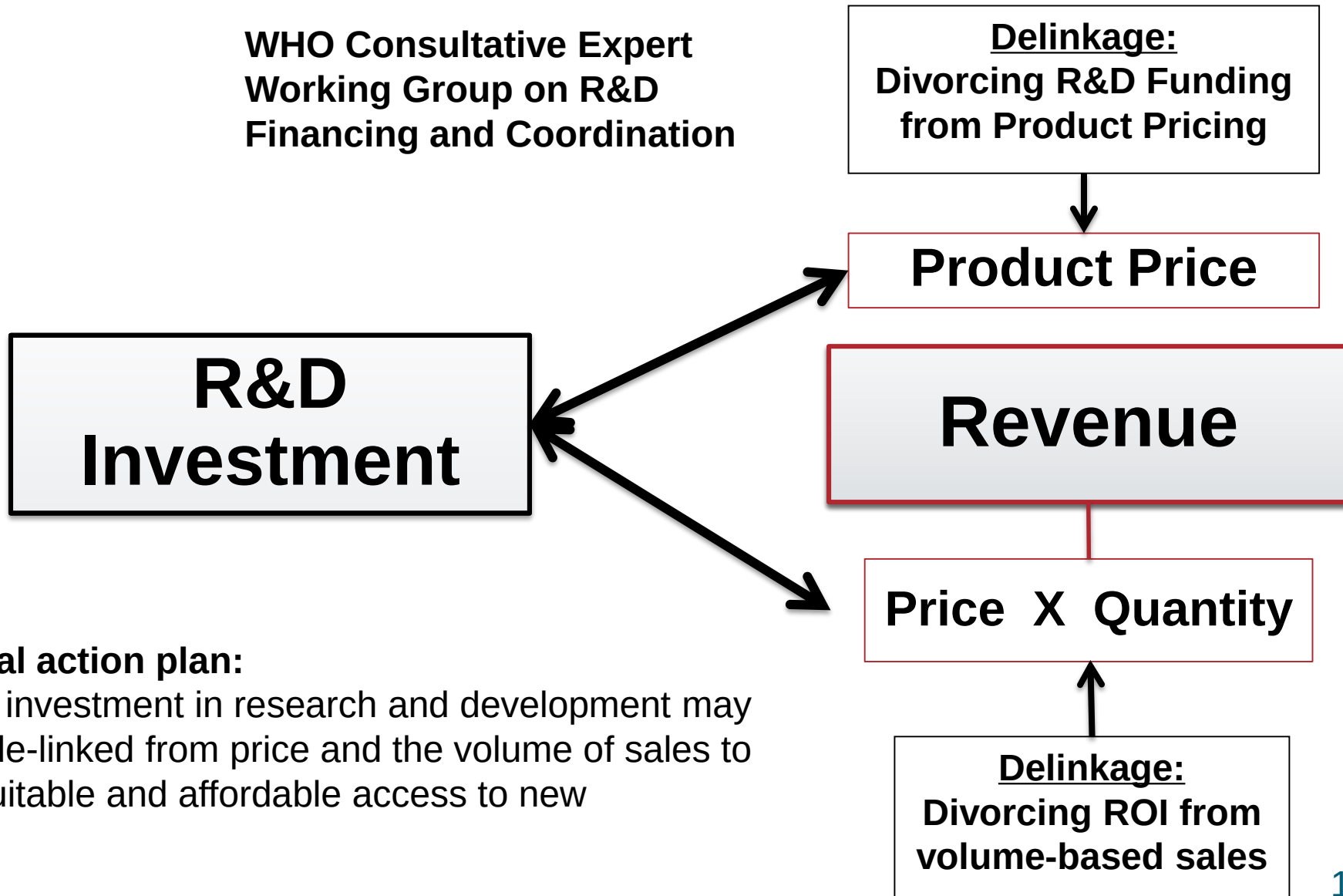
The stream of new antibiotics is struggling to keep up with emerging bacterial resistance. **Anthony So and colleagues** examine what can be done to increase innovation



Innovative financing to achieve de-linkage



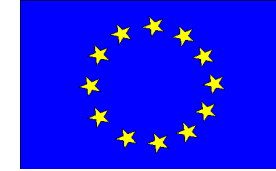
Innovative financing to achieve de-linkage



WHO Global action plan:

“The cost of investment in research and development may need to be de-linked from price and the volume of sales to facilitate equitable and affordable access to new medicines”

Innovative Medicines Initiative
New Drugs for Bad Bugs (ND4BB)

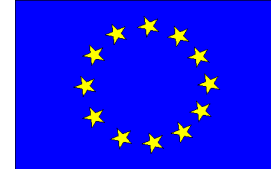


**US Biomedical Advanced
Research and Development Authority**
BARDA



Innovative Medicines Initiative

New drugs for Bad Bugs (NB4BB)



“Public investment into development of new antibiotics should come with appropriate obligations to governments, regulators, producers, and distributors with respect to the marketing and responsible use of these new products to avoid the rapid build-up of drug resistance”.

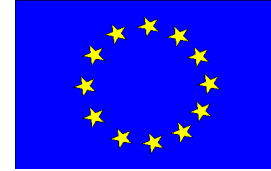
(WHO/DNDi concept note: Guiding principles)

US Biomedical Advanced Research and Development Authority

BARDA



Innovative Medicines Initiative
New drugs for Bad Bugs (NB4BB)



Both IMI and BARDA are supporting pivotal trials of the Astra-Zeneca combination avibactam-aztreonam

**US Biomedical Advanced
Research and Development Authority**
BARDA



OPEN

The Journal of Antibiotics (2015), 1–16

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www.nature.com/ja

REVIEW ARTICLE

A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics

Matthew J Renwick¹, David M Brogan^{1,2} and Elias Mossialos¹

Universal Access to Effective Antimicrobials: An Essential Feature of Global Collective Action against Antimicrobial Resistance

*Nils Daulaire, Abhay Bang, Göran Tomson, Joan N. Kalyango,
and Otto Cars*

Journal of Law, Medicine & Ethics, 2015

High Proportion of Intestinal Colonization with Successful Epidemic Clones of ESBL-Producing Enterobacteriaceae in a Neonatal Intensive Care Unit in Ecuador

