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# National Strategic Action Plan on Antimicrobial Resistance

Singapore

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- Agri-Food & Veterinary Authority of Singapore (AVA)
- Ministry of Health (MOH)
- National Environment Agency (NEA)
- National Water Agency (PUB)



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# LIST OF ABBREVIATIONS

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<b>AMR</b>	Antimicrobial Resistance
<b>ASP</b>	Antimicrobial Stewardship Programme
<b>AVA</b>	Agri-Food & Veterinary Authority of Singapore
<b>CLSI</b>	Clinical and Laboratory Standards Institute
<b>EUCAST</b>	European Committee on Antimicrobial Susceptibility Testing
<b>FAO</b>	Food and Agriculture Organization of the United Nations
<b>GAP</b>	Good Aquaculture Practices
<b>HPB</b>	Health Promotion Board
<b>MOH</b>	Ministry of Health
<b>NARCC</b>	National Antimicrobial Resistance Control Committee
<b>NAREP</b>	National Antimicrobial Resistance Expert Panel
<b>NASEP</b>	National Antimicrobial Stewardship Expert Panel
<b>NAT</b>	National Antimicrobial Taskforce
<b>NEA</b>	National Environment Agency
<b>NIPC</b>	National Infection Prevention and Control Committee
<b>NPHL</b>	National Public Health Laboratory
<b>OIE</b>	World Organisation for Animal Health
<b>PUB</b>	National Water Agency
<b>WHO</b>	World Health Organization

# INTRODUCTION

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Antimicrobial resistance (AMR) is a pressing threat to health globally. As microbes become increasingly resistant to antimicrobial agents, such as antibiotics, antivirals and antifungals, our ability to treat infections becomes compromised, and this erodes the health benefits achieved as a result of progressive advances in medicine and public health. Prolonged illnesses and increased mortality resulting from infections caused by drug-resistant organisms has been shown worldwide to lead to decreased productivity, higher treatment costs, and economic losses. Singapore is cognisant of the impact of AMR on health and society, and work to combat AMR has been ongoing in various sectors for several years.

Antimicrobials for human use in Singapore are regulated by the Health Sciences Authority to ensure their safety, efficacy and quality. These are largely classified as prescription only medicines and can only be obtained when prescribed by licensed healthcare professionals. In 2009, the Ministry of Health (MOH) appointed the National Antimicrobial Taskforce (NAT) to address the problem of AMR in public hospitals. In 2011, following NAT recommendations, mandatory surveillance of key drug-resistant bacteria and antimicrobial prescription in public acute hospitals was implemented. At the same time, funding was provided to support antimicrobial stewardship programmes (ASP) in all public acute hospitals, and to develop clinical decision support systems for antimicrobial stewardship. NAT was reconstituted as the National Antimicrobial Resistance Control Committee (NARCC) in 2014 to continue AMR surveillance and risk assessment in public hospitals, and broaden engagement with private hospitals and community physicians on issues related to AMR.

Veterinarians, feed mills and food farms in Singapore are licensed by the Agri-Food & Veterinary Authority (AVA). AVA specifies the types of antimicrobials that cannot be used in animal feed and food-producing animals. To ensure food safety, AVA has been screening food products for antibiotic residues since the 1990s. In 2008, AVA introduced screening for multidrug-resistant *Salmonella* in local and imported food products, followed by screening for other foodborne drug-resistant organisms.

In May 2015, the 68<sup>th</sup> World Health Assembly endorsed a Global Action Plan to tackle AMR. Countries around the world shared growing concerns about the impact of drug-resistant organisms, and Singapore joined the global call for action against AMR. This National Strategic Action Plan on Antimicrobial Resistance unifies and formalises the existing response mounted across animal, human, food, and environment sectors, while providing a roadmap to address existing gaps and prioritise future interventions.

The Strategic Action Plan serves to complement existing strategies against infectious diseases, such as tuberculosis, HIV/AIDS, and sexually transmitted infections. Through coordinated approaches and improved focus on the challenge of AMR, we hope to preserve the effectiveness of antimicrobials for as long as possible.

# APPROACH

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Using a One Health approach, the Singapore One Health Coordinating Committee convened a One Health Antimicrobial Resistance Workgroup in January 2017, comprising of representatives from MOH, AVA, the National Environment Agency (NEA), and PUB, the National Water Agency. This workgroup has compiled and coordinated efforts across animal, human, food, and environment sectors in order to develop the National Strategic Action Plan on AMR.

Singapore's National Strategic Action Plan on AMR sets the framework for the national response to AMR, especially bacterial resistance to antibiotics. It is aligned with the World Health Organization's (WHO) *Global Action Plan on Antimicrobial Resistance*, and with standards and guidelines established by intergovernmental bodies such as the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE).

The plan aims to reduce the emergence and prevent the spread of drug-resistant organisms through 5 core strategies:

- Education;
- Surveillance and Risk Assessment;
- Research;
- Prevention and Control of Infection; and
- Optimisation of Antimicrobial Use

Under each of the five strategies, initiatives already in place are described, while current gaps are articulated along with “priority areas for further action” that highlight strategic areas requiring attention. The core strategies are in turn underpinned by the principle of international collaboration, recognising that a collective effort with other countries and stakeholders is necessary for an effective response to the threat of AMR.

