# A Strategy and Action Plan for the Prevention and Containment of Antimicrobial Resistance in Malta (2020 – 2028)

MINISTRY FOR HEALTH

MINISTRY FOR AGRICULTURE, FISHERIES & ANIMAL RIGHTS

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## A ONE HEALTH RESPONSE TO THE THREAT OF AMR

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**Foreword by the Deputy Prime Minister, Minister for Health**

Since penicillin started to be used in the 1940s, antibiotics have saved countless lives and contributed to the control of infectious diseases that previously used to cause untold death and suffering. However, this medical miracle risks turning into one of the biggest public health threats of our time. Excessive and inappropriate use of antibiotics has resulted in the development of Antimicrobial Resistance (AMR) throughout the world. Infections are now no longer being cured or prevented by the same antibiotics which were so effective against them, just a decade or two ago. We face a real possibility of turning the clock back seventy years, when serious infections were untreatable. Just as worrying, medical advances like surgery and cancer treatment could be compromised since these require effective antibiotics to be successful.

Malta is not immune to this "Microbial Threat". For this reason, I am pleased to launch this Strategy outlining major actions and priority areas which will be addressed for the prevention and containment of AMR in Malta in the coming years. This Strategy and Action Plan focuses on improvements in surveillance, stewardship measures for the proper use of antibiotics, infection prevention and control as well as education and research.

AMR is not only a challenge in human healthcare but equally impacts on animal health and the environment. This complex, inter-related, problem requires concerted efforts by various stakeholders from a multitude of sectors – including healthcare specialists, veterinarians, pharmacists, educationalists, policy makers, legislative bodies, agriculture, industry and the public. The Ministry for Health is therefore proud to be leading this initiative through a 'One Health' collaboration with the Ministry for the Environment, Sustainable Development and Climate Change, with whom this Strategy was developed.

AMR can and does have an impact on people and on our health services. Working towards its prevention and containment is necessary to allow the key medicinal advances to remain effective and to ensure that we can continue to rely on antibiotics in the coming decades.

Hon Chris Fearne
Deputy Prime Minister
Minister for Health

Antimicrobial Resistance (AMR) has progressively raised concerns in many countries, including Malta. The issues encompass issues of microbes previously sensitive to antimicrobials which are now developing resistance to them. These resistant microbes may find themselves in the human body not only when they enter through direct means, but also indirectly when people consume foodstuffs from animal origin that may be contaminated with resistant microbes, e.g. meat, milk and eggs.

The foodstuffs from animal origin may also contain residues of antimicrobials administered to animals that may end up in the human body when the foodstuffs are consumed thereby contributing to the problem. For this purpose the Ministry of Agriculture Fisheries and Animal Rights in tandem with the Ministry for Health is launching a 'Strategy and Action Plan for the Prevention and Containment of Antimicrobial Resistance intended to target the years 2020 – 2025'. This reflects the wider action plans on this important issue of the Food and Agriculture Organization (FAO)'s, World Organisation for Animal Health Organisation and World Health Organisation (WHO)'s.

Antimicrobials have for the last eighty years played a crucial role in the treatment of both human and animal diseases. Their use in plants have sometimes been reported in a number of countries. However, the impudent use of antimicrobials is having an adverse effect on the health issues it intends to resolve so we should ensure that these are used properly. The use and administration of antimicrobials needs a proper holistic regulatory framework intended to prevent the abuse, misuse, and overuse of antimicrobials.

AMR will surely have long term implications which for now may be unseen (although present) for the livestock breeder who might not be able to adequately safeguard the proper health of his livestock. The magical antimicrobial which today solves some of his issues might be useless in the long term due to AMR. This will have devastating consequences both for the farmer himself whose interest is to ensure a healthy livestock and also for the consumer himself who can end up harboring microbes resistant to antimicrobials.

Thus our Ministry together with the Health Ministry has embarked on this strategy and action plan, whereby all this is sought to be avoided in the long term. All measures indicated in this strategic plan should yield positive results on the long term and mitigate an otherwise worrying situation. The strategy focuses on measures such as improved hygiene and biosecurity in farms which will help farmers in reducing risks to overall animal health, increase cost effectively and at the same time ensuring a more prudent and controlled use of antimicrobials. This could be reached through a proper awareness program amongst all those involved including livestock breeders and veterinarians. On the other end co-operation from all stakeholders is the other ingredient for the success of the plan.

Hon. Anton Refalo
Minister for Agriculture, Fisheries and Animal Rights.

**Acronyms and Abbreviations**

| | |
|---|---|
| AmpC | Amp C beta-lactamases are cephalosporinases from the functional group 1 and molecular class C in the Bush-Jacoby-Medeiros classification of beta-lactamases |
| AMR | Antimicrobial Resistance |
| ARMed | Antibiotic Resistance Surveillance & Control in the Mediterranean Region project |
| ATC | Anatomical Therapeutic Chemical |
| BURDEN | Burden of Resistance and Disease in European Nations project |
| CPD | Continuous Professional Development |
| CRE | Carbapenem resistant Enterobacteriaceae |
| DDD | Defined daily dose |
| EARS-Net | European Antimicrobial Resistance Surveillance Network |
| EARSS | European Antimicrobial Resistance Surveillance System |
| EC | European Commission |
| ECDC | European Centre for Disease Prevention and Control |
| EEA | European Economic Area |
| EFSA | European Food Safety Authority |
| ESAC | European Surveillance of Antimicrobial Consumption |
| ESAC-Net | European Surveillance of Antimicrobial Consumption Network |
| ESBL | Extended spectrum beta-lactamase |
| ESVAC | European Surveillance of Veterinary Antimicrobial Consumption |
| EU | European Union |
| HAI | Healthcare Associated Infections |
| ICD | Infection Prevention & Control Department - Mater Dei Hospital |
| ICM | Inter-sectorial coordinating mechanism |
| IMPLEMENT | Implementing Strategic Bundles for Infection Prevention & Management project |
| IPC | Infection Prevention and Control |
| MDH | Mater Dei Hospital |
| MDRO | Multi-drug-resistant organisms |
| MRSA | Methicillin-resistant *Staphylococcus aureus* |
| NAC | National Antibiotic Committee |
| OIE | World Animal Health Organisation |
| PPP | Purchasing Parity Power |
| PPS | Point Prevalence Survey |
| TESSy | European Surveillance System |
| VPRD | Veterinary and Phytosanitary Regulation Division |
| VRD | Veterinary Regulation Directorate |
| WHA | World Health Authority |
| WHO | World Health Organisation |

## Glossary

**Antibiotic resistance**
Refers to a property of bacteria that confers the capacity to grow in the presence of antibiotic levels that would normally suppress growth or kill susceptible bacteria.

**Antimicrobial**
Refers to medicine that, on application to living tissue or by systemic administration, will selectively kill or prevent or inhibit growth of susceptible organisms.

**AMR**
Refers to the ability of microorganisms, including bacteria, viruses, fungi and parasites to resist the action of antimicrobials especially of antibiotics that would normally suppress growth or kill susceptible organisms.

**Animals**
Refers to both food producing and non-food producing, including pets, pigeons and farmed fish.

**AWaRE list of antibiotics**
Refers to the Essential Medicines List issued by WHO for adults and children; this includes:

- ACCESS antibiotics which are first- and second-choice options for common infections and should be available in all countries and all facilities
- WATCH antibiotics that should be prescribed only for specific indications, since they are at higher risk of bacterial resistance.
- RESERVE antibiotics including last-resort options.

**'Critical' antibiotics (human use)**
Refers to those antibiotics used to treat serious or life-threatening infections in humans for which there are very limited or no alternative antibiotics that can be used to treat the infections if antibiotic resistance develops. The antibiotics that are in this critical class change from time to time and are influenced by the availability of newer antibiotics and the resistance rate of bacteria causing serious human infections.

**Community/primary care**
Refers to healthcare provided in the community for people making an initial approach to a medical practitioner or clinic for advice or treatment.

**Food producing animals**
Refers to land animals as well as fish that are reared for eating.

**Hospital care**
Refers to healthcare provided in a public or private licensed institution providing medical and surgical treatment and nursing care for sick or injured people.

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## Executive summary

Antibiotics are essential to medical practice because they are used to treat or prevent infectious diseases that might otherwise be lethal. Without antibiotics, lifesaving interventions such as intensive care, cancer treatment and many serious surgical procedures would not be possible because the risk of infection would be too high.

Antimicrobial Resistance (AMR) occurs when an antibiotic is no longer effective on bacteria it previously used to destroy. In common with many Mediterranean countries, the prevalence of AMR in Malta is significantly higher than several other regions within the European Union (EU), especially Scandinavia. These local challenges manifest themselves in both Human Health – in hospital and community settings, as well as in veterinary practice. The greatest challenge resides in the increasing levels of Carbapenem Resistant Enterobacteriaceae (CRE) which can be resistant to all known antibiotics and therefore untreatable; they threaten to turn the clock to the days before Fleming discovered penicillin.

The AMR Strategy is a cross-sectoral response to the threat of AMR in Malta with the aim of controlling and possibly reversing these current AMR trends. It has been informed by a review of national and international literature as well as expert advice from key stakeholders, especially the European Centre for Disease Prevention and Control (ECDC). The Strategy aligns with the World Health Organisation (WHO) Global Action Plan on Antimicrobial Resistance, the EU Action Plan on Antimicrobial Resistance as well as National legislation. It recognises the interconnectedness of humans, animals and the environment and adopts a whole of Government, a whole of society and a comprehensive One Health Approach to AMR, recognizing the complexity of the issue.

The main strategic aims of the AMR Strategy are to:

1. Strengthen the infrastructure needed to address the AMR situation through adequate support of the inter-sectoral coordinating mechanism (ICM), appropriate legislation and strengthening of relevant surveillance and feedback systems in Human and Animal Health as well as the environment.
2. Foster improved awareness and education on AMR among healthcare professionals, veterinary professionals, livestock keepers, animal owners and the public, as well as the measures needed to prevent it.
3. Introduce overarching measures to ensure appropriate antibiotic prescribing and use in community, hospitals and veterinary practice and in both Human and Animal Health sectors.
4. Improve Infection Prevention and Control (IPC) through national coordination and oversight, implementation of effective IPC multi-modal strategies in all healthcare facilities (with the control of CRE designated as a national priority) and foster hygiene standards in farms to prevent cross-transmission of animal pathogens.
5. Encourage and support innovation, research and networking in areas relevant to AMR.

## 1. INTRODUCTION

Antimicrobial resistance (AMR) refers to the ability of microorganisms to resist the action of antimicrobials, occurring when such microorganisms (e.g. bacteria, fungi, viruses and parasites affecting humans, land-dwelling and aquatic animals and plants) become resistant to antimicrobials such as antibiotics, making infections or diseases caused by such microorganisms more difficult or impossible to treat. Antimicrobials play a critical role for ensuring health and productivity when judicially used. However, when imprudently used they can lead to the associated emergence and spread of antimicrobial resistant microorganisms, placing everyone at great risk.

