

The French interventional research plan developed to tackle antimicrobial resistance

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Introduction

It is widely known that, together with climate change, antimicrobial resistance (AMR) is one of the most urgent global health challenges for the next decade. Overuse of these wonder drugs, which revolutionised medicine in the late 1930s, has been accompanied by the rapid appearance of AMR strains¹. A recent report estimated that AMR could be responsible for at least 10 million deaths / year globally by 2050 if measures are not taken². For several years, in response to the global AMR challenges, many countries launched priority initiatives. In this article, we discuss the recent strategies set out by the French Government, which promptly recognised the importance of tackling this health emergency.

The French National Priority Research Programme against AMR

As the burden of AMR infections in France was recognised as one of the highest in the European Union, the One Health inter-ministerial roadmap of 2016 prompted the French Government to dedicate one of its strategic research instruments, the French National Priority Research Programme (Programme Prioritaire de Recherche - PPR), to tackling AMR³. This French national AMR PPR, which started in 2019, aims to bring together the strengths of all relevant public research expertise to reduce AMR over the next 10 years. See the professional community network involved here. To address this, the action plan promotes multidisciplinary research initiatives that take a One Health approach.

This ambitious research programme aims to reduce and optimise antibiotic use in human and veterinary medicine and to propose new public health strategies and environmental control measures. It is based on an innovative framework supporting an interconnected / integrated approach (Figure 1).

The French AMR PPR plan, which combines One Health principles with digital technology, data mining and artificial intelligence, comprises four main challenges:

1. **Dynamics and control of the emergence, transmission and dissemination of AMR.**
2. **Optimisation of antibiotic use in human and veterinary medicine.**
3. **Individual, ethnological, sociological, economic, political and cultural determinants of AMR.**
4. **Therapeutic innovation.**

Actions of the AMR PPR

To achieve the aforementioned goals, the three different actions detailed below have been already funded.

Call 1: Antibiotic resistance: understand, innovate, act

This action (€25 million) launched by the French National Research Agency (ANR) led to the selection of 11 long-term research projects (3 to 6 years) with expected impact at both the national and international level. The projects (Table 1) should undoubtedly contribute to tackling the four key AMR PPR challenges.

Several results regarding *the optimisation of antibiotic use* are expected and are detailed in Table 1. They come under the headings: dynamics and control of the emergence, transmission and dissemination of AMR / Optimisation of antibiotic use / Individual, ethnological, sociological, economic, political and cultural determinants of AMR / Therapeutic innovation. The main features of these projects are also [presented in short movies](#) (in French).

Call 2: Structuring tools

This action (€4 million) launched by Inserm aimed to structure research on AMR in metropolitan France and in overseas departments and territories while applying a One Health approach. Three projects were funded with ambitious objectives (Table 1).

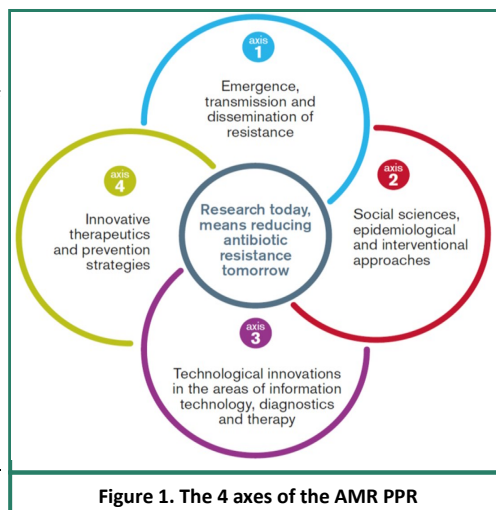


Figure 1. The 4 axes of the AMR PPR

Call 3: An Antibiotic Resistance network in partnership with LMICs

Within the framework of the AMR PPR, a budget of €1.5 million was allocated to the structuring and coordination of an AMR network in partnership with low- and middle-income countries (LMICs), designated as **the AMR-Sud network**. Since the burden of AMR is disproportionately higher in such countries, international cooperation must indeed be considered as a key element of the AMR action plan.⁵ To this aim, two complementary research projects were developed fostering collaborations within the AMR-Sud network and will be carried out in Burkina Faso, Cambodia, Côte d'Ivoire and Madagascar. The first project focuses on the transmission factors of antibiotic resistance in various environments and in the three One Health sectors (CircUs), while the other focuses on the economic and social factors of antibiotic resistance (RAMSES).

