TECHNICAL BRIEF ON WATER, SANITATION, HYGIENE AND WASTEWATER MANAGEMENT TO PREVENT INFECTIONS AND REDUCE THE SPREAD OF ANTIMICROBIAL RESISTANCE

Food and Agriculture Organization of the United Nations

WORLD ORGANISATION FOR ANIMAL HEALTH

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Acronyms

AMR	Antimicrobial resistance
API	Active pharmaceutical ingredient
ARB	Antibiotic resistant bacteria
ARGs	Antibiotic resistant genes
CAFO	Concentrated animal feeding operations
DALY	Disability adjusted life year
ESBL	Extended spectrum beta lactamase
FAO	Food and Agriculture Organization of the United Nations
GAP	Global Action Plan
GLAAS	Global Analysis and Assessment of Sanitation and Drinking-water
GLASS	Global Antimicrobial Resistance Surveillance System
GMP	Good Manufacturing Practice
HCF	Health care facility
HIA	Health care associated infection
IPC	Infection prevention and control
NAP	National action plan for AMR
OIE	World Organisation for Animal Health
SDG	Sustainable Development Goal
UNEP	United Nations Environment Programme
UNICEF	United Nations Children's Fund
WASH	Water, sanitation and hygiene
WHO	World Health Organization

Tackling AMR by including WASH and wastewater management in national policies and plans

This technical brief provides information to inform water, sanitation and hygiene (WASH) and wastewater elements within multi-sectoral antimicrobial resistance (AMR) national action plans (NAPs). It includes a summary of evidence and the co-benefits rationale for action in each sector and presents a menu of actions for consideration and refinement in each country context. The technical brief also identifies sector specific policy options and additional information, including knowledge gaps and research needs, as well as additional technical resources to support planning and implementation.

Where evidence is weak or lacking, actions proposed are cost-effective measures with wider co-benefits for health that plausibly contribute to combatting AMR.

The most relevant actions for any given country will depend on:

- the status of existing WASH and wastewater services in communities and health care facilities,
- patterns and intensity of animal and plant production,
- whether the country manufactures antimicrobials or procures them from abroad, and
- patterns of antimicrobial use in humans, animals and plants.

However, it is likely that in all countries some action is possible and needed in all sectors (Figure 1) regardless of which one can do most to prevent unnecessary use of antimicrobials and/or the spread of AMR.

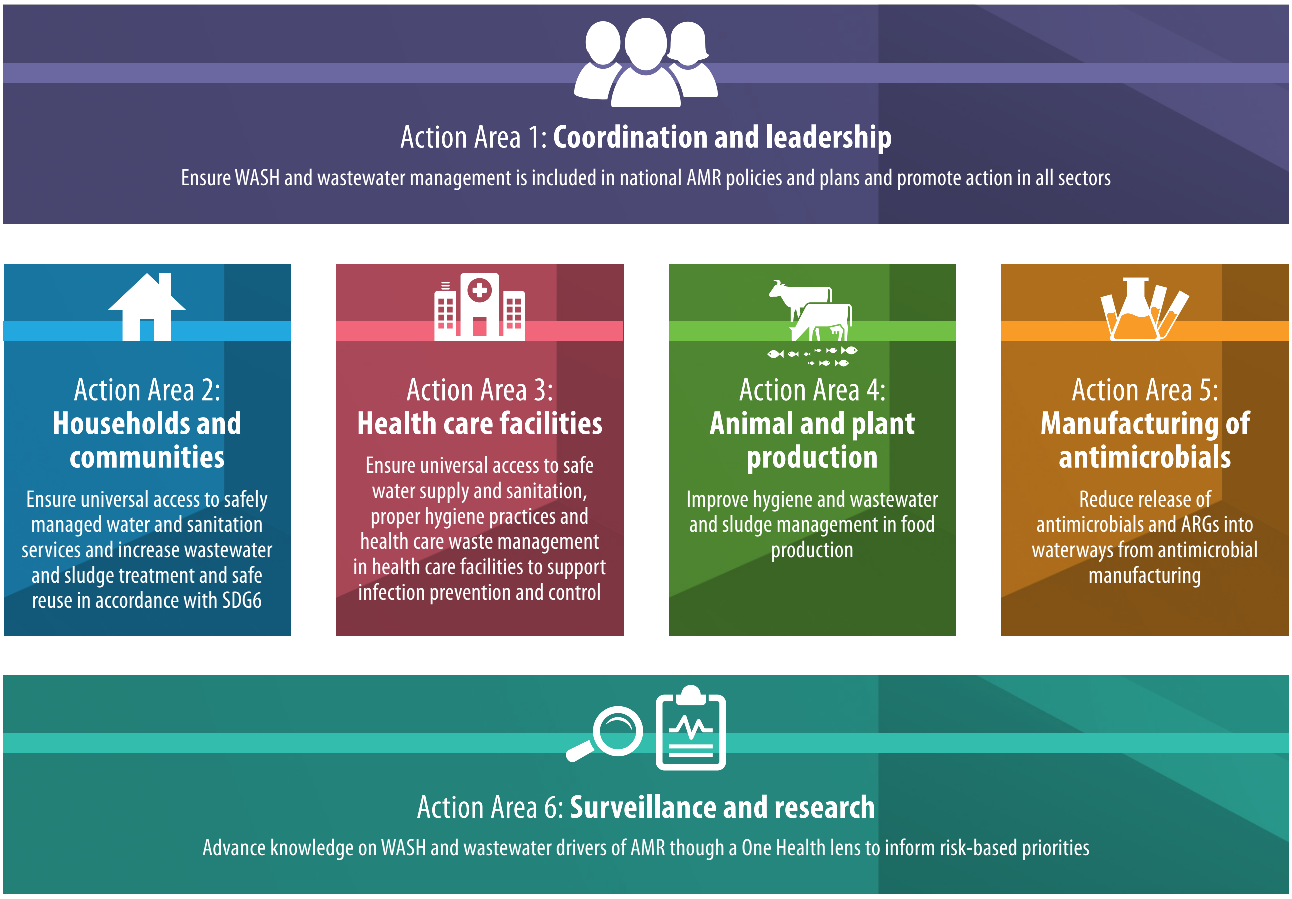


Figure 1: Actions areas for coordinated multi-sectoral action on WASH and AMR

WASH in the global context of antimicrobial resistance

The world is facing high rates of AMR. The pipeline of new antimicrobials has all but dried up, and urgent solutions to tackle AMR are sought from a wide range of stakeholders such as policymakers, engineers and scientists, health care professionals, veterinarians, farmers, donors, non-governmental organizations, and private citizens and corporations. Everyone has a role to play.

Low- and middle-income countries bear a greater burden of infectious disease and with limited resources will be most adversely affected by AMR. However, multidrug-resistant bacteria are carried in the intestinal tract of people and animals around the world, which means untreatable symptomatic infections are challenging health care systems everywhere, rendering antimicrobials less effective. As the recent COVID-19 pandemic has shown, global solutions are needed to address global public health challenges and the role of infection prevention in communities and health facilities is more important than ever.

