



THE UNIVERSITY OF
MELBOURNE

Policy Brief

Antimicrobial Regulation and Policy en Timor-Leste

Dr Alipio Gusmao Lopes

June 2023



1. Goal Statement

The goal is to have better policy and regulation to control antimicrobials (AM) through advocacy with the Ministry of Health and increasing the evidence base to inform future policy makers.

In partnership with:

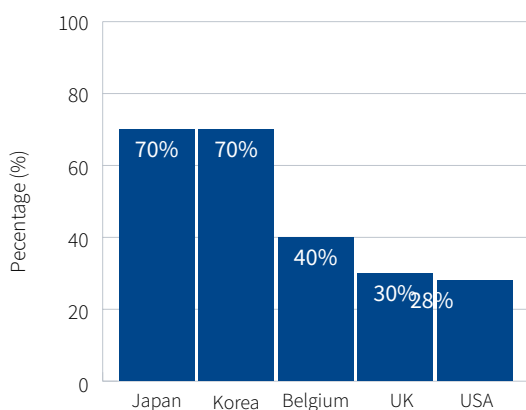


2. Scope of the Problem

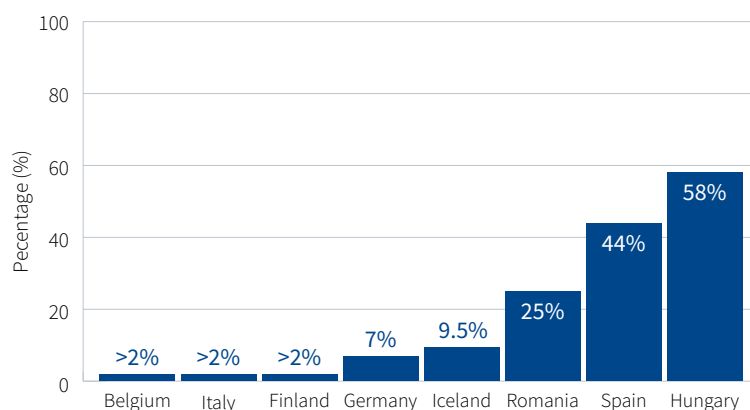
The World Health Organization has declared that antimicrobial resistance (AMR) is one of the top 10 global public health threats facing humanity⁽¹⁾. Resistance rates for many isolates are rising but are highly variable. For example, the proportion of isolates of *Staphylococcus aureus* resistant to methicillin increased from close to zero 10–15 years ago to approximately 70% in Japan and the Republic of Korea, 40% in Belgium, 30% in the United Kingdom, and 28% in the USA by 1998⁽²⁾. Recent rates of resistance in *Streptococcus pneumoniae* were less than 2% in Belgium, Italy, and Finland, but 7% in Germany, 9.5% in Iceland, 25% in Romania, 44% in Spain and 58% in Hungary⁽³⁾. Resistance to antimicrobial therapies reduces the effectiveness of these drugs, leading to increased morbidity, mortality, and health care expenditure⁽⁴⁾. The rate of development of AMR is accelerated by the use and misuse of antimicrobials⁽⁵⁾. Globally, the demand for antibiotics consumption is increasing in health care, as is evident in the 65% increase in global consumption from 21.1 billion to 34.8 billion daily doses from 2000 to 2015.

Timor-Leste should contribute to the global effort to combat AMR because it has direct and indirect impacts on development. For example, patients who do not recover when treated with an antimicrobial due to resistance will spend more time in hospital, resulting in additional treatments with higher costs. This leads to spending more money that then cannot be allocated to other healthcare needs, infrastructure development and other sectors. AMR is a rising problem for many health systems in Low-Middle Income Countries, including in Timor-Leste, given greater attention from the Ministry of Health on combating diseases like tuberculosis, dengue, malaria, and reducing maternal and child mortality rate, malnutrition and other illnesses⁽⁵⁾.