Viveka Nordberg^{1,2*}, Arturo Quizhpe Peralta^{3,4}, Telmo Galindo³, Agata Turlej-Rogacka^{5,6}, Aina Iversen^{5,6}, Christian G. Giske^{5,6}, Lars Navér^{1,2}

Availability of old antibiotics

C. Pulcini et al. CID 2012;54:268

Mecillinam iv



Pivmecillinam

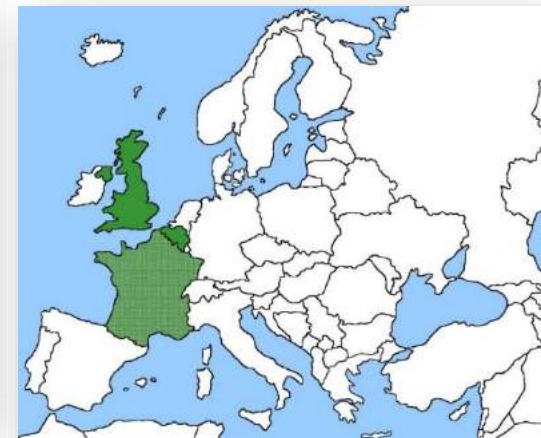


■ Available
■ Available through special system

Fosfomycin oral

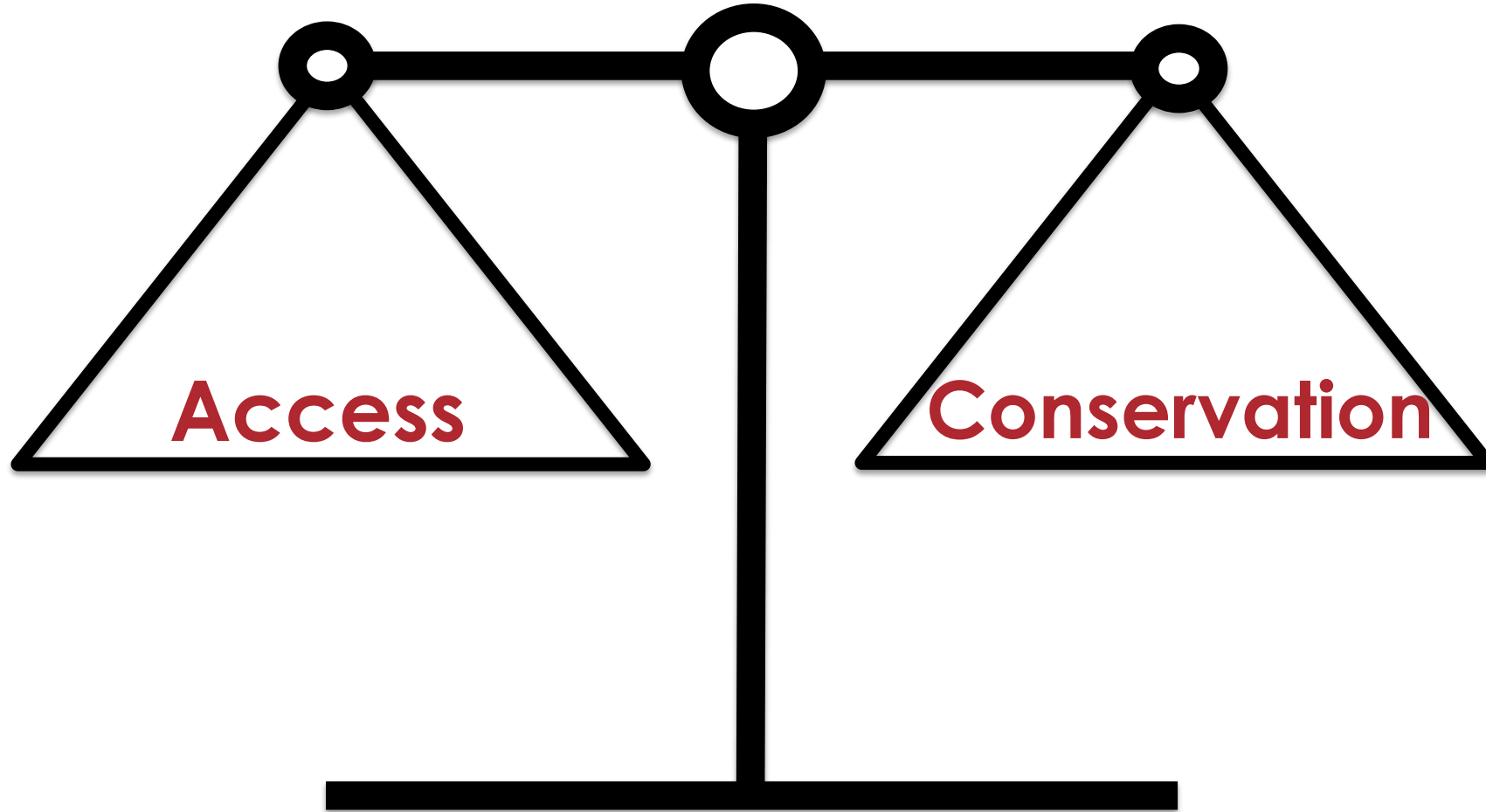


Temocillin



Ongoing Update 2015: Availability decreases, common long lasting shortages

Innovation





Antimicrobial Stewardship:

The South African Perspective

Precious Matsoso

Director General; National Department of Health;
South Africa

13th November 2015



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Why do we need an AMR strategy and implementation plan?