The response to the AMR crisis has been spearheaded through the One Health AMR Global Action Plan (GAP) *(1)*, developed by the World Health Organization (WHO) in close collaboration with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE), and formally endorsed by the three organizations' membership and the United Nations General Assembly Political Declaration at the high-level meeting of the General Assembly on AMR in 2016. The Tripartite organizations, were mandated to support the development and implementation of NAPs and AMR activities at the national, regional and global levels in collaboration with regional and multilateral development banks, relevant United Nations agencies, particularly United Nations Environment Programme (UNEP), and intergovernmental organizations as well as civil society and relevant multi-sectoral stakeholders. A central task is to support the development and implementation of national policies and actions within all sectors to combat AMR at national, regional and global levels. WASH and wastewater management contribute across all five objectives of the Global Action Plan but contribute most significantly under Objective 3 on reducing incidence of infections (Box 1).

Most countries have developed and are periodically revising their AMR NAPs. However, the important roles of WASH and wastewater management is often not addressed, or the actions selected may not be adequately informed by evidence and tailored to national contexts, or lack integration with existing WASH activities. Science-informed actions within AMR NAPs and sectors policy and plans for improving WASH and wastewater are critical because water, and potentially soil, may be major modes for AMR development and spread – especially in places with inadequate WASH. Plausible causal pathways and growing evidence suggests that effective WASH and wastewater management will reduce risks posed to human, animal and plant health by AMR.

WASH and wastewater management within this briefing covers households and communities, health care facilities, animal and plant production, and antimicrobial manufacturing including waste management for unused medicines in each setting.

Box 1: Five Objectives of the Global Action Plan on Antimicrobial Resistance

- 1: Improve awareness and understanding of antimicrobial resistance through effective communication, education and training
- 2: Strengthen the knowledge and evidence base through surveillance and research
- 3: Reduce the incidence of infection through effective, sanitation, hygiene and infection, prevention measures
- 4: Optimize the use of antimicrobial medicines in human and animal health
- 5: 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

How does WASH and wastewater contribute to antimicrobial resistance?

AMR refers to microorganisms (such as bacteria, fungi, viruses, and parasites) that can become resistant to antimicrobials through a variety of mechanisms, such as mutation or genetic exchange (acquired resistance). This can occur in microorganisms in the body of human or animal hosts, but also in environmental settings where the release of excreta and presence of antimicrobial agents and other pollutants weaken or deplete the main populations of the target bacteria allowing the remaining resistant strains to persist or flourish. In the environment, genetic material (that includes the genes that code for AMR which can also be present in naturally resistant bacteria) can be shared between bacteria under selective pressure from antimicrobials (along with other selecting agents, e.g. herbicides and pesticides), thus spreading AMR attributes across diverse populations of environmental bacteria and pathogens *(2)*.

Water, sanitation, hygiene and wastewater factors play a role in the environmental dispersal and transmission of AMR in three main ways:

a) Dispersal via water, sludge and manure potentially resulting in the transmission of **disease-causing pathogens** to humans, animals and plants increasing the need for treatment with antimicrobial agents *(3)*.

   Each year hundreds of millions of cases of diarrhoea in humans are treated with antimicrobials. Universal access to WASH could reduce this by 60%.

b) Silent transmission of resistant **microorganisms with low pathogenicity** that only become evident when they infect particularly vulnerable populations or their genes are transferred to pathogens causing infection.

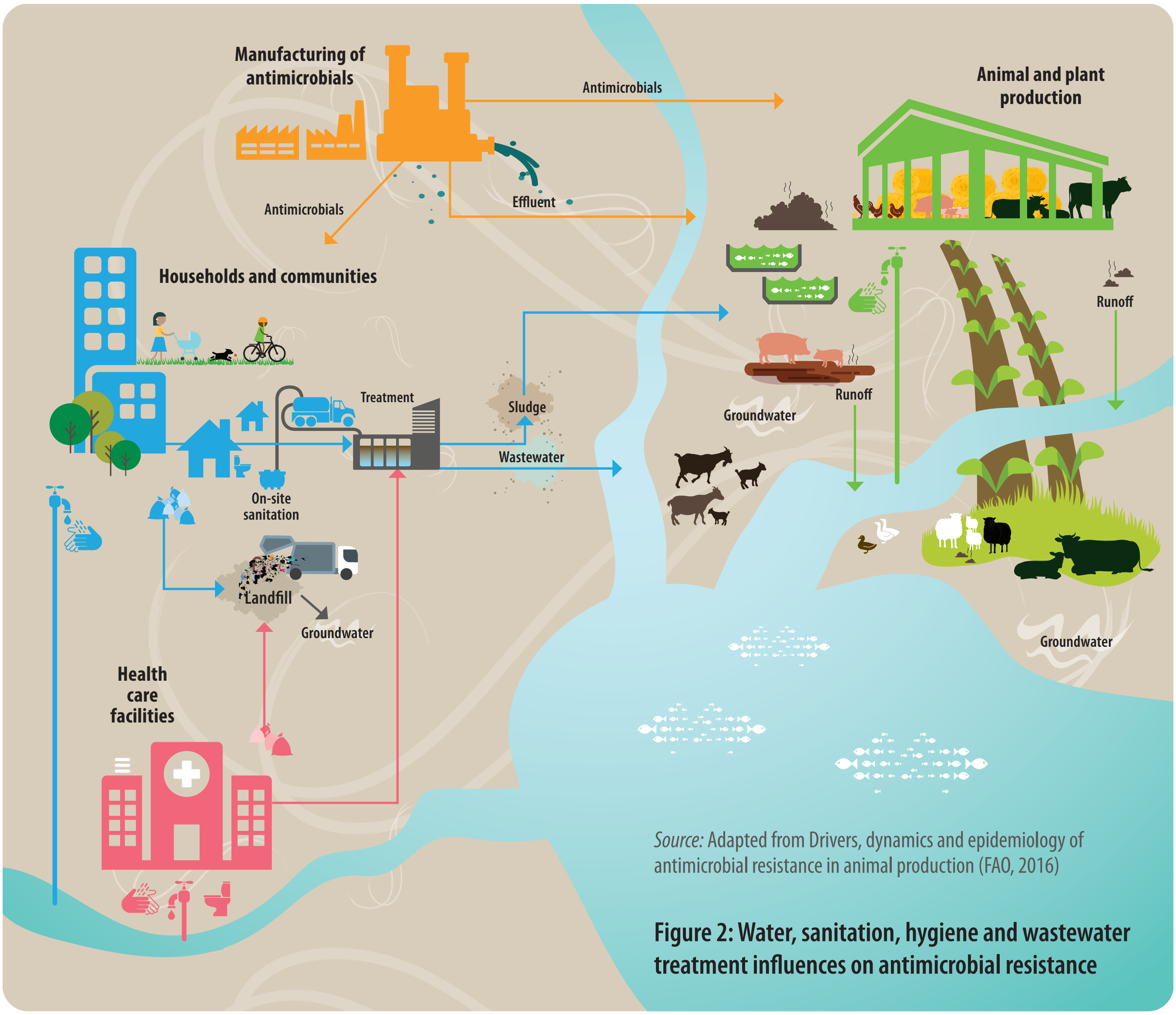
   14% of people globally carry *E. coli* in their faeces that produce extended spectrum beta-lactamase (ESBL) enzymes which provide resistance to antibiotics such as penicillins, cephalosporins, cephamycins, and to some extent carbapenems *(4)*.

c) Release of faecal and other pollutants, including **antimicrobial compounds** into the environment (excreta from use in humans or in terrestrial or aquatic animals or plants; from disposal of unused antimicrobials; or from antimicrobial manufacturing waste and wastewater) may promote resistance by creating conditions favorable to the transfer or emergence of new resistance genes.

