Antimicrobial policy interventions in food animal production in South East Asia

Flavie Goutard and colleagues call for concerted multisectoral measures through stronger policies to combat antimicrobial resistance

Antibiotics and other antimicrobial agents are widely used in food animal production for disease prevention and treatment in animals, to contain disease spread, to prevent contamination of the food chain, and to increase productivity.1 However, their wide use in humans and animals leads to the emergence of antimicrobial resistance, a general term that encompasses antibiotic resistance.2 In September 2016, the United Nations recognised the global rise of antimicrobial resistance as a threat to health and human development.3

Antimicrobial resistance will increase infectious disease outbreaks, slowing down livestock productivity and disrupting international trade. Recent projections estimated that by 2050 global livestock production would fall by 3% to 8% each year, resulting in the decline in the annual global gross domestic product of 1.1%-3.8%. Because of higher disease incidence, these falls will affect low income countries more severely, with a predicted rise of 6.2 to 18.7 million in the number of extremely poor people by 2030.4 The UN has called for a limit on the overuse of antimicrobial agents, including in animals, but an evaluation of the national animal health systems of about 130 countries, performed by the World Organisation for Animal Health (OIE) using its performance veterinary services pathway tool, showed that more than 110 of them do not yet have appropriate legislation to regulate the import, manufacture, distribution, and use of antimicrobial agents. Even where legislation does exist and is enforced, antibiotics continue to be freely circulated as common goods, and in many countries they are often counterfeited.5

Several countries in the region produce meat and aquaculture products for the global market.6 The World Health Organization South East Asia region (SEAR: Bangladesh, Bhutan, Democratic People’s Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka, Thailand, Timor-Leste) has developed intensive farming systems, leading to the rising consumption of fertilisers, antibiotics, and pesticides, of which many farmers have limited technical knowledge. The lack or weakness of regulations, adequate policies, and implementation of standards for antibiotic use in the food animal sector, together with low standards of biosecurity, hygiene, and sanitation, have accelerated the emergence and dissemination of antibiotic resistance.7

We have determined the challenges and requirements for policy interventions to combat antimicrobial resistance in food animal production in each of the SEAR countries, with a focus on antibiotic production and marketing, use, and monitoring of resistance.8 9

Methods
We reviewed several databases (PubMed, Science Direct, MEDLINE, LISTA, Web of Sciences, Scopus, and Google Scholar) to search for official documents, in English or French, published after 2010. We consulted the legislative and policy database (FAOLEX: http://faolex.fao.org/) of the Food and Agriculture Organization of the United Nations (FAO) and made contact with the FAO and OIE national focal points for veterinary products. We retrieved documents from eight countries, including 16 legal documents and 11 policies, related strategies, and action plans (table 1). For each document we extracted information on the topic (drug and medicine production and marketing, drug and medicine use, antibiotic resistance surveillance and monitoring); the competent authority in charge; the type of document (policy or legal document); the objective(s); the key components and limitations. These results were cross checked with additional information on policy implementation and law enforcement found in other non-official documents.29-31 Specific recommendations are based on the reference guides published by WHO, OIE, and FAO.8-11

Food animal sector: trends and challenges of antibiotic use
Over recent decades, profound changes in food production and feeding regimens have had a major effect on the use of antibiotics in livestock and aquaculture farms. Most SEAR countries have experienced considerable growth in population, combined with improved living standards for part of the population. In India, the national diet has radically changed, with increased meat consumption among the young urban generation.12 This growing demand for animal proteins has resulted in intensive breeding of pigs, poultry, and fish, with the routine use of antibiotics as growth promoters. Meanwhile, these countries still face high levels of infectious disease, with a lack of health advice and guidance in veterinary care. This, together with weak regulations surrounding the sale of antibiotics and surveillance, has led to the emergence, maintenance, and spread of antibiotic resistance.3

Policy related best practices and global challenges for their implementation

The region is recognising that antimicrobial resistance issues are critical and has moved to develop sound and comprehensive policies to tackle the problem. These policies are often in line with international standards (Codex, see box 1; OIE, see table 2) and trade partner requirements. However, the regulatory framework is often outdated and does not allow governments to implement and monitor the course of action defined in their policies. Furthermore, some of the objectives of these policies remain elusive and are clearly unattainable in the socioeconomic context.
All SEAR countries have sound legal requirements that establish a framework for the quality of drugs used in food animals (table 3). However, official documents do not specifically target antibiotic production and marketing, and requirements for manufacturing and licensing are poorly described. Good manufacturing practices, as well as quality assurance and control, are compulsory in several countries, although only Thailand seems fully able to carry out official checks at every level of the manufacture and distribution of veterinary medicines. Finally, the circulation of counterfeit and substandard antibiotics is poorly dealt with; control legislation (inspections) should not target solely farmers but should include each level of the drug marketing chain.