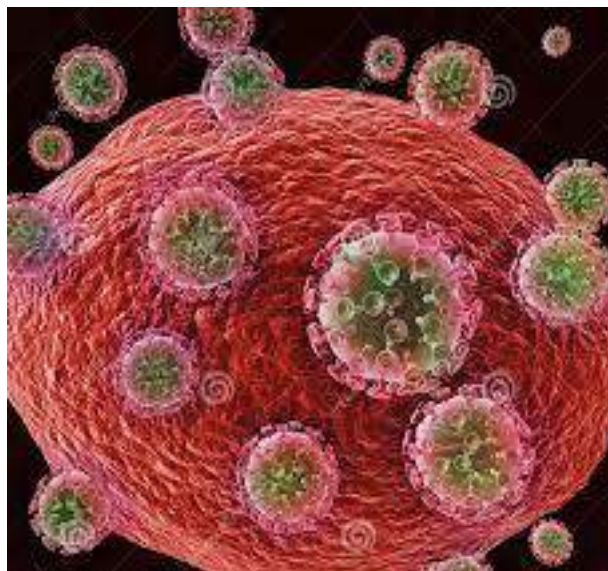


South Africa's triple burden of AMR Multidrug resistant organisms

Multidrug
resistant TB (MDR TB)

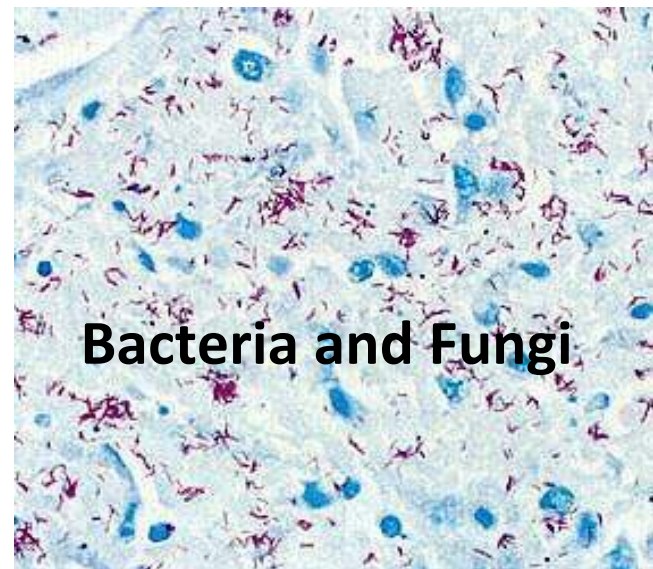


Drug resistant HIV
DRHIV



The AMR strategy and implementation plan focuses on multi drug resistant organisms

Multi drug resistant
organisms (MDR)



Bacteria and Fungi



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How serious is AMR in SA?



SAMJ situation analysis 2011

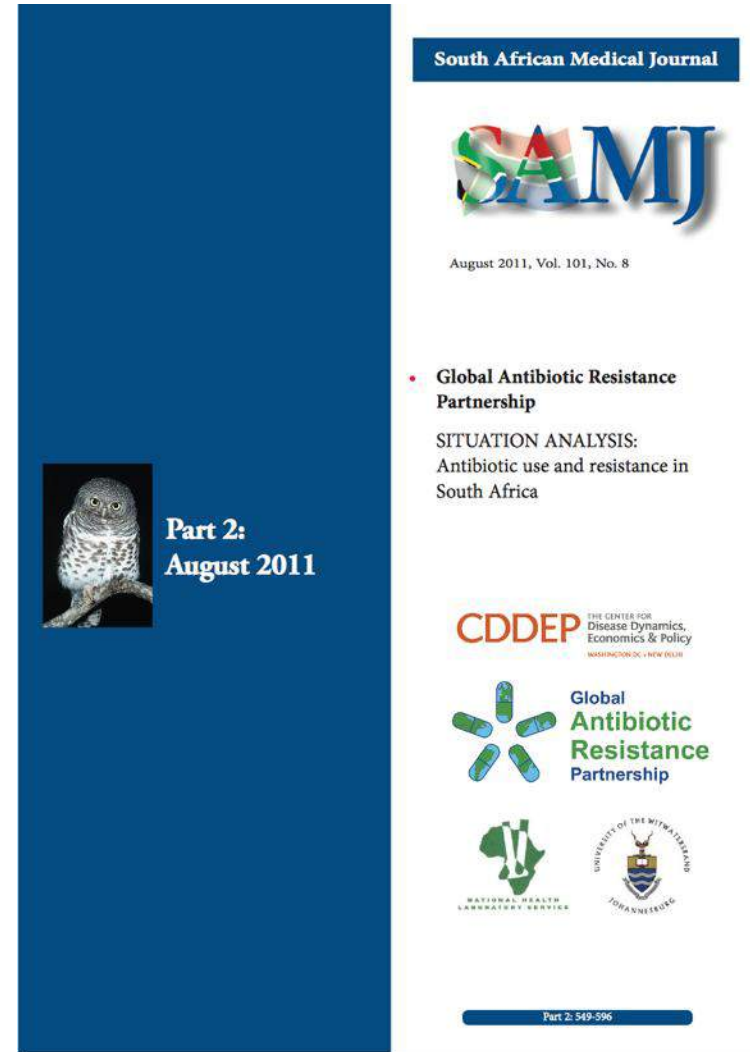
The situation analysis identified numerous concerns and resource constraints limiting implementation of good infection control practices and antimicrobial stewardship programs