To achieve the objectives of these strategies, detailed programmes and specific activities will be developed with accompanying resource requirements for successful implementation and long-term sustainability. A strong economic case is a precondition for sustainable, long-term investments to tackle the problem of AMR. Tools for assessing the economic burden of AMR are currently available using existing surveillance, epidemiological and economic data. The benefits and cost-effectiveness of action should therefore be weighed against the cost of inaction, especially when prioritising investments and resources to support implementation.

For the Strategic Action Plan on AMR, the overarching strategies to address AMR are designed with a long-term perspective. However, an interim timeframe of five years will be used for designing and implementing the initial programmes and activities, with periodic review to ensure relevance and effectiveness.

## CORE STRATEGY 01. EDUCATION

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Education is important to ensure that all stakeholders and the public have a correct understanding and perception of AMR's impact on health and society. Recognising the need for action is important to ensure continuing support for efforts to counter AMR, and having the right knowledge is essential for effective participation in activities against AMR.

Different educational messages will need to be tailored for professionals and the public, guided by socio-behavioural understanding and effective public health communication to promote behavioural change in practices that affect AMR. Professional education will include better understanding of the contributors of AMR, appropriate prescribing and infection control. Prescribing practices of doctors and veterinarians are also often linked to the attitudes and expectations of their patients. Public education will be focused on increasing awareness of AMR and its dangers, and the appropriate uses of antibiotics.

### One Health

**Coordinate a national strategy for improving awareness and understanding of AMR.** To ensure consistent messaging from a One Health perspective, member agencies will coordinate communications to the public and target audiences. Surveys will also be conducted to gauge prevailing practices and understand the drivers of antibiotic use behaviour, which will help to design effective messages and improve future communications.

**Reinforce food safety and hygiene practices.** AMR impacts all stakeholders along the food chain, from the farmer to the food handler to the consumer. NEA and AVA will continue to reinforce food safety messages and good hygiene practices for handling, cooking and storing food.

### Public

#### Ongoing Activities

MOH works with the Health Promotion Board (HPB) to promote vaccination and social hygiene measures among the public, through media campaigns. These campaigns are evaluated to assess changes in knowledge, attitude and practices. Such campaigns have focused on the general prevention of infection, but do not mention AMR specifically.

#### Priority Areas for Further Action

**Increase public awareness and understanding of AMR and the importance of using antibiotics appropriately.** The public needs to recognise the threat of AMR and learn how to prevent the spread of drug-resistant organisms. Local research has shown misunderstanding of antibiotic use among patients attending private primary care. More needs to be done to educate patients and the public in general about unnecessary antibiotic use.

MOH and HPB will work together to organise campaigns for AMR awareness, which could be coordinated with events such as the annual World Antibiotic Awareness Week and World Immunisation Week. These would include messages such as the following: antibiotics do not work for viral infections, patients should consult with doctors on the necessity of antibiotics, and vaccinations should be kept up to date to prevent infections.

## Professionals

### Ongoing Activities

Education is important for healthcare professionals to understand the threat posed by AMR and how it will impact their practice. It not only guides them for appropriate prescription and dispensation of antimicrobials, but also enables them to consider alternatives to antimicrobials for treatment and communicate these management plans with patients effectively. AMR is currently included in the education curricula of many undergraduate and graduate healthcare professional programmes. Work has also commenced to understand antibiotic prescribing in primary care from doctors' and patients' perspectives. Since 2015, activities to commemorate World Antibiotic Awareness Week have also been organised at various public hospitals and public forums.

Veterinarians also play a critical role in promoting and ensuring the responsible use of antimicrobials for animal health and welfare. AMR is included in the education curricula of veterinary tertiary programmes of veterinary colleges recognised by Singapore. In addition, AVA conducts activities regularly to raise awareness of AMR to local veterinarians, leveraging on international events such as World Veterinary Day and World Antibiotic Awareness Week. These include publication of newsletters and distribution of education posters and pamphlets targeted at the animal sector. Because veterinarians play a critical role in the control of animal diseases and in prescribing veterinary medicines, active engagement of veterinary professionals will be essential for a successful education campaign.

### Priority Areas for Further Action

**Strengthen education initiatives for health professionals**, particularly amongst doctors and pharmacists who are involved in the prescription of antimicrobials. The topics on AMR and antimicrobial prescribing can be expanded in existing undergraduate and postgraduate education programmes, and be kept up to date through continuing education programmes as new evidence emerges. New postgraduate training programmes for healthcare professionals will be established to deal with these topics as well as antimicrobial stewardship.

**Ensure up-to-date knowledge of AMR issues among veterinary professionals.** In order to ensure that local veterinary professionals are kept up-to-date on current knowledge, guidelines and regulations on AMR, AMR issues will form a part of continuing professional education development. AVA will work on capability building for veterinary professionals by putting in place programmes to ensure prudent antimicrobial use. Initiatives to improve the understanding of antimicrobial stewardship will also be introduced to the veterinary and farming sector.

## Industry

### Ongoing Activities

AVA has worked with wholesalers to restrict the sales of human therapeutic products for veterinary use to veterinarians, veterinary centres and farms. As end-users of veterinary medicines, local farmers also play an important role in contributing to a culture of responsible use of antimicrobials in animals. AVA promotes and administers schemes to farmers that encourage good animal husbandry practices and biosecurity measures, which help prevent and manage diseases. These include the Singapore Quality Egg Scheme (SQES) for the local layer farms, and Good Aquaculture Practices for Fish Farming (GAP-FF) for food fish farms. These measures aim to reduce the incidence of infections, and hence reliance on antimicrobials.