**Antibiotic production and marketing**

All SEAR countries have sound legal requirements that establish a framework for the quality of drugs used in food animals (table 3). However, official documents do not specifically target antibiotic production and marketing, and requirements for manufacturing and licensing are poorly described. Good manufacturing practices, as well as quality assurance and control, are compulsory in several countries, although only Thailand seems fully able to carry out official checks at every level of the manufacture and distribution of veterinary medicines. Finally, the circulation of counterfeit and substandard antibiotics is poorly dealt with; control legislation (inspections) should not target solely farmers but should include each level of the drug marketing chain.

**Antibiotic use**

Regulations on antibiotics in animal feed (for growth promotion or therapeutic use) and the promotion of rational antibiotic use in healthcare and veterinary settings.

### Table 1: List of official documents dealing with antibiotics (except antimicrobial residue surveillance and control) in the food animal production system from SEAR retrieved from the literature review between 2010 and 2016

| Document title | Year | Type | Development/monitoring | Use | Monitoring |
|----------------|------|------|-------------------------|-----|------------|
| National drug policy | 2005 | P | YES | - | - |
| Fish feed and animal feed act | 2010 | L | - | Yes | - |
| National livestock development policy | 2007 | P | - | Yes | - |
| National strategy for antimicrobial resistance containment (ARC) | 2011 | P | - | Yes | Yes |
| Road map of national action plan for ARC | - | P | - | Yes | Yes |
| The drug (control) ordinance | 1982 | L | Yes | - | - |
| Bhutan | | | | | |
| Medicines rules and regulations | 2012 | L | Yes | - | - |
| National action plan on antimicrobial resistance (draft) | 2015 | P | - | Yes | Yes |
| National antimicrobial policy (draft) | 2015 | P | - | Yes | Yes |
| India | | | | | |
| Advisory on use of antibiotics in poultry producing animals | 2014 | P | - | Yes | - |
| Drugs and Cosmetics Act | 1945 | L | Yes | - | - |
| Bureau of Indian Standards, poultry feed specification, 5th revision 1374-2007 | 2007 | P | - | Yes | - |
| Food safety and standards (contaminants, toxins, residues) regulations | 2011 | L | - | Yes | - |
| National livestock policy | 2013 | P | - | Yes | - |
| National policy for containment of antimicrobial resistance | 2011 | P | Yes | - | - |
| Indonesia | | | | | |
| Law No 18 on husbandry and animal health | 2009 | L | - | Yes | - |
| Manual for prime method of animal drugs manufacturing | 1999 | P | Yes | - | - |
| Regulation of the head of the agency of drug and food control no 27 | 2013 | L | Yes | - | - |
| Regulation of the head of the agency of drug and food control no 28 | 2013 | L | Yes | - | - |
| Regulation of the minister of marine affairs and fishery on fish medication | 2012 | L | Yes | - | - |
| Terms and procedures for the issuance of animal medicine business permit | 2009 | L | Yes | - | - |
| Myanmar | | | | | |
| Fisheries law directive 996 on general product standard | 1996 | L | - | Yes | - |
| Nepal | | | | | |
| Drug act | 1978 | L | Yes | - | - |
| Drug registration rules | 1981 | L | Yes | - | - |
| National drug policy | 1995 | P | Yes | - | - |
| Sri Lanka | | | | | |
| Animal Diseases Act No 59 | 1992 | L | Yes | - | - |
| Thailand | | | | | |
| Code of practice for control of the use of veterinary drugs | 2009 | L | Yes | - | - |
| Drug ACT B.E. 2510 (B.C. 1967) and its amendment | 2001 | L | Yes | - | - |

No documents were retrieved for Timor-Leste, Korea, and Maldives. L = legislation; P = policies.