More recent studies are showing similar high rates of HAI's

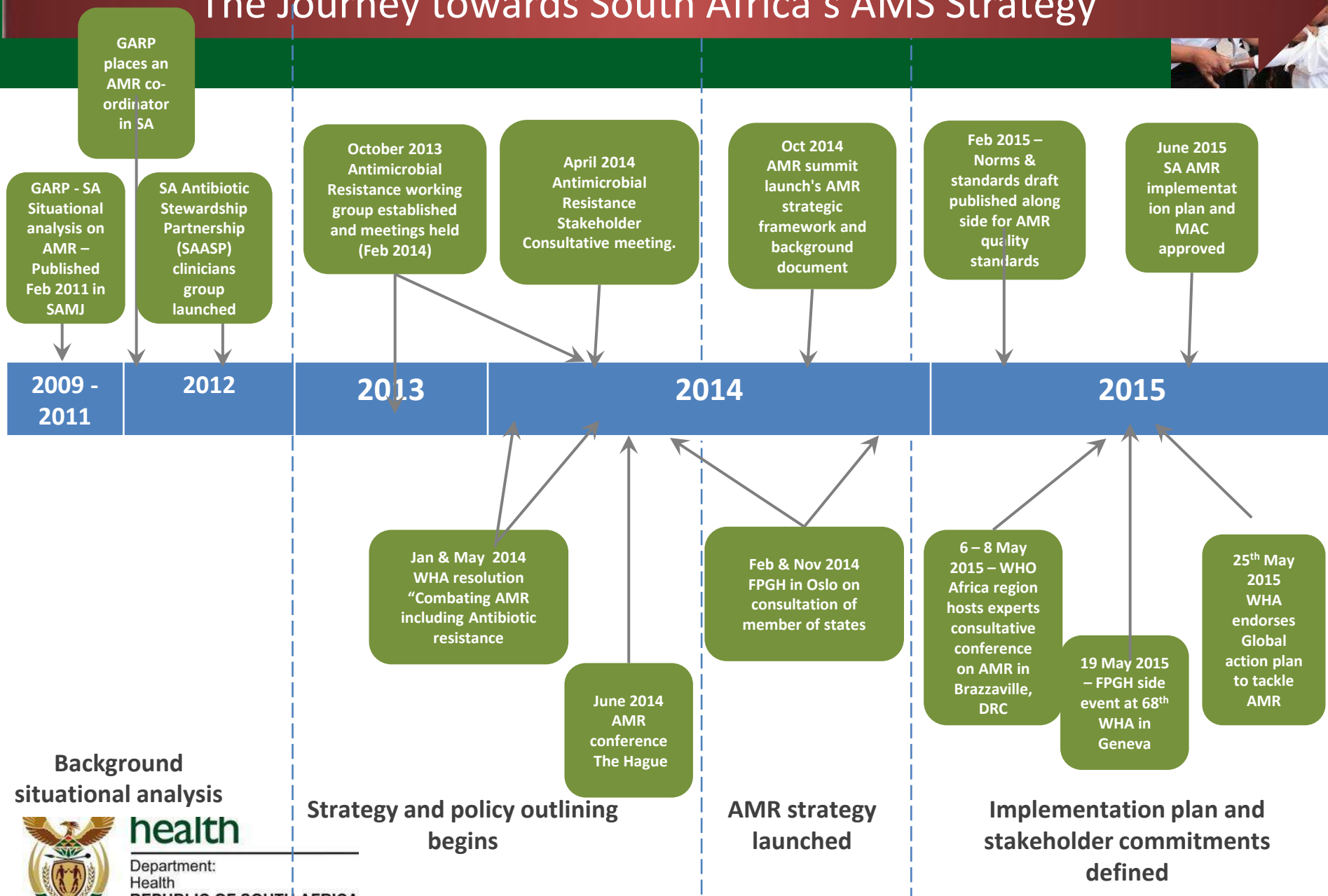


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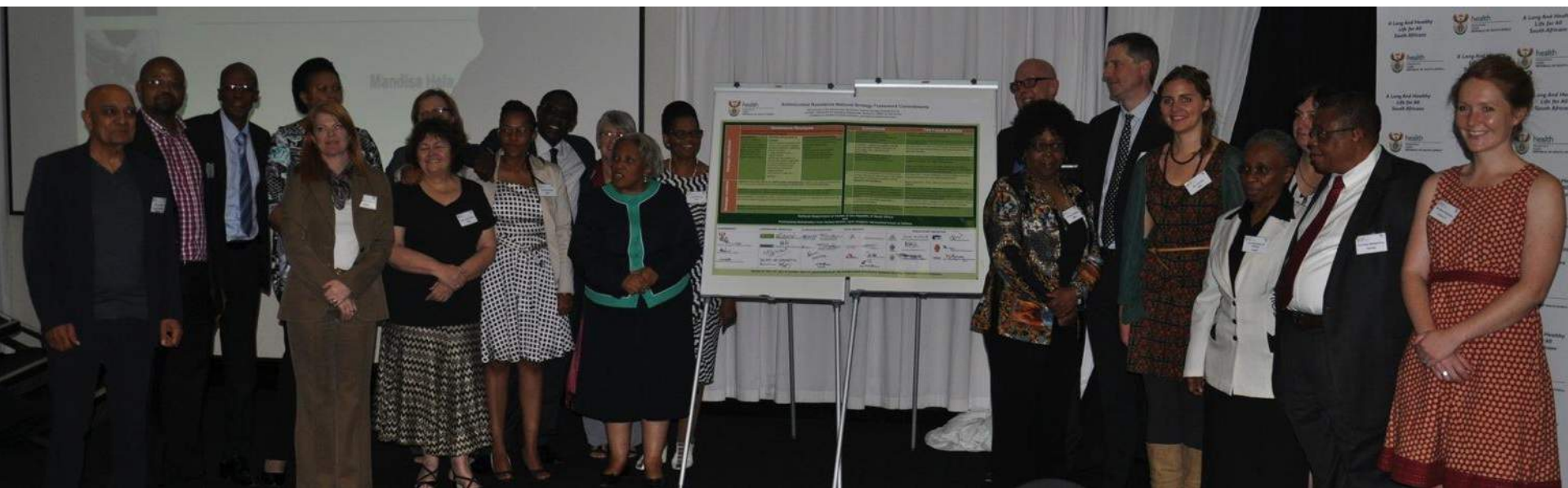
The Journey towards South Africa's AMS Strategy



The South African AMR initiative started at the summit in October 2014.



Brought together key stakeholders from government, laboratory services, clinician societies, civil societies and regulatory bodies



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The summit culminated in all stakeholders signing a commitment to



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Antimicrobial Resistance National Strategy Framework Commitments

The purpose of the Antimicrobial Resistance National Strategy framework is to provide a framework for managing Antimicrobial Resistance (AMR), to limit further increases in resistant microbial infections, and improve patient outcomes.

