

THE SWISS RECIPE FOR CONTAINING ANTIMICROBIAL RESISTANCE

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In 2015, the Swiss Federal Council adopted a national strategy to ensure the long-term efficacy of antibiotics, while preserving human and animal health. Developed through a consultation process involving all interested stakeholders (across public health, animal health, agriculture and the environment), this strategy is well matched with the WHO Global Action Plan on Antimicrobial Resistance. A range of measures are currently being implemented to monitor and contain antimicrobial resistance, appropriately use antibiotics, develop new drugs and diagnostic tools, and foster cooperation and education across the public and private sectors.

The Strategy on Antibiotic Resistance (1) was established jointly by the Federal Office of Public Health (FOPH), the Federal Food Safety and Veterinary Office (FSVO), the Federal Office for Agriculture (FOAG), the Federal Office for the Environment (FOEN), the regional authorities (cantons), and a wide array of stakeholders. Its content is therefore comprehensive and broadly supported, and grounded on a One Health approach.

Switzerland being a federal state, duties and responsibilities in the healthcare system are decentralized and divided among the federal, cantonal, and municipal levels, the cantons playing a vital role. Each of the 26 cantons has its own constitution and is responsible for licensing healthcare providers, coordinating hospital services, and subsidizing institutions. There are also multiple scientific institutions, which are active either at the federal or cantonal levels. These include universities, professional societies, associations and expert groups.

All these stakeholders and interest groups were involved in the preparation of the national strategy, with the aim of achieving a coordinated, cross-sectoral implementation. They all had the opportunity to express their viewpoints and experience in three workshops for devising the strategy. This process also took into account national AMR strategies of other countries and lessons learned in implementing them. Eventually, a public consultation was held before the strategy was adopted; the feedback from this process was summarized in a report and incorporated into the implementation.

Many of these stakeholders – in particular at cantonal level – are currently in charge of implementing the strategy. Four federal offices (FOPH, FSVO, FOAG and FOEN) are in charge of coordinating the activities, while the FOPH has the overall lead. In addition, two new permanent coordinating bodies based on the revised Law on Epidemics have been created to facilitate the cooperation between the Confederation and the cantons. In particular, a cross-sectoral One Health Coordination Body created in 2016 facilitates the adoption of any complementary laws or amendments (2).

The measures of the Strategy on Antibiotic Resistance are divided into eight fields, which are depicted in Figure 1. The following sections of this article briefly provide examples of activities currently being implemented, following the structure of WHO's Global Action Plan on AMR.

National public awareness campaign

Switzerland's inaugural National Antibiotic Awareness Week took place in November 2017. It aimed to inform stakeholders and the public about the dangers of antibiotic resistance and provide the latest information on regional and national projects (3). Universities, consumer associations and multiple stakeholder groups held their own events across the country.

During this week, pharmaSuisse (the umbrella organization of pharmacists), the Swiss Medical Association (FMH) and the FOPH jointly launched the first nation-wide initiative to improve awareness about appropriate antibiotic use.

After several focus groups, representatives of these three institutions prepared an information leaflet to be distributed to patients affected by an infectious disease, whether or not they are prescribed antibiotics. In 2018, general practitioners, specialists and a network of 1,500 pharmacies will distribute nearly a million of these leaflets, which are available in four languages. A short animated movie will provide complementary information on a dedicated website, where printed leaflets can

be ordered free of charge (4). An evaluation of this information campaign is planned for the end of 2018.

Surveillance of AMR epidemiology and antibiotic use

From 2001 to 2006, a national research programme (NRP 49) mapped antibiotic resistance in Switzerland for the first time, in humans, animals and the environment. As a product of this research programme, the Swiss Centre for Antibiotic

Figure 1: The structure of the Swiss Strategy on Antibiotic Resistance

8 fields of activity – 35 measures

The measures of the Strategy on Antibiotic Resistance concern human medicine, veterinary medicine, agriculture and the environment and are divided into eight fields of activity. The strategy follows the One Health approach.