While bacterial resistance to antibiotics has developed rapidly and has become a major threat, a slowly emerging phenomenon of resistance of other micro-organisms to antimicrobials such as antifungals, antivirals and anti-parasitic agents have also been observed. Since bacterial AMR to antibiotics constitutes the largest significant threat of AMR, the Strategy focuses on antibiotic resistance and does not encompass other antimicrobial resistance, which has so far been on the low side.

The challenge of AMR is complex and no single action will, in isolation, provide an effective response. For this reason, the Strategy is a cross-sectoral response to the threat of AMR in Malta. Its focus lies in controlling and possibly reversing current AMR trends. The Strategy sets out aims that identify the broad areas where integrated and simultaneous action is required. Progress in each area is important to ensure a comprehensive response and support progress towards the Strategy's vision.

The aims, objectives and actions needed to achieve this vision have been informed by a review of national and international literature as well as expert advice from key stakeholders. The Strategy aligns with the WHO Global Action Plan on Antimicrobial Resistance, the EU Action on Antimicrobial Resistance as well as National Legislation.

With the aim of maintaining efficacy of antibiotics for both humans and animals for the long term and to improve Human and Animal Health, the Strategy sets priorities for future actions, whilst highlighting good practice initiatives which are already being implemented to address AMR. Some actions are concerned with adapting and extending existing successful initiatives whilst others focus on identified gaps that require new areas of action.

The Strategy recognises the interconnectedness of humans, animals and the environment. In view of the complexity of the issue, it adopts a whole of Government, a whole of society and a comprehensive One Health Approach to AMR. The Strategy, therefore, underscores the need for co-ordinated action by many stakeholders in Malta who are responsible for the different actions within the Strategy including Government, private and public partners and the public across the human, animal and environment sectors. Whilst individual actions are important, many are interrelated and specific actions in one area contribute to the achievement of multiple objectives.

## 1.1. The problem of AMR

AMR occurs due to changes in bacterial genetic material which can arise either due to mutations or through the acquisition of resistance genes from other bacteria. Various resistance genes can be exchanged or acquired between different species of bacteria and can lead to the development of multi-drug-resistant organisms (MDRO). As a result of antibiotics killing off sensitive bacteria, resistant bacteria are allowed to proliferate further and therefore become predominant.

Since their discovery in the early 20$^{th}$ Century antibiotics have revolutionised medicine. Antibiotics are essential to medical practice because they can be used to treat infectious diseases that might otherwise be lethal. Infections, which had previously killed millions, suddenly became treatable. The prompt administration of antibiotics in the treatment of certain conditions has also been proven to reduce morbidity and mortality. Without antibiotics, lifesaving interventions such as intensive care, cancer treatment and many serious surgical procedures would not be possible because the risk of infection would be too high.

However, as we move towards a century of antibiotic use, the availability of antibiotics that are effective is significantly threatened by the development and spread of AMR, making the prevention and treatment of infectious diseases more difficult and challenging.

## 1.2. The burden of AMR and its significance to Public Health

The emergence and spread of microbes resistant to the most effective antimicrobial agents, places medical advances in jeopardy. The resultant higher patient morbidity and mortality, together with increasing healthcare costs, are becoming major challenges worldwide. This is especially important to consider in the context of an ageing population which is generating a greater demand for healthcare services including antibiotic use.

Whilst the health, social and economic burden due to AMR is significant, it is difficult to quantify precisely because of deficiencies in the available data for many countries. It is even more difficult to estimate the additional human burden associated with AMR such as pain and psychosocial costs. Inappropriate use of antibiotics leads to wastage and higher medication costs; second and third line antibiotics often need to be used, coupled with additional investigations, consultation time and nursing care as well as the additional burden on hospitals. In addition, patients, their family and society endure loss in income, reduced worker productivity and added family support which all contribute to the social and economic burden generated by infections due to resistant microbes. Furthermore, the social and economic burden is exacerbated by associated mortality.

Estimates from Europe indicate that every year around 25,000 deaths are attributable to infections caused by a selection of multidrug-resistant bacteria. The estimated global yearly economic burden due to infections resulting from extra healthcare costs and productivity losses due to MDROs exceeds 1.5 billion euros per year.

Recent European reports have provided new evidence on the burden of AMR in Malta. A 2019 ECDC publication estimates that 25 to 35 Maltese die every year from infections caused by AMR organisms (Cassini, et. al., 2019). OECD has recently reported that AMR is

resulting in direct costs of more than €3,000,000 a year to the Maltese economy. It estimates that, in a worst-case scenario, in which no antimicrobial treatment is effective, AMR infection could cause healthcare losses of more than 6000 hospital days, and almost 20 million euros, a year. Fig 1 demonstrates estimated average annual health care expenditure associated with AMR across OECD modelled countries. Malta is estimated to have the highest healthcare expenditure as a consequence of a 100% resistance scenario (OECD, 2018).

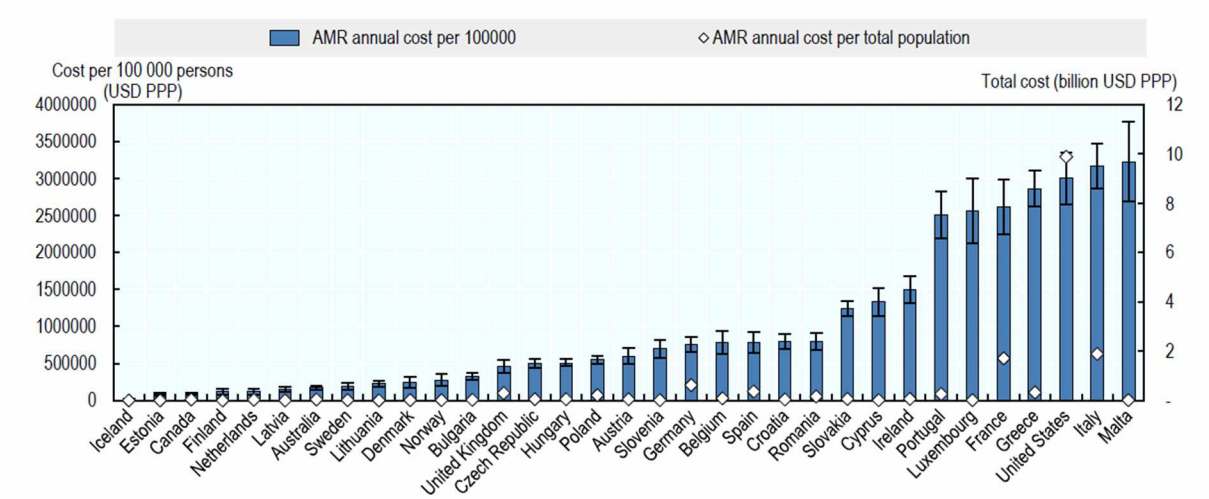

Fig 1: Average annual healthcare expenditure associated with AMR under 100% resistance scenario (OECD, 2018)

## 2. BACKGROUND

### 2.1 Global and European initiatives to counteract AMR

Recent G7, G20 fora and United Nations discussions on this subject show that the scale of the problem requires a concerted global governance effort. The increase in AMR experienced in recent decades has seen it designated as a Public Health priority by all major stakeholders. The WHO, in its Global Action Plan on Antimicrobial Resistance (2015), which was subsequently adopted by the World Animal Health Organisation (OIE) and the Food and Agriculture Organisation, the United Nations Political Declaration on AMR (2016) and the European Union One Health Action Plan against Antimicrobial Resistance (2011) as amended in 2016 through "A European One Health Action Plan against Antimicrobial Resistance (AMR)" highlight the efforts necessary to address this global treat. They have consequently, published roadmaps aiming to control AMR. These Strategies emphasise the importance of national, regional, and international collaboration for the control and spread of resistance. Through WHA 67.25 and 68.7 the WHO calls upon all member states to have in place by 2017 national action plans on AMR.

Between 2001 and 2010, European countries collected resistance data through the European Antimicrobial Resistance Surveillance System (EARSS). As of 2011, EARSS, whose new acronym is EARS-Net, has become fully integrated in the ECDC database (TESSy). The EU additionally established the European Surveillance of Antimicrobial Consumption (ESAC) to monitor the consumption of antibiotics in both the inpatient and outpatient sectors.

Northern European countries tend to report a lower resistance prevalence compared to countries in the south and east of Europe. These geographical differences in AMR could be

explained by differences in IPC practices and antibiotic consumption. For instance, the antibiotic consumption rate in the community tends to be low in Scandinavian countries whereas Southern European countries have high levels of antibiotic use. Compared to other European countries, broad-spectrum antibiotics are also prescribed more frequently in Mediterranean countries, in both community and hospital settings.

## 3. CURRENT SITUATION OF AMR IN HUMAN HEALTH IN MALTA

### 3.1 AMR Epidemiology

Malta is not immune to the significant challenge of AMR. Indeed, in common with most Mediterranean countries, several drug-bug resistance combinations are locally prevalent in significantly greater proportions than other EU regions, especially northern countries, which tend to report lower resistance. These local challenges manifest themselves in Human Health – at hospital and community settings – as well as in the animal sector. More details on the status of AMR in key pathogens, relevant to human and Animal Health, can be found in Appendix I.

### 3.2 Antimicrobial Consumption

Several local datasets have provided indicative trends and levels of use of antimicrobial agents both in the community as well as in the hospital setting. The data suggests that major challenges are present in the community, possibly due to a culture of over-prescribing antibiotics as well as to doctors acceding to patient demands. Whilst non-prescribed use of antibiotics has reduced drastically in the past decade (from over 18% in 2002 to around 1% of total usage as reported by the 2016 Eurobarometer survey), the same cannot be said for inappropriate prescribing. Almost half of the Maltese participants in the same survey reported being prescribed at least one course of antibiotics during 2015. Most respondents reported that it was prescribed for a cold, influenza or sore throat - conditions for which antibiotics are not normally indicated. The Eurobarometer results have been confirmed by other local post-graduate dissertations. Most antibiotics prescribed in the community are highly broad spectrum in nature; with co-amoxiclav, cefuroxime and ciprofloxacin being the three most commonly prescribed. These are well known to be greater drivers of resistance than the narrower spectrum equivalents.

Trends of consumption of antibiotics within Mater Dei Hospital (MDH), (the main hospital in the country), have stabilised in recent years, especially in high consuming units such as Intensive Care, Nephrology and Haematology, where antibiotic stewardship programmes have been introduced with some success. Nevertheless, use per capita is well above the European average. Additionally, the over-use of broad-spectrum products (especially carbapenems) remains a challenge together with excessively prolonged and unnecessary use of antibiotics for surgical prophylaxis.