Minimising the discharge of antimicrobial waste is also essential, as antimicrobials in the environment increase the selection pressure for the development and expansion of the environmental antimicrobial gene reservoir, which could eventually be adopted by human or animal pathogens. Awareness of waste management issues is currently generated at the planning and design stage of facility development. During this stage, environmental requirements such as proper disposal of toxic industrial waste (which include pathogenic wastes and pharmaceutical wastes) and discharge of trade effluent are communicated. Stakeholders include pharmaceutical industries, hospitals, vet clinics and farms.

### Priority Areas for Further Action

**Strengthen awareness of proper disposal of waste with antimicrobials.** Messages on proper waste disposal will be coordinated with national campaigns for AMR awareness, which serves to further educate and remind all stakeholders of the importance of proper disposal of waste with antimicrobials. As a component of antimicrobial stewardship programmes, educational materials will also incorporate such messages. Future education materials will be guided by data and information gained from surveillance and risk assessment activities, which will be described in the following section.

**Increase awareness on AMR and prudent antimicrobial use among stakeholders in the veterinary sector.** Awareness campaigns will be expanded beyond veterinarians and farmers to include all relevant stakeholders in the sector, such as pet owners, feed manufacturers, distributors of veterinary drugs, veterinary technicians and para-professionals. Extending beyond AMR awareness, education efforts will promote prudent and responsible use of antimicrobials in animals, and emphasise infection control as a tool to reduce the spread of disease.

# SURVEILLANCE &

## CORE STRATEGY 02. RISK ASSESSMENT

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Detection of AMR through surveillance, coupled with risk assessment, enables a timely and appropriate response to be mounted. The monitoring of resistance trends will require surveillance data on AMR patterns in specific organisms, good epidemiological information of infections with drug-resistant organisms, antimicrobial utilisation and health outcomes. The collection of information coupled with risk assessment analyses also supports a better understanding of AMR, and will be useful in estimating the socioeconomic burden of AMR. Such data will be needed for measuring outcomes of programmes and initiatives, and assessing the overall impact of this Strategic Action Plan.

### One Health

**Integrate surveillance for antimicrobial resistance and antimicrobial utilisation across sectors for human, animals, food and environment.** Surveillance in the human, animal, food and environment sectors are currently conducted independently by the respective agencies, and while there are overlaps in certain areas, gaps exist in areas especially in the integration of AMR testing and data sharing across sectors. Agencies will work together to incorporate relevant information from existing separate surveillance activities on a single coherent platform. This will shed light on how specific resistance develops and spreads between humans and animals, through food, water and the environment.

Better sharing of information and data among agencies will also enable timely implementation of control measures to limit the spread of resistant organisms. Integrated surveillance across the human, animal, food and environment sectors will therefore be established, in cooperation with regional and international AMR initiatives. Where applicable, this would include coordination in sampling, laboratory methods and data reporting across sectors for priority pathogens and antimicrobials.

**Establish a national coordinating body.** This will facilitate One Health agencies' analysis and coordination of surveillance data and evaluate the effectiveness of control measures, which can be used to review the National Strategic Action Plan and its programmes. This builds on the existing One Health information sharing platform by convening a dedicated group to focus on facilitating AMR surveillance between One Health agencies. Risk assessment will also be conducted at this platform to inform control measures and research priorities.

**Publication and reporting.** Relevant surveillance data will be shared at the national, regional and international levels. This will contribute to the international understanding of AMR, and also help Singapore to benchmark internally and with other countries to identify areas for improvement.

### Human

#### Ongoing Activities

Surveillance of infections with drug-resistant organisms and antimicrobial stewardship and utilisation is conducted in public hospitals under the National Antimicrobial Resistance Control Committee (NARCC). Under NARCC, there are two expert panels, the National Antimicrobial Resistance Expert Panel (NAREP) and the National Antimicrobial Stewardship Expert Panel (NASEP), which provide

guidance to the main NARCC committee on matters pertaining to antimicrobial resistance and stewardship. The NARCC framework also allows for collection and reporting of national aggregate data on antimicrobial resistance. All public hospital laboratories and the National Public Health Laboratory (NPHL) have the capability to detect and characterise drug-resistant organisms. National laboratory surveillance covering mainly public hospitals is undertaken for priority drug-resistant organisms.

### Priority Areas for Further Action

**Harmonise laboratory methodologies and data reporting for characterisation of AMR organisms with relevant drug combinations in hospitals.** This will enable easier monitoring and interpretation of trends at the national level, and should be aligned with international guidelines, including that of WHO, the Clinical and Laboratory Standards Institute (CLSI) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST). NPHL will be established as the national AMR reference laboratory, to perform diagnostic reference functions and provide laboratory testing support for both public and private laboratories.

**Extend surveillance to cover private hospitals and the community.** Existing surveillance covers only public hospitals, and private hospitals will be included in future surveillance programmes, with microbiology laboratory support extended to private hospitals. The reporting of AMR and infection control indicators by all hospitals will be required through licensing, accreditation and quality assurance frameworks. Routine healthcare-associated infection point-prevalence studies (currently funded as research) could also be established as another surveillance mechanism in both public and private hospitals. In the community setting, surveys of antimicrobial utilisation and resistance could be conducted to examine the extent and severity of the problem in the community. This could be achieved through testing in sentinel primary care clinics.

