What do the various noncommercial actors in the antibiotic R&D ecosystem do?

Guest speakers:Laura Marin, Erin Duffy & Peter BeyerModerator:Herman GoossensHost:Shirine Derakhshani (GARDP)

22 January 2024







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Laura Marin

Head Joint Programming Initiative on Antimicrobial Resistance – JPIAMR (Sweden)



Peter Beyer

Deputy Executive Director Global Antibiotic Research & Development Partnership – GARDP (Switzerland)



Erin Duffy Chief of Research & Development *Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator – CARB-X (USA)*



Moderator:

Herman Goossens

Emeritus Professor of Medical Microbiology University of Antwerp (Belgium) &

Chair of the Scientific Advisory Committee GARDP (Switzerland)

Laura Marin



Laura Marin heads the Secretariat of the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) initiative hosted by the Swedish Research Council. She also leads the preparations of the future One Health AMR Partnership.

Previously she was responsible for Science Policy and Member Relations at the European Science Foundation. Earlier on she was team leader of the European Science Open Forum in 2008 and Director of Operations at the Catalan Foundation for Research and Innovation.

She has several years of experience in Brussels and Germany managing research and innovation projects and facilitating numerous fora on science policy.

"What do the various non-commercial actors in the antibiotic R&D ecosystem do?"

Joint Programming Initiative on Antimicrobial Resistance

The JPIAMR funding portfolio and the discovery pipeline

Laura Marin, Head of Secretariat - JPIAMR Swedish Research Council

22 January 2024





JPIAMR supporting AMR research globally



JPIAMR: A global One Health AMR Research Funder



JPIAMR funding mechanisms

	Call for Research Projects	Call for Research Networks		
Nature of the call	Project calls support multi-national translational research collaborations for AMR research scientists that includes (but not limited to) basic research, pre-clinical and phase 1 clinical trials	Networks of AMR experts, scientists and policy makers to enhance resource alignment, capacity building and maximise existing and future efforts to combat AMR through multinational collaborations		
Expected outputs and outcomes	Research findings	White papers, views, guidelines, and/or best practice frameworks, and others		
Application process	2-stage application	1-stage application		
Size of the consortium	3-7 researchers from at least 3 JPIAMR (or fundable) countries	Typically 15 partners from at least 10 different countries		
Funding amount and details	 Coordinator and partners funded by their national funding agencies Funding amount according to national guidelines 	 Coordinator is funded by their national funding agency Funding amount 50-200k€ (call dependent) 		



ANR Interventions 2024

Participating countries: Australia, Belgium, Canada, France, Germany, Hungary, Ireland, Israel, Italy, Latvia, Lithuania, Moldova, Netherlands, Norway, Poland, Spain, Sweden, Switzerland, United Kingdom.

Estimated budget: € **17.7** Million Call closes on March 14, 2024 Info webinar on January 24, 2024 <u>www.jpiamr.eu</u>



Therapeutics

JPIAMR Therapeutics discovery pipeline



Details related to the main findings and the impact generated by the projects and networks in the area of therapeutics can be found in the following report <u>JPIAMR therapeutics</u> discovery pipeline: Outputs, outcomes and impact of the funded projects and networks in the Therapeutics priority topic of the JPIAMR-SRIA (May 2022, pdf 0,8 MB)



Therapeutics

Overview of the JPIAMR discovery pipeline



Therapeutics

Approach and mode of action of leads in the JPIAMR discovery pipeline



Others include nanobiotics, non-anitbiotic bactericidal agent



Mode of action



Outcomes of some of the JPIAMR supported Therapeutics projects



New leads

- 2 Biofilm-disrupting agents
- 1 Secretion system inhibitor
- 1 Peptidoglycan fragment analog
- 2 β-lactamase inhibitor
- Combinations of antibiotics and nonantibiotics
- 3 flavodoxin inhibitors
- 2 compounds targeting TolC of efflux pump system
- Multiple ribosome-targeting antibiotics
- 1 siderophore-antibiotic conjugate
- 2 siderophore based PET probes to detect bacteria with high sensitivity

Therapeutic indications

Treat infections caused by

- Pseudomonas aeruginosa
- Mycobacterium tuberculosis
- Counteract β-lactam resistance
- Pneumonia

8 Patents

- 1 β-lactamase inhibitor
- 1 anti-tubercular agent
- 3 Combinations of antibiotics and non-antibiotics
- 1 Bacteriophage(s) targeting capsular deficient Klebsiella pneumoniae
- In vitro screening assays for transtranslation in ESKAPE pathogens
- 1 siderophore-based conjugate (theranostic composition having both, therapeutic as well as diagnostic activities)

