GOING MACRO ON MICRO:
EMERGING THEMES IN MICROBIOLOGY

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TABLE OF CONTENTS

1 Introduction

4 One World, One Health: taking action to control AMR

6 A threatening future ahead: are we prepared?

9 An urgent case: AMR-research and restructuring public health systems and policies

11 Diagnostic tools for all: developing cost-efficient and accessible solutions

13 References

INTRODUCTION

Humanity is currently facing several health threats, namely re-emerging infectious diseases, antimicrobial resistance (AMR), global changes, and malnutrition.

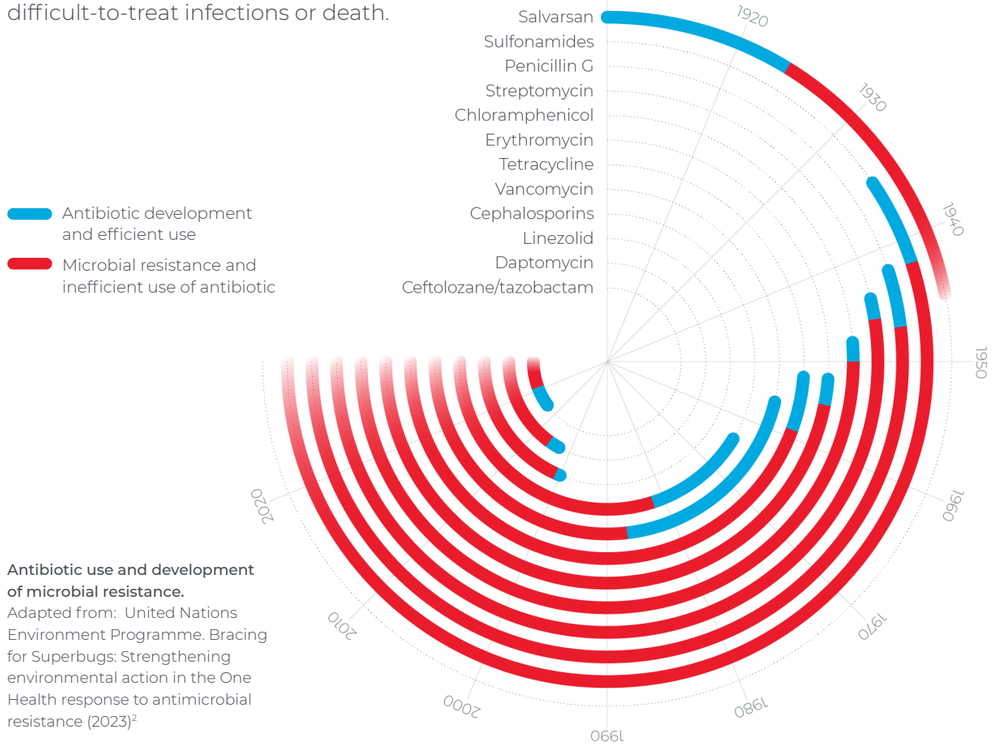
Important milestones have been achieved throughout human history that notably improved our health such as vaccination and antimicrobials. While these have allowed for many subsequent advances in healthcare, several events and environmental factors have also paved the way for the global rise of other health issues.

Most notably, the **overuse and misuse of antimicrobials** as well as poor infection prevention and control practices have contributed to the emergence and spread of resistant microorganisms. AMR renders treatment ineffective, leading to more difficult-to-treat infections or death.

This resistance can occur in different types of microorganisms from fungi to parasites, viruses, and bacteria, and can be acquired from many sources, such as other people, animals, food, and the environment.

The speed and extent of AMR is a deeply concerning global issue, especially with the continued emergence of organisms resistant to multiple classes of antibiotics, raising the burden of healthcare-associated infections that increase healthcare costs, treatment failures, and deaths.

It is estimated that, if left uncontrolled, by 2050, AMR infections could cause 10 million deaths per year, more than cancer or traffic accidents[1].