Isolates of *Staphylococcus aureus* resistant to methicillin⁽²⁾



Recent rates of resistance in *Streptococcus pneumoniae*⁽³⁾



3. Antimicrobial Resistance, Consumption and Use in Timor-Leste

There is limited available data on AMR in Timor-Leste. Resistance to third-generation cephalosporins was reported in 2% of *Escherichia coli* isolates, methicillin resistance in 25% of *S. aureus* isolates and resistance, or non-susceptibility, to penicillin in 4% of *Streptococcus pneumoniae* isolates⁽⁶⁾. This poor and contrasting evidence would suggest a lower prevalence of antibiotic resistance in Timor-Leste compared with other countries in the region⁽⁷⁾. However, the very limited amount of data collected with different sampling methods does not allow any meaningful conclusions. A recent study has shown high rates of resistance in Gram-negative isolates from urine samples, suggesting that antibiotic resistance may be more widespread. Marr et al stated that in Timor-Leste a total of 154 urine isolates and 57 skin isolates were analyzed. Of the *Enterobacteriaceae*, 35% were resistant to ceftriaxone with an extended-spectrum β -lactamase (ESBL)-producing phenotype. Carbapenem resistance was not observed in any of the Gram-negative isolates. Of the *S. aureus* isolates, 11% were of the community-associated methicillin-resistant *S. aureus* (CA-MRSA) phenotype⁽⁸⁾.

Timor-Leste has an estimated total consumption rate of 28.44 Dose Inhabitants per Day (DID)/1000 inhabitants/day. Data from National Hospital Guido Valadares indicated that only 42.9% of prescriptions from medical doctors were compliant with guidelines, 35.7 % were non-compliant and 21.4 % were not accessible. In addition, appropriate use of AM was 60.7%, inappropriate use of AM was 35.7% and 3.6% was not accessible⁽⁹⁾.



4. Policy on Importation and Regulation of Antimicrobials in Timor-Leste

Regulation and policy is vital to ensure the implementation of activities to control AMR in Timor-Leste, because in Timor-Leste it is easy to access antimicrobials even in small shops. There are some regulations, and policy has been in place related to AMR as part of Timor-Leste's contribution to the global efforts in combating AMR through the development of National Action Plans. Timor-Leste has had two National Action Plans (2017-2020 and 2022-2027), but their implementation has been constrained by policy and regulation. Specific challenges include the importation of antimicrobials, licensing, supply, monitoring and evaluation.

The use of drugs of low potency and effectiveness has resulted from poor manufacturing or counterfeiting. Substandard medicines have been identified in Timor-Leste, some of them changing colors, structure and composition. In 2021 there was cooperation with the Therapeutic Goods Administration (TGA) of Australia to test Amoxicillin tablets. The TGA found that only half of tablets tested were Amoxicillin. This also negatively affects the conditions of patients treated with these medicines. In addition, inappropriate use by professionals also contributes to microbial modification and difficult to treat infections, leading to morbidity and mortality. In the case of increased resistance, the government needs to allocate more resources to obtaining new antimicrobials, resulting in affected development of the country due to budgetary restraints for development.

Importation of antimicrobials for use in human health in Timor-Leste is divided into two components: firstly, importation for public health systems and secondly, importation for private clinics. For the public health system, procurement is undertaken by wholesaler Serviço Autónomo de Medicamentos e Equipamentos de Saúde (SAMES) (in English Autonomous Service of Medicines and Health Equipment) through tenderization. In the private system, procurement depends on the licensing list of medicines that the private clinic has. They can import for three years before renewing the licensing process.

In article 3, of the Decree Law number 12/2004 Pharmaceutical Activities, the section on Licensing states that activities of import, storage, sales in bulk, sales in retail, and export of medicines for human use may only be exercised by entities duly registered in accordance with the applicable law for registration of businesses and duly licensed by the Regulating Commission of Pharmaceutical Activities. However, SAMES has not yet registered to obtain a license from the Ministry of Health (National Directorate of pharmacy and Medicines as Regulating Commission of Pharmaceutical Activities) to import the medicines.