### 3.3 Healthcare Associated Infections

Data about the prevalence of healthcare associated infections (HAI) is available only for MDH. Results from the 2011-2012 European Point Prevalence Survey (PPS), undertaken by ECDC, placed the prevalence of HAI in Maltese hospitals at the lower half of the European median; the actual prevalence was lower than what could be predicted from patient characteristics and case mix. In addition, significant improvement has been registered in the incidence of bloodstream infections in intensive care as well as several types of surgical site infections, especially those related to prosthetic hip and knee replacement surgery.

## 4. Current Situation of AMR in Animal Health AND Plant Health in Malta

### 4.1 AMR Epidemiology

Information on AMR in isolates of animal origin remains extremely sparse and restricted to a very limited set of isolates tested annually at the National Veterinary Laboratory, in compliance with EU minimal requirements. Yet, even from this limited information, it appears that AMR in animals is a significant problem. The level of resistance to ciprofloxacin in *Salmonella* spp. in local broiler flocks tested in 2016 was 50%, while 48.8% of the isolates were resistant to nalidixic acid. This trend is consistent with the average occurrence of resistance in the EU for these antibiotics. 2.5% of the isolates were resistant to cefotaxime and 1.3% were resistant to ceftazidime. At the same time, 67.7 of *E. coli* strains from the same source were also resistant to ciprofloxacin and 64.5% were resistant to nalidixic acid.

In May 2017 Malta undertook a surface waters monitoring exercise covering the testing for all substances listed in Directive 2015/495/EU, which established a watchlist of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC. This data was also reported to the EU Commission. Another monitoring exercise will follow up and cover an updated list of substances as per Implementing Decision 2018/840/EC. Action targeting pharmaceuticals in the environment is also being developed and addressed at EU level. Article 8 of Directive 2008/105/EC (amended by Directive 2013/39/EU) obliges the European Commission to develop a strategic approach to water pollution from pharmaceutical substances. The Strategy, which is in its final stages of drafting, includes tackling antimicrobial resistance as a key aim.

### 4.2 Antimicrobial Consumption

Detailed information on antibiotic use in animals in Malta is also significantly limited. Malta started providing sales data of antimicrobials to the European Medicines Authority's European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) network in 2018 for the year 2017. Antimicrobials are used in different species for various conditions including when the indication is not listed in the product specification for a particular species (off label use or cascade use).

Critically important antibiotics for human medicine also exist in formulations for use in veterinary medicine. Amongst others, they are said to be used to treat urinary disease in cats, respiratory disease in cattle, diarrhoea in cattle and swine, locomotion disorders in cattle, post-partum dysgalactia syndrome in swine and dental disease in dogs. Metaphylactic use of antibiotics is reportedly resorted to at times, in the rearing of broilers.

Regulation 60 of Subsidiary Legislation 437.47 requires all antimicrobial Veterinary Medicinal Products to be obtained following a veterinarian's prescription. These pharmaceuticals are also allegedly sourced from a range of sources including from other farmers, visiting veterinarians, from other Member States, direct personal imports and from retail outlets not approved by the Veterinary Services. The quantities of antimicrobials sourced in such ways is not known. These issues also present challenges for the implementation of policies for the prudent use of antimicrobials.

### 4.2.1 Aquatic farming

The aquatic sector benefits from the prudent use of antimicrobials in terms of improving on-farm biosecurity and husbandry (e.g. use of vaccines and disinfectants), treating chronic diseases (that cause reduced growth, low food conversion rate and poor survival thus leading to reduced production) and epizootic diseases that can cause mass mortalities. Nevertheless, there are some local concerns regarding threats posed by abuse, overuse, misuse, environmental and ecological issues, antimicrobial residues and AMR.

## 4.3 Plant Health

There is a global increase in concern that overuse or misuse of antimicrobials to manage plant pests is creating a selection pressure in the production environment, which can accelerate the development and spread of AMR in the environment. It is not only the antimicrobials that should be regarded as environmental contaminants, but also the genes that confer AMR. Many countries do not approve antibiotics as active ingredients in pesticides, and such pesticides are, so far, not known to be imported into Malta, reducing the potential risk of AMR development and so far keeping the development of pest resistance to pesticides.

# 5. EXISTING ACTIVITIES TO ADDRESS AMR IN MALTA

## 5.1 Legislation regulating Human Health and Animal Sector

Legislation directly related to AMR is limited. Current legislation requires that all antibiotics used for human patients (including topical formulations) as well as food animals, should be Prescription Only Medicines.

Subsidiary Legislation 465.08 of 2008 established the National Antibiotic Committee (NAC), a committee that serves as the Intersectoral Coordinating Mechanism for Malta. The NAC has representation from various professional groups involved in the prescribing and dispensing of antibiotics although it does not include participation of non-prescribers or the

public. Most of its past activities have focused on Human Health. Animal Health interventions have been minimal. The main role of the NAC has been primarily educational, both in terms of guideline development as well as educational campaigns aimed at both healthcare professionals as well as the public. It is legally empowered to collect wholesaler antibiotic sales data.

The NAC is limited in its output due to lack of adequate resources both financial and human. Ad hoc funds have been provided over the years, especially in activities related to European Antibiotic Awareness Day; this has allowed a basic level of activity to be maintained on a yearly basis. Other than to undertake collection and analysis of data related to ambulatory-care antibiotic consumption, no administrative support is available to the NAC.

Various legislation is in place in relation to Animal Health as per EU/EC regulations, directives, actions and decisions. EU guidelines have been adopted and adapted as needed. However, there is lack of legislation covering prescription, distribution, marketing, dispensing and retail of all veterinary medicinal products including antibiotics for animals. This is a barrier that is considered a central issue by both veterinary regulators and practitioners. In addition, tools to enforce the current Veterinary Services Act are either lacking or not sufficiently robust.

There is anecdotal information of the ease of availability of antibiotics and other pharmaceuticals for livestock over the counter by both veterinary pharmacies as well as retail outlets not approved by the Veterinary Services. This has resulted in a situation where veterinarians are not being called to farms except in last resort situations, with farmers preferring to carry out 'do-it-yourself' care on their animals. This situation is of concern from an AMR as well as from an animal welfare point of view. The lack of veterinary presence on farms is also resulting in a lack of crucial input in farm management issues, such as vaccination programmes as well as general farm practices. This often results in the development of medical problems in calves and cows such as diarrhoea and mastitis which go untreated or not properly treated, as highlighted, in particular, by those veterinarians who are ready to offer farm veterinary services.

One possible historic reason for this situation can be traced to a past system where the farmers' co-operative employed veterinarians to offer a veterinary service to dairy farms without cost to farmers. This potentially led to an ingrained culture among farmers that made them unwilling and/or unable to afford to pay for veterinary services themselves when this free service ceased.

The Regulation on transmissible animal diseases ("Animal Health Law") of March 2016 sets out a legal basis for monitoring animal pathogens resistant to antibiotics. This is supplemented by the regulations on veterinary medicines and on medicated feed.

Subsidiary Legislation 437.47 obliges the Marketing Authorisation Holder to comply with any request from the VPRD to provide information about the volume of sales or prescription of veterinary medicinal products. Compliance is generally satisfactory for data that is currently requested.

Challenges in human and financial resources at the VPRD together with ever increasing complexity of regulatory controls constitute a major challenge to achieve effective implementation.

Major legislative lacunas exist in both human and animal sectors. In Human Health and Animal Health, Legislative provisions directly relevant to AMR prevention are lacking. The absence of legal notices covering patient safety and infection prevention and control exacerbates the situation. In animal health there are no regulations to cover antibiotic formulations that consider AMR.

## 5.2 Interventions to address AMR in Human Health

### 5.2.1 AMR surveillance

The surveillance of AMR at MDH is already well established and on par (if not above average) to that performed in most EU hospitals. This relates both to day to day surveillance and outbreak detection as well as monitoring of trends. Regular feedback of data is communicated to decision makers as well as healthcare workers. Other public hospitals are also notified in real time of AMR isolates of concern. Epidemiology of AMR in these hospitals can be extracted from the central MDH laboratory database, however, the frequency of specimen taking is significantly lower than in MDH and therefore accurate epidemiological conclusions are more difficult to achieve.

Information about AMR in the community is less robust. While data about community samples sent for culture and sensitivity at the Microbiology Laboratory at MDH is available, these tend to originate from patients failing first line treatment in the community and are therefore skewed towards higher resistance profiles. There is currently no requirement for private laboratories and/or hospitals to report AMR to the National Antibiotic Committee.

### 5.2.2 Surveillance of Antimicrobial Consumption

Surveillance of antibiotic use has also been long established at MDH, where historical trends of consumption are available by Anatomical Therapeutic Chemical (ATC) Classification System, against bed day denominators. In addition, audits of restricted antibiotics, especially carbapenems, have been undertaken using hospital guidelines as the gold comparative standard. Indicators of overuse and misuse have been established. Knowledge about antibiotic use patterns in other hospitals is not generally available.

Community consumption is more problematic. In the absence of a national reimbursement system or electronic prescribing infrastructure, obtaining data at prescriber/pharmacy level has proven close to impossible. As a compromise, wholesaler distribution statistics are collected on a yearly basis and used as a proxy.

Both hospital and community data sets are submitted on a yearly basis to the ESAC-Net network coordinated by ECDC. However, since the method of data collection of ambulatory care consumption differs from that of most EU countries participating in this network (who have access to reimbursement data), benchmarking can only be done on an approximate basis. The results of the Eurobarometer Surveys on antibiotic use, where a standard methodology is utilised across all countries, are more accurate.

### 5.2.3 Infection Prevention and Control (IPC)

The Infection Control Department (ICD) at MDH coordinates all activities related to the prevention and control of HAI in the hospital. It also provides technical assistance, when requested by other public hospitals, each of which now have an appointed Practice Nurse in IPC. The ICD has developed a comprehensive set of policies and Standard Operating Procedures that are also used by the other public hospitals, is active in IPC education and organises an annual national conference. The Unit also adopts a Plan-Do-Study-Act approach utilising Root Cause Analysis tools to identify and address causative factors for serious infections, such as MRSA bacteraemia. In addition, a strong emphasis is placed on process audits including hand hygiene facilities and performance, management of central lines, peripheral venous cannula care, compliance with contact precautions, and environmental cleaning amongst others. A formal IPC setup in other hospitals and clinics is not required nor regulated.