   Up to 80% of the antimicrobial dose administered can be excreted as the active compound or metabolites depending on the class of antimicrobial and how it is used, and wastewater treatment is often insufficient or not possible. Similarly, antimicrobials in water downstream of some antimicrobial manufacturing sites have been found at concentrations higher than in the blood of patients taking medicines *(5)*.

Natural AMR is common among environmental bacteria, including in pristine locations relatively untouched by modern anthropogenic activities, such as caves, permafrost, and glaciers. However, use of antimicrobial agents such as antibiotics in humans, terrestrial and aquatic animals and companion animals and plants has been associated with the evolution and amplification of antimicrobial resistant pathogens and the antimicrobial resistance genes (ARGs) that they carry. Anthropogenic activities are increasing the importance of the environment as a pathway for AMR human exposure. For example, human consumption of antimicrobials can result in antimicrobial resistant pathogens and ARGs being discharged to waterways via open defecation, raw and treated sewage, and liquid effluent from septic tanks and pit toilets. Wastewater discharges from sites where use of antimicrobials can be high, such as hospitals, intensive livestock farms and aquaculture systems are likely to contain particularly elevated concentrations of antimicrobials, antimicrobial resistant bacteria (ARB) and ARGs which might influence AMR spread depending on dilution in the receiving water.

Similarly, the use of antimicrobials in terrestrial and aquatic animals and plants can also contribute to the spread of antimicrobial compounds and their metabolites and clinically-relevant ARGs to waterways via point source pollution (e.g. discharge from feedlots or aquaculture ponds) or diffuse pollution (e.g. manure-treated fields) (Figure 2).



Source: Adapted from Drivers, dynamics and epidemiology of antimicrobial resistance in animal production (FAO, 2016)

Figure 2: Water, sanitation, hygiene and wastewater treatment influences on antimicrobial resistance

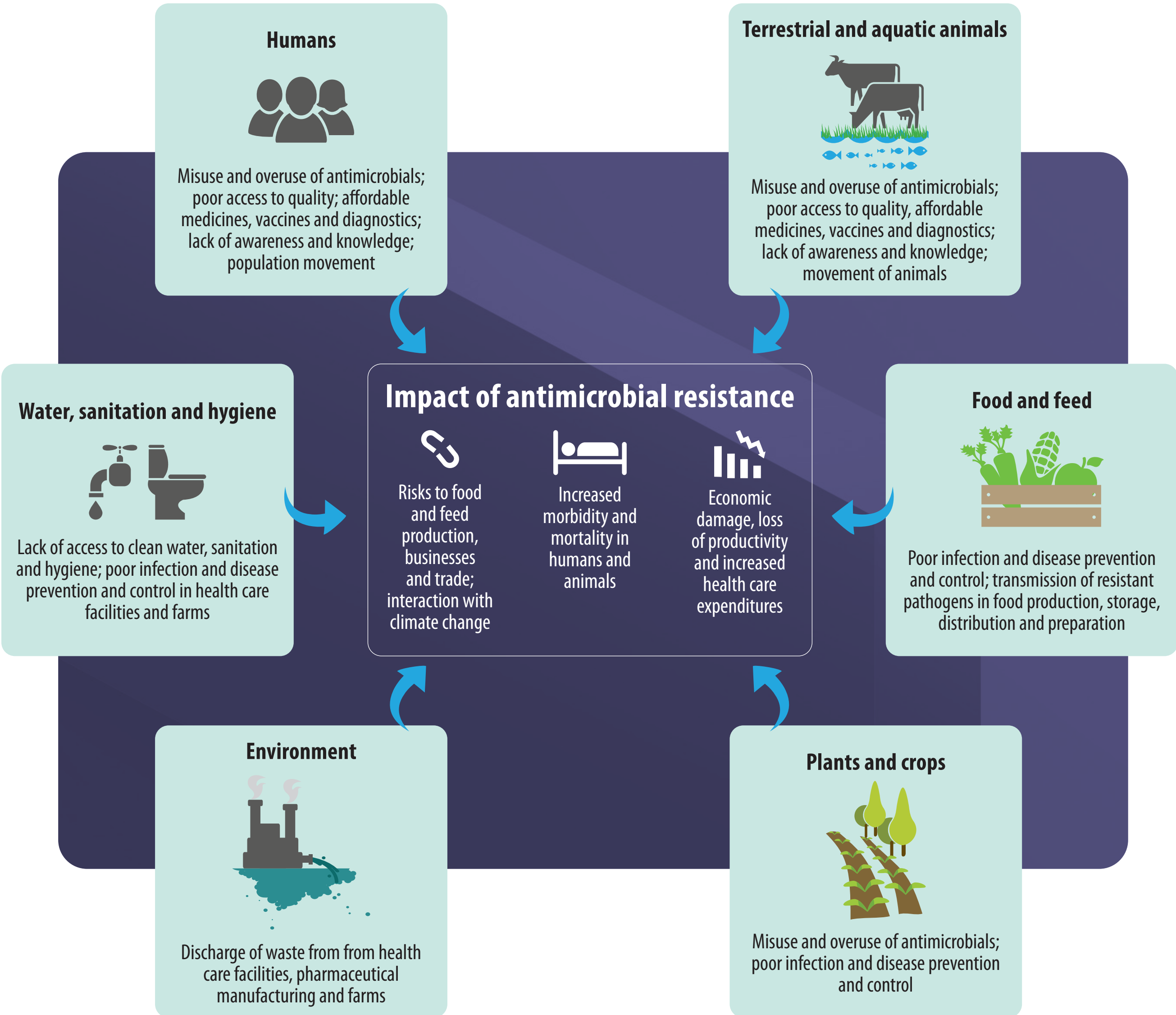
Treatment of wastewater will always be needed to reduce levels of ARBs, ARGs and antimicrobial compounds and their metabolites released to the environment as a result of use in humans and some animals. However, wastewater treatment, depending upon how advanced it is, may not be able to reduce AM concentrations in effluent to levels that remove the risk of promoting AMR acquisition and persistence in the environment. Furthermore, excreta from most terrestrial and aquatic animals are generally not treated but collection and manure management might have a negative impact on survival of pathogens and stability of antimicrobials. This means that antimicrobials, ARB and ARGs may be applied to soils through manure and added to marine and freshwater from aquaculture systems.

Antimicrobials applied to plants inevitably also enter the environment. Therefore, measures to reduce the level of environmental pollution need to be taken as far as possible at source by avoiding misuse and overuse of antimicrobials and other selecting agents *(6, 7)* in all sectors. It is important to note that even with the responsible and prudent use of antimicrobials, some active antimicrobial compounds and their metabolites will still reach the environment, although in lower amounts than when antimicrobials are misused and overused.

Exposure to AMR pathogens may occur when humans come into contact with contaminated water downstream of point or diffuse sources. For example, consumption of contaminated drinking water, recreational water use, or contact with of contaminated water, including as aerosols during irrigation, toilet flushing, or industrial processes (e.g. cooling), may all serve as possible routes of exposure to AMR microorganisms and other pathogens. The direct use of inadequately treated wastewater could also be a contributory factor. Consumption of food products contaminated by resistant pathogens or containing antimicrobial residues can also facilitate the spread of AMR from animal and plant sources. Attributing the weighted cause of AMR development to particular factors, such as those directly linked with human use versus animal or plant use versus the environment is difficult, because of overlaps between factors and because of insufficient data on the processes involved.