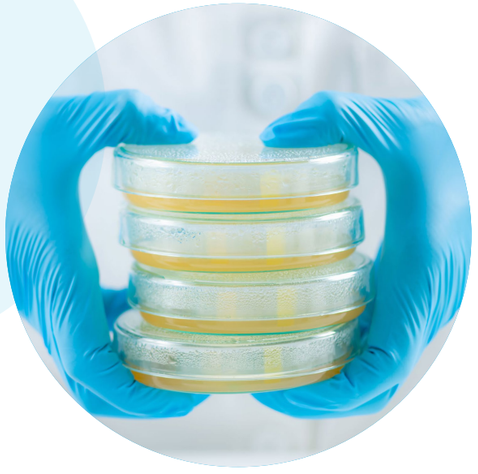


Antibiotic use and development of microbial resistance.
Adapted from: United Nations Environment Programme. Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance (2023)[2]

A SYSTEMIC ISSUE CALLS FOR A SYSTEMIC APPROACH

Systemic shocks that impact society at all levels —the COVID-19 pandemic, military conflicts, or climate change— remind us that a comprehensive strategy and transdisciplinary collaboration are required to face major threats like AMR.

AMR must be addressed under the **One Health** concept: acknowledging the connections among human, animal, and environmental health, and promoting collaboration across sectors, disciplines, and communities, working locally, nationally, and globally.



This approach entails:

- **Improving antimicrobial stewardship** to preserve the currently available antimicrobials for use against the right pathogens
- **Drug discovery** and development of new antimicrobials
- **Better education** and a change in people's behaviour on antimicrobials' use and consumption
- **Scientific research and innovation** on new tools and portable methods to enhance our knowledge and obtain reliable data to aid policymaking on AMR monitoring, prevention, and control.

"Microbiology plays several specific roles in understanding and tackling antimicrobial resistance. It is vital in the diagnosis of microorganisms causing infection and the subsequent testing of their sensitivity to antimicrobials. It enables us to then collect data on these microorganisms from an epidemiological standpoint. Microbiology also allows for the monitoring and prompt reporting of the most critical microorganisms in terms of aggressiveness and resistance to antimicrobials. This process and the data it produces helps significantly in consultation at all levels of healthcare, as well as the training of professionals and further research and study in the sector."

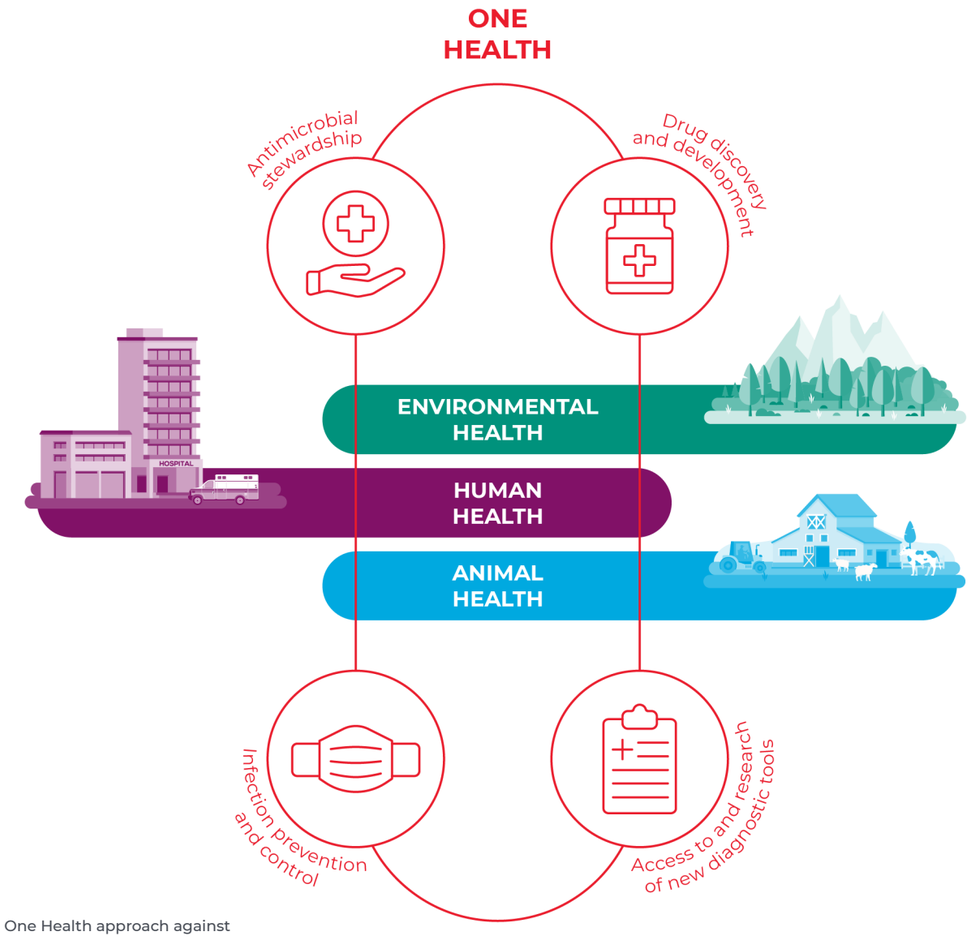
Dr Giancarlo Basaglia, Head of the Department of Microbiology and Virology at the Western Friuli Health Authority (AS FO), Italy

