



Strategic priority for AMR

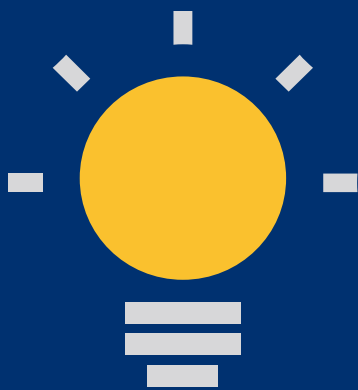
launching a new program

ASM / ESCMID Conference on Drug
Development to Meet the Challenge of
Antimicrobial Resistance

Boston

07 September 2014

Wellcome's framework for supporting science



Advancing ideas
We support great ideas
and inspired thinking



Seizing opportunities
We bring ideas together
to make a difference



Driving reform
We change ways of working
so more ideas can flourish

Wellcome's new strategic framework

Seizing opportunities

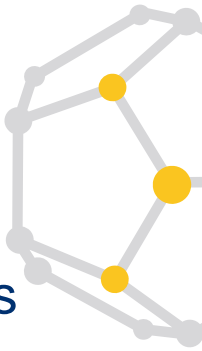
We bring ideas together to make a big difference

We identify times when our concerted intervention can accelerate progress towards better health.

We identify a critical need and set ambitious goals.

We connect experts from different disciplines, build partnerships, and lead advocacy, policy development, communications and public engagement.

We do this by providing focused, intensive support that creates a step change over five to ten years.



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Drug Resistant Infections **Why a priority area?**

The thoughtless person playing with penicillin is morally responsible for the death of the man from penicillin-resistant organism.

Hope this evil can be averted.

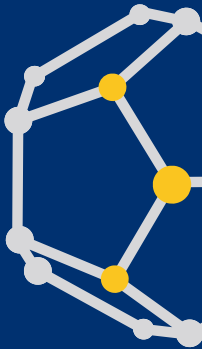
Alexander Fleming **1945**

Drug-resistant infections are a challenge on the scale of climate change.

Jeremy Farrar **2016**

Antimicrobial resistance is a slow-motion tsunami. It is a global crisis that must be managed with the utmost urgency.

Margaret Chan **2016**



Wellcome's priority area focused on AMR

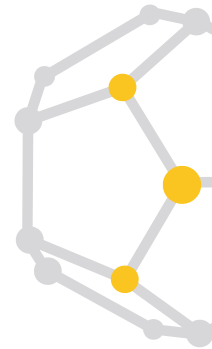
Will be

- Outcome / objective led
- Targeting research activities to deliver outcomes
- Commissioning work and inviting requests for proposals
- Influencing & advocating
- Building and catalysing partnerships

Response-mode funding (*Advancing Ideas*) will still support AMR research as it always has