Further research is needed to better understand the circumstances that promote the development and spread of AMR in the environment, which sources and exposure routes are most relevant in a variety of contexts and how best to prevent the spread and transmission to humans and animals *(8, 9)*. However, existing drinking-water treatment technologies as well as sanitation improvements, wastewater treatment, manure management where possible and hygiene interventions are critical barriers to the spread of AMR, similar to their barrier function for transmission of other faecally transmitted pathogens. In addition, prevention of infections that would overwise be treated by antimicrobials will limit antimicrobial prescription and use.

These WASH and wastewater barriers therefore need to be included in plans and strategies to combat AMR as part of a comprehensive approach to addressing multiple drivers of AMR (Figure 3).



Source: Adapted from Inter-Agency Coordination Group (2019). No time to wait: Securing the future from drug-resistant infections. Report to the Secretary-General of the United Nations.

Figure 3: Water, sanitation, hygiene and wastewater contribute as drivers of antimicrobial resistance

Global status of WASH and wastewater management

WASH in households and communities

WASH-related disease

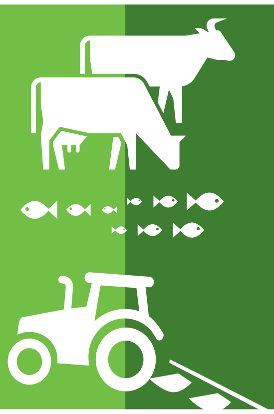
- Worldwide, in 2016, 1.9 million deaths and the loss of 123 million disability adjusted life years (DALYs) could have been prevented with adequate WASH. The WASH-attributable disease burden amounts to 4.6% of global DALYs and 3.3% of global deaths. The burden of deaths among children under 5 is 13% *(10)*.
- Almost 830 000 of WASH-related deaths are from diarrhoeal disease.

Water supply *(11)*

- Globally, at least 2 billion people use a drinking water source contaminated with faeces.
- 71% of the global population (5.3 billion people) used a safely managed drinking-water service – that is, one located on premises, available when needed, and free from contamination.
- 90% of the global population (6.8 billion people) used at least a basic service. A basic service is an improved drinking-water source that can be accessed within 30 minutes (roundtrip).
- 785 million people lack even a basic drinking-water service, including 144 million people who are dependent on surface water.

WASH in health care facilities

- Around 1 in 4 health care facilities lack basic water services – that is, an improved water source located on the premises. That means 2 million people are going to health care facilities without an on-site protected source of water *(12)*. The proportion may rise during periods of water scarcity.
- Around 1 in 5 health care facilities have no sanitation service. That means over 1.5 billion people are going to health care facilities without toilets *(12)*.
- Globally, 42% of health care facilities lack hand hygiene facilities at the point of care and 40% do not have systems to segregate waste *(12)*.



Animal and plant production

- It is estimated that globally higher quantities of antimicrobials are used in terrestrial and aquatic animals than in humans. Use is higher in countries where antimicrobials are used for growth promotion and/or where animals are raised intensively.
- Antimicrobials can be excreted virtually unchanged as the parent compound since frequently they are only partially metabolized in livestock and poultry *(18)*.
- If no action is taken, antimicrobial use is predicted to rise by more than 50% from 2015–2030 largely driven by consumer demand for livestock products *(19)*.

Manufacturing of antimicrobials

- The majority of antimicrobials, particularly generics, and active pharmaceutical ingredients (APIs) are manufactured in India and China *(23)*.
- Antimicrobial compounds and their metabolites can be found in the wastewaters from manufacturing sites for medicines and APIs. In extreme cases, levels of antimicrobial compounds in water downstream of manufacturing sites have been found at concentrations higher than therapeutic concentrations in the blood of patients taking medicines *(5)*.

Sanitation and domestic wastewater treatment *(11)*

- Globally 2 billion people still do not have basic sanitation facilities such as private toilets or improved latrines.
- Of these, 673 million still defecate in the open, for example in street gutters, behind bushes or into open bodies of water.
- 74% of the world's population (5.5 billion people) use at least a basic sanitation service – use of an improved toilet that is not shared with other households.
- 45% of the global population (3.4 billion people) use a safely managed sanitation service of which two thirds are connected to sewers from which wastewater is treated.* The remaining third use toilets or latrines where excreta are disposed of in situ.

Hygiene *(11)*

- Nearly three quarters of the population in least developed countries lack handwashing facilities with soap and water.
- 60% of the global population has basic handwashing facilities with soap and water available at home. Many high-income countries lack data on hygiene.
- 3 billion people still lack basic handwashing facilities at home. 1.6 billion have limited facilities lacking soap or water, and 1.4 billion have no facility at all.

*To secondary level or higher or primary treatment with a long ocean outfall.

- Compared to hospitals, smaller health centres and clinics are twice as likely to lack water or sanitation services *(12)*.
- More people die every year from unsafe care than lack of care. Between 5.7 and 8.4 million deaths are attributable to poor quality care each year. WASH is fundamental to the provision of safe, quality care *(13)*.
- An estimated 15% of patients in low- and middle-income countries acquire one or more infections during a hospital stay *(14)*. Infections associated with unclean births account for 26% of neonatal deaths and 11% of maternal mortality; together these account for more than 1 million deaths each year *(15, 16)*.
- Almost one third of sepsis-related neonatal deaths worldwide each year may be attributable to resistant pathogens *(17)*.

- Both treated and untreated manure and wastewater from livestock operations are commonly used as a fertilizer and soil conditioner on farms to support food and feed production. When not managed properly, wastewater and manure, also from grazing animals, can contribute to pollution of ground and surface waters.
- Cropland in peri-urban areas irrigated by mostly untreated urban wastewater has reached about 36 million hectares globally, equivalent to the size of Germany *(20)*.
- By 2025, half of the world's population will be living in water-stressed areas increasing the demand for direct and indirect use of wastewater.
- At least 10% of the world's population is thought to consume food from plants irrigated by wastewater *(21)*.
- Soils are contaminated by antimicrobial treatments used for disease control in plant production, and by active antimicrobial compounds and their metabolites in manure and wastes applied to cropland without proper management as organic fertilizers *(22)*.

- Currently there are no global effluent water quality guidelines based on health risk assessment or best available technologies.
- Voluntary industry initiatives are establishing a common framework for managing discharge of antimicrobial compounds into waterways and applying it across manufacturing and supply chains among their members *(24)*.
- Countries are introducing measures to limit emissions. For example, by introducing measures to restrict antibiotic emissions from manufacturing plants, by including waste antibiotic residue in the national hazardous waste list, and by adding emission control as part of antimicrobial procurement criteria.
- The Good Manufacturing Practice (GMP) initiative focuses on the quality standards appropriate to their intended use and as required by the product specification. GMP is considering options to strengthen environmental aspect within inspections.

Action area 1: **Coordination and leadership**

Ensure WASH and wastewater management is included in national AMR policies and plans and promote action in all sectors

Key evidence and co-benefits

- Coordinated leadership to engage WASH and wastewater actors in AMR and vice versa can be a powerful lever to increase investment and accelerate action on WASH and wastewater with wide co-benefits for health, wellbeing and the environment.
- There is not yet concrete evidence on what proportion of AMR risks come from human, animal, plant and environmental sectors. Nonetheless, improvement in WASH and wastewater management in each sector, as set out in the subsequent Action Areas 2–5, can be pursued as cost-effective measures with wider co-benefits for health and plausibly minimize AMR. Lack of scientific certainty should not be used as a reason for postponing cost-effective measures to combat AMR and reduce discharges of ARB, ARGs and antimicrobials to the environment.
- Research needs to increase the evidence base for action in each action area are summarized in Action Area 6.
- Actions in Areas 2–5 are typically led by different sectors within the AMR coordination platform with their own budgets. As such, actions are complementary and can be pursued concurrently by selecting the most relevant actions for each sector.