Facing antibiotic resistance with accurate microbiology solutions

Identifying infections and their physiological mechanisms to determine the medications that are most effective to treat them, as well as inform on prevention strategies, are crucial to prevent microbial resistance and manage the threat of AMR.

Diagnostic testing helps clinicians prescribe the appropriate medications at the right time and in the right dosage.

Robust, easy-to-use, cost-efficient, and portable technologies for surveillance and testing are needed, especially in low-resource settings, to equip microbiology laboratories to detect AMR and promote targeted therapies.



One Health approach against antimicrobial resistance.

ONE WORLD, ONE HEALTH:
TAKING ACTION TO CONTROL AMR

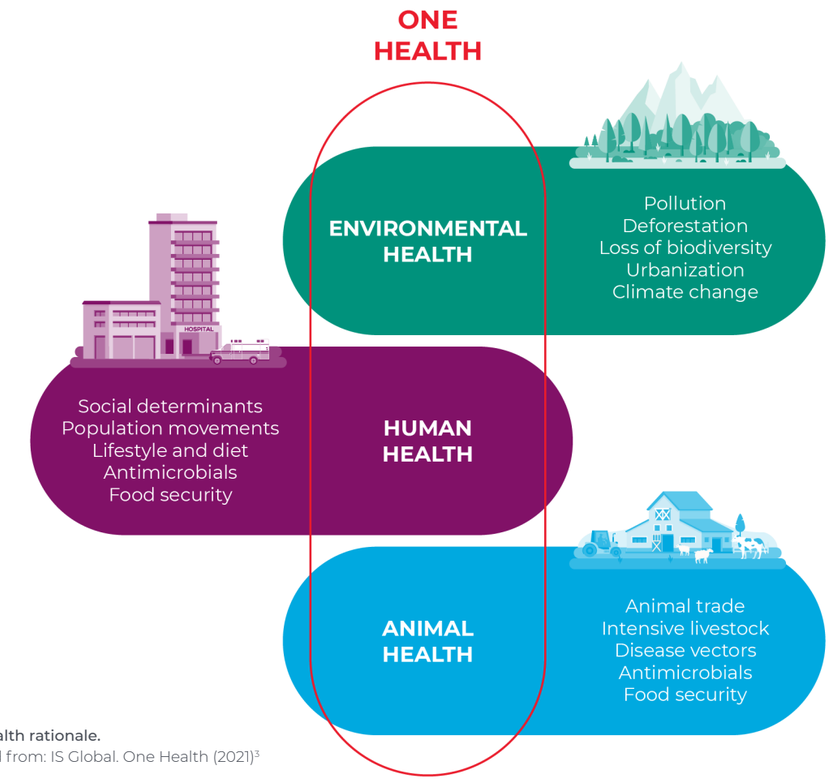
The imminent and complex threat of AMR calls for **coordinated and unified efforts** across sectors, disciplines, and communities at local, national, and international levels.