Not a broad funding scheme for AMR

Not pulling all AMR activities under one umbrella



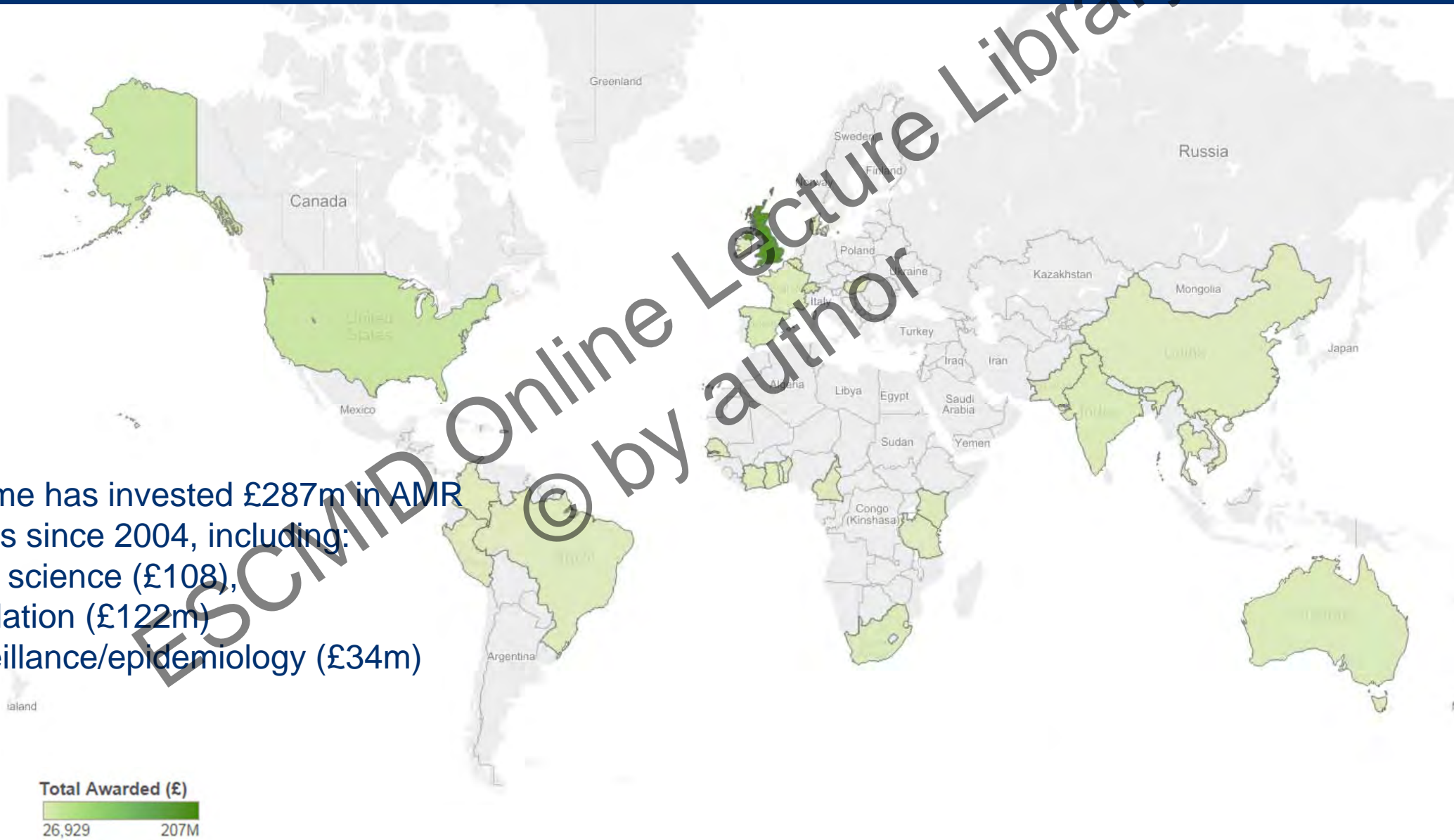
**A look at Wellcome's support
to advance ideas**

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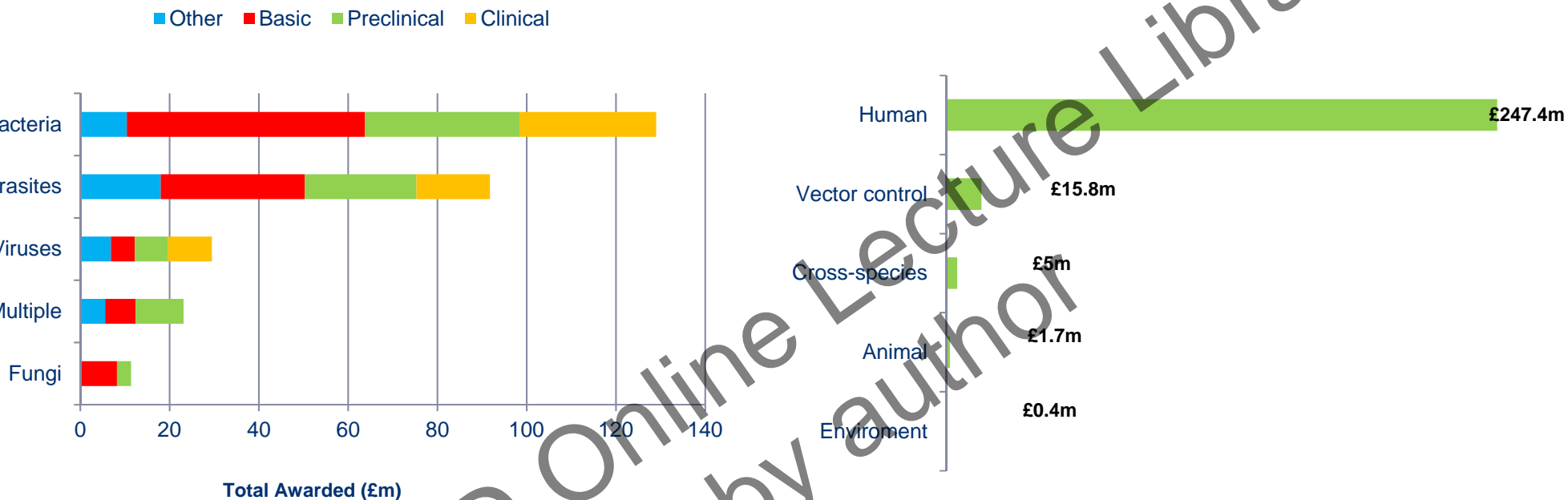
Funding research globally to tackle AMR

Some countries have invested £287m in AMR research since 2004, including:

- Basic science (£108m)
- Translation (£122m)
- Surveillance/epidemiology (£34m)



Funding since 2004 Pathogen type and stage of development

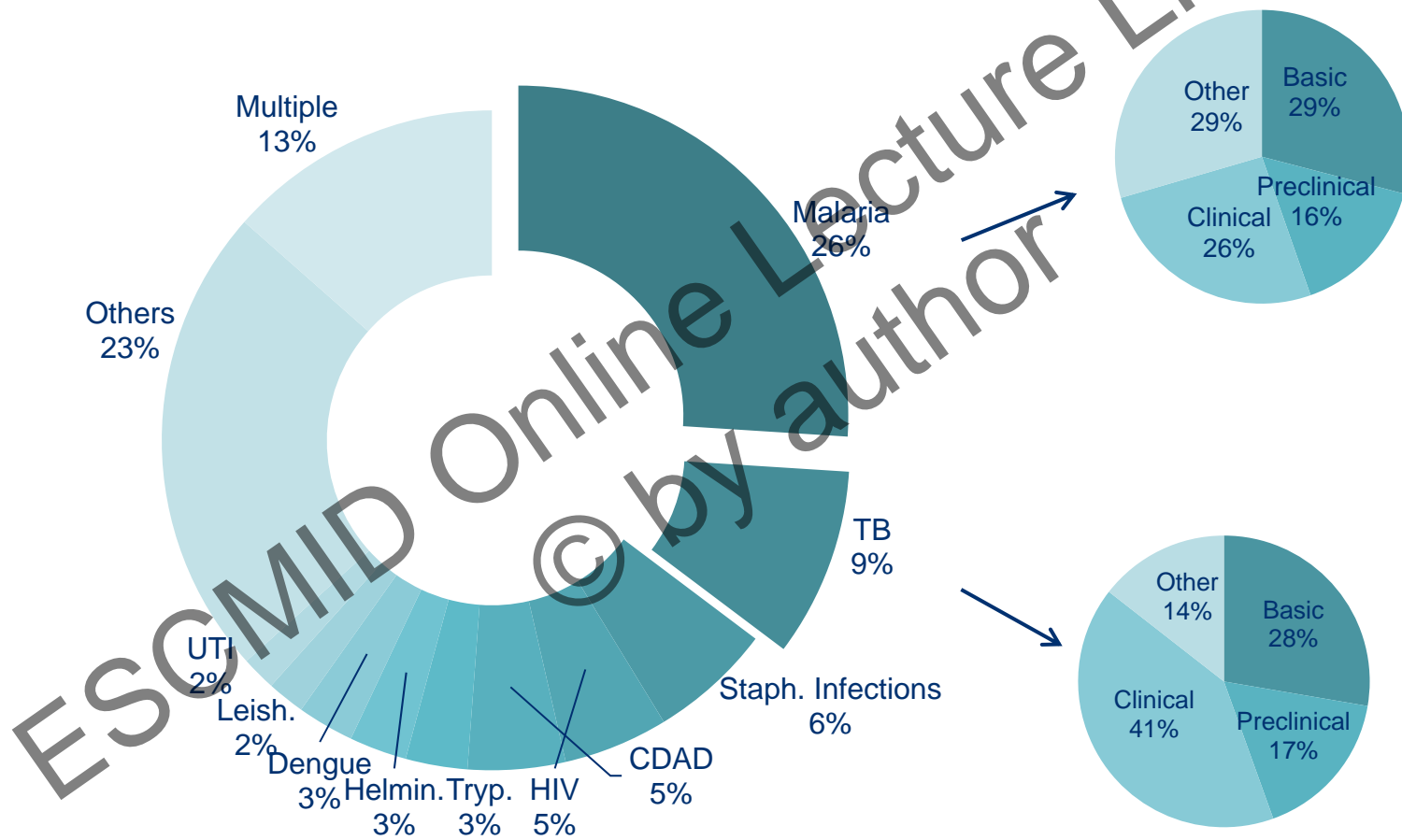


Significant investment in translational research for therapeutics in a smaller number of projects compared to basic science.

Notably there has been little support for diagnostic development and almost nothing in public engagement.