WASH and wastewater actions

- Ensure representatives from Action Areas 2–5 are included in AMR national multi-stakeholder platforms. Representatives will include government departments (e.g. environmental health, water and sanitation service providers, water resources management, irrigation, pollution control and researchers) and non-government stakeholders (e.g. private sector and civil society).
- Develop and update national and regional AMR action plans based on a national risk assessment (Action Area 6) to address priority national risks and international obligations. They should also reflect actions in AMR-sensitive sector policies and plans.
- Support implementation of multilateral actions across the health, water, sanitation, animal, plant, and industrial sectors through AMR-sensitive strategies, policies, planning, legal frameworks and standards.
- Encourage practical and affordable surveillance systems both to track AMR spread within environmental media and for early detection of exposure pathways and risks *(25)*.
- Support workforce education with a combination of clinical and non-clinical skills to implement WASH and wastewater management across all sectors.

Additional information

Multi-sectoral AMR committees are important to engage actors responsible for WASH service delivery and effective wastewater management to identify and accelerate environment related risk-reduction measures for AMR.

The AMR GAP identified multi-sectoral working groups as critical to a successful One Health approach[1] to addressing AMR. Currently, 50% of countries (covering more than 90% of the world's population) report having a multisectoral AMR working group *(26)*. However, more that 40% of current NAP committees do not include experts working on WASH and wastewater management primarily because many countries struggle with multi-sectoral engagement and planning. Consequently, attention gravitates towards more familiar health sector activities.

Baseline assessment of WASH and wastewater status is needed to identify the most useful country-specific WASH and wastewater actions using an AMR lens. National and sub-national data on WASH status in communities and health facilities as well as the status of wastewater treatment under Sustainable Development Goal 6 (SDG6) is available from the WHO/UNICEF Joint Monitoring Programme and the SDG6 data portal. Many countries also have up-to-date national WASH and wastewater data on sector planning, financing and implementation collected though the Global Analysis and Assessment of Sanitation and Drinking-water (GLAAS) and TrackFin initiative which tracks financial inputs and expenditures for WASH at national and sub-national level. GLAAS data can help with identifying existing water- and sanitation-sector coordination mechanisms, and thus with identifying entry points for the implementation of environmental aspects of AMR policy and planning.

Surveillance data from the Global Antimicrobial Resistance Surveillance System (GLASS) and other national health surveillance data can be used to target WASH and wastewater investments to areas and health care facilities with highest incidence of WASH-related diseases and resistant infections.

Regional strategies on environmental dimensions of AMR should also inform NAP priorities where such strategies exist e.g. in Europe *(27)*.

Resources to support action

- Water, sanitation, hygiene and health: A primer for health professionals www.who.int/water_sanitation_health/publications/water_sanitation_hygiene-primer-for-health-professionals/en/
- WHO /UNICEF Joint Monitoring Programme (JMP) website www.washdata.org
- UN-Water SDG6 data portal www.sdg6data.org
- GLAAS country data and external support agency (ESA) data www.who.int/water_sanitation_health/monitoring/investments/glaas-2018-2019-cycle/en/
- TrackFin initiative www.who.int/water_sanitation_health/monitoring/investments/trackfin/en/
- Global Antimicrobial Resistance Surveillance System (GLASS report) www.who.int/glass/resources/publications/en/

[1] One Health is an approach to designing and implementing programmes, policies, legislation and research in which multiple sectors communicate and work together to achieve better public health outcomes. In the case of AMR key collaborating sectors are human, animal and plant health and environment, particularly WASH and wastewater management.

Action area 2: **Households and communities**

Ensure universal access to safely managed water and sanitation services and increase wastewater and sludge treatment and safe reuse in accordance with SDG6

Key evidence and co-benefits

- Access to safe water and sanitation is a human right *(28)*.
- SDG targets for universal access to safe WASH by 2030 offer health co-benefits beyond combatting AMR. Safe WASH in communities reduces faecal-oral infections, contributes to better nutrition and improves social and economic wellbeing and is a precondition for development *(29)*.
- Antimicrobial use explains some AMR variation, but levels of AMR are also strongly correlated with socio-economic, health and environmental factors, especially low levels of sanitation which correlate with higher levels of AMR *(30, 31)*.
- Globally hundreds of millions of cases of diarrhoea are treated each year with antibiotics. Safe WASH in communities can prevent infection and avoid 60% of WASH-related antibiotic use *(3)*.
- Safely managed water supply and sanitation reduces transmission of faecal-oral pathogens. Resistant faecal-oral pathogens follow the same paths as non-resistant strains. Sanitation and drinking-water treatment technologies are similarly effective *(32)* against resistant and non-resistant strains.
- Available studies of pharmaceuticals in drinking-water sources and supplies indicate that the very low levels typically found are unlikely to pose a risk human health (although where hotspots have been identified, further investigation may be needed and further research is needed on the potential effects of chronic exposure and in relation to vulnerable groups) *(33)*.
- Therefore, efforts to limit AMR emergence and spread in environmental media should focus primarily on improving management of sanitation systems and treatment of wastewater and sludge *(34, 35)*. Nonetheless improvements in drinking-water quality and research on AMR risk for drinking-water remain important.

WASH and wastewater actions

- Rapidly accelerate WASH investments in countries without universal access to safely managed water and sanitation services.
- Target stepwise improvements based on national level risk assessment targeting investments to areas of highest risk (e.g. unserved communities and areas of recurrent WASH-related disease) to achieve safely managed sanitation for all.
- In all countries implement the core recommendations of the WHO Guidelines on Sanitation and Health *(2)*.
  - Sanitation improvements should cover entire communities with a minimum level of service (safe toilet and safe containment) with progressive improvement to reach safely managed services for all.
  - A mix of sewered on-site (pits, septic tanks and container-based collection with on- or off-site treatment of sludge) technologies is needed to respond to context-specific, geographical, social and economic conditions.
  - Implement local-level risk assessment (i.e. sanitation safety planning) to improve and sustain sanitation services and support safe use of wastewater in agriculture and aquaculture *(36)*.
  - Ensure the health sector fulfils core functions for sanitation – especially ensuring WASH promotion and monitoring of WASH status is included into health services and surveillance systems and sharing WASH related disease data to inform targeting on sanitation investments.
- Once safe sanitation for all is achieved, deploy advanced wastewater treatment technologies to highest risk areas.