There are no wholesaler systems in place for importation of antimicrobials in animal health, and in the public sector, imported medicines are based on needs identified by the Ministry of Agriculture and Fisheries (MAF). Sometimes veterinarians buy (and prescribe) antibiotics for human use, which is illegal, based on Decree Law number 12/2004 Pharmaceutical Activities, as stated in article 13, which indicates that prescriptions shall be signed by the prescriber and contain the following details:

a) Name and address of the prescriber and respective number of registration with the Ministry of Health.

Supplies, medicines and antimicrobials for public health systems are supplied by SAMES to all health facilities, and prescriptions from health professionals are mandatory. Timor-Leste is lacking data on comprehensive population-based surveillance of antimicrobial resistance; the challenges are high due to weak laboratory capacity, poor health systems governance, lack of health information systems, and limited resources. Currently Timor-Leste does not have any regulation in place to control antimicrobials use in private and public sector.

5. Past Policy

As a member state of WHO, each country should have National Action Plans for antimicrobial resistance. Timor-Leste had the first version of the National Action Plan (NAP) for AMR for 2015-2020 and the new version of the NAP (2020-2025) has been approved. National Action Plan version 2015-2020 had very general statements and did not assign specific responsibilities to relevant ministries: Ministry of Health, Ministry of Agriculture and Fisheries, Secretary Estate of Environmental and Ministry of Education. However, the new version (2020-2025) is more specific and defines clear roles in the implementation of activities to the relevant ministries.



6. Current Policy

In 2021, we engaged all stakeholders to revise the first edition of the NAP. The World Health Organization contributed by hiring technical experts to support writing the document. A number of workshops have been delivered to finalize the document with Ministry of Agriculture and Fisheries, Estate of Environment, international agencies and other relevant stakeholders. The document was approved by the respective ministries in 2022. From the critical review, we found that all activities mentioned in the NAPs should be implemented. The activities are as follows:

1. Ministry of Health and Ministry of Agriculture and Fisheries should control AMU to all private clinics and farmers with the development of regulations and policy.
2. Engage the Ministries of Education to include information about AMR as part of the curriculum of education for school children in Timor-Leste.
3. The Ministry of Education should provide basic information on how to prevent AMR in Timor-Leste through inclusion in education curricula.
4. Continue with AMR stewardship activities for all health facilities.
5. The Estate of Environmental must provide the same information to respective areas to control and prevent AMR.
6. The Ministry of Health and Ministry of Agriculture and Fisheries should have regulation and policy in place to control AM in the private sector.
7. Activities in the National Action Plan should be adopted by the Ministry of Health, Ministry of Agriculture and Fisheries, Ministry of Education and Estate of Environmental to be regular activities and should be allocated budgets for AMR.
8. Continuously support and develop rational use of antimicrobials.



7. Recommendations

7.1. Regulation:

7.1.1. Licensing and regulation of providers in order to ensure antibiotics are only prescribed to those who need them

- In Timor-Leste, the company should have licensing for importation, and have to register at Public Business and Trade Institute (in Tetum, Servisu Rejistrasaun no Verifikasaun Emprezarial, SERVE. IP) then register to Ministry of Health and Ministry of Agriculture and Fisheries for Pharmaceutical Products especially for AM. Some companies currently import illegally—the regulation needs to be enforced.
- Sufficient human resources should be allocated to control importation in border areas.
- Pharmacists should be placed in border areas to control all the medicines that enter through border areas.
- Register all items and supply samples to the Ministry of Health with all the documents including certificates for analysis (CoA), Good Manufacture Product (GMP) etc.
- SAMES is not currently registering imported medicines; SAMES should also be required to register with the Ministry of Health, specifically to the National Directorate for Pharmacy and Medicines as Regulating Commission of Pharmaceutical Activities.
- Decree Law number 12/2004 Pharmaceutical Activities should be modified and harmonized with current regulation relating to SAMES and importation.
- Legislation should be established to require the following information to be provided:
 - Certificate of analysis
 - Manufacturing certificate
 - Amounts/quantity of medication
- SAMES should be required to provide information about medications imported from other countries.