MONITORING

The antibiotic resistance situation and consumption must be monitored systematically in all sectors. This is the only way that correlations between usage, the nature of the antibiotics and the development of resistance can be identified, so that the success of the measures taken can be assessed.

PREVENTION

Lower antibiotic use contributes the most to fighting resistance. The time-honoured saying “prevention is better than cure” applies: the fewer people and animals that suffer from infections, the fewer antibiotics need to be used. Preventive measures such as better hygiene, targeted diagnostics, vaccination and optimized animal husbandry can reduce the use of antibiotics to what is strictly necessary.

APPROPRIATE USE OF ANTIBIOTICS

The excessive and inappropriate use of antibiotics is primarily responsible for the increase in resistance. Clear guidelines on prescription, dispensing and use in human and veterinary medicine are needed, especially for newly developed antibiotics or those classified as critical.

RESISTANCE CONTROL

Resistance must be identified quickly and its further spread prevented. In human medicine, the risk of bringing resistance into hospitals or nursing homes when patients are admitted needs to be reduced – notably by preventive screening. The focus in veterinary medicine is on limiting the spread of resistant pathogens between herds.

RESEARCH AND DEVELOPMENT

An understanding of causes and correlations is the basis for effective measures. Targeted and interdisciplinary research fills gaps in our knowledge. New findings will lay the foundations for product development, for example in diagnostics or in the field of antimicrobial substances.

COOPERATION

Cooperation is needed to tackle the problem successfully. This is why multidisciplinary and cross-sector coordination is essential. A coordinating and expert body is supervising the implementation of the strategy. International networking and knowledge exchange will also continue to be encouraged.

INFORMATION AND EDUCATION

The general public also has an important role to play. Information at all levels aims to raise the awareness of individuals so that they realise their own responsibility in dealing with antibiotics. The aim among professionals is to increase their specific knowledge about resistance, preventive measures, diagnostics and the correct use of antibiotics.

GENERAL CONDITIONS

The general conditions have to be right for antibiotics to remain effective in the future. Appropriate measures, e.g. at the political or legislative level, should support the development of new antibiotics and their sensible use. The question of finding incentives in animal husbandry which will lead to better animal health and less antibiotic use is also being examined.

Resistance (anresis.ch) was established in 2004 to monitor AMR in the human population. Anresis.ch brings together a representative network of 22 microbiology laboratories covering more than 60% of inpatients and about 30% of outpatients. It maintains an open online database with updated resistance data, and publishes surveillance results monthly for the FOPH Bulletin and through a dedicated website for specialists (5).

Figure 2 below illustrates the evolution in Switzerland of various forms of resistance in pathogenic bacteria responsible for invasive infections of the brain or bloodstream.

The declaration of cases of resistance to last-resort antibiotics (carbapenems) is mandatory since 2016. A *National Reference Centre for Emerging Antibiotic Resistance* was created in 2016 to help any laboratory – free of charge – in the identification of new or emerging forms of antibiotic resistance (6). The Swiss cantons have also set up a nationwide network of laboratories, which closely collaborate with the Federal authorities and the National Reference Centres on bacterial pathogens.

In the veterinary sector, a system aligned with European provisions (7) was established in 2006 to enable continuous monitoring of antimicrobial resistance in livestock animals and meat. Since 2009, data on sales of veterinary antimicrobials and results of resistance monitoring have been published yearly. More recently, a pilot project has been launched to further analyse resistant pathogens causing infections in livestock and pets.

Since 2013, data on the use of antibiotics in livestock and on resistance in animals and meat has been published every other year in a joint report, together with data from the human sector (8). The next Swiss Antibiotic Resistance Report (to be published in November 2018) will feature new surveillance results from 1) pilot projects to enhance surveillance of infections caused by resistant bacteria (e.g., in long-term healthcare facilities), 2) pathogens causing infections in livestock and pets, and 3) resistant microorganisms in rivers and lakes. The analysis of all these data in a One Health perspective will be strengthened.