Outcomes relating to Wellcome-funded activities were not captured making it difficult to conclude the impact of investment

NT funding since 2004 Pathogen

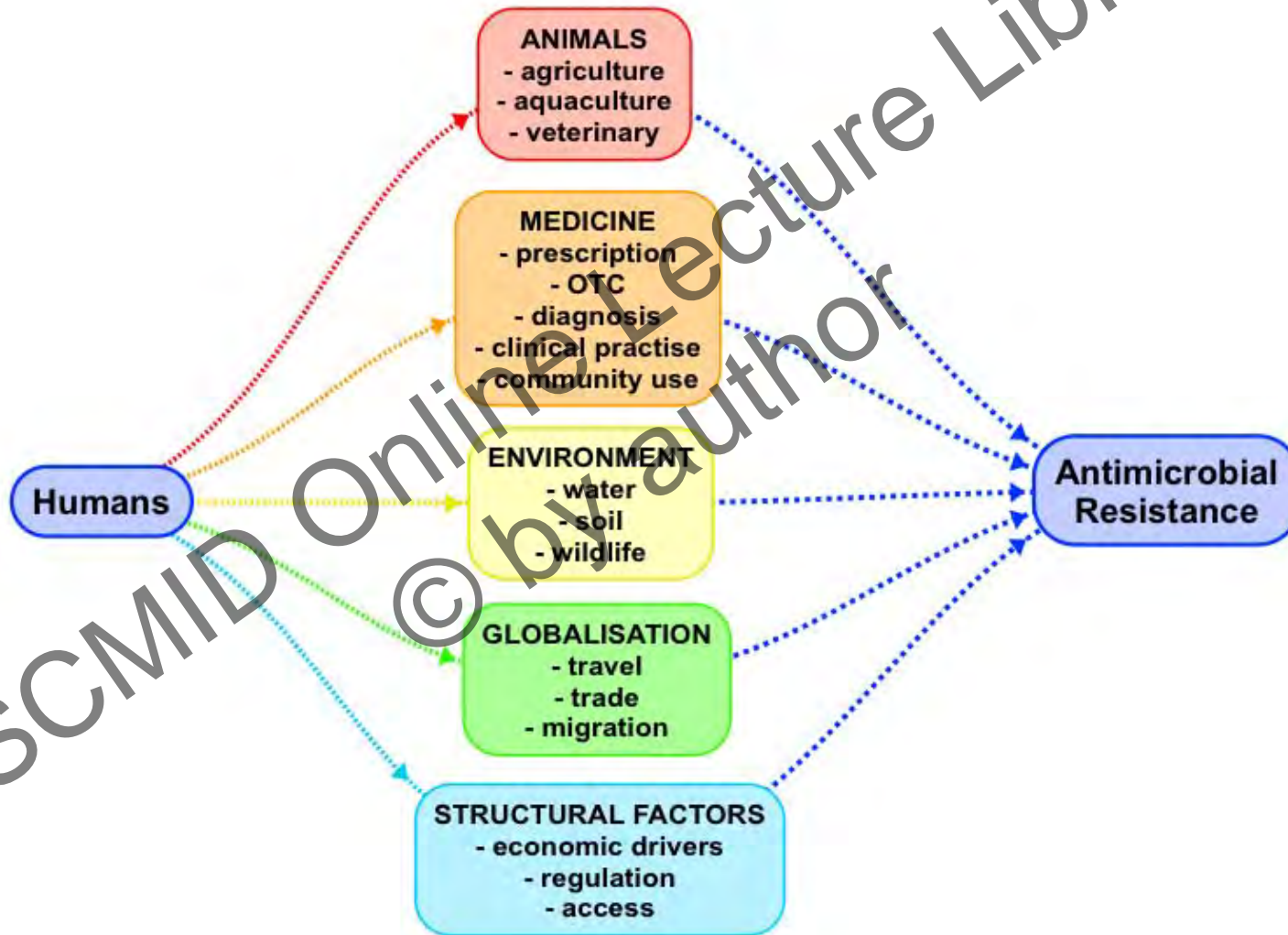


Funding has been heavily weighted toward malaria and to a lesser extent TB

The opportunity to be seized

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A complex problem with multiple drivers



Global Call to Action

Concerted efforts to tackle drug-resistance threat world-wide

World Health Organization

- WHO Strategic and Technical Advisory Group on AMR (2013-2016)
- Global Action Plan WHA68.7 (2015)

United Nations

- High-Level Meeting at UNGA (2016)
- Political Declaration 16-16108 (2016)
- IACG (2016 – present)

Trans-Atlantic Task Force on AMR (TATFAR) (2009-present)

Joint Programming Initiative on AMR (JPIAMR) (2014-present)

WHO Global Action Plan

to ensure treatment and prevention of infectious diseases with quality-assured, safe and effective medicines

GLOBAL ACTION PLAN

- Improve awareness and understanding of antimicrobial resistance
- Strengthen knowledge through surveillance and research
- Reduce the incidence of infection
- Optimize the use of antimicrobial agents
- Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions



Recommendations for tackling AMR on ten fronts



Review on Antimicrobial Resistance

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Developing Wellcome Trust's strategic priority

Seeking to transform the response to the threat of AMR by improving treatments, enabling policy and engaging communities

Near-term goals

Understanding emergence and transmission of AMR

Increased pipeline of new therapeutics and diagnostics, and optimisation of existing Tx

Accelerating development of new treatments for patients

Coordinating activities toward common goals

Long-term goals

- Paradigm shift in preventing and treating infections

- Coordinated international response to make healthcare systems resilient to threat of resistance

- Public mandate for change

The moment to act is now



Drug-Resistant Infection is a global health threat that undermines the progress made in the fight against infectious disease in the last century.