## Animal

### Ongoing Activities

Antimicrobial utilisation in the animal sector is monitored by AVA. Quantitative data from the sales of antimicrobials to farms and veterinary establishments are reported annually to OIE. Singapore's poultry farms are also required to maintain a record of antibiotic use under the Singapore Quality Egg Scheme.

Local farms are closely monitored for the occurrence of major livestock diseases and pathogens of concern to public health, such as *Salmonella* Enteritidis in local poultry farms. Antimicrobial resistance profiles are determined when such organisms are isolated. Bacterial isolates from pets may also be screened for resistance at the request of the veterinarian, to guide appropriate treatment. When foodborne pathogens or pathogens of public health concern are found, especially those with significant antimicrobial resistant profiles, strategies such as isolation and selective treatments will be introduced to the farms or pet owners to manage the disease.

### Priority Areas for Further Action

**Expand the AMR surveillance programme to include all animal production sectors,** namely poultry, ruminant and aquaculture (food fish) farms. Apart from surveying bacterial pathogens, surveillance of resistance will also be extended to appropriate indicator or commensal bacteria. Surveillance priorities will be set using a risk-based approach, taking into account antimicrobials of veterinary and human health importance in the OIE List of Antimicrobials of Veterinary Importance and the WHO List of Critically Important Antimicrobials (CIA) respectively.

**Harmonise surveillance for antimicrobial resistance with antimicrobial utilisation on farms.** Integrating data on drug-resistant organisms from local food-producing animals with data on antimicrobial usage

on these farms will help elucidate relationships between usage and observed resistance. Information from surveillance will be used to assess the impact of animal husbandry practices on the development of resistance, monitor effectiveness of interventions, guide policies for antimicrobial use in food-animals, and develop appropriate education and mitigation measures at the farm level.

## Food

### Ongoing Activities

More than 90% of Singapore's food is imported and is monitored from source to consumer. Food safety is overseen by two One Health agencies: AVA has oversight on the upstream processes from source to import and processing, while NEA oversees food safety at the consumer interface, i.e. at kitchens and retail.

Food products in Singapore, such as meat, dairy products, eggs and egg products, honey, and drinking water are routinely tested by AVA for the presence of antibiotic residues. Animal feed used at food farms is also regularly tested for antibiotic residues or banned substances. Products that exceed the maximum residue limits for a specific substance, or found to contain any banned substance at all, are prohibited for sale.

In addition to screening food for harmful foodborne bacteria such as *Salmonella*, AVA monitors imported meat and meat products for the presence of antibiotic-resistant bacteria, such as Methicillin-resistant *Staphylococcus aureus* (MRSA), ESBL-producing *E. coli* and multi-drug resistant (MDR) *Salmonella*. Surveys are ongoing to determine the baseline microorganism community and the diversity of the environmental gene reservoir of ubiquitous microorganisms in food.

### Priority Areas for Further Action

**Enhance laboratory capacity for testing of AMR and antibiotic residues in food products.** Existing capabilities will be strengthened and periodically reviewed to ensure test methods and scope remain current and relevant. This includes identifying a core panel of relevant antimicrobials for surveillance to determine AMR in the food chain. AMR surveillance of food products will also be harmonised with surveillance of food-producing animals in local farms.

**Strengthen national surveillance of drug-resistant organisms in food products to include retail food and meat, and to assess risk to consumers.** The respective agencies will identify common indicators between imported and retail food, and develop surveillance programmes that will help identify the risk factors and trends in the prevalence of drug-resistant organisms along the food chain. The methodology for AMR surveillance in food will be harmonised, so as to generate comparable data across sectors. This provides a framework for assessing potential risks associated with exposure to drug-resistant organisms among consumers.

## Environment

### Ongoing Activities

Surveys are ongoing to determine the baseline microorganism community and the diversity of environmental gene reservoirs of ubiquitous microorganisms in water catchments, water and used-water treatment processes, urban water bodies and urban pests. This is done by measuring antibiotic concentrations, drug-resistant organisms and/or antimicrobial resistance genes. These surveys will provide data for risk assessment, and to provide a baseline for monitoring the trend and dynamics of gene reservoirs in the environment.

## Priority Areas for Further Action

**Develop a systematic environmental surveillance system** to allow for better understanding of the dynamics and prevalence of AMR in the environment, including water bodies, water and used water treatment processes, and trade effluents. Surveillance methodology and approach will be harmonised with other sectors for ease of interpretation.

**Conduct risk assessment** using the data collected from surveys, which will be interpreted against knowledge and data from literature. The risk assessment will provide evidence for follow up actions on surveillance and for development of educational materials as described in the 'Education' strategy. The assessment is also expected to guide policy and operations in the longer term.

A better understanding of AMR, including risk factors for the emergence and spread of drug-resistant organisms, and how to stop them, is fundamental to controlling it. Research may also provide information where gaps in evidence exist to support the other core strategies. Internationally, there is a need for more research to develop new vaccines, medicines or alternative treatments for bacterial infections, as well as new or improved rapid or point-of-care diagnostic tests to enable appropriate use of antimicrobials. Identification and prioritisation of research needs are important to ensure that key questions and important evidence gaps are addressed in a manner that is relevant and resource-efficient. Research collaborations adopting a One Health approach are to be encouraged.