**Box 1: Codex texts on foodborne antimicrobial resistance related best practices for resistance containment in food animal sectors—Codex Alimentarius Commission**

**Guidelines for risk analysis of foodborne antimicrobial resistance (CAC/GL 77-2011, adopted 2011)**

These guidelines aim to

- Provide science-based guidance on processes and methodology for risk analysis and its application to foodborne AMR (antimicrobial resistance) related to non-human use of antimicrobial agents
- Assess the risk to human health associated with the presence in food and animal feed, including aquaculture, and the transmission through food and animal feed, of AMR microorganisms and determinants, to provide advice on appropriate risk management activities to reduce such risk
- Address the risk associated with different sectors of antimicrobial agent use such as veterinary applications, plant protection or food processing

**Code of practice to minimise and contain antimicrobial resistance (CAC/RCP 61-2005, adopted 2005)**

This code provides recommendations to regulatory authorities and operators involved in the authorisation, manufacture, sale and supply, prescription, and use of antimicrobials in food producing people, in order to prevent or reduce the selection of antimicrobial resistant microorganisms in humans and animals.

These two texts, together with specific standards of importance to animal production, have supported the development of the Global Action Plan on Antimicrobial Resistance (adopted in May 2015), developed by WHO in collaboration with FAO and OIE.
are clearly emerging as priorities for the region. Many countries have already developed policies to ban all use of antibiotics as growth promoters or feed additives, but few yet have the capacity to ensure their implementation (table 4). Policy interventions focus on good practices among health professionals and users, prescriber awareness, and disease prevention and diagnostics, while research on alternatives is overlooked.

**Surveillance of antibiotic resistance and monitoring of use**

While recognised as essential in providing the necessary data to fight effectively against antibiotic resistance, surveillance in the food animal sector is at a preliminary stage of development in the region (table 5). Most of the updated documents for surveillance of antibiotic use and antibiotic resistance concentrate only on humans, without considering the animal health sector. Ideally, policies should drive the development of surveillance of the use of antibiotics for terrestrial and aquatic animal health (and plant health), on resistance in clinical isolates from diseased animals, and in commensal and zoonotic bacteria hosted by food producing animals.

**Priority actions for best practice policies at regional level**

At the time of writing, all but one country in the region has developed and finalised a national action plan for the containment of antimicrobial resistance in line with the global action plan endorsed by the World Health Assembly in 2015. Currently, only two countries have had their national action plan endorsed by the highest level of the government. Here, we outline priority actions for regions to design and implement.

**Coordinated regional collaboration for better food and health security**

Priority should be placed on strengthening the regional One Health tripartite partnership (FAO, OIE, and WHO), establishing an antimicrobial resistance regional secretariat to focus on changes in policy and practices expected at country level. Its main contribution would be to provide a mechanism that facilitates and empowers multisectoral collaboration to combat antibiotic resistance in food animal production. A synergistic approach through a joint regional action plan and continuous communication between regional partners would have a trickle-down effect on SEAR nations. Joint understanding of risks, activities, and recommendations issued by the regional tripartite partnership would drive the organisations’ country offices and their respective national counterparts to communicate, exchange, and collaborate.

A regional secretariat could organise the joint monitoring of progress towards implementation of a national action plan, promote best practices on policies, and provide evidence to deal with country specific barriers and challenges concerning policy enforcement. Actions would enable emphasis to be placed on best practices within policies, with the rules and

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**Table 2 | OIE standards and guidelines related to antimicrobial agents and veterinary public health**

| Chapter | Guideline | Version |
|---------|-----------|---------|
| Terrestrial Animal Health Code | Harmonisation of national antimicrobial resistance surveillance and monitoring programmes | Revision adopted in 2012 |
| Chapter 6.7 | Monitoring of the quantities and usage patterns of antimicrobial agents used in food producing animals | Revision adopted in 2012 |
| Chapter 6.9 | Mandatory authorisation for business operators | Revision adopted in 2012 |
| Chapter 6.10 | Risk analysis for antimicrobial resistance arising from the use of antimicrobials in animals | Revision adopted in 2014 |