Our strategy will deliver a reduction in the impact of AMR

- Epidemiology of Drug-Resistant Infection
- New treatments
- Accelerating clinical assessment
- Global governance

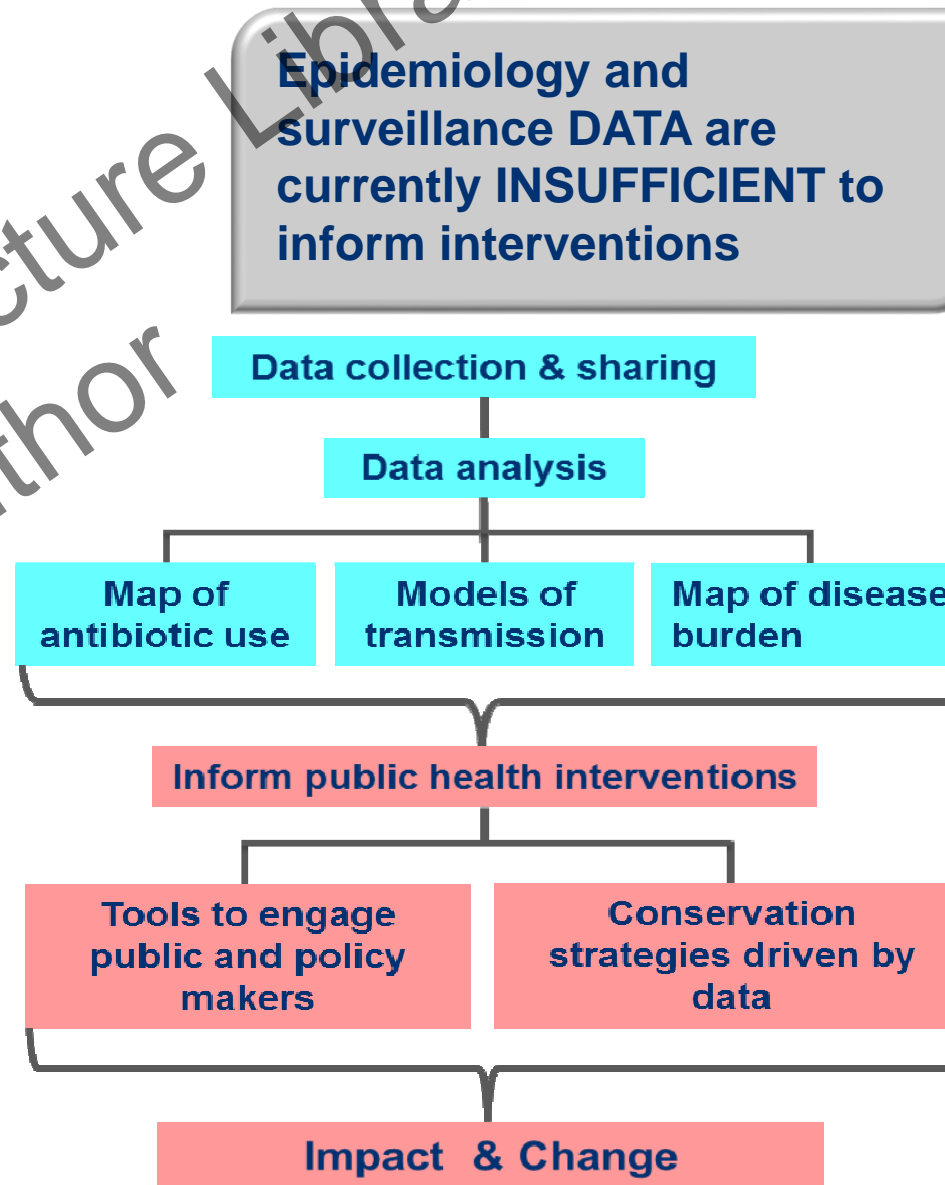
Epidemiology of AMR

Outcome

Robust epidemiology generated and used in global and national strategies

Activities proposed:

Global analysis of surveillance and mapping data
Levers for global change



New treatments

Outcome

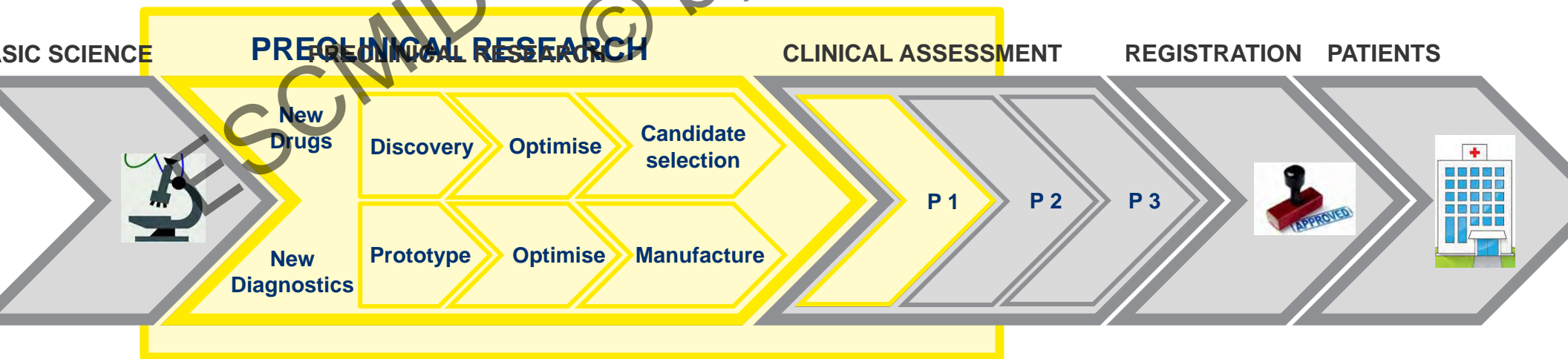
Accelerated discovery of new treatments

The current PIPELINE is **INADEQUATE** to meet future needs

Activities proposed:

CARB-X with partner commitments \$250 million from BARDA, NIH, FDA

Other areas to address access and conservation, e.g. GARDP



Accelerating clinical assessment

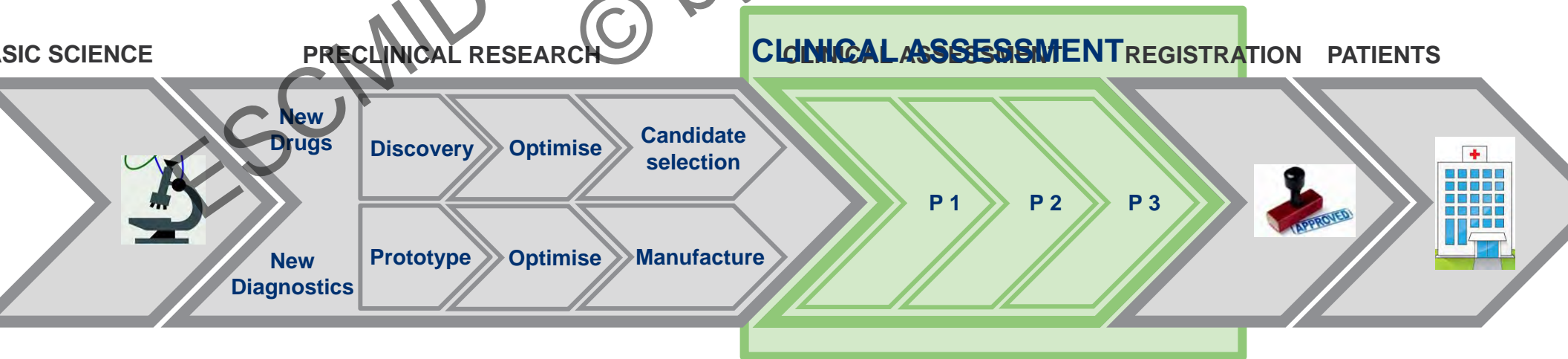
Outcome

Accelerated clinical development of new drugs
and improved use of existing drugs

Clinical DEVELOPMENT is
a significant BOTTLENECK
in the delivery of new
treatments

Activities proposed:

Global clinical trial networks (GCTN) to support design, operation and interpretation
Continuous master protocols (CMP) to accelerate registration of new treatments