- Providers in the private and public sectors to be regulated by Ministry of Health, Public Business and Trade Institute:
 - » Have an office in Timor-Leste to do pharmaceutical activities
 - » Appropriate storage conditions, including temperature
 - » Appropriate HR—pharmacist on staff to ensure appropriate prescribing
 - » License from Public Business and Trade Institute
 - » Inform Ministry of Health of the proposed activities
 - » MoH issues a certificate of approval for proposed activities
 - » License is then issued
 - » To import medicines, letter to be provided to Ministry of Health with all the documentation:
 - What medicine,
 - Where produced, and
 - Appropriate certificates

7.1.2. Procurement of antimicrobials should be regulated to ensure that those who need these drugs receive the appropriate treatment

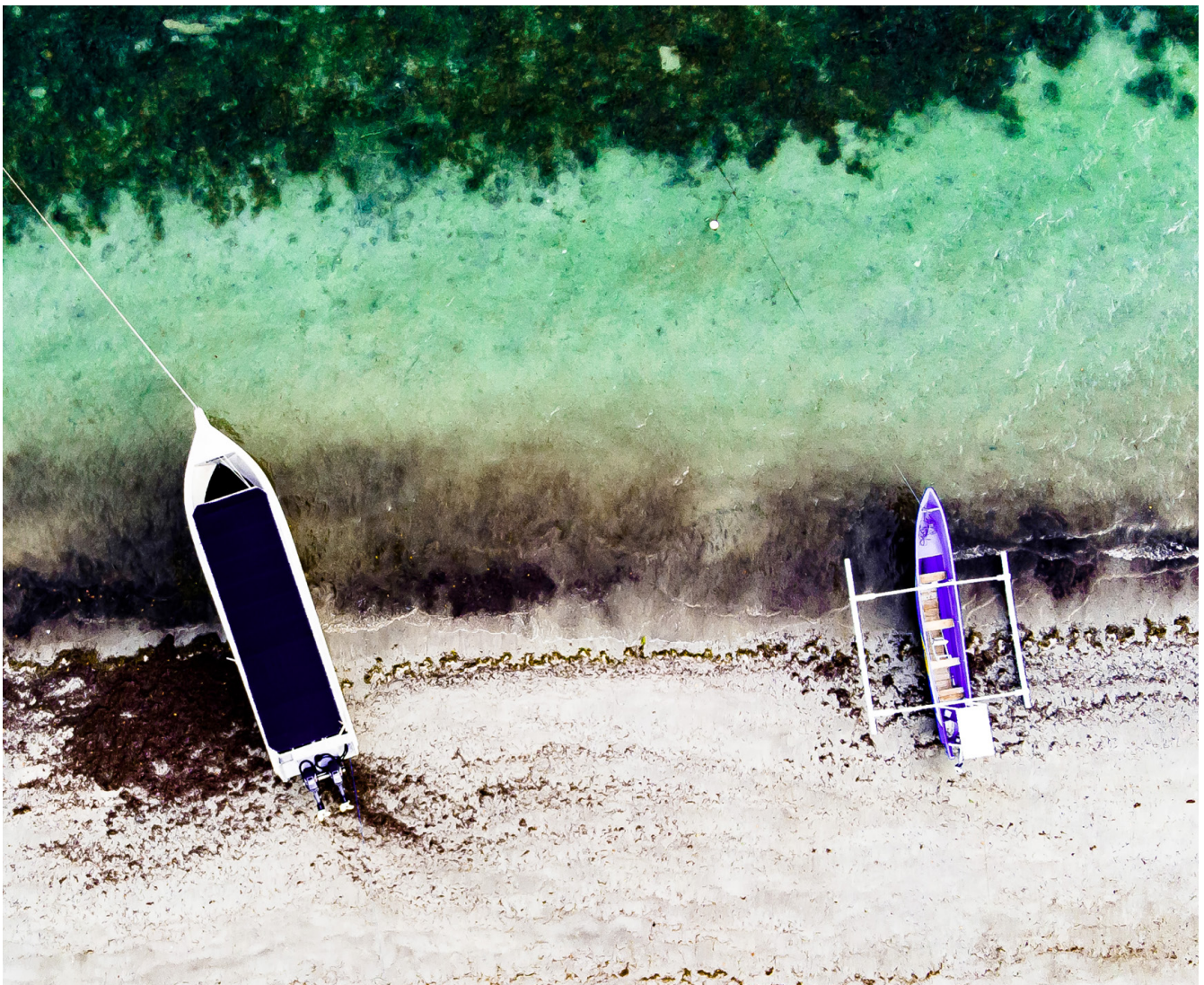
The Ministry of Health should strengthen current regulation, to increase transparency of all procurement processes, should consistent with the list of quantifications, if there are any changes to the list of quantification of pharmaceutical products within procurement, the Ministry of Health (Directorate for Pharmacy and Medicines) should be informed.