To promote this collaboration, the European Commission launched, in 2017, the **One Health Action Plan Against AMR**.

One Health recognizes that people's health is closely connected to that of animals and the environment. This approach involves varying levels of society to prevent, predict, detect, and respond to global health threats, such as AMR.

"The synergism [between animal and human health] occurs because antibiotic-resistant bacteria can spread rapidly through communities, food, and the environment— making it difficult to control and treat."

Carolina de Queiroz M Pereira, Marketing Specialist Latin America, Beckman Coulter



One Health rationale.
Adapted from: IS Global. One Health (2021)[3]

Applied to AMR, One Health recommends the **implementation of surveillance and control measures across human, animal, and natural environments**.

These systematic monitoring schemes are essential to assess the AMR status (occurrence, sources, reservoirs, and dissemination), the risks of AMR evolving and spreading, and the risk of transmission to humans.

Scientific research and innovation are key in this fight:

- To gather more knowledge on AMR acquisition, transmission, and dissemination
- To develop new methods and portable tools that simplify and promote the feasibility needed to implement global AMR monitoring schemes.

"Scientists in both worlds - animal and human health have been working for years towards the same goal - understanding the resistance patterns and developing quick detection and response tools to prevent the spread of pathogens. However, there have not been enough meaningful interactions or exchange of ideas between the animal and human health experts. The monitoring and stewardship of antimicrobial resistance must cross sectors and fields for it to succeed. Sharing best practices and aligning on the approaches is, in my opinion essential, if we want to keep the situation under control."

Agnieszka Jagiello-Johnstone, Senior Commercial Marketing Manager, Europe, Beckman Coulter Microbiology

Global monitoring based on comparable methods and reliable data can aid authorities and policymakers to accurately define guidelines and recommendations on antimicrobial consumption and AMR-monitoring procedures. Overall, this will enhance the prevention and remediation of AMR dissemination, creating long-term and sustainable solutions.

A THREATENING FUTURE AHEAD: ARE WE PREPARED?

Bacterial resistance is on the rise and diminishing the number of antibiotics that can be used to treat infections. At the same time, not enough new antibiotics are being developed. Therefore, existing antibiotics must be used more responsibly and managed carefully to extend their lifespan while being made available to the patients who truly need them.

"Unfortunately, we are in an unequal fight —the pharmaceutical industry takes many years to discover a new antibiotic, and in a few months, the bacteria are already developing resistance mechanisms."

Carolina de Queiroz M Pereira, Marketing Specialist Latin America, Beckman Coulter

"The only way to completely prevent antibiotic resistance is to not use antibiotics. Obviously, we know that's not really an option, because there are a lot of patients who need them. So, we're left with, 'how can we minimize antibiotic resistance as much as possible?'"

Eric Myers, System Pharmacy Specialist, Infectious Diseases, Adventist Health

Antimicrobial stewardship (AMS) is the effort to measure and improve how antibiotics are prescribed by clinicians and used by patients. Improving the prescription and use of antibiotics is key to effectively treat infections, protect patients from possible harm and improve their treatment outcomes, combat AMR, and reduce healthcare costs.

The implementation of AMS programmes with other policies to reduce the overuse of antibiotics and promote hospital hygiene could save up to **1.6 million lives by 2050 and US$ 4.8 billion per year**[4].