	Governance Structures			Commitments	Time Frames & Actions
	Strengthen, coordinate and institutionalise interdisciplinary efforts through national and health establishment level governance structures				
Strategic objectives	Surveillance Optimise surveillance and early detection of antimicrobial resistances to enable reporting of local, regional, and national resistance patterns to optimise empiric and targeted antibiotic choice	Infection Prevention & Control Enhance infection prevention and control of the spread of resistant microbes to patients in healthcare settings, focusing on improvement in hand hygiene and the identification and isolation of patients with resistant organisms. Community measures include preventing infection through wide-reaching vaccination programmes and improvements in water and sanitation.	Antimicrobial Stewardship Promote appropriate use of antimicrobials in human and animal health through antimicrobial stewardship including: • Effective policies and protocols • Stewardship at point-of-care • National prescribing guidelines • Appropriate antibiotic choice	1. To collaborate as intersectoral, interdisciplinary organisations and departments to strengthen, co-ordinate and institutionalise efforts to address Antimicrobial Resistance	Short term – March 2015: Establishment and initial meeting of National Ministerial Advisory Committee Short to medium term 2015 - 2019: Strengthen governance at Health Establishment levels
				2. To establish a national surveillance system to track and report resistant organisms and Antimicrobial use in agriculture and human health	Short term 2015 - Develop an Antimicrobial Resistance map for South Africa through data sharing between the private and public sector laboratory services
Strategic enablers				3. To enhance the processes, structures, resources and supplies needed for effective Infection Prevention & Control	Short term 2015 - Ensure the equipment and Infection Prevention & Control resources required to practice effective hand hygiene are available at all times in all Health Establishments Medium term 2016 – 2019 – All Health Establishments meeting compliance of the National Core Standards relating to Antimicrobial Stewardship and Infection Prevention & Control
	Legislative and policy reform for health systems strengthening to support the quality of antimicrobials in the country and to enable control over prescribing of antimicrobials in the animal health sector.			4. To promote the appropriate use of Antimicrobials in human and animal health through antimicrobial stewardship in facilities and suitable enabling legislation and regulations	Short term 2015 – Ensure availability of Antimicrobials according to Essential Medicines List in all Health Establishments Medium term 2016 – 2019 – Review of antimicrobials use in feed additives
	Education of all levels of health providers in human health and agriculture in the critical concepts of antimicrobial stewardship, infection control, infectious diseases, microbiology and pharmacology.			5. To build the expertise and strengthen the competency of health and veterinary professionals and improve the staffing levels of the workforce in Antimicrobial Resistance and Infection Prevention & Control	Medium term 2016 – 2019 - Development of strategy and operational plan for the integration and implementation of Antimicrobial Resistance and Infection Prevention & Control training into the undergraduate and post graduate medical curriculums of health care professionals in South Africa
	Communication to educate the public, create awareness of the dangers of inappropriate antimicrobial use and enhance patient advocacy to combat antimicrobial resistance.			6. To increase the community awareness of Antimicrobial Resistance	Short term 2014 – 2015 – Design of an awareness campaign relating to Antimicrobial Resistance based on past successful campaigns
	Research into novel diagnostics, such as point of care testing, new antimicrobials and implementation of treatment guidelines (treatment duration, antimicrobial consumption).			7. To promote research into novel diagnostics and clinical trials in Infection Prevention & Control and Antimicrobial Resistance	Long term 2019 – 2024 – Defined research opportunities

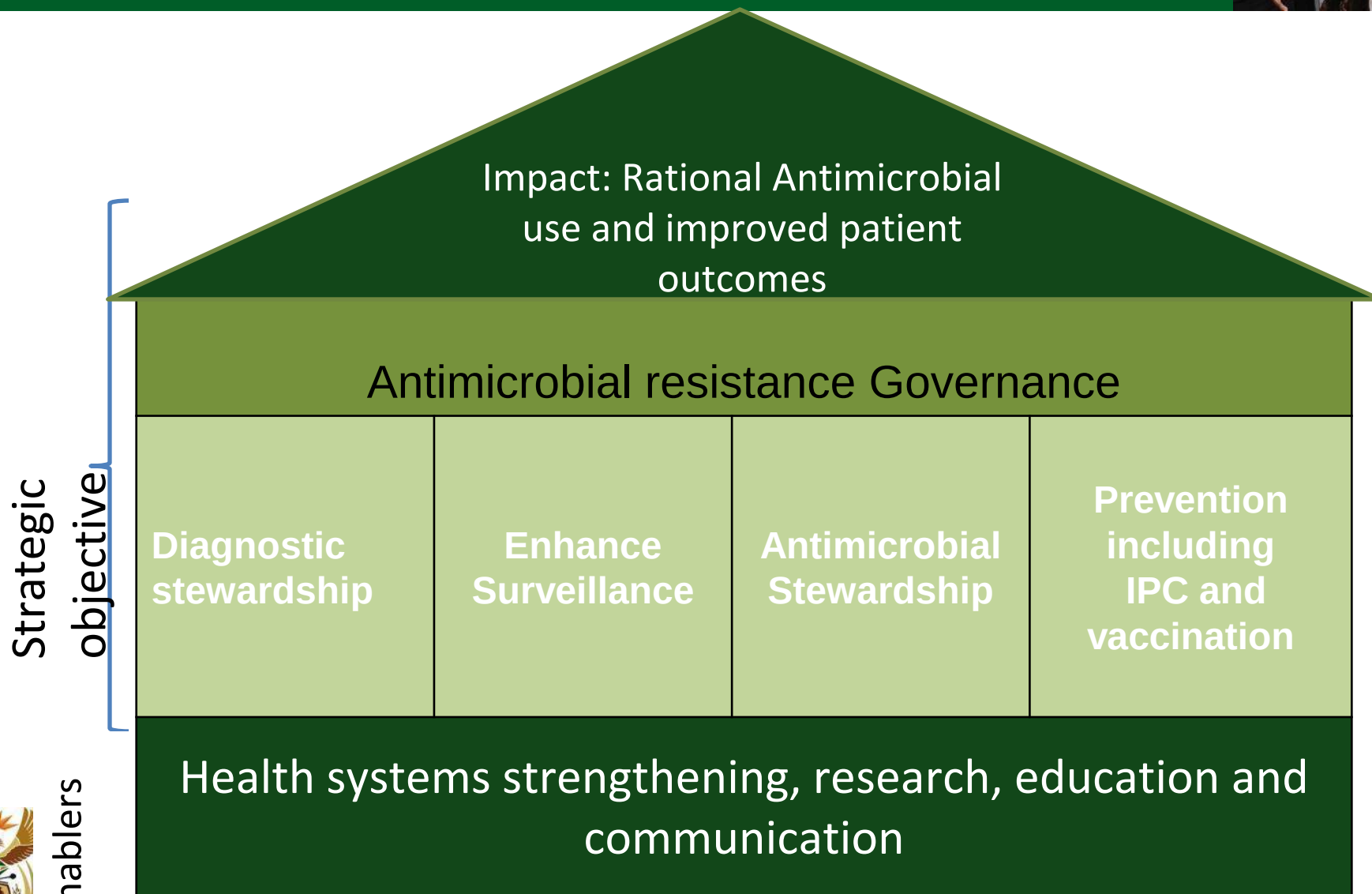
National Department of Health of the Republic of South Africa
and

