



# Regulation and antimicrobial resistance (AMR)

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*“Our future health depends on forming an international legal framework that resolves – or at least substantially reduces – the problem of antimicrobial resistance”. 1*

## Key messages

- Most high-income countries (HICs) have reinforced their regulation of antibiotics, particularly through “prescription-only status”, and have a system for monitoring antibiotic use and AMR though this is not the case in low- and middle-income countries (LMICs)
- Poor enforcement is a problem in both HIC and LMIC countries, highlighting institutional weakness in regulatory enforcement
- Some countries had success with using integrated strategies to reduce the consumption of antimicrobials, particularly antibiotics
- Country experience shows that top-down initiatives alone, such as reinforcing market regulations, cannot effectively address AMR. A reduction of AMR consumption seems to be best achieved by combining regulatory activities with bottom-up initiatives, particularly educational activities and the engagement of important stakeholders
- In 2015 at the 68th World Health Assembly, Member States committed to have a National Action Plans in place in two years. The WHO has a database of which countries have developed National Action Plans; many have not yet done so, or are still in the process of completing them<sup>2</sup>
- The recent UN General Assembly's political declaration on AMR is a sign that political commitment for action is firming. In the long term a binding global framework of AMR may be a logical step

## Introduction

On 21 September 2016 at the UN General Assembly, Heads of State committed to taking a broad coordinated approach to address the root causes of Antimicrobial Resistance (AMR). Countries reaffirmed their commitment to develop national action plans on AMR, based on the Global Action Plan on Antimicrobial Resistance, and pledged to strengthen regulation of antimicrobials.

## Regulation of safe antimicrobial use in human medicine

Strengthening drug regulation is essential to control antimicrobial use and prevent AMR. Areas of current focus include the regulation of the pharmaceutical market, imposing



restrictions and controls on prescribing and dispensing, and controlling marketing activities aimed at prescribers, other health-care practitioners and users.

Most developed countries categorize antimicrobial drugs with a "prescription-only" status.<sup>3</sup> In countries with these controls, antimicrobial agents are dispensed only in registered outlets, by qualified personnel.

Some countries choose stricter regulation than others, while others, often for economic reasons may choose to liberalise their regulatory approach with a knock-on effect for the effective regulation of antimicrobials. The World Medicines Situation 2011 reported, some governments operate a "race to the bottom" in drug regulation: "Many governments, including India, Brazil and China are rolling back on other elements of regulation, such as monitoring and oversight policies, and are increasingly relying on market competition forces which makes it harder to oversee drug policies and to monitor availability and prices."<sup>4</sup>

### **Top down and bottom up approaches**

Most success to date in the reduction of antimicrobial consumption highlights the need for a combination of top-down and bottom-up initiatives. Antibiotic consumption in Sweden has decreased substantially since the mid- 1990s. Sweden now has a relatively low use of antibiotics per capita and favourable resistance conditions. Sweden acted early to initiate long-term and structured measures, characterised by work on both national and local levels coordinated by the Strama network.<sup>5</sup>

Another example is the Thailand Antibiotic Smart Use initiative, which was initiated by civil societies, it involves strong engagement of local stakeholders and use of financial incentives to reduce antibiotic use. The Chinese government used a similar financial incentive reform in its three-year antibiotic resistance containment program of 2011. The allocation of hospital funds is based on the achievement of antibiotic use reduction targets. Noncompliant hospitals risk being downgraded and noncompliant staff face dismissal. After the program began, prescribing of antimicrobials decreased by 10 to 12 percent for both hospitalized patients and outpatients from 2010 to 2012.<sup>6</sup>

### **Regulating antimicrobial use in food production**

Another problem is the *routine* use of antibiotics as a substitute for good animal husbandry and hygienic conditions. Antimicrobial agents are used for animals to treat and prevent infection. They are also used at low doses in animal food as "growth promoters", in the aim of productivity improvement.

In Sweden, growth promoters have been prohibited since 1986. Antibiotics can only be used to prevent or treat infections, under veterinary prescription only. After this reform, national antimicrobial consumption has reduced by approximately 50%.<sup>7</sup> Denmark saw a similar decrease after its 1998 Act totally banned feed additives for pigs. Applying the precautionary



principle, a 2006 European Directive withdrew the use of antibiotics as growth promoters across the European Union.

## **Surveillance of antimicrobial use and AMR**

The 2014 WHO report<sup>8</sup> reveals serious gaps related to surveillance of AMR. Out of 194 member states, only 129 countries provided surveillance data. Only two WHO regions have regional surveillance systems.