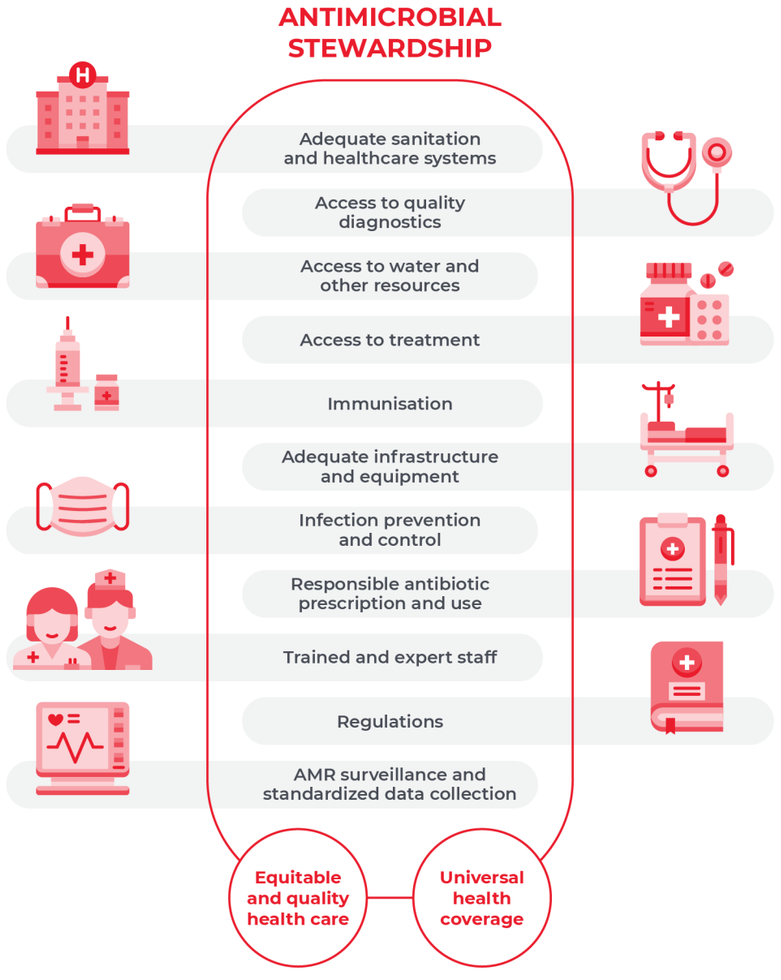
"Essentially, [minimizing antibiotic resistance] comes down to using as little antibiotics as we possibly can. My institution is focusing on the duration of therapy because it can be very difficult for a stewardship team to swoop in and convince a physician that they shouldn't be using antibiotics at all. But once they have come up with a diagnosis and have given an antibiotic, we can at least try to use the minimally effective duration […]."

Eric Myers, System Pharmacy Specialist, Infectious Diseases, Adventist Health

AMS takes responsibility for the health and well-being of the population and guides health systems at a local, national, and global level. Under the One Health concept, AMS also applies to the use of antimicrobials in the animal and agriculture sectors.

Ultimately, the goal is to promote a behavioural change in antibiotic prescribing practices for more responsible use of these agents.

Since there is not a "one size fits all" approach to optimize antibiotic use, AMS programs are flexible and adapt to the complexity and variability of different settings and facilities. These frameworks provide a set of key principles that complement existing guidelines and standards from key healthcare organisations.



Antimicrobial stewardship, infection management, and health systems strengthening.
Adapted from: World Health Organization. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a practical toolkit (2019).[5]

Embracing diagnostic stewardship

Past antibiotic stewardship programs have not paid enough attention to diagnostic stewardship. Providers often treat a positive-culture infection with antibiotics, even when the patient doesn't necessarily have symptoms consistent with infection.

The appropriate use of diagnostics is key for an effective antibiotic stewardship program and to mitigate issues instead of dealing with them later (such as trying to limit antibiotic overuse).

"There are some examples of healthcare settings which have written treatment guidelines based upon the diagnostics used in their institution. And this can be very specific. They know what kind of results a doctor would get, and you can teach doctors to use antibiotics based on a very specific test result. I think those kinds of treatment guidelines are really helpful."