Participating Stakeholders from Various Sectors, each Company represented herein as follows:

GOVERNMENT	LABORATORY SERVICES	CLINICIAN SOCIETIES	CIVIL SOCIETY	REGULATORY SOCIETIES
 Department of Agriculture, Forestry and Fisheries National Department of Health Department of Science and Technology	 National Health Laboratory Services AMPATH (on behalf of Private Labs) SALGA IVD DIAGNOSTICS BHE (on behalf of BHE)	 SAASP fidssa SAHWSOC L. M. M. P. S. S. A.	 TAC SECTION27 MSH Medicins Sans Frontières	 OHSC mce South African Pharmacy Council HPCSA Health Professionals Council of South Africa

Signed on this 16th day of October 2014 in Johannesburg as The Antimicrobial Resistance National Strategy Framework Commitments

Pillars of the South African AMR Strategy Framework



Objectives of the South African AMR Strategy Framework



Strategic objective

Strategic Enablers

- **1:** Strengthen, coordinate and **institutionalize interdisciplinary efforts** through national and health establishment level governance structures
- **2:** Improve the **appropriate use of diagnostics** to identify pathogens and guide treatment
- **3:** **Optimise surveillance and early detection** of antimicrobial resistances to enable reporting
- **4:** **Enhance infection prevention and control** of the spread of resistant microbes to patients in healthcare settings, wide-reaching vaccination programmes and improvements in water and sanitation; and
- **5:** Promote **appropriate use** of antimicrobials in human and animal health through **antimicrobial stewardship**.

- **Legislative and policy reform for health systems strengthening** to support the quality of antimicrobials and to enable control over prescribing of antimicrobials in the animal health sector
- **Education** of all levels of health providers in human health and agriculture in the critical concepts of antimicrobial stewardship, infection control, infectious diseases, microbiology and pharmacology
- **Communication** to educate the public, create awareness and enhance patient advocacy of the dangers of inappropriate antimicrobial use
- **Research** into novel diagnostics such as point of care testing and clinical trials of treatment duration, antimicrobial consumption plus new antimicrobials.



Implementation plan for AMR



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**IMPLEMENTATION PLAN FOR THE ANTIMICROBIAL RESISTANCE
STRATEGY FRAMEWORK IN SOUTH AFRICA: 2014–2019**

November 2015

Implementation plan has been approved

Each province must report quarterly on progress



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Implementation plan Monitoring & Evaluation