### 5.2.4 Education

Education on AMR of healthcare professionals at undergraduate levels is somewhat heterogeneous. In the MD course run by the University of Malta, there has been a significant increase in IPC related lectures and tutorials (medical students receive more than 15 hours on IPC) but at the same time there has been a reduction in contact time on antimicrobial agent pharmacology. Undergraduate teaching in Pharmacy also dedicates a considerable (proportionally greater) quantity of lectures to infection prevention (including vaccination) and, as expected, pharmacology of antimicrobial agents. Historically, undergraduate education in nursing has always had a strong component of IPC; however, in recent years, coverage was reduced; topics have been interspersed in various modules and not always taught by specialists in the field. Unfortunately, the situation is even worse in the allied health sciences, where undergraduate instruction in AMR and IPC is sparse, at best.

Post graduate education in AMR and antibiotic prescribing is generally unstructured other than in the Specialist Training Programme for family doctors, where at least one session is dedicated to antibiotic prescribing. There are no AMR related CPD requirements for any healthcare profession and, not surprisingly, activities are often sub-optimal. Family doctors are the professional group most exposed to CPD activities related to infectious disease management and antibiotic prescribing. Unfortunately, although normally organised under the umbrella of a professional society, these activities are invariably sponsored by industry and often include a promotional introduction by the sponsor.

Education of the public has so far been primarily in relation to the European Antibiotic Awareness Day. The lack of a dedicated budget and resources causes planning challenges. Dissemination of information has relied on billboards as well as media opportunities through radio and TV talk shows. Despite their restricted nature, these activities have had an impact that appears to outweigh the level of investment. Nevertheless, there are still major challenges in public education and awareness. According to the 2015 Eurobarometer survey only 27% of Maltese were aware that antibiotics do not kill viruses, and 39% knew of their ineffectiveness against colds and flu. Education on AMR, appropriate use of antibiotics and infection prevention in schools is almost completely lacking.

### 5.2.5 Research

Over the past decade, the MDH-ICD has participated in various EU funded research programmes including ARMed (as project coordinator), BURDEN and IMPLEMENT. The paucity of funding opportunities means that local research initiatives are largely restricted to ad-hoc studies undertaken as part of undergraduate and postgraduate dissertations, especially B.Sc. Medical Laboratory Science and M.Sc. Biomedical studies (Microbiology). Although limited in scope, the data generated by these studies have, however, provided invaluable information on local AMR epidemiology.

## 5.3 Interventions to address AMR in Animal Health and the Environment

### 5.3.1 AMR surveillance

AMR surveillance in animals is currently very restricted and carried out by the National Veterinary Laboratory only on resistance of *Salmonella* species in poultry (layers and broilers) and swine as well as for *E. coli* under Decision 2013/652. Surveillance on bovine species reared in Malta is not compulsory because calves are not slaughtered. Other species such as rabbit, ovine and caprine are not targeted as this is not an EU requirement. National legislation allows for the slaughtering of small numbers of rabbits on farms without the presence of the official veterinarian on site. However, it does except the farm from being monitored if they are registered with the Food Safety Commission.

There are currently no laboratories in Malta that can provide a suitable service for performing routine diagnostic and susceptibility tests. Consequently, samples must be sent to other countries for analysis but this is rarely done due to the costs involved, logistical issues (e.g. ensuring suitable conditions for sample transport) and time taken to receive the result. Consequently, obtaining a realistic picture of AMR has proved to be challenging.

Currently, surface water is periodically monitored for pollutants of concern, including antibiotics, by the Environment and Resource Authority (ERA). The Life IP project is currently ongoing and aims to identify emerging pollutants including in groundwater, run-off and polished water. No monitoring of air, soil, irrigation water and forage crops is being undertaken for antibiotic residues.

### 5.3.2 Surveillance of Antimicrobial Consumption

Each year all registered local distributors of veterinary medicinal products and distributors of medicated feed are required to supply the VPRD with information on the sales of antibiotics for that year. The single licensed medicated feeding mill in Malta also supplies VPRD with information on the sales of medicated premix for each medicated feedstuff manufactured. This is used as a proxy for consumption.

The data received have been of variable quality. As of 2017 the process for data collection, reporting and evaluation has been reviewed and data analysis intensified. As of 2018 the data collected is more reflective of the local situation. Since 2016, Malta started giving sales

data on antimicrobials to the OIE and also started participating in the ESVAC project on the sales of antimicrobials in 2018.

The situation is complicated by possible use of antimicrobials intended for human medicine, but which are used in animals under the cascade (provided for by Articles 10 and 11 of Directive 2001/82/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to veterinary medicinal products) which allows for off-label use. This can be tackled by eventually measuring antimicrobial use at farm level using several additional tools, for example through electronic prescription. Such tools will also help for non-food producing animals since the cascade is more readily used in the prescription of treatment for these animals.

### 5.3.3 Education

Previous local experience with educational initiatives targeting veterinarians and farmers did not yield the expected results in terms of compliance with the regulatory requirements, other than some improvement in the dairy sector. It is not clear whether the improvement in the diary sector was due to the success of these educational initiatives or the "cross-compliance programme". This programme links direct payments through the Common Agricultural Policy to compliance by farmers with basic standards concerning the environment, food safety, animal and plant health and animal welfare.

The website of the VPRD includes a risk-based scoring tool that evaluates the quality of biosecurity of a herd. The tool can help with the reduction of antimicrobial usage and to improve the general land-dwelling Animal Health situation. Farmers can make use of this tool to assess the biosecurity level in their farms. The website also includes a comprehensive formulary of Veterinary Medicinal Products to be used for specific diseases in companion animals (including racing pigeons) listing the first and subsequent line of treatment. The suggested treatments only include the currently authorised veterinary medicinal products in Malta. An explanation of scientific factors related to the possible spread of AMR in humans from companion animals and the proven efficacious treatment for specific diseases is also included.

At present there is no undergraduate university course for veterinarians in Malta. A leading vocational education and training institution provides a course leading to B.Sc. in Animal Management and Veterinary Nursing. Efforts have been made to include or increase emphasis on subjects related with AMR in this course. Furthermore, there is a proposal to include veterinary medicinal products (with an emphasis on AMR) in the undergraduate programme leading to a degree in pharmacy to bridge some of the gap between education and industry thus enhancing interest in the subject.

Circulars have been issued as guidance on prudent use of critically important antimicrobials by VPRD. These guidelines are addressed to pharmacists, wholesale dealers and veterinarians and are publicly available on the VPRD website.

The Veterinary Surgeon Council has issued a series of documents as a guide for Professional Conduct which draws attention to the legal and ethical obligations related to the prudent use of veterinary medicinal products. It is obligatory to adhere to this guidance and sanctions may be taken against veterinarians who do not follow it. In addition, the Malta

Veterinary Association, a non-profit body, issues information to its members on the prudent use of antimicrobials as part of its activities to promote professional knowledge, science and practice.

## 6. RELEVANT STAKEHOLDERS

The control and prevention of the development and spread of AMR depends on various professionals and entities, in both public and private sectors, spanning the Human Health and Animal Health sectors as well as the agricultural, aquaculture and environmental sectors. In addition, Government commitment is also paramount for the success of this AMR Strategy.

Key stakeholders in the implementation of this Strategy include:

- Ministries responsible for Human Health, Animal Health, Plant Health and Education
- National Antibiotic Committee
- Public Health authorities
- Professionals involved in antibiotic prescribing and dispensing for humans and animals
- Healthcare workers providing patient care
- Medicines Authority
- Farmers, animal owners and stakeholders involved in animal sectors and aquaculture
- Hospital-based entities (public and private)
- Professional Organisations
- Community practitioners
- Public
- Long-term care facilities
- Pharmaceutical Industry and wholesalers
- Schools and child-care facilities
- Pharmacies
- Universities and educational institutions responsible for training of professionals

## 7. FRAMEWORK FOR ACTION

### 7.1 Vision

The vision is to create a society in which antimicrobials are available, recognised and managed as a valuable shared resource, maintaining their efficacy through appropriate use so that infections in humans and animals remain treatable, lives are not threatened, and communities continue to benefit from the advances that antimicrobials enable.

### 7.2 Guiding Principle

The guiding principle leading the Strategy is that of One Health. This principle recognises the inextricable link between humans, animals and the environment and emphasis that achieving optimal health outcomes for people and animals requires the collaboration and cooperation of Human Health, Animal Health and the environment. Interdisciplinary collaboration which needs to be facilitated at various levels including national, through a whole of government approach, and international is critical between the numerous stakeholders.

## 7.3 Aim of the Strategy

The aim of this Strategy is to provide a plan of action for Malta, designed to ensure the efficacy of antibiotics for the long term. This focuses on the appropriate use of antibiotics and minimising the development and spread of AMR, thereby improving Human and Animal Health.

## 7.4 Overall Objectives

- Review current relevant legislation to strengthen governance to prevent and counteract AMR and address the gaps in legislation and regulation to ensure leadership, engagement and accountability for actions to combat antimicrobial resistance.
- Implement effective One Health antimicrobial stewardship practices across Human and Animal Health settings to ensure the appropriate and prudent prescribing, dispensing and administering of antimicrobials.
- Develop nationally coordinated One Health surveillance of AMR and antimicrobial usage.
- Improve infection prevention and control measures across Human Health and Animal Health settings to help prevent infections and the spread of AMR.
- Increase awareness and understanding of the use of antibiotics to treat and prevent infections through education and training.
- Agree on a national research agenda and promote investment to prevent, detect and contain antimicrobial resistance.
- Strengthen international partnerships and collaboration on regional and global efforts to respond to AMR.

## 7.5 Strategic Priority Areas for Action

The Strategy provides a framework to guide actions on AMR and use of antibiotics. It coordinates activities across stakeholder groups where all stakeholders must work under the Strategy to change those practices that are contributing to the inappropriate use of antibiotics and the increasing development of resistance in Malta. The Strategy aims to build on the current strengths and address areas where deficits have been identified for each objective (Appendix 2). In order to achieve full implementation of the Strategy, a number of pre-requisites (such as improved legislation and adequate infrastructure that enhances enforcement, electronic prescribing) are required.

Implementation and evaluation of the Strategy will be supported by an Implementation Plan that provides the detail of specific actions, targets, time frames and indicators. The Plan will be developed during 2018-2019 in consultation with stakeholders. Implementation will take a staged approach over the period 2018–2025.

The Objectives and their Priority Action areas are outlined below.

**Objective 1: Legislation and infrastructure**

***Ensure the necessary legislation and infrastructure to address AMR and implement effective strategies.***

The following actions are required to ensure a more robust legislative framework:

1.1 Review and update legislation relevant to antimicrobial usage and antimicrobial resistance and its enforcement.

1.2 Develop a regulatory framework for a One Health Approach in implementing this Strategy.

1.3 Strengthen enforcement and monitoring of compliance with relevant legislation.

1.4 Review the role of the NAC by regulating for more robust responsibilities, accompanied by appropriate funding and resources for its effective functioning.

1.5 Introduce appropriate legislation to establish minimum standards for infection prevention and control in Human Healthcare and residential care institutions.