Dr Jean Patel, Principal Scientific Affairs, Beckman Coulter Microbiology

AN URGENT CASE: AMR-RESEARCH AND RESTRUCTURING PUBLIC HEALTH SYSTEMS AND POLICIES

Humanitarian crises cause **massive migrations of populations into neighbouring countries**, posing several societal and health challenges. For instance, the sudden influx of people can pressure healthcare systems and create new difficulties in infectious disease control. As these migrations occur more frequently in the context of globalization, a coordinated and timely response is crucial.

The main concerns are epidemic outbreaks in refugees, such as a new wave of COVID-19, or the resurgence of diseases considered eradicated, such as polio. Moreover, the spread of multidrug-resistant organisms (MDRO), like the tuberculosis bacteria (MDR-TB), is becoming a pressing issue because these organisms are resistant to multiple classes of antibiotics, causing infections that are very hard to treat.

From a medical point of view, transit and host countries must adopt urgent measures to prevent outbreaks in refugees and protect the indigenous population.

Migrants are a group with an increased risk of developing diseases due to poor nutrition, reduced general health status and access to adequate healthcare, and overcrowded temporary living conditions. Moreover, these populations are often barred from public health services access and information. These conditions increase the risk of contagion and adverse evolution.

Transit and host countries must protect and provide solutions to migrants' health problems. Their experiences and situations should be understood to establish evidence-based measures, responses, and actions, to protect and respond specifically to their needs.

To prevent onward transmission, professionals must be aware of the increased prevalence of MDRO associated with migrations and follow infection prevention and control measures. These guidelines generally recommend screening for MDRO in individuals with reported hospitalisation in countries with high AMR rates. Moreover, further research is required to determine additional resistance patterns of MDRO, including novel combinations of antibiotics, to develop new options to treat MDRO infections.

Overall, host countries need to become a source of stability and health care for refugees. Measures should not only focus on preventing the transmission of diseases and outbreaks but also on developing efficient and sustainable interconnected health services systems.

UKRAINE – CASE STUDY

Ukraine has been facing serious public health problems such as SARS-CoV-2 infection, high levels of MDR (e.g., MDR-TB), and an ineffective vaccination program. These issues increase the risks of developing epidemics in transit and host countries.

Immunity against several diseases in Ukraine is low, and consequently, the population is vulnerable to preventable diseases.

Infectious diseases vulnerabilities among people fleeing Ukraine:

- SARS-CoV-2: large proportion of unvaccinated population and undiagnosed cases, and lack of efficient preventive measures
- Tuberculosis: high prevalence and high risk of MDR-TB
- Human immunodeficiency virus (HIV): second highest prevalence of infection in the European Region (as defined by the World Health Organisation, WHO)
- Measles: current outbreak
- Polio: high risk.

The prevalence of MDRO in Ukraine is high[6].

The massive migration included the medical evacuation of over 1,000 patients from Ukrainian hospitals to hospitals in other countries. This is a risk factor for the acquisition of MDRO. For instance, there has been an emergence of MDRO in the Netherlands in patients receiving hospital care and originating from Ukraine[7]. Similarly, there has been an increase in NDM1-producing Klebsiella pneumoniae in Germany coinciding with the arrival of refugees and evacuated patients[6].

DIAGNOSTIC TOOLS FOR ALL: DEVELOPING COST-EFFICIENT AND ACCESSIBLE SOLUTIONS

AMR poses a uniquely dangerous threat to those living in low- and middle-income countries (LMICs) and could even reverse the recent progress towards controlling infectious diseases.

In LMICs, the impact of AMR is greater than in other countries because of the already high prevalence of infectious diseases associated with inadequate sanitation, poor healthcare systems, and limited access to resources and safe water. The lack of access to quality diagnostics is also a major contributor to the burden of disease.

To tackle AMR, it is key to measure the impact of AMR control efforts and use diagnostic tools and evidence-based treatments to ensure the optimal use of antimicrobial agents. To do so, representative and comparable data on drug-resistant bacterial infections is needed.