### One Health

**Set up a national coordinating body to coordinate AMR research in line with a national AMR research agenda.** To focus research activity and accelerate research in areas of importance, a collective national research agenda will be developed, together with all stakeholders, including those in research and industry. This will increase collaborations between researchers working on AMR in humans, animals, food, and the environment, and create multi-disciplinary research projects with results that can be translated into practice. A national research coordinating group will be needed to have general oversight of the research, and have dedicated funding for inter-agency collaborative AMR research that fits the national AMR research agenda. Joint establishment of a common research database will also facilitate sharing of AMR information for future collaboration.

Priority research areas for cross-sectoral collaboration have been identified as follows:

- Determine transmission pathways between sectors (human, animal, food, and the environment), and determine the implications of cross-sectoral transmission on efforts to control AMR
- Advanced methods of surveillance of AMR (including genomic analysis) and antimicrobial use
- Socio-behavioural research to understand baseline attitudes, practices and knowledge of AMR, and determine how best to change behaviour to facilitate control of AMR.
- Socioeconomic impact of AMR

### Human

#### Ongoing Activities

Funding for research on AMR has been made available through various institutions and funding streams, including the National Medical Research Council, the National Research Foundation, the Communicable Disease Public Health Research Grant, and the Industry Alignment Fund. Existing research projects include surveillance of healthcare-associated infections in public and private hospitals, cohort and genomic studies of extensively drug-resistant organisms, and development of new diagnostics and therapeutics.

The National Medical Research Council recently awarded a collaborative AMR centre grant involving multiple academic institutions and public hospitals.

## Priority Areas for Further Action

AMR was recognised as one of the top three infectious disease focus areas for research under the government-funded Research, Innovation and Enterprise 2020 (RIE2020) Plan. Areas recommended for further research support include:

- Better surveillance of AMR and antimicrobial consumption in hospitals, community and food sources;
- Socio-behavioural research to study antimicrobial prescription patterns and the link to transmission of drug-resistant organisms, and also to determine the most effective method(s) for reducing misuse and overuse of antimicrobials;
- Modelling and evaluation of hospital-based and community-based interventions in the above areas;
- Basic science research to understand the factors affecting the rising rates of local drug-resistant organisms; and
- Applied research on infection control in both acute care and intermediate- and long-term care (ILTC) settings, including health services research and operations research to redesign processes and protocols, and trial of novel human-use and surface/material technologies to reduce AMR

In addition to RIE2020, there are other important areas of action for AMR research, including:

- Mapping out AMR research done in Singapore and providing an avenue for researchers to collaborate on projects addressing the focus areas described above;
- Harnessing existing research programmes and research centres of excellence to include AMR research in their body of work;
- Defining and funding more areas for One Health research in AMR;
- Health systems research on AMR to determine the drivers of AMR in the local healthcare system for potential intervention;
- Integrating genomics into routine infection prevention and control; and
- Participating in regional and international collaborative research in AMR, tapping on existing research networks and funding.

## Animal

### Ongoing Activities

There are several local research groups and biomedical companies involved in the development of rapid, on-site test kits to detect animal bacterial pathogens to aid diagnosis and guide appropriate treatment of animals.

Several feed producers, vaccine developers and academic institutions based in Singapore also carry out research into developing viable alternatives for the farming industry, such as vaccines, pre- and probiotics, compounds to improve gut health and food absorption, and technologies for pathogen control to reduce reliance on antimicrobials.

## Priority Areas for Further Action

**Establish baseline AMR data for target bacteria in local poultry, dairy and food fish farms.** Baseline data of resistant bacteria is required to monitor changing trends in resistance and assess impact of interventions on farms. Baseline AMR data can be obtained through surveillance programmes or cross-sectional studies, as appropriate.

**Facilitate applied research into the development of viable alternatives to reduce overall use of antimicrobials in livestock.** Alternatives include new vaccines, products, animal management systems and husbandry practices. Collection of scientific evidence to support the use of such alternatives can encourage uptake, especially in conjunction with cost-benefit studies.

## Environment

Research studies to understand environmental gene reservoirs of ubiquitous, non-pathogenic microorganisms and its association with phenotypic expression, have been initiated. Several local research groups have been conducting independent AMR research including short-term studies on the prevalence of drug-resistant organisms in raw and cooked ready-to-eat food samples, crops and meat. The mechanisms of AMR in foodborne pathogens are also being investigated. Coupled with similar studies in the animal and human sector, these studies are expected to contribute to reducing the research gaps described under One Health.

People can become exposed to drug-resistant organisms through the food chain. However, more clarity is needed on the role of food in the context of AMR. Little is currently known about the occurrence, effects, biodegradation and significance associated with the release and accumulation of antimicrobials in the environment. There is a need to understand how antimicrobials (including disinfectants) may contribute to the selection and spread of drug-resistant organisms in the natural environment and throughout the water and used-water treatment processes. This information will be necessary for sound risk assessment, management and mitigation measures to be successfully implemented, so as to control the spread of drug-resistant organisms between human, animal, food and environment sectors.