Finally, in 2016 a five-year *National Research Programme on Antimicrobial Resistance* (NRP72) was launched; it aims at enhancing our knowledge of antibiotic resistance development and transmission (9).

Infection prevention and control

The NOSO Strategy for the monitoring, prevention and control of healthcare-associated infections was adopted in 2016 (10). Long before the adoption of this strategy, national guidelines were already published in this field, for instance for reprocessing medical devices and for antimicrobial prophylaxis in surgery. And more than half of all hospitals (164 at the latest

count) already take part in a National Surgical Site Infection Surveillance Programme.

Currently, infection prevention and control policies and operational plans are available at all health facilities. They include hand hygiene measures and recommendations regarding isolation of colonized or infected patients. A network of public health and academic partners is in place to develop and evaluate these prevention interventions.

As for the *Strategy on Antibiotic Resistance*, one of the goals of the NOSO Strategy is to enhance the adoption of common practices across the country, and to fill in the gaps. For instance, there is no healthcare-associated infections prevention & control plan available for residential healthcare facilities. And it is still unclear whether (and how) such facilities may screen for multidrug-resistant organisms, or if they have specific plans to prevent and combat outbreaks caused by these pathogens.

These two closely related strategies will allow for the development of screening and outbreak management guidelines for multidrug-resistant organisms, and for the monitoring of adherence to those guidelines.

In the veterinary sector, there are officially endorsed animal health schemes for cattle and pigs. There are programmes in place, designed and delivered by stakeholders, which identify and promote good practice in livestock production and healthy animals as a way to reduce the use of antimicrobials. Animal health services have also stepped up their advisory services and activities to encourage infection prevention; as a result, a number of infectious diseases have been eradicated (e.g., enzootic pneumonia and actinobacillosis in pigs, and *Salmonella enteritidis* in chickens).

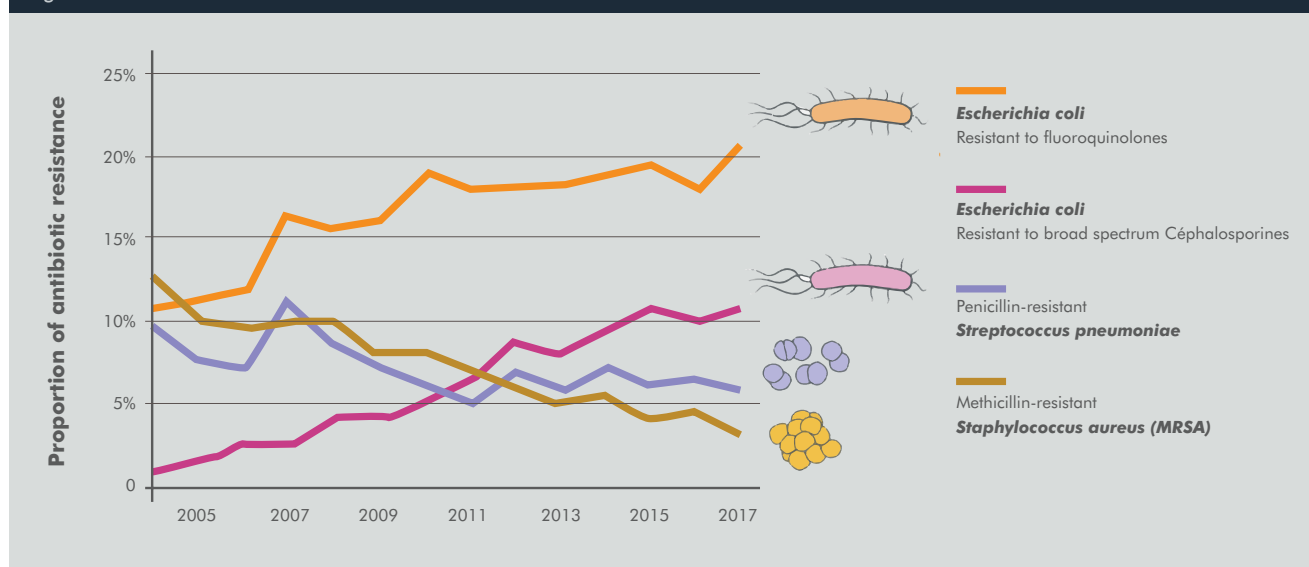
Finally, antibiotic residues in rivers and lakes are also monitored across the country. To curb the entry of these residues into the environment, wastewater treatment plants will be upgraded with additional treatment steps. With this upgrade, Switzerland is assuming a pioneering role, which has attracted considerable international interest.