- Some but not all studies have found that biological processes in wastewater treatment plants promote gene transfer and higher proportion of resistant bacteria in effluent. However, well-functioning secondary biological treatment processes reduce bacterial concentrations 3 log10-units or 99.9% and therefore the benefits of treatment outweigh the risk.
- Since typical secondary wastewater treatment effluents still contain some pathogens (~10^3–10^5 per litre), risk reduction measures (e.g. limiting recreational use or irrigation of fresh produce) to prevent exposure in the disposal/end use stage need to be considered.
- Tertiary processes which include a disinfection step inactivate most pathogens but reducing ARGs in effluent may require higher doses and might still transfer ARG to non-resistant bacteria in receiving waters.
- Unused and expired medicines are commonly disposed of with general waste or discarded into toilets. Source control (e.g. consumer education and take-back schemes for unused medicines) is needed to reduce pharmaceutical compounds in leachate from landfills and dumpsites and in wastewater effluent and sludge from sanitation systems.
- Develop mechanisms to return unused antimicrobials from households (e.g. to pharmacies) for safe disposal and develop behaviour-change approaches to ensure return mechanisms are used by the public.
- Efforts to improve drinking water safety should follow the WHO Guidelines on drinking-water quality, prioritizing implementation of water safety plans and strengthened surveillance. As part of water safety plans, water suppliers should ensure that control measures are effective and should optimize water treatment processes for microbial safety, which will incidentally minimize the risks from AMR. Routine monitoring of antimicrobial resistant bacteria in drinking water is not recommended because *E. coli* as the recommended indicator organism of faecal contamination is also predictive of contamination with ARBs. Investigative studies may periodically measure concentrations of ARB, ARGs or AM compounds and their metabolites.
- Incorporate AMR risks into Water Safety Plans and Sanitation Safety Plans.

Resources to support action

- WHO /UNICEF Joint Monitoring Programme (JMP) (2019), Progress on household drinking water, sanitation and hygiene 2000-2017: Special focus on inequalities www.washdata.org
- WHO / UN-Water (2019), National systems to support drinking-water, sanitation and hygiene - Global status report 2019 www.who.int/water_sanitation_health/publications/glaas-report-2019/en/
- WHO (2018), Progress of wastewater treatment: Piloting the monitoring methodology and initial findings for SDG6.3.1 www.who.int/water_sanitation_health/publications/progress-of-wastewater-treatment/en/
- WHO / UN-Water (2019), National systems to support drinking-water, sanitation and hygiene - Global status report 2019 www.who.int/water_sanitation_health/publications/glaas-report-2019/en/
- WHO (2018), WHO Guidelines on Sanitation and Health www.who.int/water_sanitation_health/sanitation-waste/sanitation/sanitation-guidelines/en/
- WHO resources on Sanitation Safety Planning www.who.int/water_sanitation_health/sanitation-waste/wastewater/sanitation-safety-planning/en/
- WHO resources on Water Safety Planning https://www.who.int/water_sanitation_health/water-quality/safety-planning/en/
- WHO (2017), Guidelines on Drinking-water Quality www.who.int/water_sanitation_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/
- WHO (2009), Water safety plan manual (WSP manual): Step-by-step risk management for drinking-water suppliers www.who.int/water_sanitation_health/publications/publication_9789241562638/en/
- WHO (2012), Pharmaceuticals in drinking-water https://www.who.int/water_sanitation_health/publications/pharmaceuticals-in-drinking-water/en/

Action area 3: **Health care facilities**

Ensure universal access to safe water supply and sanitation, proper hygiene practices and health care waste management in health care facilities (HCFs) to support infection prevention and control

Key evidence and co-benefits

- WASH services are essential for preventing a wide range of hospital-associated infections in addition to WASH-related faecal-oral infections in communities (Action Area 1).
- In addition to their vital curative role, antimicrobials are often used as a "quick fix" for fractured health systems, including poor water and sanitation infrastructure *(37)*. Conversely, investments in WASH-related inventions are "best-buys" in reducing AMR in HCFs *(38)*.
- 15% of patients in low- and middle-income countries acquire infections during a hospital stay.
- Prophylactic use of antibiotics during child birth is common in many countries where WASH is inadequate and infectious disease risks are high. In some countries, 90% of women giving birth vaginally receive antibiotics in hospital *(39)*.
- Known WASH and infection prevention and control (IPC) interventions in health care facilities are on the whole effective against AMR. AMR adds urgency to ensure universal WASH in HCF as called for by the 2019 World Health Assembly Resolution (WHA72.7).
- Frequent hand washing remains the most important intervention in infection control *(40)*.
- Wastewater from HCF frequently has higher concentrations of ARB, ARGs and antimicrobial compounds and their metabolites, particularly related to antimicrobials of last resort, than wastewater from communities *(41)* which can create AMR "hotspots" if not adequately treated. However, due to the higher volume of wastewater from communities, the overall load entering the environment from communities is higher *(32)*.
- Unused and expired medicines are commonly disposed of with general waste or discarded into wastewater systems, thus polluting waterbodies and groundwater. Source control is needed to reduce the need for treatment downstream.

WASH and wastewater actions

- Follow WHO/UNICEF's eight practical steps to achieve WASH in HCFs including conducting national assessments and analyses, setting targets and standards, and developing the health workforce for WASH in HCFs *(42)*.
- HCFs without access to WASH should prioritize immediate low-cost interventions such as basic hand hygiene stations, regular cleaning, improved drinking-water, and improved and accessible toilets.
- Increase isolation of patients between units or points of exposure to reduce local transmission.
- Focus attention on possible in-facility reservoirs of infectious bacteria and AMR, such as plumbing (including showers), water sinks, surfaces, and infectious waste disposal bins.
- HCF wastewater treatment may not be essential where wastewater goes to central community secondary wastewater treatment or where additional barriers to AMR spread and exposure exist.
- If wastewater from HCFs does not go to a central community secondary treatment plant, pre-treatment is needed to reduce pathogen and AMR concentrations before release into the environment. Treatment technologies should be chosen to minimise AMR releases, not necessarily relying on traditional domestic waste treatment options. In some instance pre-treatment may be required or desirable regardless of downstream treatment levels.
- Minimize antimicrobial waste through good anti-microbial inventory control and develop supportive policies, plans and accountability mechanisms. Antimicrobial waste should be segregated from other wastes, and encapsulated and buried, incinerated or returned to the manufacturer.
- Incorporate information on environmental risks of AMR in guidelines and training for healthcare professionals.

Additional information

Health care associated infections (HAI) are one of the most common adverse events in care delivery and a major public health problem with an impact on morbidity, mortality and quality of life *(43)*. Water, sanitation and hygiene, both independently and in combination support infection prevention and control and reduce HAI. However, influencing factors such as resource constraints, behavioural variations, and cultural practices impinge on the outcomes, which result in AMR generation.

Within health care facilities, resistant bacteria and fungi transmit to and from HCF environmental reservoirs (such as sinks, surfaces, equipment and plumbing systems). Among the ARBs are carbapenem-resistant *Enterobacteriaceae (44)*; carbapenems are a mainstay for the treatment of antibiotic-resistant bacterial infections.

Resources to support action

- WASH in health care facilities website - The issue, commitments, resources and stories at www.washinhcf.org
- WHO (2019) WHA72.7 Resolution on water, sanitation and hygiene in health care facilities https://www.washinhcf.org/wp-content/uploads/2019/07/A72_R7-en.pdf
- WHO /UNICEF (2016), Flyer -Tackling Antimicrobial resistance: Supporting national measures to address infection prevention and control and water, sanitation and hygiene in health care settings www.who.int/water_sanitation_health/facilities/amr-ipc-wash-flyer-nov16.pdf
- WHO /UNICEF (2019), Access to WASH in Health care Facilities: Global Baseline report www.who.int/water_sanitation_health/publications/wash-in-health-care-facilities-global-report/en/
- WHO /UNICEF (2019), WASH in health care facilities: Practical steps to achieve universal access to quality care www.who.int/water_sanitation_health/publications/wash-in-health-care-facilities/en/
- WHO /UNICEF (2018), Water and sanitation for health facility improvement tool (WASH FIT): A practical guide for improving quality of care through water, sanitation and hygiene in health care facilities www.who.int/water_sanitation_health/publications/water-and-sanitation-for-health-facility-improvement-tool/en/
- WHO (2014), Safe management of health care wastes from health care activities https://www.who.int/water_sanitation_health/publications/wastemanag/en/