Yet, these countries often lack standardized data collection practises and robust data management related to AMR and have insufficient infrastructure, equipment, and expertise. Moreover, access to high-quality and innovative diagnostic tools and treatments for infectious diseases are limited. Overall, this leads to inaccuracies and underreporting, and to distrust and underuse of laboratory services by clinicians, who often treat infections empirically.

Therefore, efficient, affordable, and user-friendly tools are urgently needed to rapidly detect infections and AMR and improve local surveillance and patient care, especially in LMICs.

THE MINI-LAB: SUCCESSFUL AMR DIAGNOSTIC STEWARDSHIP IN LOW-RESOURCE LABORATORIES

Because of the unlikeliness of innovative and efficient diagnostic tools being available soon for LMICs, **Medecins Sans Frontieres (MSF) developed the Mini-Lab**. The Mini-Lab is an all-in-one transportable clinical bacteriology laboratory for low-resource settings.

This rapid, easy-to-use, affordable, and effective diagnostic technology can identify pathogens, provide antimicrobial susceptibiilty testing (AST), and surveillance of AMR. It has minimal infrastructure requirements and low maintenance needs, bridging the gaps identified in LMICs and providing an opportunity to document AMR in difficult contexts where no data are available.

Key features of the Mini-Lab

- Box-Bench platform, easy to protect, transport, and setup
- Safe, low maintenance, and robust equipment with streamlined supplies and inventory to the strictly necessary
- Systematic internal quality control to detect random errors and minimise false results
- Accessible, visual, and detailed guides and user manuals covering the entire life cycle of the Mini-Lab (from installation to testing) for end-users to be fully autonomous
- On-site and distance training, including continuous education
- FAQ and help easily accessible
- Decision-support system to guide end-users, compensating for the lack of microbiology experience of the lab technicians working in the Mini-Lab
- Identification test and AST microplates from Beckman Coulter Microbiology

Put to the test

- **MSF Drouillard Hospital, Haiti (2019-2020)[8]**
  The Mini-Lab was tested at MSF Drouillard burn hospital. This first pilot field test showed that the Mini-Lab was easy to use even by non-expert laboratory technicians, who improved their competencies quickly.
- **District Hospital Carnot, Central African Republic (2021-2022)[8]**
  More recently, the performance, usability, and robustness of the Mini-Lab were evaluated in the District Hospital Carnot. The Mini-Lab showed good performance and easiness of use by technicians without prior experience and technical skills were quickly acquired and improved[11].

The Mini-Lab is deployed and used within the MSF movement.

REFERENCES

1. O'Neill, J. Tackling drug-resistant infections globally: final report and recommendations. (2016).

2. United Nations Environment Programme. Bracing for Superbugs: Strengthening environmental action in the One Health response to antimicrobial resistance. (2023).

3. IS Global. One Health. IS Global https://www.isglobal.org/en/-/one-health-una-sola-salud- (2021).

4. OECD. Stemming the Superbug Tide: just a few dollars more. https://www.oecd-ilibrary.org/content/publication/9789264307599-en (2018) doi:10.1787/9789264307599-en.

5. World Health Organization. Antimicrobial stewardship programmes in health-care facilities in low- and middle-income countries: a practical toolkit. (2019).

6. Sandfort, M. et al. Increase in NDM-1 and NDM-1/OXA-48-producing Klebsiella pneumoniae in Germany associated with the war in Ukraine, 2022. Eurosurveillance 27, 2200926 (2022).

7. Zwittink, R. D. et al. Multidrug-resistant organisms in patients from Ukraine in the Netherlands, March to August 2022. Eurosurveillance 27, 2200896 (2022).

8. Ronat, J.-B. et al. AMR in low-resource settings: Médecins Sans Frontières bridges surveillance gaps by developing a turnkey solution, the Mini-Lab. Clin. Microbiol. Infect. 27, 1414–1421 (2021).

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