7.1.3. Legislation regarding the supply of antimicrobials

- The current legislation, for example Decree Law number 12/2004, is insufficient because there is no regulation for specific prescribing of antimicrobials.
- Ministry of Health should strengthen the current system and revise Decree Law number 12/2004 to provide more details regarding regulation of antimicrobials for supply and distribution.

8. Key Organizations/Individuals

- **Ministry of Health** has the role of revising Decree Law number 12/2004 to include all needs related to antimicrobial resistance and allocate resources to NAP activities.
- **Ministry of Agriculture and Fisheries** has a role to regulate all private companies that import medicines, including AM
- **Fleming Fund** has a role to continue supporting training or other non-financial support relating to AMR
- **WHO** has a role to finance the activities with the government of Timor-Leste
- **OIE** has a role to support programs that have been written in the Timor-Leste NAP AMR
- **Menzies School of Health Research** has a role to support programs that have been written in the Timor-Leste NAP AMR
- **FAO** has a role to support programs that have been written in the Timor-Leste NAP AMR
- **The University of Melbourne** has a role to support programs that have been written in the Timor-Leste NAP AMR



References

1. UN Department of Economic and Social Affairs. The UN Sustainable Development Goals: The 17 goals [Available from: <https://sdgs.un.org/goals>].
2. Appelbaum PC. Antimicrobial resistance in *Streptococcus pneumoniae*: an overview. *Clin Infect Dis*. 1992;15⁽¹⁾:77-83.
3. Coast J, Smith RD, Millar MR. Superbugs: should antimicrobial resistance be included as a cost in economic evaluation? *Health Econ*. 1996;5⁽³⁾:217-26.
4. World Health Organization. Anti-Infective Drug Resistance S, Containment T. WHO global strategy for containment of antimicrobial resistance. Geneva: World Health Organization; 2001.
5. The Review on Antimicrobial Resistance Chaired by Jim O'Neill. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations. 2014.
6. The path of least resistance : main report / Standing Medical Advisory Committee Sub-Group on Antimicrobial Resistance. Wetherby: [Department of Health]; 1998.
7. Browne AJ, Chipeta MG, Haines-Woodhouse G, Kumaran EPA, Hamadani BHK, Zarea S, et al. Global antibiotic consumption and usage in humans, 2000–18: a spatial modelling study. *The Lancet Planetary Health*. 2021;5(12):e893-e904.
8. Marr I, Sarmiento N, O'Brien M, Lee K, Gusmao C, de Castro G, et al. Antimicrobial resistance in urine and skin isolates in Timor-Leste. *J Glob Antimicrob Resist*. 2018;13:135-8.
9. Tebano G, la Martire G, Sarmiento N, Francis JR. Antibiotic resistance in Timor-Leste: a systematic review of evidence. *Journal of Antimicrobial Chemotherapy*. 2018;73⁽⁴⁾:1110-1.
10. Agata Esperito Santo presentation on Closing Workshop Presentations Timor Leste Cohort 1 Fellows AMU/C Surveillance Fellowship Human Health – NHGV (2022)