1.6 Introduce, with urgency, legislation that would regulate on antimicrobial use in veterinary practice so as to ensure full compliance with all EU Medicine Veterinary legislation and EU Directive 2001/82/EC.

1.6.1 In so doing, establish the need of a prescription for all antibiotics used in animal health and other important requirements in the regulation of veterinary medicinal products.

1.7 Develop a framework to ensure adherence to legal obligations in line with local and EU requirements relating to correct antibiotic use under veterinary oversight, and infection prevention on farms.

1.7.1 Identify, through a consultative process, the respective roles and responsibilities of key stakeholders in complying with these requirements and develop the legal framework for animal health plans on farms, which are commensurate with their scale of activity.

1.8 Review and/or establish legislation to ensure adequate wastewater treatment systems to prevent discharge of antibiotics into the environment.

**Objective 2: Stewardship**

***Implement effective antimicrobial stewardship practices across Human Health and Animal Health settings to ensure the appropriate and prudent prescribing, dispensing, administering and disposal of antimicrobials*.**

The following actions are required for effective antimicrobial stewardship:

2.1 Introduce and/or improve evidence-based, easily accessible, national antibiotic guidelines, in both human (community, hospital settings as well as long term care facilities) and animal health (both treatment and metaphylaxis).

2.1.1 Ensure that all antibiotics recommended in the national guidelines, especially narrow-spectrum formulations, are stocked by, and can be easily obtained from, all pharmacies (both public and private).

2.2 Ensure that antibiotics listed within the WATCH and RESERVE groups of the AWaRE list of antibiotics, issued by WHO, are targeted by stewardship programmes, at national and institutional levels.

2.3 Set and monitor qualitative and quantitative targets for improvement of prescribing at national level and introduce systems to identify, benchmark and follow up high-end prescribers in community, hospital and veterinary settings.

2.4 Introduce specific measures to improve antibiotic prescribing and use in the community, hospitals and veterinary practice (including delayed prescribing in the case of human medicine), and formal systems of access by primary care stakeholders to specialists in infectious diseases/microbiology for both human and animal health.

2.4.1 Facilitate the use of rapid, point-of-care diagnostics to reduce the ambiguity of infection management.

2.4.2 Review rules to promote splitting antimicrobial packs in a legal and safe manner, to reduce the risk of antibiotic left-overs at home.

2.5 Establish programmes of clinical audits and peer reviews on antibiotic prescribing among doctors and veterinarians, in a blame free culture and with commensurate incentives for participation.

2.6 Ensure that any electronic prescribing systems include antimicrobial prescribing and link to clinical indication, microbiological and consumption data.

2.7 Fast track the procurement of new antibiotics, effective against currently resistant organisms, and ensure their judicious use by gatekeeping through infectious disease specialists and microbiologists.

2.8 Review existing accreditation and quality assurance programmes of public and private microbiology laboratories to ensure they appropriately support and encourage compliance with best practice AMR approaches.

2.9 Develop a system for safe disposal of antibiotics in the community.

2.10 Encourage farmers' cooperatives and other similar associations to explore models for the provision of farm veterinary services to achieve more cost-effective economies of scale.

2.11 Explore the possibility to introduce and incentivise vaccination programmes in farmed animals, possibly linked to quality schemes.

2.12 Ensure proper mechanisms to enhance the prevention of the introduction of pests and to ensure the implementation of good agricultural practices and integrated pest management (IPM), thereby continuing to discourage the use of antibiotics in crop production and plant protection.

2.13 Develop and implement strategies to minimize the contamination of plants and plant products with bacteria.

**Objective 3: Surveillance**

***Strengthen relevant surveillance and feedback systems on antibiotic use and resistance in human and Animal Health as well as the environment.***

Coordinated surveillance is essential to understand the magnitude, distribution and impact of resistant organisms and antimicrobial usage, identify emerging resistance and trends, and determine associations between usage and resistance. Such data will inform immediate actions as well as provide evidence to evaluate policies and set priorities.

The areas of priority for action include:

3.1 Strengthen reference laboratory capacity (both human and animal) in the country and increase access to microbiology support for primary care and veterinary services.

3.1.1 Establish molecular typing capability for key resistant organisms.

3.2 Strengthen surveillance systems of antibiotic resistance, especially in primary care and in veterinary practice.

3.3 Focus surveillance on priority organisms and drug-bug combinations most relevant to Human Health (Table 1). Regularly review and update the list in response to the changing incidence of resistant organisms.

| Rationale | Species |
|---|---|
| Impact in both hospital and community | Enterobacteriaceae (primarily *Escherichia coli* and *Klebsiell*a *pneumoniae*)<br>*Staphylococcus aureus* |
| Impact mainly in hospital | *Acinetobacter baumanii*<br>*Pseudomonas aeruginosa*<br>*Clostridium difficile* |
| Impact mainly in community | *Streptococcus pneumoniae*<br>*Salmonella* species<br>*Campylobacter jejuni*<br>*Mycobacterium tuberculosis*<br>*Neisseria gonorrhoeae* |

Table 1: List of priority organisms AMR surveillance in Human Health (based on WHO recommendations for global AMR surveillance)

3.4 Establish and implement a nationally representative and coordinated programme for surveillance of antimicrobial usage in hospitals, the community, environment, animal and aquatic medicine and agriculture, in both food and non-food, and aquatic production, including by sector and by antibiotic (broad and narrow).

3.4.1 Establish a comprehensive programme for at-source monitoring of antimicrobial residues in food animals.

3.4.2 Establish a comprehensive programme for at-source monitoring of antimicrobial residues in the environment, including soils and irrigation water.

3.5 Strengthen systems to feedback data on antimicrobial resistance and antibiotic consumption used in human and animal care and produce an annual AMR report for Malta.

3.6 In primary human care, establish a sentinel AMR surveillance system with timely feedback and trend analysis.

3.7 Explore the possibility of enhancing diagnostic services and sensitivity testing for animals.

3.8 Re-introduce veterinary post-mortem services for surveillance of notifiable diseases and necessary testing, as appropriate. Increase sampling of antibiotic residues in carcasses, and food as an indicator of abuse of antimicrobials.

3.9 Establish a sentinel AMR surveillance programme in animals to capture data generated from routine tests undertaken by veterinarians, slaughter houses as well as the public health laboratory. This will allow a better understanding of AMR epidemiology within animals, especially in areas not covered by mandatory EU testing requirements.

3.10 Introduce a programme of antibiotic residue testing in meats available for sale in retail outlets (e.g. butchers, supermarkets) including products such as rabbit meat which are not covered in EU testing programmes.

**Objective 4: Infection Prevention and Control**

***Improve infection prevention and control measures across Human Health and Animal Health settings to help prevent infections and the spread of antimicrobial resistance.***

Malta has been implementing several actions related to IPC including the introduction of dedicated IPC personnel in acute care and rehabilitation hospitals and the introduction of a focal point of IPC expertise in MDH. These actions have led to several success stories of improved processes and outcomes within tertiary care. However, additional actions need to be implemented, particularly in community and environment settings.

Further priority actions include:

4.1 Implement and enforce national IPC regulations that include minimum/core infection prevention and control standards for primary, tertiary, rehabilitation and residential settings, and establish plans to monitor and evaluate their effectiveness.

4.2 Establish national IPC coordination and oversight including national IPC guidelines and a healthcare associated infection surveillance programme, covering all public and private healthcare entities.

4.3 Implement IPC multi-modal strategies commensurate for all healthcare facilities, through a properly functioning IPC programme managed by dedicated, trained professionals with clear structures of administrative responsibility and accountability for its implementation.

4.4 Establish structure, process and outcome Key Performance Indicators (KPIs) to allow monitoring and evaluation of IPC activities and structures of healthcare facilities at national and institutional level, to ensure uniformity in competence and output.

4.5 Designate the control of CRE as a national priority and address it through specific, funded, interventions outlined in a CRE Action Plan for Malta that includes expanded screening and improved intervention protocols.

4.6 Establish specific programmes of Infection Prevention and Control in the community, including follow-up of discharged patients colonised with MDROs and support to primary care physicians.

4.6 Improve hygiene standards in farms to prevent cross-transmission of animal pathogens.

**Objective 5: Training, Continuous Professional Development and Education**

***Through education and training, increase awareness and understanding of AMR, its implications, and actions to combat it.***

Education of all stakeholders involved in combatting AMR is a critical component of any Strategy. Unless all the players are aware of the problem, and the solutions available, it will be impossible to achieve urgency – the first and essential component of behaviour change.

The following actions will be implemented:

5.1 Enhance the knowledge and awareness on AMR among healthcare and veterinary professionals by ensuring the availability of continuing professional education activities, on AMR and prudent use of antibiotics, not sponsored by industry.

5.1.1 Include a minimum of one continued medical education (CME) session on antibiotic use per year as part of any reaccreditation schemes for all those professionals who

prescribe and dispense antibiotics, with an emphasis on multidisciplinary events to enhance inter-professional communication and improved outcomes.

5.1.2 Facilitate educational activities on AMR and antibiotic use for other professions including nursing and allied health.

5.2 Review professional training during undergraduate and postgraduate medical training and programmes.

5.2.1 Ensure inclusion of AMR, prudent antibiotic use and infection prevention and control as a defined contact time during undergraduate courses for healthcare professionals, with particular attention to avoiding fragmentation or inconsistencies through improved inter-linking or centralised modules.

5.2.2 Include AMR training in all post-graduate training and continuing professional development of specialists.

5.3 Provide health and veterinary professionals with communication resources and behaviour change training to support informed decision-making regarding treatment and to support efforts to educate clients regarding appropriate antibiotic use and effective infection prevention and control practices each time they prescribe, dispense or provide advice about antibiotics.

5.4 Explore the establishment of academic detailing systems to enhance knowledge of evidence based antibiotic prescribing amongst doctors and veterinarians.

5.5 Undertake specific awareness and education campaigns to veterinarians, including safe disposal of waste generated by veterinary practice, appropriate use of disinfectants in clinics and infection prevention and control measures.

5.6 Address literacy, on AMR and correct antibiotic use among both the public and journalists by developing and implementing regular campaigns making full use of conventional and social media platforms.

5.7 Set up a help-line dedicated to infections and antibiotic use, manned by appropriate healthcare professionals, to allow the public to phone and discuss basic issues so as to provide reassurance and support.

5.8 Educate employers on the cost-effectiveness of adequate home rest in mild infections, so as to avoid cross transmission in the work place.

5.9 Expand educational Animal Health campaigns aimed specifically at farmers, animal and pet owners emphasising the risks of non-prescribed use of antibiotics or acquisition of antibiotics from unlicensed sources as well as the benefits and cost-effectiveness of greater hygiene.