Global governance

Outcome

Effective global governance framework for DRI

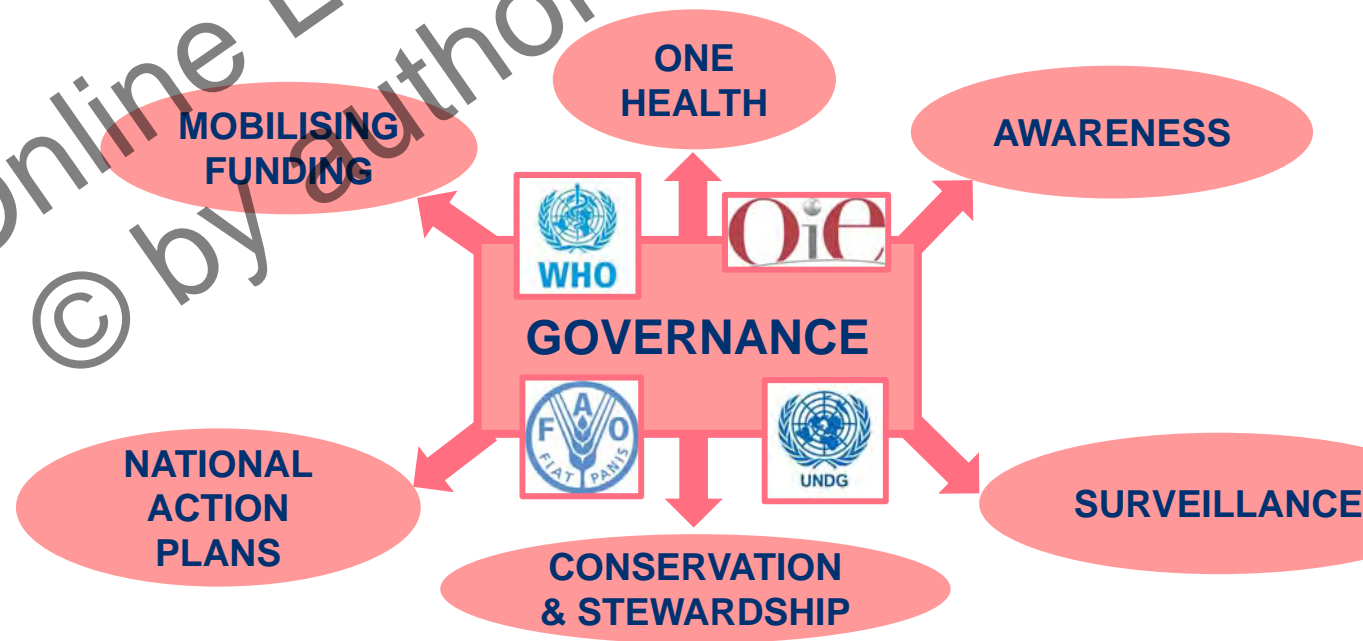
LACK of an effective global GOVERNANCE and coordination framework

Activities proposed:

Coordinate global action

Support multilateral action

Incentivise R&D



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CARB-X and accelerating development of new treatments

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Accelerating projects globally

CARB-X

Xccelerating global antibacterial innovation

Investing to develop new antibiotics and other life-saving products to treat drug-resistant bacteria



What is CARB-X?

Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator

Created in response to US government's 2015 Combating Antibiotic Resistant Bacteria (CARB) initiative and UK government's call in 2016 for concerted global effort to tackle antibiotic resistance

Headquartered at Boston University

Launched July 28, 2016, by the US Department of Health and Human Services

- Biomedical Advanced Research and Development Authority, a component of the Office of the Assistant Secretary for Preparedness and Response (ASPR/BARDA)
- National Institute of Allergy and Infectious Diseases, part of the National Institutes of Health (NIAID/NIH)

Mission: Accelerate a portfolio of high-quality antibacterial products towards clinical development, focusing on the priority drug-resistant bacteria identified by the WHO and CDC

Funded over 5 years by Wellcome Trust (\$155M) and BARDA (\$250M). NIAID provides preclinical services (\$50M)



Partners include the Broad Institute of MIT and Harvard, the Massachusetts Biotechnology Council (MassBio), the California Life Sciences Institute (CLSI), and RTI International

New Treatments

CARB-X accelerating R&D to combat the rising threat of serious drug-resistant bacterial infections



Urgent public health need

Antibiotic resistance kills an estimated 700,000 people each year world-wide. No new classes for drug-resistant Gram-negative bacteria have been approved in decades.



New global partnership model

CARB-X represents a new non-profit public-private partnership model to accelerate the development of life-saving antibiotics, vaccines and rapid diagnostics.



Turning science into products

Non-dilutive funding and accelerator support help companies with promising early research become life-saving antibiotics, vaccines and rapid diagnostics to treat serious drug-resistant bacterial infections.



CARB-X's first year results

18 companies in 6 countries; 8 are pursuing new classes against Gram-negative bacteria; 10 new molecular targets; 5 non-traditional products; one rapid POC diagnostic.