Future development

- 1 project supported by CARB-X (NAPCLI, Call 2014, β-lactamase inhibitor)
- 1 project in collaboration with TB Alliance
- 1 project received H2020-EU funding

JPIAMR Therapeutics Networks

The 6 Ways Innovative Products Address Patient Needs to Combat AMR: White Paper from BEAM Alliance









Support regulatory shift to evaluate innovative therapeutics based on category of products rather than individual products

International Research Alliance for Antibiotic Discovery & Development Focus: early stages of antibiotic discovery and development Implement a global cooperative platform to exchange scientific data, translational knowledge and interdisciplinary expert advice

https://beam-alliance.eu/wp-content/uploads/2019/10/beam-alliance-a-new-vision-to-support-amr-innovation.pdf

Network addressing antifungal resistance

CycleDrug: using repurposed agents (drug cycling) and combination therapy strategies



Diagnostics

The Diagnostics project portfolio





www.jpiamr.eu twitter.com/JPIAMR facebook.com/JPIAMR

2 projects on rapid diagnosis of fungal infection

Approaches and indications of the JPIAMR diagnostic innovations

	Pathogen ID	AST	RDT	Indications
AntiRYB	•••		•••	Yeast biosensors for specific bacterial species and pathogen detection
IDAREMS	•••	•••	•••	Tool for clinical diagnosis of blood stream infection
K-STaR	•••	•••	•••	Combination of Nanopore and K-mer based sequencing approaches
MAGITICS	•••	•••		Machine learning and strategies for predicting MIC; Digital diagnostics
SAMPAN	•••	•••	•••	Detection in human-water interface
TARGET	•••	•••	•••	Bacterial and viral detection in lower respiratory tract infection
SENSIF	•••		•••	AI-based methods for periprosthetic joint infection diagnosis
ERADIAMR	•••	•••	$\bullet \bullet \bullet$	Nanomotion technology platform and single-cell microfluidics-microscopy

AST: Antimicrobial Susceptibility Testing RDT: Rapid Diagnostic Tests





2011-2025

Evolution

Official launch of JPIAMR

JPIAMR supported AMR research

Over 30 states collaborating 170 M€ Total investment

1730 Researchers from77 different countries

173 projects and networks 42% OH projects

2023

OHAMR SRIA draft OHAMR Roadmap draft JPIAMR/OHAMR transition strategy



Joint co-fund between the European Commission and Member States Estimated budget 330 M€

OH AM R

2025-2032

Launch OHAMR

Last JPIAMR call

2024

•••

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The AMR Challenge





Joint Programming Initiative on Antimicrobial Resistance

Erin Duffy



Erin Duffy is the Chief of Research & Development at CARB-X.

CARB-X is a global biopharmaceutical accelerator for the discovery and early development of products to prevent, diagnose and treat bacterial infections.

Most of her professional growth was with Melinta Therapeutics (founded as Rib-X Pharmaceuticals) where ultimately she became Executive Vice President, Chief Scientific Officer and Research & Development site head.

Her entry into the pharmaceutical sector began with Pfizer Central Research. Erin's formal training was at Yale University, where she completed a PhD in physical-organic chemistry and an HHMI postdoctoral fellowship in computational structural biology.





How CARB-X Contributes to the Antibiotic R&D Ecosystem

Erin M Duffy, PhD, Chief of R&D January 22, 2024

The global partnership accelerating early-stage antibacterial R&D

Federal Ministry of Education

and Research

BILL& MELINDA

GATES foundation

novo nordisk

Canada



- Three pillars: therapeutics, preventatives and diagnostics
- Non-dilutive funding <u>and</u> comprehensive support model
- All programs enter through active funding calls
- Focused on performance characteristics, pathogens + infectious syndromes with highest morbidity and mortality rates attributable to/associated with AMR
- Created the world's most scientifically-diverse discovery & early-development portfolio, with <u>significant progress</u>:



CARB-X is a crucial link in the antibacterial innovation chain



What CARB-X Supports in our "Link of the Innovation Chain"



Pv

 Antigen/composition discovery through FIH

Dx

 Feasibility through alpha-prototype development





Funding early-stage R&D is indispensable AND urgent

- Early-stage R&D is where the most promising projects, but also the most vulnerable product developers, are:
 - The AMR Action Fund has struggled to find investment opportunities, with its CEO <u>acknowledging</u> publicly that the clinical pipeline is "much thinner" than he had originally realized (Jan 2023)
 - The World Health Organization <u>found</u> that "the *clinical* pipeline and recently approved antibiotics are insufficient to tackle the challenge of AMR." By contrast, "[t]he *preclinical* pipeline is innovative and includes a large number of non-traditional approaches" (May 2022)
 - Yet, "[t]he *preclinical* antibacterial pipeline continues to rely on micro (< 10 employees) and small (< 50 employees) companies and academic institutions," and the "analysis of groups with programmes in the *preclinical* antibacterial pipeline clearly indicates significant volatility and turnover" (May 2022)

CARB-X

• Without a healthy early-stage pipeline, there will be no R&D projects to develop clinically and no treatments to make accessible.