# PREVENTION &

## CORE STRATEGY 04. CONTROL OF INFECTION

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Every infection prevented means one less opportunity for antimicrobial use, and for organisms to develop resistance. Vaccines prevent humans and animals from getting infected, conferring protection against certain diseases that are difficult to treat or do not yet have effective treatment. Vaccination is therefore an important and cost-effective strategy to limit the spread of AMR.

Equally important are infection prevention and control measures, which are required to minimise infection risks and limit emergence and spread of drug-resistant organisms among humans and animals. Prevention and reduction of infections among patients translate to a decreased need for antimicrobial prescription. When good animal husbandry practices are applied, food-producing animals become less susceptible to disease and the need for antimicrobial use in animals decreases. Prevention of AMR also requires rapid detection and control of outbreaks, to stop transmission of resistant organisms in healthcare settings and the community.

### Human

#### Ongoing Activities

There are national immunisation policies and guidelines for children (National Childhood and Adolescent Immunisation Schedule), healthcare workers, and travellers (for specific diseases). Adult vaccination guidelines were also published in 2016 by local professional organisations.

Most of the serious and difficult-to-treat drug-resistant infections occur in hospitals, and more potent antimicrobials are used extensively in hospitals to treat them. To prevent the spread of such severe infections, measures to prevent and control infections is critical in hospitals. Hospitals currently have in place Infection Prevention and Control programmes that look into preventing the spread of infections, in particular multidrug-resistant organisms. MOH works with the National Infection Prevention and Control Committee (NIPC) to publish the National Infection Control Guidelines. In addition, hospitals report infection control indicators routinely to MOH. MOH and NIPC review these indicators regularly and institutions will be consulted if any peculiar trend is observed.

In the event of an outbreak of AMR infections in healthcare institutions, epidemiology teams based in public hospitals and the healthcare epidemiology team in MOH are available and ready to respond.

#### Priority Areas for Further Action

**Enhance infection prevention and control measures in hospitals.** A strong infection prevention and control programme is pivotal in containing multidrug-resistant organisms in the hospital setting to prevent nosocomial acquisition and spread of AMR. Infection prevention and control measures in hospitals are constantly being reviewed and strengthened. Good infection control practices are shared among hospitals for adaptation and adoption. Infection control indicators will continue to be tracked to monitor the effectiveness of prevention and control measures implemented.

**Increase uptake of vaccination.** Vaccinations reduce the number of infections, thereby reducing the potential need for and exposure to antimicrobials. To encourage vaccination among adults, the National

Adult Immunisation Schedule has been established. This will be accompanied by the monitoring of vaccine uptake and introduction of measures to encourage uptake.

## Animal

### Ongoing Activities

AVA works with farms to promote and implement biosecurity and best practices to prevent and control disease outbreaks. Strict biosecurity requirements and good animal husbandry practices in accordance with national guidelines are required for farms, which are all licensed by AVA. At the regional level, guidelines for good animal husbandry practices and good aquaculture practices (GAP) have also been developed for poultry and aquaculture farms through the ASEAN Sectoral Working Group for Livestock and Fisheries. AVA will be looking into harmonising our national GAP standards with the ASEAN guidelines in the near future.

The use of quality vaccines and alternatives to antimicrobials for the prevention of disease is encouraged. Veterinary vaccines used in Singapore must first be registered with AVA to ensure the safety, efficacy of the vaccines. Dogs and cats imported and sold in pet shops in Singapore are required to undergo mandatory vaccination, while routine vaccination is practised in equine, companion animal sectors and major food-producing animal sectors. Vaccination is increasingly being applied in aquaculture to control diseases, including the use of autogenous vaccines against fish bacterial pathogens.

### Priority Areas for Further Action

**Improve animal health management practices in local food animal establishments.** Good animal management practices reduce the occurrence of infectious diseases in animals, leading to a reduced need for veterinary antimicrobials. Strengthening disease prevention and welfare regulations and guidelines, and promotion of best practice guidelines on good animal husbandry and GAP will reduce reliance on antimicrobials.

**Promote and facilitate the use of vaccines and alternatives to antimicrobials in livestock, pets and fish.** The availability of safe, effective and affordable alternatives to prevent and control infection will reduce reliance on antimicrobials. It is important to highlight the benefits of vaccination to the farming industry and provide access to safe and effective vaccines for disease prevention. Vaccine evaluation and pharmacovigilance processes will also be reviewed to facilitate import while ensuring that vaccines are safe for use. Vaccine and feed companies will also be encouraged to develop monitoring and management strategies with farms, to reduce the reliance of antimicrobials.

## Environment

### Ongoing Activities

NEA regulates the food retail industry and Environmental Public Health (EPH) (Food Hygiene) regulations ensure that good food safety hygiene standards are maintained, with the purpose of preventing foodborne diseases. NEA's environmental hygiene programme and EPH (Cooling Towers and Water Fountains) regulations are also in place to maintain hygiene standards for cooling towers, swimming pools, water features or fountains and recreational waters, with the purpose of safeguarding public health and prevention of waterborne diseases.