Action area 4: **Animal and plant production**

Improve hygiene and wastewater and sludge management in food production

Key evidence and co-benefits

- Food animals produce about four times more faecal matter, in total, than humans *(45)* .
- If not managed appropriately wastewaters and manure from intensive livestock raising and from aquaculture systems can be a source of pathogens, ARB, ARGs antimicrobial compounds and their metabolites.
- 10% to over 80% of antimicrobials administered to animals is absorbed or metabolized depending on the animal species treated and the particular antimicrobial used, with the remainder excreted as active compounds through urine and faeces *(22)*.
- Antimicrobials could have negative effects on the functional, structural and genetic diversity of soil microbial communities, even causing temporary loss of soil functionality, at least at concentrations in the mg/kg range *(46)*.
- Waste streams from humans, animals and plants that have been treated with antimicrobials are also enriched with resistant microorganisms and ARGs.
- Although acquired AMR in livestock, aquaculture and plant production systems primarily derives from antimicrobial use, spread of AMR is fueled by inadequate waste management, pollution, and other non-use factors *(47, 48)*.
- Relative contributions to AMR from antimicrobial use in humans, animals and plants and related wastes varies from region to region, depending upon local human, animal and plant health, and livestock, aquaculture and plant production practices.
- Use of antimicrobials for non-veterinary medical use, such as in animal and fish feed as a growth promoter or to mitigate effects of poor husbandry practices, might increase AMR in wastes and manure from such operations.

WASH and wastewater actions

- Use of antimicrobials and other chemical supplements should be minimised to the extent possible in livestock, aquaculture and plant production operations in line with good production practices and animal health and welfare standards.
- Antimicrobials should only be used in animal, fish and plant production systems when needed for animal and plant health and welfare, such as the prevention, treatment and control of infectious disease, in a responsible and prudent manner.
- Apply good husbandry practices and veterinary oversight in terrestrial and aquatic animal production.
- If circumstances demand higher antimicrobial use in intensive livestock and fish production systems, animal and aquaculture waste management and treatment should be considered aiming at large reduction in pathogens and stability of antimicrobials in wastewater systems as an important part of animal and aquaculture WASH.
- Implement responsible and prudent use of anti-microbials in livestock farming and collect and treat waste whenever possible.
- Practice integrated manure management to optimize handling of terrestrial animal manure from collection, through storage and treatment up to application (crops and aquaculture). Through this process it is possible to negative impact on survival of pathogens and stability of antimicrobials and to prevent nutrient losses to a large extent under the site-specific circumstances.
- Collect and treat the wastewater and manure produced in large-scale livestock operations and in aquaculture systems before reusing or disposing of them.
- Promote improved manure treatment practices and manure treatment facilities, and develop and implement national standards.

- ➜ Runoff waste from slaughterhouses is a potential source of contamination of antimicrobial compounds and their metabolites and possibly ARBs.
- ➜ Aquaculture ponds can release antimicrobial compounds into the aquatic environment through the leaching from unconsumed feeds, intentional or unintentional release of effluent water and the presence of residues in faecal material *(49)*.

- ➜ The multiple barrier concept should be adopted whenever wastewaters are used in plant irrigation and aquaculture. The number of barriers (one to three) depends on the level of wastewater treatment and nature and use of the plant.
- ➜ Ensure maximum use of integrated pest management to minimise the use of antimicrobials in plant production.
- ➜ Develop mechanisms to return unused antimicrobials from farms to the supplier for safe disposal and develop behaviour change approaches to ensure return mechanisms are used.

Additional information

Most of the existing actions to mitigate/stop antimicrobials and ARB reaching the environment from farming are focused on the responsible and prudent use of antimicrobials by veterinarians and livestock and fish farmers, and on the management of the livestock itself. Even if those measures are successfully implemented, some antimicrobials will still reach the environment because of their presence in plant production, in excreta and aquaculture systems after prudent application. Controlling point sources of antimicrobials from animal and plant production, including activities such as composting waste from concentrated animal feeding operations (CAFO) containing antimicrobials, may be easier than controlling non-point sources such as the use of fungicides on cropland.

There are several options for properly managing waste (wastewater and manure) from animal and aquaculture production systems to make them safe to be reused or disposed of. Some of those options can even result in benefits to farmers, for example by generating biogas from waste, or allowing water reuse in agricultural activities. In all cases as a co-benefit the aim should be to eliminate or drastically reduce the concentration of AM compounds and resistant organisms in the waste, and options should be selected on a case-by-case basis. Finally, more research and investment in the development and application of new techniques *(50, 51)* is needed.

Resources to support action

- Drivers, dynamics and epidemiology of antimicrobial resistance in animal production (FAO, 2016) http://www.fao.org/feed-safety/resources/resources-details/en/c/452608/
- FAO 2019. Prudent and efficient use of antimicrobials in pigs and poultry. FAO Animal Production and Health Manual 23. http://www.fao.org/3/ca6729en/CA6729EN.pdf
- OIE List of Antimicrobial Agents of Veterinary Importance (July 2019) www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_OIE_List_antimicrobials_July2019.pdf
- The OIE Strategy on Antimicrobial Resistance and Prudent Use of Antimicrobials www.oie.int/fileadmin/Home/eng/Media_Center/docs/pdf/PortailAMR/EN_OIE-AMRstrategy.pdf
- OIE Annual report on Antimicrobial agents intended for use in animals - Better understanding of the global situation – 4th report https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/A_Fourth_Annual_Report_AMU.pdf
- OIE terrestrial animal health code: Chapter 6.10 Responsible and prudent use of antimicrobial agents in veterinary medicine www.oie.int/en/standard-setting/terrestrial-code/access-online/
- OIE aquatic animal health code: Chapter 6.2 Principles for responsible and prudent use of antimicrobial agents in aquatic animals www.oie.int/en/standard-setting/aquatic-code/access-online/

Action area 5: **Manufacturing of antimicrobials**

Reduce releases of antimicrobials and ARGs into waterways from antimicrobial manufacturing

Key evidence and co-benefits

- Inadequate waste management prevails along many supply chains in the local and international manufacturing of antimicrobials *(52, 53)*.
- Untreated wastewater and sludge discharges from antimicrobial production can be a hotspot for ARGs development *(54, 55)*.
- High concentrations of antimicrobials downstream of active pharmaceutical ingredient manufacturing plants can select for AMR in the local environment *(56, 57)*.
- Pre-treatment of production wastewater to remove antimicrobials is the best way to control the development of ARGs *(58)*.
- Inadequate public data exist on AM manufacturing processes, including waste treatment and management, which makes it difficult to develop mitigation interventions *(23, 57, 59)*.
- Currently there are no internationally agreed guideline values for acceptable levels of antimicrobial compounds in wastewater effluent and sludge from manufacturing processes.
- Voluntary industry initiatives are establishing a common framework for managing antimicrobial discharge and apply it across manufacturing and supply chains among their members.
- The GMP initiative currently focuses on the quality standards appropriate to the intended use of antimicrobials and as required by the product specification. GMP is considering options to strengthen and broaden the environmental component of inspections.