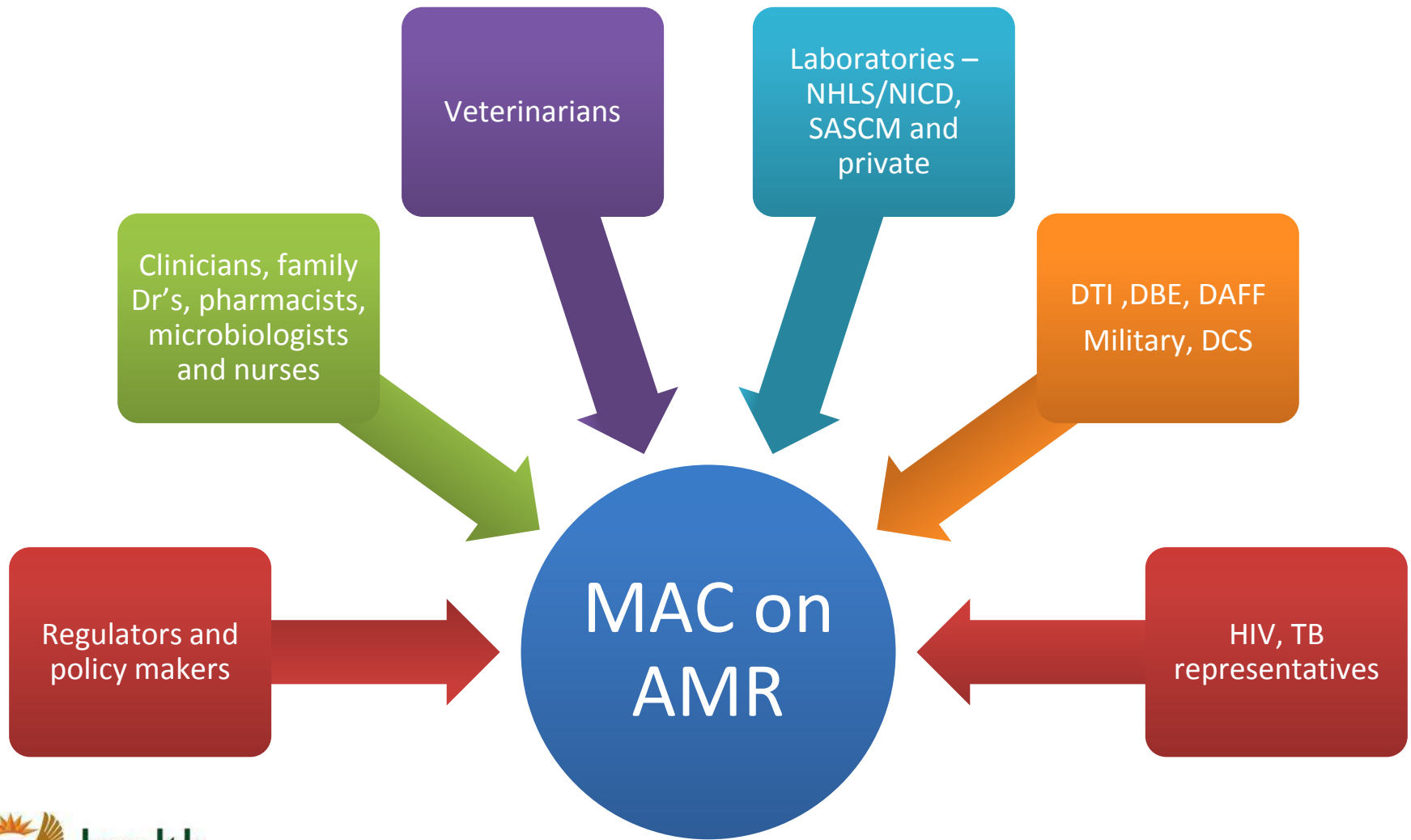


Indicators for monitoring impact:

- Reduction in key resistant organisms:
 - *Escherichia coli*—bacterial bladder infections (UTI's) and common infections in the community
 - *Staphylococcus aureus*—common cause of skin and soft tissue infections as well as bacteraemia in people of all ages
 - *Klebsiella pneumoniae*—common cause of severe infections of patients in hospitals that require treatment with carbapenem).
- Reduction in national consumption of antibiotics linked to key resistant organisms
- Reduction in maternal mortality from infectious diseases
- Reduction in neonatal mortality from infectious diseases



Ministerial Advisory Committee on AMR being appointed

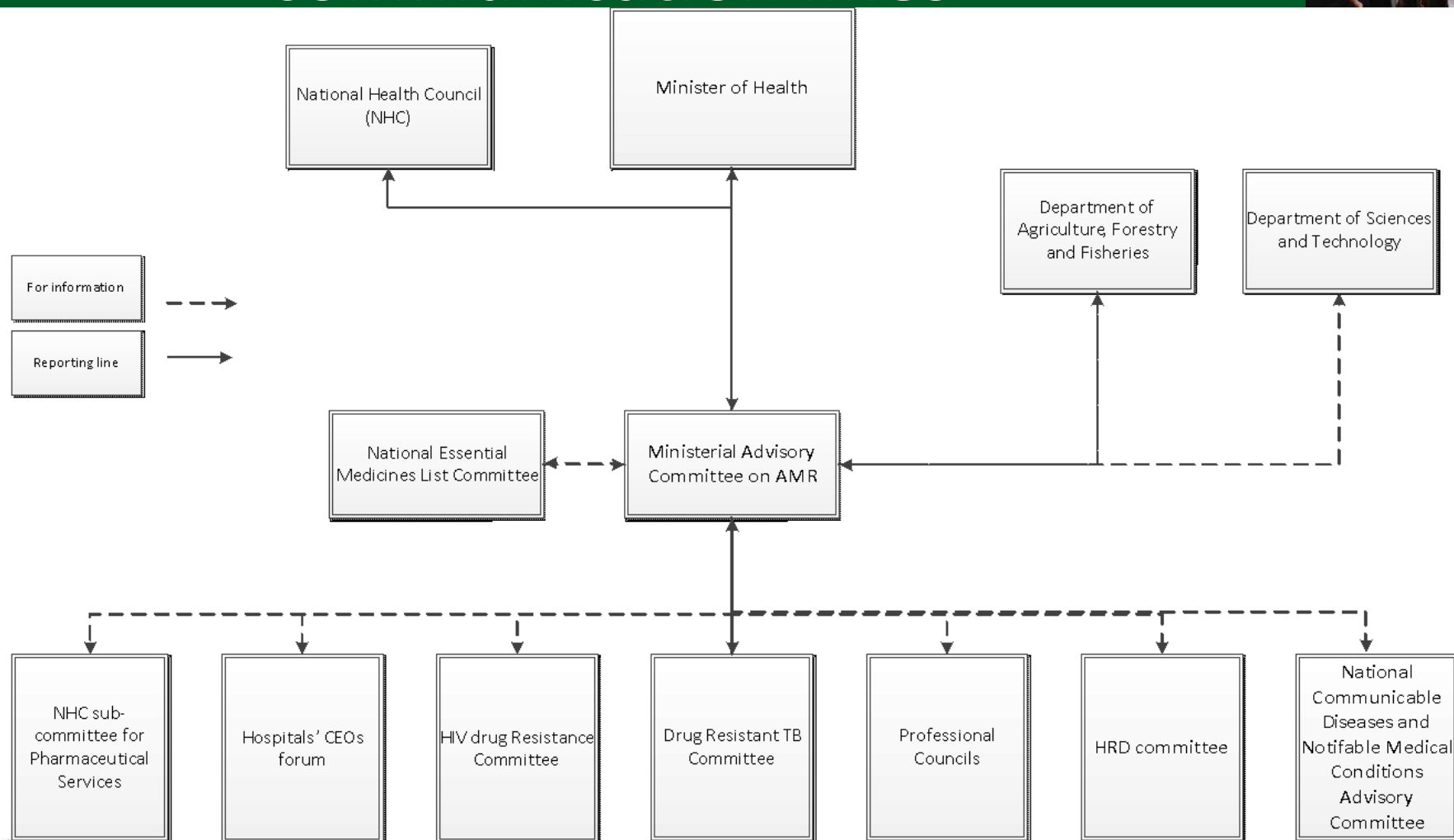


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NHC has approved the MAC and the
call for nominations is imminent

AMR MAC: Proposed reporting and communication lines



Partnerships



- Partnership between the following parties which:
 - Center for Disease Dynamics Economics and Policy (CDDEP)
 - South African Society of Clinical Microbiologists (SASCM)
 - National Institute for Communicable Disease (NICD)
 - South African Antibiotic Stewardship Programme (SAASP)
 - Best Care Always!