5.10 Include topics on AMR, hygiene and antibiotic use in the curricula of primary and secondary schools to ensure children are educated about the problem from an early age.

**Objective 6: Research and Performance Measurement**

***Strengthen the research agenda through consensus, coordination and collaboration.***

Research initiatives are essential to strengthen the knowledge and evidence base of AMR. In addition, research can provide the basis for devising and implementing more effective interventions to address AMR. It is therefore of great importance that research is actively promoted and supported.

The following will be priority areas:

6.1 Agree on a national research agenda to address issues related to AMR.

6.2 Develop local research into the behavioural drivers of AMR that impact local practices.

6.3 Coordinate national AMR research activities and the sharing of information.

6.4 Explore and identify opportunities to increase support for research and development, including possible funding sources.

**Objective 7: International partnerships and collaboration**

***Strengthen international partnerships and collaboration on regional, European and global efforts to respond to antimicrobial resistance.***

The increasing movement of people, animals, foods and other products has the potential to facilitate the movement of resistant pathogens across borders faster and further than ever before. Growth in tourism, including the travel of people to another country to obtain medical treatment in that country, has accelerated the international spread of AMR, further highlighting the global nature of the problem.

Malta's AMR Strategy will be less effective if it is not aligned with international efforts. To support global efforts to reduce the spread of resistant organisms, Malta must continue to actively collaborate with European countries, especially those in the Mediterranean as well as international organisations through strategic policy support, regulatory action and coordinated initiatives.

Priority will be given to:

7.1 Continue to actively engage with European and International Fora.

7.2. Participate in international surveillance initiatives.

## 8. WAY FORWARD

The Strategy supports a collaborative effort through a One Health Approach to enhance those practices that encourage the appropriate and prudent use of antibiotics, change those practices that have contributed to the development of resistance and implement new initiatives to reduce inappropriate antibiotic usage and resistance. It builds on the good practices already being implemented by integrating new and existing programmes and initiatives into a unified national response.

Implementation of the priority areas identified will take a staged approach over the life of the Strategy. It will involve many stakeholders and require a high level of cross sectoral cooperation at both the national and international levels. The Strategy can only be successful if all stakeholders heed its call to action and actively look for opportunities to develop new whilst strengthen existing partnerships to support the achievement of the Strategy's objectives.

The Strategy will be regularly reviewed and updated so that it remains reflective of the work that is underway, and action plans for the future.

**Owners:** Intersectoral Co-Ordinating Mechanism (Superintendence of Public Health through the National Antimicrobial Committee)

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## APPENDIX 1: LOCAL AMR EPIDEMIOLOGY

### 1. Human Health

Malta is not immune from the significant challenges from AMR that all countries are facing, which – unless effectively addressed – will have significant patient safety consequences. In common with most Mediterranean countries, several drug-bug resistance combinations are locally prevalent in greater proportions than other EU regions, especially Scandinavia, that tend to report low resistance. Furthermore, these local challenges manifest themselves in both hospital as well as community settings.

### 1.1 Hospital

***Staphylococcus aureus***

For over a decade, since its initial participation in EARSS and now EARS-Net, Malta has reported one of the highest prevalence of MRSA in Europe. Indeed, the proportion of MRSA, isolated from blood cultures was, for many years, greater than 50% as can be seen in Fig 1 below.

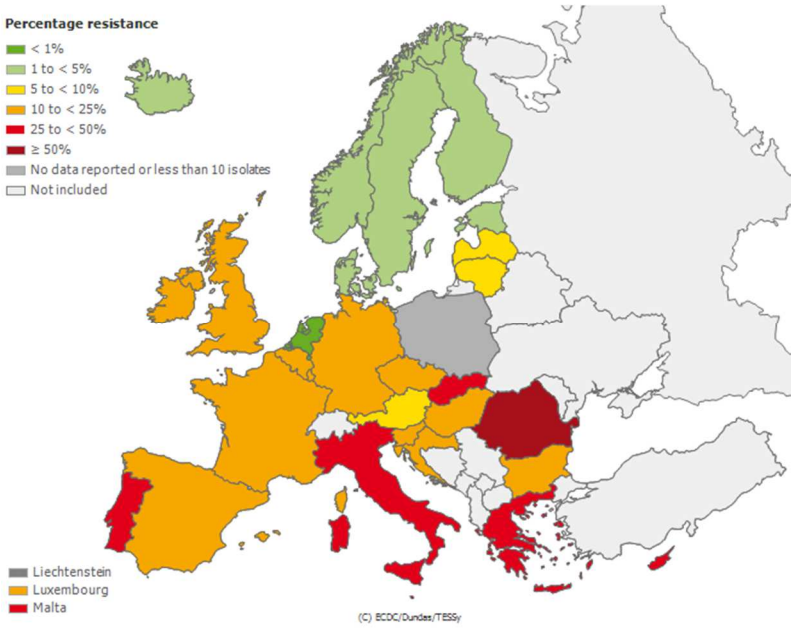


*Fig 1 Proportion of MRSA in Staphylococcus aureus isolated from blood cultures within European countries participating in the EARS-Net network (source: ECDC 2015)*

However, over the past years, a significant improvement in MRSA bacteraemia incidence has been achieved in MDH, following the launch of a hospital wide AMR Strategy in 2010. The cornerstone of the initiative was a policy of Root Cause Analysis and subsequent corrective action. As a result, the median yearly incidence of MRSA bacteraemia has reduced by more than 70% since the start of the campaign (Fig 2).

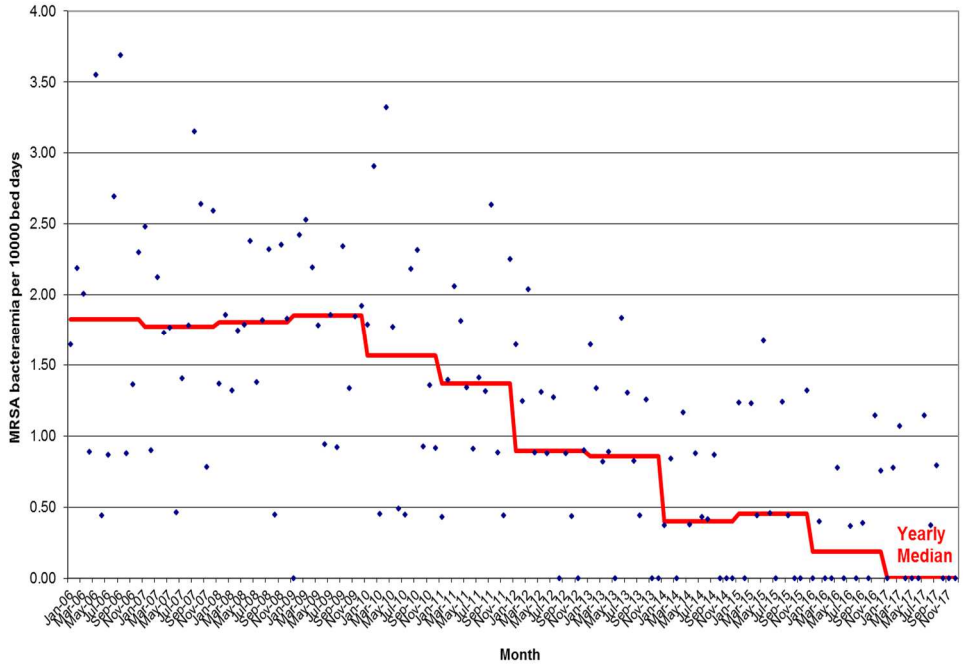


*Fig 2: Incidence of healthcare associated MRSA in Mater Dei Hospital (source: Infection Control Department 2018)*

### *Clostridium difficile*

*Clostridium difficile* is traditionally regarded, as only secondary to MRSA in terms of healthcare transmission importance. Nevertheless, for as yet unknown reasons, the incidence of *C. difficile* in Malta has historically been significantly lower than most of European countries, despite a high level of antibiotic use.

### *Acinetobacter baumannii*

Multi-resistant *Acinetobacter baumannii* is highly prevalent in many Mediterranean countries, especially in the Balkans. This organism was also regularly isolated from patients in the Intensive Therapy Unit (ITU) of St. Luke's Hospital, where several outbreaks were reported. However, since the migration to MDH and as a direct consequence of numerous initiatives within this department to improve infection prevention and control practices, incidence of MDR *A. baumannii* has reduced significantly.

### *Carbapenem-resistant Enterobacteriaceae*

Carbapenem-resistant Enterobacteriaceae (CRE), especially *Klebsiella pneumoniae*, have been reported in several European hospitals. In Malta, the local threat from these organisms is higher than that reported in most EU countries. Indeed, Malta is one of only three EU countries that are regarded as endemic for CRE. In addition, New Delhi Metallo beta-

lactamase producing (NDM-1) strains of CRE, almost resistant to all antibiotics, are locally increasing in incidence; at least one outbreak has been reported.

CRE infections have, almost certainly, become Malta's greatest AMR threat. In fact, the high prevalence has led to the CRE situation in Malta being referred to as endemic (Fig 3). Extensive Drug Resistant (XDR) strains are increasing on a yearly basis and Pandrug resistant (PDR) isolates of Klebsiella pneumoniae – resistant to all known antibiotics – have started to be detected. The extent of resistance of Klebsiella pneumoniae is demonstrated in Figs 4 and 5 below.