To protect water resources, the sewerage and drainage systems in Singapore have been designed to be separate, which prevents cross-contamination between surface water and used water. The deep

tunnel sewers in the Deep Tunnel Sewerage System convey used water by gravity to centralised water reclamation plants, which further minimises the risk of cross-contamination. PUB also conducts preventive checks and carries out repairs on defective sewers to reduce infiltration and exfiltration. Treated effluents from the water reclamation plants are either discharged to the sea, or channelled for NEWater production. The reverse osmosis and ultra-violet disinfection processes in NEWater treatment can effectively remove antibiotics and bacterial pathogens. To minimise the risks of pathogen transmission from infectious individuals through the sewerage system, hospitals are required to dose hypochlorite disinfectant at their last inspection chamber (the discharge point to public sewer) or at the inspection chamber serving isolation wards.

The risk of acquiring drug-resistant organisms is further reduced by stringent regulations that mandate the proper collection, treatment and disposal of pathogenic waste and pharmaceutical wastes (including antibiotics), through licensed Toxic Industrial Waste Collectors. NEA conducts routine inspection on facilities of these licensees to ensure compliance. For trade effluent discharges into the sewerage system, PUB enforces the Sewerage and Drainage Act and the Sewerage and Drainage (Trade Effluent) regulations and all trade effluent discharged into the public sewerage system must be done with the written consent of PUB, and must comply within stipulated water quality limits.

### Priority Areas for Further Action

**Enhance surveillance and programmes for food safety.** The food hygiene programme is under constant improvement to reduce the risk of contamination of food. Education of food handlers will be enhanced so that food handlers can continue to play their part in maintaining high hygiene standards. Surveillance of pathogens in food and the environment will also be enhanced, so as to enable prompt mitigation of emerging risks.

# OPTIMISATION OF CORE STRATEGY 05. ANTIMICROBIAL USE

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Inappropriate use of antimicrobials across the human and animal sectors has been the biggest driver of development of resistance in organisms. Resistance to one particular antimicrobial agent commonly leads to resistance against an entire class of antimicrobials, thereby exacerbating the problem. Infections with organisms resistant against last-line antimicrobials have already been seen in patients in Singapore. Measures must therefore be urgently taken to conserve currently available antimicrobials.

Proper regulation of health products and medicines not only ensures access to safe and quality antimicrobials, but also prevents AMR through judicious use. The implementation of antimicrobial stewardship programmes also promotes rational prescribing practices – use of the right drug at the right time, in the right dose and for the right duration. These programmes, through optimising treatment, slow the emergence of resistance and minimise healthcare costs. Prescribing of antimicrobials is also often done when the nature of infection is unknown, and the availability of rapid diagnostics will be useful in guiding antimicrobial use.

## Human

### Ongoing Activities

Therapeutic products which include products containing antimicrobial agents are regulated under the Health Products Act and its subsidiary legislations. Specifically, antibiotics are classified as prescription only medicine and hence can only be obtained when they are prescribed by licensed healthcare professionals.

Antimicrobial stewardship programmes (ASPs) have been implemented in all public acute hospitals since 2011. This includes the establishment of ASP teams, consisting of physicians, microbiologists, pharmacists and executive personnel, as well as the development of computerised decision support systems to guide clinicians in making appropriate antimicrobial drug choices. Antimicrobial usage, appropriate antimicrobial use and ASP intervention acceptance rates are reported bi-yearly.

### Priority Areas for Further Action

**Strengthen antimicrobial stewardship in hospitals.** A review of existing ASPs in hospitals will be conducted to enhance their effectiveness, as well as to develop guidelines based on identified good practices. These guidelines can then be used when extending ASPs to private hospitals. All hospitals (both public and private) will be required to implement ASPs, including the monitoring of antimicrobial use, through licensing, accreditation and quality assurance frameworks.

**Ensure appropriate antimicrobial use in the community.** Local studies have found that the majority of primary care doctors believed antibiotics were over-prescribed in primary care. Guidelines on the appropriate use of antimicrobial medicines in community hospitals, ambulatory facilities (e.g. dialysis centres), and primary care clinics will be issued to improve prescribing practices and guide antimicrobial use. Incentives will also be explored to encourage doctors to optimise antimicrobial use.

# Animal

## Ongoing Activities

Prudent use principles recognise that antimicrobials are essential for animal health and welfare and must be used in a responsible, appropriate and targeted manner to prevent overuse and misuse of antimicrobials in agriculture, and reduce the development of resistance, particularly against medically-important antimicrobials. Non-therapeutic use of antimicrobials, such as for growth promotion in the absence of risk analysis, is not considered prudent use.

Antimicrobials are not used for growth promotion in Singapore farms. Certain antimicrobials such as nitrofurans, chloramphenicol and avoparcin are prohibited for use in feed and all food-producing livestock and aquaculture farms. This is supported by legislation. Antibiotics, including permitted drugs, are not allowed in animals ready for slaughter. AVA enforces strict limits on antimicrobial residues in food products. Regulatory action is taken when drug residues exceed the maximum residue levels or when prohibited substances are at all present.

Currently, farmers are allowed to administer antimicrobials to their animals without a veterinary prescription. However, AVA has in place licensing conditions for the manufacture of animal feed and has issued Directives to farms to ban the use of certain antimicrobials in food-producing animals. AVA is in the process of strengthening legislation to regulate veterinary use of human therapeutic products, to implement a system of veterinary drug registration, and to require veterinary prescription for all veterinary antimicrobials, including those used in livestock and aquaculture.