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AMR MAC:

Proposed membership



Core members (25)	Co-opted members
Department of Agriculture, Forestry and Fisheries Department of Science and Technology Department of Health: • Sector Wide Procurement; • Communicable Diseases; National Health Laboratory Services National Institute for Communicable Disease Microbiologists/Pathologists Infectious Disease Specialist Infection Control Specialist Veterinarian Paediatrician specialised in Infectious Diseases Hospital (clinical) Pharmacist Community Pharmacists District Pharmacist Information systems or data warehouse specialist (communicable diseases) Family Physicians Epidemiologist Health Economist	Nominated representatives from: • Basic Education • Trade and Industry • Correctional Services • Military Services Department of Health: Hospital Services and Health Workforce Primary Health Care HIV drug resistance committee TB drug resistance committee Malaria committee Regulatory bodies: Medical Control Council South African Nurses Council Health Professional Council of South Africa South African Pharmacy Council South African Veterinary Council Others: Civil Societies



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SA's Antibiotic Resistance picture



- Antibiotic-resistant bacteria are increasing in prevalence worldwide, resulting in infections that are difficult and expensive to treat.
- Laboratory surveillance data in South Africa show that from 2012 to 2014 (Drug-Bug combinations for tracking):
 - *Escherichia coli* (*E coli*) resistant to fluroquinolone is at 27% over this period;
 - **Staphylococcus aureus** – MRSA rate is 30%, though slight decline has been noted (from 35% in 2012 to 28% in 2014).
 - **Klebsiella pneumoniae** carbapenems resistant is at 3.2% rate and showed increase from 2.9% to 4.2% over this period.
- All three organisms-antibiotic combinations show no statistically significant change in proportion of resistance from 2012 to 2014



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CDDEP THE CENTER FOR
Disease Dynamics,
Economics & Policy
WASHINGTON DC • NEW DELHI

sascm
South African Society
for Clinical Microbiology

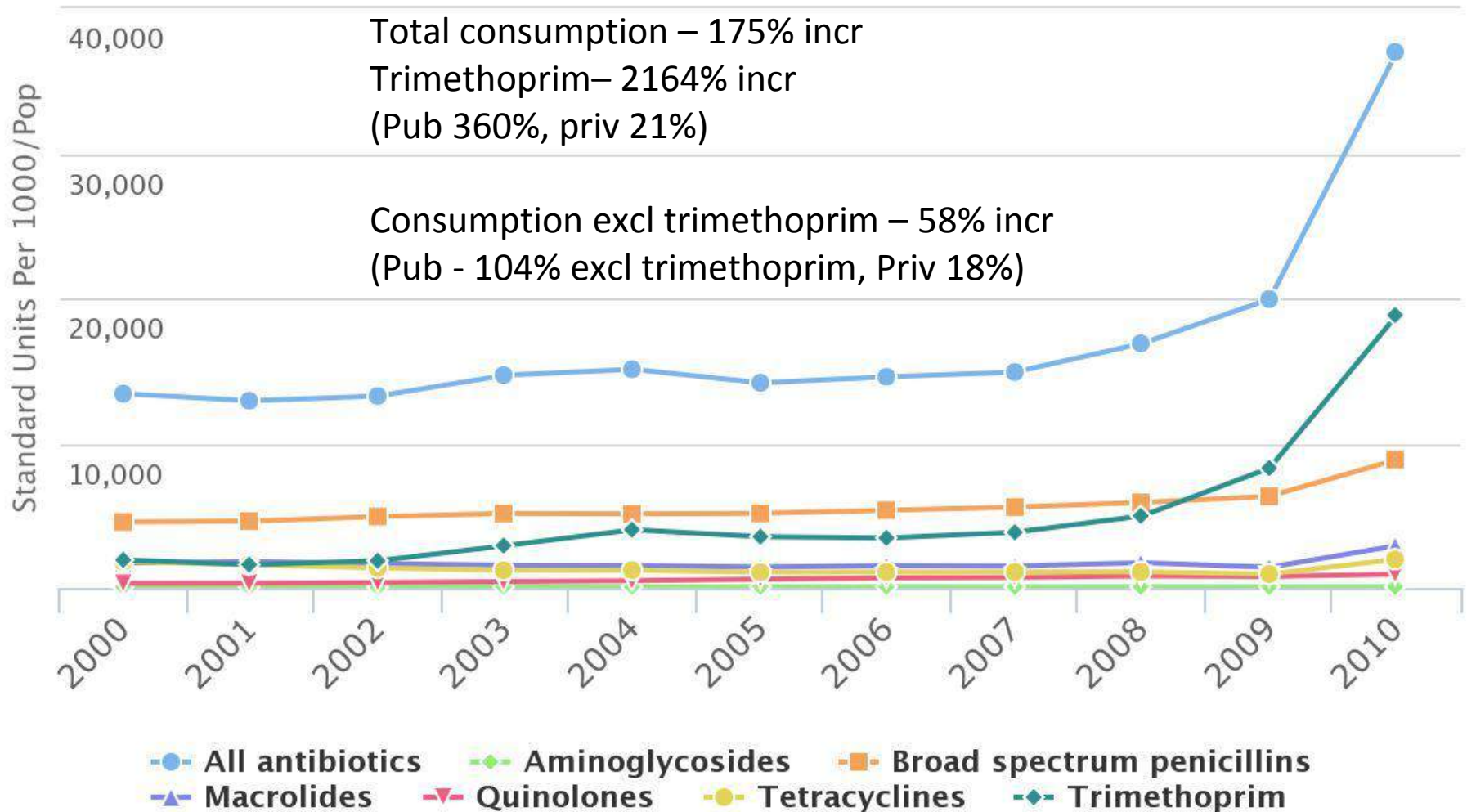
SAASP
SOUTH AFRICAN ANTIBIOTIC
STEWARDSHIP PROGRAMME

SA's consumption alone increased by 175% when trimethoprim is included



Antibiotic Use in South Africa

Source: IMS Health



Next steps and activities



- Line item AMR surveillance data to be collected by all the labs by province and by facility
- Animal health consumption and surveillance data to be sourced through partnerships with the Dpt of Agriculture (DAFF) and the Veterinary Societies
- Province departments being tasked to set out their implementation plans against the national AMR strategy



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Thank you

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