Reinvigorating the pipeline

Focused on supporting early stage projects to get them to a stage when they can attract new private or public investment

Drugs and Therapeutics



Diagnostics



Global reach: CARB-X funds 18 projects in 6 countries



North America

Forge Therapeutics
San Diego, CA

Cidara Therapeutics Inc.
San Diego, CA

Achaogen Inc.
South San Francisco, CA

Contrafect Corporation
Yonkers, NY

VenatoRx Pharmaceuticals
Malvern, PA

Spero Therapeutics LLC
Cambridge, MA

Visterra Inc.
Cambridge, MA

Tetraphase
Pharmaceuticals Inc.
Watertown, MA

Entasis Therapeutics Inc.
Waltham, MA

Microbiotix Inc.
Worcester, MA

Europe and Asia

Iterum Therapeutics Ltd.
Dublin, Ireland

Proteus IRC
Edinburgh, Scotland

Redx Pharma Plc
Alderley Park, UK

Oppilotech Ltd.
London, UK

Eligochem Ltd.
Sandwich, UK

Antabio
Labège, France

Debiopharm International S.A.
Lausanne, Switzerland

Bugworks Research India Pvt Ltd.
Bangalore, India

Great science knows no boundaries

18 early stage R&D projects investigating 8 new classes of antibiotics, 5 non-traditional antibiotics, 10 new molecular targets and a rapid diagnostic

Company/Research Team	Project	Novelty*			Project description	Urgency/Priority**	Bacteria Targeted / Stage of Early Development			
		New Class	Non-traditional	New Target			Hit to Lead	Lead Optimization	Pre-Clinical	Phase 3
Achaogen	AKAO-LpxC	✓		✓	LpxC Inhibitor	✓	<i>Pseudomonas aeruginosa</i>			
Antabio	PEI		✓	✓	Pseudomonas Elastase inhibitor	✓	<i>Pseudomonas aeruginosa</i>			
Bugworks Research	Gyrox	✓			Gyrase-topoisomerase inhibitor	✓	Gram-negative activity			
Cidara Therapeutics	CD201		✓	✓	Bifunctional immunotherapy	✓	Acinetobacter + <i>P. aeruginosa</i> + Enterobacteriaceae			
ContraFect	Gram-negative lysins		✓	✓	Recombinant lysin protein	✓	<i>P. aeruginosa</i>			
Debiopharm	Debio 1453	✓		✓	Narrow-spectrum inhibitors of FabI	✓	<i>Neisseria Gonorrhoeae</i>			
Eligochem	Helical AMP	✓			Helical Antimicrobial Peptide	✓	Gram-negative activity			
Entasis Therapeutics	ETX0282 CPDP				Oral Gram-negative combination	✓	Gram-negative activity			
Forge Therapeutics	FG-LpxC	✓		✓	LpxC Inhibitor	✓	Gram-negative activity			
Iterm	Sulopenem				Oral and IV penem	✓	Gram-negative activity			
Microbiotix	T3SS Inhibitor	✓		✓	Virulence modifier	✓	<i>Pseudomonas aeruginosa</i>			
Oppilotech	LPS	✓		✓	Targets synthesis of LPS	✓	Gram-negative activity			
Redx Pharma	NBTI	✓			Dual-acting topoisomerase inhibitor	✓	Acin. + <i>P. aerug</i> + Enterobacteriaceae			
Spero Therapeutics	SPR741			✓	Potentiator	✓	Gram-negative activity			
Tetraphase Pharm	TP-6076				Next-generation tetracycline	✓	Acinetobacter + Enterobacteriaceae			
VenatoRx	VNRX-PBP	✓			β-lactamase Resistant PBP Inhibitor	✓	Entero-bacteriaceae			
Visterra	VIS705		✓	✓	Antibody-drug conjugate	✓	<i>Pseudomonas aeruginosa</i>			

Company/Research Team	Project	Project description	Development Stage			
			Feasibility Demonstration	Optimization and Preparation for Development	Product Development	System Integration and Testing
Proteus	Rapid POC Diagnostic	Optical bacterial imaging	POC Diagnostic			

* Novelty characterizations of new class and new target are established by CARB-X following the Pew Charitable Trusts pipeline analysis model. Pew defines a novel chemical class as a group of antibiotics that share a new common core molecular structure. Non-traditional products include lysins and monoclonal antibodies.
 ** Urgent and priority drug-resistant bacteria are determined by the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO).
 ✓ Urgent/Critical priority ⚠ Serious/High priority ⚡ Serious/Medium priority.
 Stage of development is approximate as of July 2017.

Wellcome Trust priority on AMR

Wellcome seeks to achieve a **TRANSFORMATIVE IMPACT** on AMR through the delivery of a coordinated and interconnected set of activities

Wellcome has:

- ✓ Invested over £287m in DRI-related research since 2004
- ✓ Shown capacity to integrate and coordinate activities of disparate stakeholders

We are building:

In-house team dedicated to the Wellcome DRI Priority Platform

A joint Strategic approach with Vaccines initiative

Projected budget £175m



Thank you

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