The funding gap in push funding for early-stage AMR R&D

- <u>AMR Review</u> (2015): "a global AMR Innovation Fund of around 2 billion USD over 5 years" = USD 400 M annually (when CARB-X did not exist)
- <u>GUARD</u> (2017): a Global Research Fund with USD 87.5 M for preclinical development and USD 85 M for Phase 1 studies = additional USD 172.5 M annually
- <u>Drive-AB</u> (2018): "additional annual global push funding in the range of USD 200 million to USD 500 million would particularly benefit early-stage research" = additional USD 200-500 M annually
- <u>WHO/Global AMR R&D Hub</u> (2023): drew "renewed attention to a significant funding gap in the preclinical stages of R&D" and highlighted that "the most promising pre-clinical antibacterial R&D projects need additional push funding to replenish a weak clinical pipeline."
- <u>Swedish Presidency of the EU</u> (2023): "There remains a very significant funding gap for early-stage product development ..."
- <u>DG HERA</u> (2023): "push funding should complement pull models, acting where the pull models are least efficient: in the early phases of development" and "there is relative consensus on the need to provide additional push funding, in a range between USD 250 and USD 400 million on an annual basis, and at a global level ..."

Summary: additional USD 172.5-500 M annually





How Programs Enter Portfolio: Active Funding Calls

- 8 funding calls (2016-2020)
 - First 4 "all-comer" calls, predicated on a product focused on one or more priority pathogens
 - Last 4 thematic (non-traditional products; vaccines & biotherapeutics; rapid diagnostics and Gram-negative-targeting therapeutics)
- 1 omnibus solicitation (2022-2023)
 - 3 funding themes (oral therapeutics; vaccines against top etiologies for neonatal sepsis; cross-pillar gonorrhea products)
 - 3 sequential intakes to allow for package-building or resubmission
- New rounds to be shaped by recent Strategic Review





Stages and Evaluation of Applications

- non-confidential <u>Expression of Interest</u> (EOI)
 - reviewed by CARB-X R&D for responsiveness
- confidential written proposal/project narrative + budget workbook
 - juried by sub-teams of external Advisory Board
- presentation to virtual advisory board (invitation only)
 - juried by full external Advisory Board
- negotiations to enter CARB-X portfolio
 - recommended by Advisory Board and CARB-X R&D
 - decided by CARB-X Investment Committee





Application Outcomes



CARB-X



A Unique and Layered Support Model



Portfolio Responsive to Global Burden of Disease





=omnibus =first 92 projects

Collaborators, The Lancet,

dark grey = global deaths

with AMR in 2019

CARB-X

indication;

A Look at Portfolio Acceleration Tools



CARB-X Advances Projects Closer to Patients



CARB-X graduates remaining active with follow-on funding

Company	Pillar	Product	Stage	Follow-on Funding	Notes
Clarametyx	Тх	CMTX-101	Ph1B	Series A	\$33M, including the CF Foundation
GSK	Tx	GSK3882347	Ph1B	GSK	Successful FIH gained internal support
Seres	Pv	SER-155	Ph1B	current investors	IND-effective gained internal support
Vedanta	Pv	VE303, VE707	Ph3	Series D + BARDA	Series D (\$81M including AMRAF, BMGF, Global Health Fund), BARDA (\$7.4M upfront; \$23.8M option)
Pattern Biosciences	Dx	Pneumonia Action Panel	α-development clinical studies	Series C	\$29.0M including AMRAF
Specific Diagnostics	Dx	Vitek REVEAL	CE mark; 510(k) filed	bioMerieux	\$416.8M acquisition
T2 Biosystems	Dx	T2 Resistance	CE mark	BARDA	\$5.9M upfront; \$18.5M in 3 exercised options

JNIVERSITY



Most Novo REPAIR companies were co-funded with CARB-X





✓ current or formerly-funded program(s) specifically listed as part of the goals of the financing
 ✓* formerly-funded CARB-X program as part of a newco active preclinical portfolio



AMRAF selected 5 companies with prior CARB-X funding





current or graduated CARB-X program(s) specifically listed as part of the goals of the financing
 formerly-funded CARB-X program as part of Company active preclinical portfolio



Stewardship and access are vital to sustainability

CARB-X is not just about funding innovation

- Innovation delivers new solutions to address the global threat of drugresistance
- Access supports patient care and helps control the spread of drug-resistant bacteria
- Stewardship helps reduce misuse and overuse of innovative products and promotes responsible use