## Priority Areas for Further Action

**Establish a robust regulatory framework for supply chain control of all antimicrobials.** A sound regulatory framework will ensure responsible supply and use of antimicrobials along the entire supply chain. This will be achieved by veterinary drug registration and supply chain control covering import, manufacture, distribution and sale.

**Strengthen the system to ensure prudent use of antimicrobials in veterinary medicine and reduce inappropriate use of antimicrobials in food-producing animals.** This will be achieved through: (i) establishing a roadmap to progress towards veterinary prescription for drugs used in all animal sectors; (ii) establishing national guidelines for prudent use of antimicrobials in livestock and veterinary medicine (such as restricting the use of critically important antimicrobials for human and animal health); (iii) developing antimicrobial stewardship programmes; and (iv) enhancing communication and education efforts to instil a culture of responsible antimicrobial use in animals.

# INTERNATIONAL COLLABORATION

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The World Economic Forum has identified AMR as a global risk beyond the capacity of any organisation or nation to manage or mitigate alone. The spread of drug-resistant organisms is facilitated by the international movement of people, animals, food and other products. Singapore is particularly susceptible to the risk of AMR, being an international travel hub and having over 90% of its food imported. Resistance to last-line antimicrobials is already occurring in Singapore and other parts of the world. Singapore therefore supports global efforts to minimise the emergence and spread of AMR, through international partnerships and engagement with countries in the region.

**International benchmarking.** Participation in global surveillance networks, such as the WHO global AMR surveillance system (GLASS) and OIE global database on the use of antimicrobial agents in animals, will contribute to international understanding of AMR and antimicrobial utilisation. At the same time, this enables comparison of Singapore's efforts in controlling AMR with other countries and may highlight areas for improvement. Singapore can also learn from best practices of countries that are successful in combating AMR in specific areas.

**International partnerships.** Singapore supports WHO in addressing the global impact of AMR on human health and participates in the implementation of the Global Action Plan. Singapore is a member of the Association of Southeast Asian Nations (ASEAN) and supports member states to improve health systems by sharing technical expertise and experience, and this complements the National Strategic Action Plan objectives. AVA plays an active role as the lead for AMR in the ASEAN Livestock sector, where there is joint development of regional guidelines; harmonisation of veterinary drug requirements; strengthening of regional laboratory capacity; and collaboration with international agencies such as FAO and OIE. During the 38th Meeting of ASEAN Ministers for Agriculture and Forestry, which was held in Singapore in 2016, an agreement was reached to strengthen regional cooperation in mitigating the impact of AMR.

**International research collaborations.** On the research front, tapping on partnerships with international health research funding agencies will enable more efficient use of research funding and resources. PUB is currently a member of the Global Water Research Coalition, and is party to the antimicrobial resistance initiative. Singapore researchers are also partners in multiple international initiatives, including global point prevalence surveys on human antimicrobial use and resistance, and projects with Wellcome Trust-funded research units in the region.

The investment in new medicines, vaccines, diagnostic tools and other products to counter AMR is a long-term one, and partnerships with industry will be vital to ensuring sustainability. Support is needed on two levels: to promote prudent use of antimicrobials to prolong their effectiveness; and to develop new medicines and technologies to overcome AMR. Singapore will look to foster partnerships with industry and facilitate their research and development efforts.

International collaborations coupled with Singapore's commitment to combating AMR will be essential to the implementation of the Strategic Action Plan.

# CONCLUSION

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The Strategic Action Plan maps out key areas for understanding and controlling AMR, and for mitigating its impact on Singapore, within and between human, animal, food and environment sectors. Programmes and activities described under priority areas for further action will be introduced in a phased, incremental approach.

Goals for the next five years, implementation steps, funding priorities, as well as monitoring and evaluation indicators will be detailed subsequently. Surveillance initiatives will be used to establish baseline measurements and monitor trends in antimicrobial utilisation and resistance for evaluation and action. As part of the monitoring and evaluation process, key process indicators and outcome indicators will be developed and monitored to determine the success of the various programmes and activities.

To achieve the objectives and outcomes of the Strategic Action Plan, coordinated action from a wide range of stakeholders is required, and additional partners will be involved, together with community engagement, in the implementation.

# GLOSSARY

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<b>Antibiotic Resistance</b>	The ability of a bacterium to grow or survive in the presence of an antibiotic at a concentration that is usually sufficient to inhibit or kill bacteria of the same species and that exceeds concentrations achievable in the human / animal. It is a subset of antimicrobial resistance.
<b>Antimicrobial Resistance</b>	The ability of a microorganism to grow or survive in the presence of an antimicrobial at a concentration that is usually sufficient to inhibit or kill microorganisms of the same species and that exceeds concentrations achievable in the human / animal. Includes resistance to antibiotics, antivirals, antifungals etc.
<b>Antimicrobial Stewardship</b>	The use of coordinated interventions to improve and measure the use of antimicrobials by promoting optimal drug regimen, dose, duration and route. The aim is for optimal clinical outcome and to limit selection of resistant strains. This is a key component of a multi-faceted approach to preventing antimicrobial resistance.
<b>Healthcare Associated / Acquired Infections</b>	Infections acquired as a result of medical intervention e.g. in hospitals or in other clinical settings
<b>One Health</b>	The One Health concept recognises that human health, animal health, and the environment are interdependent and bound to the health of the ecosystems in which they exist.