WASH and wastewater actions

- Foster cooperation across public and private sectors to enhance commitment to and innovation for reducing pollution throughout the supply chain using a combination of technological, behavioural, market-based and regulatory mechanisms.
- Promote and incentivize investment in life cycle analysis, green technology and efficient operation of wastewater and sludge treatment within antimicrobial manufacturing operations – e.g. by revising national generic substitution systems so that not only low(est) price but also pollution control during manufacturing is valued when determining which antibiotic products should be reimbursed to the consumer.
- Strengthen procurement systems to include aspects of waste stream analyses and waste management within supply chains.
- Develop antimicrobial manufacturing pollution standards, based on best available treatment technology and strengthen the capacity of environmental authorities to issue and enforce adequate discharge permits. Where feasible, incorporate checks on permit compliance and treatment technologies in third-party inspections of manufacturing practice.
- Establish a recommended list of technologies for industrial operators to guide waste management decisions.
- Strengthen on-site inspections and the assessment of manufacturers' dossiers under GMP environmental procedures.
- Contribute to and promote wider membership of the pharmaceutical industry's own stewardship framework.
- Promote greater public access to waste and wastewater management data from AM manufacturers.
- Support the development of pharmaceuticals intrinsically less harmful for the environment taking into consideration public health priority needs and access to medicines principles.

Additional information

Currently little data is available on the disposal of wastewater from manufacturing of antimicrobials and their active pharmaceutical ingredients. Some studies in low or low-middle income countries, indicate that pharmaceutical plant wastewater is often discharged to waterways with limited or no treatment or to municipal wastewater treatment plants that are typically not designed for treating high concentrations of antimicrobials. Hotspots of extremely high concentrations of antimicrobials have been documented downstream of manufacturing sites in emerging economies *(56, 57, 60)* but emission of residual drugs can be quite significant even in Europe, despite strong focus on surface water quality *(61, 62)*.

Improvements in pollution control in those countries that are the major manufacturers of antimicrobials and API will have the greatest potential to reduce the global risk of AMR from manufacturing but there is a clear need for improved pollution control also in other countries as well.

Reducing antibiotic concentrations in manufacturing wastewater using enhanced hydrolysis pre-treatment is an effective approach to control the development of ARGs during biological wastewater treatment *(58)* and has been successfully applied in full-scale plants in China *(63)* to implement limits on waste antibiotic residues included in the National Hazardous Waste List in 2008 and 2016. Countries primarily acting as consumers can support improvements internationally (e.g. though research and development, technology transfer and incentivising cleaner production in procurement policies) while also improving the environmental performance of any domestic manufacturing facilities, targeting no net increase in releases of antimicrobials to the environment.

Resources to support action

- WHO Good Manufacturing Practices for pharmaceutical products: main principles https://www.who.int/medicines/areas/quality_safety/quality_assurance/production/en/
- AMR Industry Alliance Roadmap www.amrindustryalliance.org/industry-roadmap-for-progress-on-combating-antimicrobial-resistance/
- OECD Report: Pharmaceutical residues in fresh water www.oecd.org/environment/pharmaceutical-residues-in-freshwater-c936f42d-en.htm

Action area 6: **Surveillance and research**

Advance knowledge on WASH and wastewater drivers of AMR though a One Health lens to inform risk-based priorities

Coordinated leadership across sectors

- Raise awareness among politicians and health officials of the importance of all WASH and wastewater management actions (Action Areas 1–5) to combat AMR, evoking the existing evidence and co-benefit arguments presented.
- Conduct a national risk assessment to identify and quantify primary sources occurrence, and transport of antimicrobials and ARGs in different geographies and sectors (communities, HCF, livestock and plant production and manufacturing) to identify priorty WASH and wastewater risks and hotspots and associated risk-reduction interventions to be addressed and targetted in AMR NAPs and sectoral policy.
- Involve WASH, wastewater, sludge and solid waste-management professionals in the review of existing sectoral policies and plans and the selection of risk-reduction actions, and determine their feasibility and cost effectiveness to address priority risks.
- Incorporate surveillance in wastewater (from sectors below) into national AMR surveillance activities according to the recommendations of GLASS and strengthen national surveillance mechanisms and regulatory authorities for wastewater aspects of AMR. Currently several methods and applications of wastewater surveillance are under consideration including ESBL *E. coli* as part of a human-animal-environment One Health protocol *(25)*, metagenomics and nuclear techniques.
- If feasible, quantify relative exposure of humans, animals and plants from identified environmental sources of antimicrobials, ARGs and ARB.
- Establish and support a national research agenda based on knowledge gaps identified in the national risk assesment above.

Examples of sectoral research priorities of global interest

Households and communities

- Quantify the number and context of barriers including WASH, needed to reduce AMR spread.
- Determine the efficiency of different water and wastewater treatment technologies, both onsite and offsite, at removing ARB, ARGs and antimicrobial compounds and their metabolites, and use the information to assess the potential and the worth of upgrading existing plants to more advanced technologies.
- Develop a cost-benefit analysis approach for various intervention options. Develop criteria and guidance for wastewater-treatment plant operators and municipalities on AMR risk and provide practical guidance on and tools to incorporate risk reduction in operations.

Health care facilities

- Compliance with WHO/UNICEF surveillance of WASH aspects.
- Determine the need for additional AMR related barriers, including local wastewater treatment at HCFs.
- Identify HCFs where wastewater treatment is needed to reduce AMR exposure.
- Stimulate the development of innovative WASH and wastewater technologies tailored to different contexts and trialled with user involvement.
- Conduct/support operational research on behaviour-change approaches to increase compliance with WASH and IPC measures in different contexts.
- Strengthen accountability and rewards for staff, patients and community members to demand better services.

Animal and plant production

- Identify best practices to decrease ARB, and antimicrobial compounds and their metabolites in animal waste before application to crop and pasture lands.
- Quantify the stability and subsequent impact on local environments from antimicrobials used in animals, aquaculture and plant production.
- Improve the understanding of how ARB, ARG, anitimicrobial compounds and their metabilites move (in soil and water).
- Identify innovative surveillance approaches to AMR in the environment.
- Determine best practices when and how to apply antimicrobials to minimise spread from aquaculture and plant production systems.
- Identify cost effective best management options to mitigate/stop ARB, ARG development and movement via wastewater from terrestrial and aquatic animal, manure runoff from plants.

Manufacturing of antimicrobials

- Conduct risk assessment to identify acceptable environmental concentrations or minimum selective concentrations.
- Identify best available treatment technology for groups of antimicrobial agents.
- Support research into designing "greener" pharmaceuticals.

Resources to support action

- Towards a research agenda for water, sanitation and antimicrobial resistance https://iwaponline.com/jwh/article/15/2/175-184/28255
- European Union Strategic Approach to Pharmaceuticals in the Environment https://ec.europa.eu/environment/water/water-dangersub/pdf/strategic_approach_pharmaceuticals_env.PDF

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Improvements in water sanitation and hygiene (WASH) and wastewater management in all sectors are critical elements of preventing infections and reducing the spread of antimicrobial resistance (AMR) as identified in the Global Action Plan to combat AMR. Yet, at present, WASH and wastewater management actors and improvement actions are under-represented in AMR multi-stakeholder platforms and national action plans (NAPs).

This technical brief provides a summary of evidence and the co-benefits rationale for WASH and wastewater management actions within NAPs as well as in sector specific policy to combat AMR.

Evidence and actions are presented in the domains of:

Coordination and leadership	**Households and communities**	**Health care facilities**	**Animal and plant production**	**Manufacturing of antimicrobials**	**Surveillance and reserarch**

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