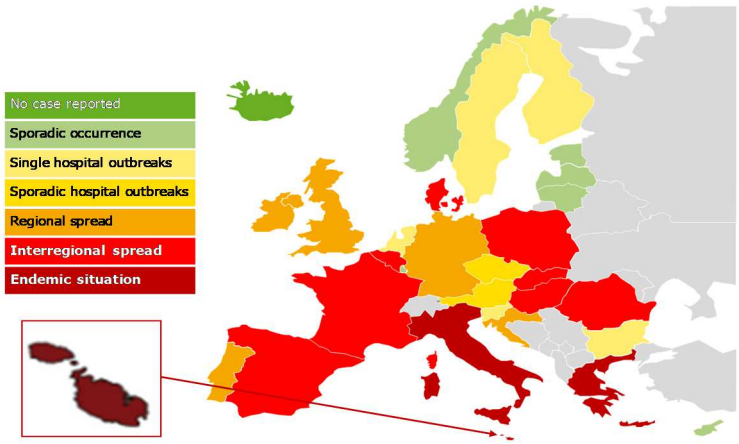


*Fig 3: Prevalence of CRE in European countries; countries in brown report the highest levels and are deemed as endemic for these organisms (source: ECDC 2015)*

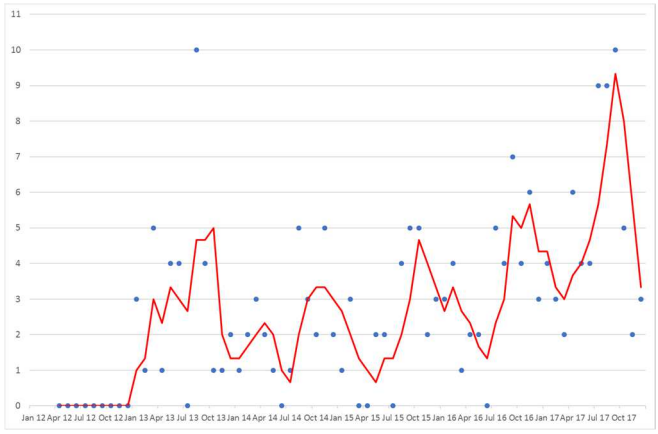


Fig 4: Yearly isolates of imipenem resistant Klebsiella pneumoniae in Mater Dei Hospital (source: Infection Control Department, 2018)

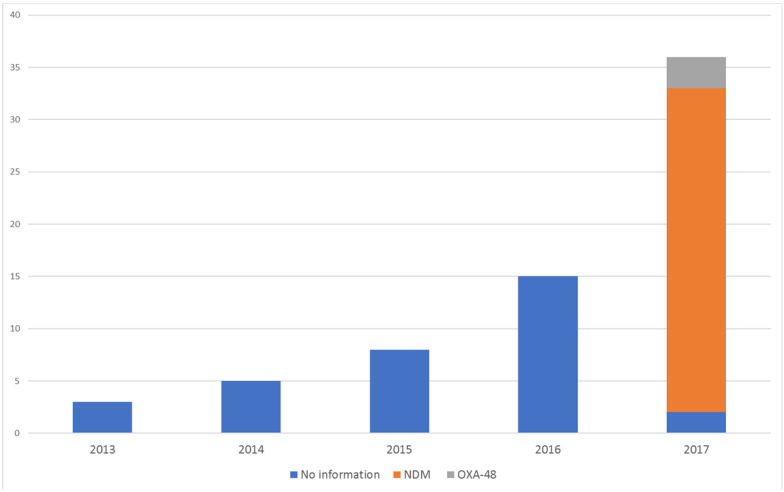


Fig 5: Yearly isolates of XDR Klebsiella pneumoniae (resistant to all antibiotics except colistin) in Mater Dei Hospital (source: Infection Control Department 2018)

## 1.2 COMMUNITY

### *Staphylococcus aureus*

Incidence of MRSA in the community setting has reached worrying levels. Approximately 30% of *S. aureus* isolates from samples sent from health centres are meticillin resistant. A study looking at MRSA carriage rate amongst healthy individuals, without any hospital treatment in the previous year, found carriage to be above 8%; this is one of the highest recorded levels in the literature. Misuse and overuse of antibiotics in the community are thought to be responsible for such high MRSA levels, including abuse of topical antibiotics.

### *Escherichia coli*

Community strains of *E. coli* exhibit high resistance levels to ciprofloxacin; substantial proportions also exhibit evidence of extended spectrum beta-lactamase (ESBL) production. Antibiotic misuse and overuse is thought to be the major driver behind such trends and an association has been shown between *E. coli* resistance and the consumption of beta-lactam antibiotics and quinolones in the community.

### *Streptococcus pneumoniae*

*Streptococcus pneumoniae* is the most important community pathogen causing lower and upper respiratory tract infections. Although it remains relatively sensitive to penicillin, local resistance to macrolides is a concern.

## 1.3 Antibiotic consumption

The current knowledge base on trends and levels of use of antimicrobial agents suggests that major challenges are present in the community. Nevertheless, non-prescribed use of antibiotics has reduced drastically from more than 18% in 2002 to around 1%, as reported by the 2016 Eurobarometer survey. However, the same cannot be said for inappropriate prescribing. Almost half of the Maltese participants in the same survey reported being

prescribed at least one antibiotic during 2015 as seen in Fig 6 below; more worryingly, the vast majority of them said that it had been prescribed for a cold, flu or sore throat - conditions for which antibiotics are not normally indicated. The vast majority of antibiotics prescribed in the community are broad spectrum in nature; co-amoxiclav, cefuroxime and ciprofloxacin are the three most common; these are greater drivers of resistance than their narrower spectrum equivalents.

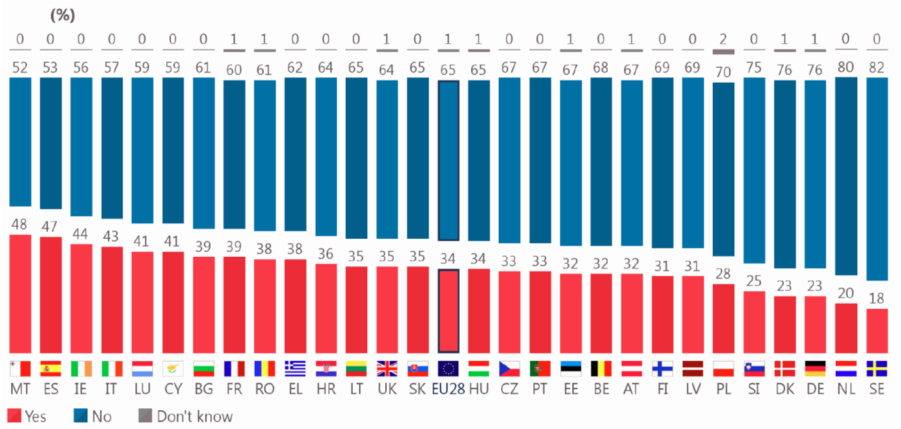


Fig 6: Proportion of EU citizens who took at least one oral antibiotic (in tablet, powder or syrup form) from April 2015 to March 2016 (source: Special Eurobarometer 445)

Trends of antibiotic consumption within MDH have stabilized in recent years, especially in high consuming units such as intensive care, nephrology and haematology, where antibiotic stewardship programmes have been successfully introduced. Nevertheless, Fig 7 clearly shows that use per capita is well above the European average. Additionally, the over-use of broad-spectrum products (especially carbapenems) remains a challenge together with excessively prolonged and unnecessary use of antibiotics for surgical prophylaxis.

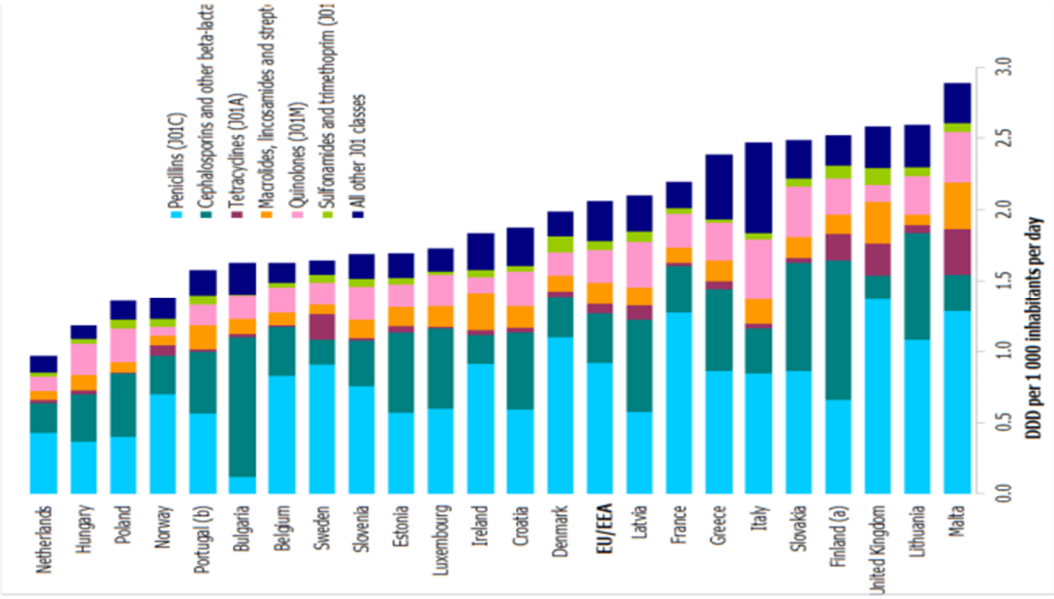


Fig 7: Consumption of antibacterials for systemic use (ATC group J01) in the hospital sector in EU/EEA countries at group level 3, expressed as DDD per 1 000 inhabitants per day (source: ECDC 2017)

## 1.4 Healthcare associated infections

Data about the prevalence of HAI is mainly available only for MDH, the sole tertiary care hospital that provides the bulk of hospital care in the country (>90%). Results from the 2011-2012 European Point Prevalence Survey (PPS), undertaken by ECDC, placed the prevalence of HAI in Maltese hospitals at the lower half of the European median (Fig 8); the actual prevalence was lower than what could be predicted from patient characteristics and case mix. In addition, significant improvement has been registered in the incidence of bloodstream infections in intensive care as well as several types of surgical site infections, especially those related to prosthetic hip and knee replacement surgery.

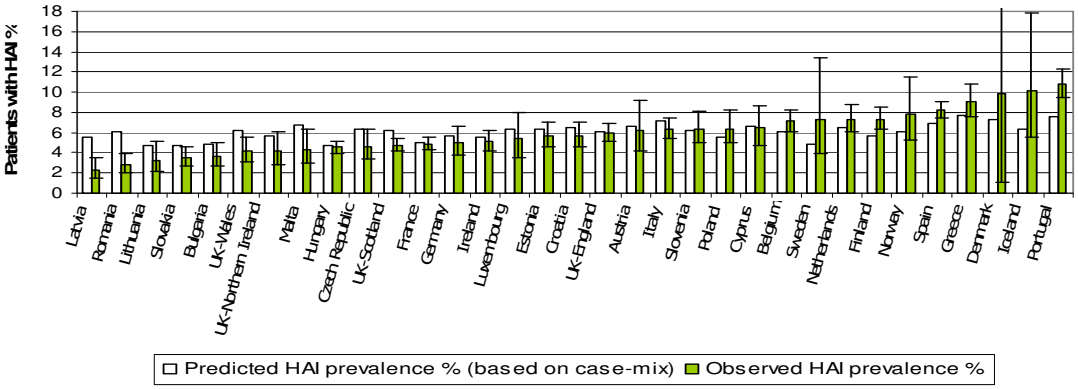


Fig 8: Observed HAI prevalence with 95% confidence intervals and predicted HAI prevalence based on case mix and hospital characteristics, by country (source: ECDC PPS 2011–2012)