**Table 3 | Country specific analysis of policies, legislation, and regulation for antibiotic production and marketing**

| Topic | Main findings/objectives | Gaps identified | Country specific features |
|-------|--------------------------|-----------------|--------------------------|
| General | Existence of official documents framing antimicrobial production and marketing in 7 countries (4 policy documents and 11 legal instruments) joint documents for human and veterinary sectors, issued by the public health authorities | Antibiotic management poorly addressed as a specific issue Legislation outdated regarding the emerging issue of antibiotic resistance Inadequacy between policy interventions and available legal instruments Drugs management mainly addressed in human sector | India: specific document dealing with antibiotic management (human drugs) Indonesia, Thailand: specific documents for veterinary drugs Licensing requirements more or less strict depending on the country |
| Drug commercialisation | Mandatory registration and authorisation Administrative and quality requirements for authorisation, Authorisation cancellation or suspension conditions, Active list for illegal substances | Licensing criteria and procedure poorly described | Nepal, Bangladesh: science based assessment of drugs before introduction to market |
| Drug production and manufacture | Compulsory registration for companies, mandatory implementation and compliance with good manufacturing practice, quality assurance and control | Official control measures carried out by competent authorities not commonly addressed | Bhutan, Bangladesh, India, Thailand: provisions for inspections of manufacturers |
| Drug distribution, sale, and storage | Mandatory authorisation for business operators Mandatory compliance with quality and ethical requirements Quality assessment, licensing of veterinary drugs Specific requirement for importation and exportation Assessment of veterinary drug quality before being put on the market | Official control measures carried out by competent authorities not commonly addressed | Bhutan, Bangladesh, India, Thailand: provisions for inspections of sellers |
Moreover, in a region such as SEAR, one Health approach has been used for some policy decisions (table 4, table 5). For example, documents covering drug production and marketing are often common to human and veterinary sectors, and several countries are developing their national action plans by including multiple sectors.

Increase antibiotic resistance surveillance and monitoring of use
Surveillance that generates reliable data is essential for sound global strategies and public health actions to contain antibiotic resistance and is urgently needed to improve policy development in SEAR. Veterinary services are trying to stretch their resources and capacities beyond the ongoing surveillance of transboundary animal diseases to include antibiotic resistance surveillance, which requires a main active form of surveillance. There are various approaches to surveillance: drug resistance of pathogenic or commensal bacteria, antibiotic use for disease treatment, and non-therapeutic use. Understanding what each approach entails will allow the countries to prioritise and eventually help shape policies.

One priority action for the region should be to set up an integrated surveillance system for drug resistant pathogens, together with a harmonised monitoring system of antibiotic use. The standardisation of data sharing and data collection methods and antibiotic resistance testing, between sectors and countries, should enable each government to implement early effective control measures and to monitor the effectiveness of their policies.

Sharing standards for antibiotic use in animal food production
Since the introduction of the global action plan on antimicrobial resistance, there has been an international agreement to ban antibiotics as growth promoters in the absence of risk analysis. Several SEAR countries have already banned antibiotic additives in feed. However, food safety standards used for export products are often higher than those for products intended only for local consumption.

Table 4 | Country specific analysis of policies, legislation, and regulation for antibiotic use

| Topic | Main findings/objectives | Gaps identified | Country specific features |
|-------|--------------------------|----------------|-------------------------|
| General | Existence of official documents framing AMR in 2 countries (4 policy documents) | Inadequacy between policy interventions and available legal instruments | India, Nepal, Bhutan: national roadmaps to ban non-therapeutic use of antibiotics in feed but no regulatory framework for implementation |
| | Development of surveillance protocol | Disproportionate national policy objectives regarding the local socioeconomic context | Indonesia, Thailand: Code of practices for control of veterinary drugs use (in line with Codex) |
| | Development of national strains repository | Policy interventions focusing on good practices, users and prescribers’ awareness, disease prevention and spread | Bangladesh, Bhutan, India, Thailand, and Nepal: intersectoral policies to contain AMR |
| | Prevention of AMR | Lack of official controls to ensure law enforcement | India: regulation for judicious use by veterinarians, but no provisions for implementation and monitoring |
| | Promotion of AST before prescription | Antibiotics still used as growth promoters or in animal feed for therapeutic use | Sri Lanka, Maldives: ban of all antibiotics as growth promoters and in medicated feed |
| | Licensing of veterinary pharmacists | Policy interventions focusing on good practices, users and prescribers’ awareness, disease prevention and spread | Thailand: ban of all antibiotics as growth promoters, total prohibition of medicated feed in aquaculture, regular official controls on use |
| | Education of awareness of sellers and users | Policy interventions focusing on good practices, users and prescribers’ awareness, disease prevention and spread | Bangladesh: ban on antibiotics in feed additive |