Clear information on the burden of AMR is urgently needed for policy makers.<sup>9</sup> Every state needs to set up systems for monitoring antimicrobials use. The absence of local epidemiological data across the world can lead to delayed revision of treatment guidelines, and increasing empirical use of antimicrobials by prescribers. Surveillance systems based on legal duty of reporting data need to be set up to address AMR.

Although most High income countries (HIC) already perform routine surveillance for antimicrobials use human medicine, collected data in veterinary medicine and food production is limited.

In LMICs, data are still not available, except when they are collected through surveys. In 2014, it was reported that global consumption of antibiotics had increased by 36% between 2000 and 2010. Brazil, Russia, India, China, South Africa and French West Africa were responsible for 76% of this growth.<sup>10</sup> WHO, OIE and FAO have been mandated to create a global database for monitoring the use of antimicrobial agents, within the framework of the WHO's Global Action Plan on antimicrobial resistance.

In 2015, WHO developed the Global Antimicrobial Resistance Surveillance System (GLASS) to foster standardized AMR surveillance globally.<sup>11</sup>

The UN General Assembly declaration on AMR is an important political step forward towards a broad coordinated approach to address AMR. It is now important that this political intent is implemented.

Further coordinated global action is required to support countries to take national legal action to strengthen AMR regulation. Analysis of various legal tools needs to be conducted to assess their compatibility with the current policy landscape, e.g. with the operation of the to-be-established UN Inter-agency task force group mentioned in the recent UN political declaration. A combination of different proposals emerging from UN High-level meeting on AMR and from other stakeholders, may be required: e.g. Global Antibiotic Conservation Fund, GARD-P, Global development and stewardship framework and others. Additional options to be explored include the development of a new WHO regulation, under Article 21 of WHO's Constitution, or the development of a new international treaty negotiated under the auspices of the United Nations General Assembly.<sup>12</sup>



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<sup>1</sup> S.J Hoffman, K Outterson, J-A Røttingen, O Cars, C Clift, Z Rizvi, F Rotberg, G Tomson & A Zorzet (2015) 'An international legal framework to address antimicrobial resistance', *Bull World Health Organisation*, 93:66.

<sup>2</sup> <http://www.who.int/antimicrobial-resistance/national-action-plans/library/en/>

<sup>3</sup> J.P Metlay, J.H Powers, M.N Dudley, K. Christiansen, R.G Finch (2006), on behalf of the Second Colloquium of the International Forum on Antibiotic Resistance, 'Antimicrobial Drug Resistance, Regulation, and Research', *Emerging Infectious disease*, 12 (2): 183-190

<sup>4</sup> WHO (2011) 'World Medicines Situation 2011 - Options for financing and optimizing medicines in resource-poor countries', 3<sup>rd</sup> edition, available: <http://apps.who.int/medicinedocs/documents/s20054en/s20054en.pdf>

<sup>5</sup> <https://www.folkhalsomyndigheten.se/pagefiles/17351/Swedish-work-on-containment-of-antibiotic-resistance.pdf>

<sup>6</sup> O. J. Dyar, C. Obua, C. Chandy, Y. Xiao, C.S. Lundborg, & C. Pulcini, (2016) 'Using antibiotics responsibly: are we there yet?' *Future Microbiology*, 11 (8): 1057-1071

<sup>7</sup> WHO (1997) 'The medical impact of the use of antimicrobials in food animals', Report and proceedings of a WHO meeting in Berlin 13–17 October 1997, Geneva: World Health Organisation, Document WHO/EMC/ZOO/97.4.

<sup>8</sup> WHO (2014) 'Antimicrobial Resistance Global report on Surveillance', World Health Organisation; Available from: <http://www.who.int/drugresistance/documents/surveillance-report/en/>

<sup>9</sup> R. Laxminarayan, et al (2013), 'Antibiotic resistance—the need for global solutions' *Lancet Infectious Diseases*, 13 (12): 1057–98

<sup>10</sup> T.P. Van Boeckel, et al. (2014) 'Global antibiotic consumption 2000 to 2010: an analysis of national pharmaceutical sales data', *Lancet Infectious Diseases*, 14 (8): 742 – 750.

<sup>11</sup> <http://www.who.int/drugresistance/surveillance/glass-enrolment/en/>

<sup>12</sup> Hoffman, K Outterson et al, op cit.