# 2. Animal Health

## 2.1 AMR Epidemiology

Information on AMR in isolates of animal origin remains extremely sparse and restricted to a limited set of isolates tested annually at the National Veterinary Laboratory in compliance with Commission Implementing Decision 652/2013 (EU). In 2017 samples were collected from fattening pigs and analysed for Salmonella spp., Commensal Indicator Escherichia coli and for ESBL-, AmpC- or Carbapenemase producing Escherichia coli. 17 Salmonella spp. were isolated from 186 swine carcasses tested. 74 Escherichia coli isolates were cultured from 74 caecal samples collected at the slaughterhouse. 20 isolates of presumptive ESBL-, AmpC- and Carbapenemase- producing Escherichia coli were isolated from the initial 112 swine caecal samples tested. These isolates were then tested for antimicrobial resistance against a panel of antimicrobial substances as prescribed by Decision 652/2013.

| | **Salmonella Spp.** (*A total of 17 isolates tested*) | | **E-Coli** (*A total of 74 isolates tested*) | | **Presumptive ESBL-, AmpC- or Carbapenemase- producing E-coli** (*A total of 20 isolates tested*) | |
|---|---|---|---|---|---|---|
| **Antimicrobial substance** | **n** | **% Res** | **n** | **% Res** | **n** | **% Res** |
| Ampicillin | 3 | 17.7 | 13 | 17.6 | 20 | 100 |
| Cefotaxime | 0 | 0 | 0 | 0 | 20 | 100 |
| Ceftazidime | 0 | 0 | 0 | 0 | 19 | 95 |
| Meropenem | 0 | 0 | 0 | 0 | 0 | 0 |
| Nalidixic Acid | 0 | 0 | 4 | 5.4 | 7 | 35 |
| Ciprofloxacin | 0 | 0 | 8 | 10.8 | 17 | 85 |
| Tetracycline | 7 | 41.2 | 45 | 60.8 | 17 | 85 |
| Colistin | 0 | 0 | 1 | 1.4 | 0 | 0 |
| Gentamicin | 0 | 0 | 1 | 1.4 | 2 | 10 |
| Trimethoprim | 1 | 5.9 | 26 | 35.1 | 16 | 80 |
| Sulfamethoxazole | 12 | 70.6 | 40 | 54.1 | 17 | 85 |
| Chloramphenicol | 0 | 0 | 5 | 6.8 | 8 | 40 |
| Azithromycin | 0 | 0 | 0 | 0 | 0 | 0 |
| Tigecycline | 0 | 0 | 0 | 0 | 0 | 0 |

Table 1: The number of resistant isolates per antimicrobial substance collected from swine in 2017 n: number of resistant isolates

Isolates showing resistance to cefotaxime, ceftazidime or meropenem are then further submitted to extended susceptibility testing against another panel of antimicrobial substances as detailed. Following the results obtained against the first panel of antimicrobial substances, all ESBL-, AmpC- and Carbapenemase- producing Escherichia coli were further submitted to extended susceptibility testing.

Table 1 above and Fig 9 below detail the number of resistant isolates cultured from swine in 2017.

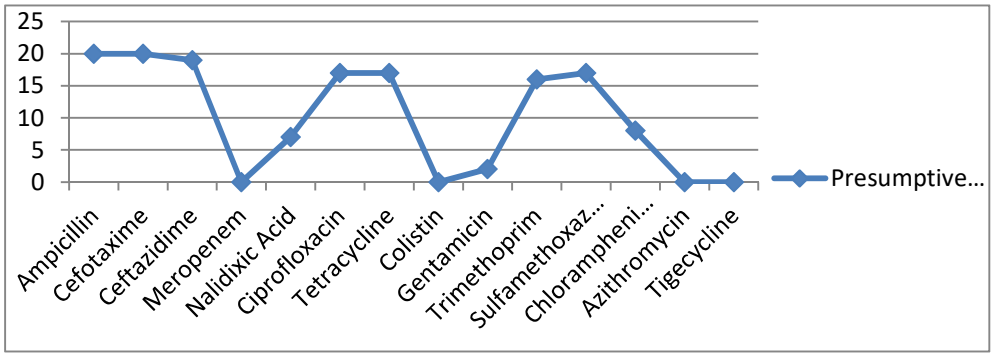


Fig 9: Number of resistant isolates of ESBL-, AmpC- and Carbapenemase- producing Escherichia coli per antimicrobial substance. Isolates cultured from caecal samples from swine during 2017

There are currently no laboratories in Malta that can provide a suitable service for performing routine diagnostic and susceptibility tests. As a result, samples must be sent to other countries for analysis but this is rarely done due to the costs, logistical issues (e.g. ensuring suitable conditions for sample transport) and time taken to receive the result.

Malta is not currently carrying out testing under Commission Implementing Decision 2015/495/EU 6 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring in the field of water policy pursuant to Directive 2008/105/EC of the European

Parliament and of the Council. No other activities are underway which could address environmental aspects of AMR.

## 2.2 Antibiotic consumption

Table 2 below provides 2017 Data on the Consumption of Antibiotics in the animal sector.

| Class | Tons | Kilograms |
|---|---|---|
| Penicillins | 0.3965746 | 396.5746 |
| First-generation cephalosporins | 0.0133516 | 13.3516 |
| Third-generation cephalosporins | 0.0035203 | 3.5203 |
| Tetracyclines | 0.191127 | 191.127 |
| Macrolides | 0.176398 | 176.398 |
| Fluoroquinolones | 0.279796 | 279.796 |
| Other quinolones | 0.015 | 15 |
| Amphenicols | 0.021081 | 21.081 |
| Trimethoprim and derivatives | 0.022585 | 22.585 |
| Pleuromutilins | 0.446814 | 446.814 |
| Lincosamides | 0.006943 | 6.943 |
| Polymyxins | 0.067294 | 67.294 |
| Streptomycins | 0.063938 | 63.938 |
| Nitrofuran derivatives | 0.004036 | 4.036 |
| Other aminoglycosides | 0.020232 | 20.232 |
| Imidazole derivatives | 0.006058 | 6.058 |
| Sulfonamides | 0.170072 | 170.072 |
| Other antibacterials | 0.269552 | 269.552 |
| | | |
| **Total** | **2.1743725** | **2174.3725** |

The data supplied above covers injections, oral paste, oral solutions, oral powder, tablets, capsules, intramammary, intrauterine and premixes. The data collected includes antibiotics used for the following species: Cattle, Pigs, Poultry, Sheep, Goat, Rabbits, Cats, Dogs Horse, Cage Birds and Racing Pigeons.

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## APPENDIX 2: CURRENT STRENGTHS AND DEFICITS IN ADDRESSING AMR IN MALTA

### 1 Legislation and infrastructure

Current strengths:

- Presence of an ICM in the form of the NAC.
- Impact of previous initiatives aimed at over-the-counter (OTC) and public awareness, albeit on a limited scale.

Current deficits:

- Absence of a budget inhibits effective planning of NAC initiatives.
- Limited consultation / involvement of professional associations/stakeholders expected to implement parts of the action plan.
- The personal capacity of NAC membership could result in limited involvement of professional associations and other stakeholders.
- Lack of appointed administrative support reduces the execution of NAC activities and functions, since the voluntary NAC members already have other major commitments.
- Lack of effective legislation, especially setting minimum IPC standards for hospitals and nursing homes.
- Absence of appropriate legislation in Animal Health that provides the necessary tools for effective intervention and regulation, especially in food animal husbandry.
- Ubiquitous definitions of prescription-only medicine for antibiotics which are neither used for treatment of humans nor used in animals and their food.
- Insufficient tools to ensure enforcement of 'prescription-only' dispensing of antimicrobials for veterinary use.

### 2. Antibiotic stewardship

Current strengths:

- A dedicated pool of specialists in antibiotic management.
- Strong antibiotic stewardship programmes (including guideline development) in hospital care, especially at MDH.

Current deficits:

- Evidence of inappropriate prescribing in the community for primarily viral infections such as colds, flu and sore throat.
- Unnecessary prescribing of broad spectrum formulations in ambulatory care, partly as a result of unavailability of older narrow spectrum antibiotics in private pharmacies.
- Excessive reliance on "last-resort" antibiotics at hospital level, especially carbapenems and glycopeptides.
- Major challenges in veterinary practice with anecdotal evidence of acquisition of antibiotics from unlicensed sources and direct medication of animals by farmers.

### 3. Surveillance

Current strengths:

- Extensive surveillance data on antimicrobial resistance in governmental hospitals.
- Robust antibiotic consumption data for MDH, the main hospital in the country.
- Audited IPC outcome and process indicators for MDH, including trends of incidence of multi-resistant organisms such as MRSA and CRE, and hand hygiene compliance, such as use of alcohol hand rub.

Current deficits:

- Surveillance of AMR in community infections and residential care is weak; available data invariably originates from samples taken from infections after lack of response to primary treatment, resulting in a bias towards resistance.
- Data on antibiotic consumption is restricted to global wholesaler statistics. The predominance of the private nature of general practice coupled with the lack of electronic prescribing and electronic dispensing records makes it impossible to identify and address doctors who prescribe significantly more antibiotics than their peers.
- Absence of e-prescribing systems in both community, hospital and veterinary settings makes it impossible to study consumption at patient and diagnosis level.
- There are major lacunae in veterinary practice, where information on AMR prevalence and antibiotic use is sub-optimal.
- Feedback of surveillance data to users, especially to community practitioners, is sub-optimal.

### 4. Infection Prevention and Control

Current strengths:

- Presence of dedicated Infection Prevention and Control (IPC) personnel in acute care and rehabilitation hospitals.
- Focal point of IPC expertise in MDH.
- Several success stories of improved processes and outcomes, especially at tertiary care.

Current deficits:

- Considerable heterogeneity in IPC activities among acute care and rehabilitation hospitals.
- Lack of national standardisation, coordination and oversight.
- Sub-optimal ownership and accountability structures to support implementation.

### 5. Training, Continuous Professional Development and Education

Current strengths:

- Coverage of IPC and antibiotic stewardship in some undergraduate courses.
- Past NAC experience in organising activities for European Antibiotic Awareness Day.
- Successful interventions to reduce over-the-counter acquisition of antibiotics.

Current deficits:

- Low level of knowledge about antibiotics among the public.
- Lack of appointed administrative support reduces the execution of NAC activities.
- Inadequate inclusion of AMR in post graduate training.

### 6. Research and Performance Measurement

Current strengths:

- Interest in under and postgraduate students to undertake dissertations and audits on AMR related topics.
- Experienced and enthusiastic researchers, willing to dedicate time over and above clinical duties.

Current deficits:

- Economies of scale make large research projects difficult.
- Budgetary constraints even for smaller research projects.
- Lack of infrastructure and paucity of dedicated research personnel for AMR research.

### 7. International partnerships and collaboration

Current strengths:

- Participation in EU networks has provided opportunities to network with peers and to learn from successful experiences in other countries.

Current deficits:

- Lack of focused initiatives with countries in the Mediterranean region who share many of the infrastructural, cultural and logistical challenges that are key factors in driving AMR locally.