Table 5 | Country specific analysis of policies, legislation, and regulation for antibiotic resistance surveillance and monitoring of antimicrobial use

| Topic | Main findings | Gaps identified | Country specific features |
|-------|--------------|----------------|-------------------------|
| General | Existence of official documents framing AMR or antimicrobial use in veterinary sectors (3 policy documents and 7 legal instruments) | Topic poorly addressed in official documents | Bangladesh: development of a national strategy to contain AMR, including monitoring of resistance and use |
| | Development of documents in line with international standards (OIE, European regulation) | No legal framework to implement the monitoring objectives when they exist | India: monitoring of AMR in food animals not yet part of the national policy on AMR containment |
| | Monitoring and evaluation of impact of promotion on consumption, Data dissemination to users and prescribers | Lack of cross-sectoral approach in the updated documents | Thailand: project developing a policy for monitoring use |
| | Monitoring and evaluation of impact of promotion on consumption, Data dissemination to users and prescribers | Lack of cross-sectoral approach in the updated documents | India: monitoring of AMR in food animals not yet part of the national policy on AMR containment |
| | Appropriate laboratory capabilities and networking | Topic poorly addressed in official documents | Bangladesh: development of a national strategy to contain AMR, including monitoring of resistance and use |
| | Development of surveillance protocol | No legal framework to implement the monitoring objectives when they exist | India: monitoring of AMR in food animals not yet part of the national policy on AMR containment |
| | Harmonised AST results reporting system | Lack of official controls to ensure law enforcement | Thailand: project developing a policy for monitoring use |
| | Prioritisation of bacteria to be monitored | Antibiotics still used as growth promoters or in animal feed for therapeutic use | Sri Lanka, Maldives: ban of all antibiotics as growth promoters and in medicated feed |
| | Dissemination of data to stakeholders | Policy interventions focusing on good practices, users and prescribers’ awareness, disease prevention and spread | Thailand: ban of all antibiotics as growth promoters, total prohibition of medicated feed in aquaculture, regular official controls on use |
| | Development of good pharmacist practices | Antibiotics still used as growth promoters or in animal feed for therapeutic use | Bangladesh: ban on antibiotics in feed additive |
| | Improvement of labelling and traceability | Policy interventions focusing on good practices, users and prescribers’ awareness, disease prevention and spread | Indonesia, India, Thailand: restriction on the use of antibiotics intended for human treatment |

| AMR=antibiotic resistance; AMU=antimicrobial use; AST=antimicrobial susceptibility testing. |
which may be poorly enforced. WHO, OIE, and FAO should support SEAR countries to achieve a total ban on antibiotic use in food animals. This will help to detect any increase in animal diseases and to avoid farmers reaching for poor quality antibiotics. Particular attention should be given to the potential effect of new or changed regulatory policies on producers and consumers.17 The tripartite alliance could propose standardised assessment of benefits, costs, and effectiveness of reforms, to ensure the development of tailored solutions taking into account specific political, economic, and social factors.17

Understanding pathways of antimicrobial resistance transmission and drivers of antibiotic use

Risk analysis, as recommended by the Codex Alimentarius and OIE guidelines,121315 is an essential tool to evaluate the risk to human health of antimicrobial resistance transmission from animal feed, to identify risk mitigation strategies, and to communicate on the complexity of this risk and the actions to be taken. However, risk analysis mainly focuses on the risk of introducing new veterinary drugs on to national markets. Critical data on risk factors for the emergence and transmission of resistance and pathways of transmission of resistant pathogens or resistance genes (foods, environments, contacts) are still fragmented. WHO, OIE, and FAO have an important role in providing more examples of risk analysis studies to assess the potential effect of the emergence and transmission of antimicrobial resistance on animal, human, and environmen
tal health, including technical support to deal with risk management options, stakeholders communication, and the perception of risk by end users. Educational efforts for providers—for example, veterinarians and farmers—must be con
tinuous, and appropriate materials and effective communication strategies must be developed.18

Conclusion

SEAR is lagging behind other parts of the world regarding the introduction of policies to combat antibiotic resistance, including surveillance, training of professionals and farmers, and the establishment of independent national drug regulatory authorities. Given the political and eco
nomic context, many countries have been unable to enforce policies that are in place, including bans on over-the-counter veterinary medicines and growth promoters. The reasons for this include low awareness, competing priorities and costs of policy, and a limited understanding of the relation between resistance in animals, humans, and the environment. Tackling all these issues will lay a solid ground for policy and its enforcement. The One Health approach, driven by WHO, OIE, and FAO, will facilitate the development of global actions across sectors, while recognising specific environmental constraints of each country in the region.17

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