Acronym and project title	Coordinator	PI institution
Call 1- Antibiotic resistance: understand, innovate, act		
ANORUTI Analysis of NOn-Response to antibiotics <i>in vivo</i> : application to Escherichia coli Urinary Tract Infection	Bruno Fantin	Inserm UMR 1137, Université de Paris IAME
DREAM Dynamics of REsistance to Antibiotics within the human gut, Microbiota: combining diet informed population cohort and quantitative <i>in vitro</i> gut studies	Olivier Tenaillon	Inserm UMR1137, IAME, Université Paris, Université Paris Nord
DYASPEO Dynamics of AMR spread, persistence and evolution between humans, animals and their environment	Jean-Yves Madec	Anses EPA
MicroFlu4AMR Characterisation and high-throughput screening of bacterial communities in the soil: mechanisms of antibiotic resistance and discovery of new antibiotics	Andrew Griffiths	ESPCI Paris EPA
Mustart Multiparametric Strategies against Antibiotic Resistance in Tuberculosis	Alain Baulard	Institut Pasteur de Lille, IPL Autre Fondation de recherche reconnue d'utilité publique
NAILR	Vincent Cattoir	Université de Rennes 1 UR1 EPSCP
NASPEC Narrow spectrum antibiotics to fight the emergence of bacterial resistance	Michel Arthur	Université de Paris ; EPSCP
OrA-NEAT Development and evaluation of a tailored antibiotic stewardship programme in nursing homes based on an in-depth qualitative assessment of organisations, health professionals' attitudes, and needs	Nelly Agrinier	Université de Lorraine -APEMAC EPSCP
PHAG-ONE Development, production and clinical use of therapeutic phages to treat infections due to antibiotic resistant bacteria	Frédéric Laurent	Hospices civils de Lyon HCL Autre CHU
Seq2Diag Whole genome sequencing and artificial intelligence to characterise and diagnose antibiotic resistance and capacity to escape treatment	Philippe Glaser	Institut Pasteur IP Autre Fondation de recherche
TheraEPI Epigenetic-based Therapy to bypass resistance	Paola B. Arimondo	Institut Pasteur IP Autre Fondation de recherche
Call 2- Structuring Tools		
ABRomics-PF A numerical platform on antimicrobial resistance to store, integrate, analyse and share multi-omics data	Claudine Médigue Philippe Glaser	French Institute of Bioinformatics (IFB), Institut Pasteur (IP)
PROMISE Professional community network on antimicrobial resistance	Marie-Cécile Ploy Bruno François	Inserm UMR 1092, CHU and CIC1435 of Limoges
DOSA Digital Observatory of Social dimensions of Antimicrobial resistance	Nicolas Fortané	Inrae CNRS UMR IRISSO, Université Paris-Dauphine

Call 4: Call for junior and senior researcher positions

The AMR PPR funding (€7.5 million) will also provide the opportunity to attract outstanding senior scientists recognised as leaders in the field of AMR and motivated to develop, in France, multi-disciplinary research projects of excellence favouring a One Health approach. The aim of this programme is also to recruit promising young scientists to set up and lead a research team within an established French laboratory. The selection process is ongoing.

Conclusion

Over the past decade, the frequency and spectrum of antibiotic-resistant microorganisms have increased dramatically worldwide and some infections have proven untreatable with antimicrobial drugs^{1,2}. As summarised above, the French government has taken AMR seriously and the scientific community is now mobilised in a One Health approach, integrating aspects of molecular epidemiology to understand on a global scale the evolution of AMR in the host (human / animal) and the associated environment³. In addition to the fundamental and clinical research focusing on emergence, transmission, dissemination, prevention, control, and therapeutic and diagnostic innovation, the PPR aims to strengthen the social sciences and digital sciences. While the first will allow the identification of underlying drivers of antibiotic misuse, raising awareness and encouraging behavioural changes at all levels, the latter will fill a research gap in the development of digital capabilities and machine

learning. This national strategy intends to fully integrate international research agendas and WHO priorities, and to strengthen ongoing international cooperation (e.g. European Joint Programming Initiative on Antimicrobial Resistance, European Innovative Medicines Initiative, EU Joint Action on Antimicrobial Resistance and Healthcare Associated Infections). Furthermore, an appropriate communication strategy has been developed: a dedicated website for the scientific community, the [National Antibiotic Resistance Portal](#).

This tool is a common, cross-sectoral and interactive entry point, identifying public and private actors, platforms, networks, and research coordination activities, and listing research projects and scientific events focusing on antibiotic resistance. This portal is highly visited by many actors not only in France but also abroad and will undoubtedly contribute to strengthening France's place in the global AMR landscape.

References

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