CARB-X



Development Guide for Stewardship & Access

World's **first practical guidance** on strategies and activities to support Stewardship and Access for companies bringing new antibacterial products to market

> Final consensus on stewardship & access language (March 2018)

Public presentation of CARB-X S&A contractual provisions (Ghana Call to Action workshop, Nov. 2018)



Wellcome Trust collaborative process to develop Development Guide for Product Developers (March 2019) Completion (Jan. 2021) Public rollout (March 2021)

> Stewardship & Access Plan (SAP) Development Guide

Contractual stewardship & access language proposed (March 2017)

The Guide is useful as a benchmark to the broader antibacterial R&D community

CARBER (C) STREE UK Government (CARBER CARBER) CARBER (C) STREE (Severations) BILLe-MELINDA GATES (Severations) BILLe-MELINDA BILL





Lean and efficient CARB-X



Leverage extensive network of >100 global subject-matter experts & 4 organizations in our Global Accelerator Network



Performance-based milestones which gate project funding decisions



Leverage BU infrastructure (payroll, compliance, databases, security, space)



Prudent fund management per funder requirements





Lean and efficient CARB-X

95% of CARB-X funding goes directly to product developers via financial grants, in-kind support or R&D expertise









CARB-X Product Developers







Thank you emduffy@bu.edu

Peter Beyer



Peter Beyer is the Deputy Executive Director at the Global Antibiotic Research & Development Partnership (GARDP). Prior to joining GARDP, he was at the World Health Organization (WHO) where he led the unit responsible for developing global initiatives to foster the development and access to new antimicrobial treatments. He was instrumental in setting up GARDP as well as the AMR Action Fund.

Peter chairs the Expert Advisory Group of the Medicines Patent Pool that assesses the terms and conditions of all proposed license agreements. Peter is a trained lawyer and was admitted to the bar in Berlin in 2002. He holds a PhD from the University of Freiburg, Germany on European environmental law and has extensive experience in international negotiations.

2024-2028 STRATEGY

Putting public health needs at the centre of antibiotic drug development

GARD P

GARDP in the antibiotic R&D and access landscape



GARDP response: A public health-driven approach







COLLABORATION AND LICENSE AGREEMENTS

We de-risk antibiotic drug development projects:

- Negotiate collaboration and license agreements with pharmaceutical companies
- In exchange for our expertise and financial support, we seek the rights to manufacture and distribute treatments in hard-hit regions
- Sublicense these rights to manufacturers for registration and distribution to facilitate access





EQUAL PARTNERSHIP



Our public-private partnership approach involves working with experts in many low- and middle-income countries and all key stakeholders from the get-go:

- Work with partners to coordinate efforts in the antibiotic pipeline of drug development and access
- Offer a range of skills, financial support, and scientific resources, as well as geographic reach



Developing critical new treatments 2024-2028



Achieving success 2024-2028

CURRENT PORTFOLIO

Continue developing up to 5 TREATMENTS

Facilitate initial access for at least 3 TREATMENTS

EXPANDED PORTFOLIO

Begin developing at least 1 NEW TREATMENT

Launch critical partnerships for ECOSYSTEM OF ANTIBIOTIC R&D AND ACCESS



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Moderator:

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Emeritus Professor of Medical Microbiology University of Antwerp (Belgium) &

Chair of the Scientific Advisory Committee GARDP (Switzerland)

Upcoming webinars – 14 February



Wednesday 14 February 2024 14:00 - 15:00 CET



revive.gardp.org/webinars

Upcoming webinars – 27 February

AMR DISCUSSIONS

What does the future look like if pull incentives to support antibiotic R&D are insufficient?

MODERATOR:



LAURA JUNG Medical doctor & AMR researcher, Leipzig University Medical Center, Division of Infectious Diseases and Tropical Medicine, Leipzig, Germany

SPEAKERS:



AARON KESSELHEIM Professor of Medicine Brigham and Women's Hospital and Harvard Medical School, Boston, USA



RADHA RANGARAJAN Director, CSIR-Central Drug Research Institute, Lucknow, India



CEO,

HENRY SKINNER AMR Action Fund. Boston, USA ٧Ļ Register

now!

SARD P

27 February 2024, 14:30-15:30 CET / 08:30-09:30 am EST / 07:00-08:00 pm IST

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Antimicrobial Chemotherapy Conference

6-7 February, 2024 I Online Conference

This free, virtual conference is jointly organised by GARDP and BSAC. For ACC2024, the collaborating organisations are Ecraid and NADP.



Programme and registration here: www.acc-conference.com

www.acc-conference.com

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Thank you for joining us