Regulation to limit antibiotics use in agriculture

Back in 1999, Switzerland banned the addition of antibiotics to animal feed as growth promoters. Other legal requirements were introduced in 2004, such as a prohibition on the administration of antibiotics to livestock without a prescription by a veterinarian. A regulation on the use of antibiotics in veterinary medicine was adopted to curb the use of antibiotics for prophylactic treatment. Since 2016, the sale of critically important antimicrobials for human medicine has also been restricted in veterinary medicine.

Antibiotic prescription guidelines are available online for the most frequent infections affecting pigs and cattle (12). Currently, only “sales data” on antibiotics for veterinary use

Figure 2: Evolution of some resistant bacterial strains in Switzerland Source: anresis.ch



are available; a system to collect “veterinary prescription data” at species level is under construction.

Antibiotic stewardship programmes in hospitals and in the community

The Swiss Centre for Antibiotic Resistance also monitors antibiotic use. For inpatients, consumption has been monitored since 2006 through a sentinel network of hospital pharmacies. Yearly data from 65 hospitals (or hospital networks) are collected on a voluntary basis, representing 56% of acute care hospitals (excluding psychiatric and rehabilitation centres). The participating hospitals receive a yearly benchmarking report, allowing them to compare their results with those of similar-sized institutions. From 2018, this qualitative and quantitative feedback will be provided on a monthly basis.

Swiss hospitals are at very different stages of antibiotic stewardship implementation. Comprehensive programmes are only implemented in about one third of acute-care hospitals, which may be related to a lack of funding or personnel. Whereas prescription guidelines are available in the majority of them, levels of adherence to those guidelines are not systematically measured.

The roll-out of modular national antimicrobial stewardship guidelines is planned to improve the current situation and generalize stewardship programmes in Swiss hospitals, while offering flexibility to account for local healthcare structure and resources. Swissnoso is in charge of preparing these guidelines, in collaboration with hospital pharmacists, insurance representatives, the Swiss Medical Association (FMH), and the Swiss Hospital Association (13). The stewardship guidelines will be prepared in accordance with the Global Framework for Development & Stewardship to Combat Antimicrobial Resistance currently being developed by FAO, OIE and WHO.

Box 1: International commitment

In May 2018, Switzerland joined the G20’s Global Collaboration Hub on AMR Research and Development, a new high-level global partnership aimed at maximizing the impact of existing and new initiatives in antimicrobial research and product development.

With a view to promoting the R&D of new antibiotics and diagnostic tools at the international level, Switzerland extended in 2017 its financial support to the Global Antibiotic Research and Development Partnership GARDP, launched by the Drugs for Neglected Diseases initiative DNDi.

Switzerland supported, with the international community, the adoption in 2015 of the Global Plan of Action to Combat AMR - developed by WHO in collaboration with FAO and OIE - and of the 2016 Political Declaration of the UN high-level meeting on AMR.

Switzerland is participating in other international initiatives such as WHO’s Global Antimicrobial Resistance Surveillance System (GLASS), the Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR) and the EU Joint Programming Initiative on Antimicrobial Resistance (JPIAMR).

In a bid to strengthen international cooperation against AMR, Switzerland also joined the Global Health Security Agenda initiative, launched by the United States of America to combat communicable diseases. In this context it published in 2015 a comparative study of various national AMR strategies, with the aim to define best practices (14).

Finally, to enhance the implementation of the national strategy, a Swiss interministerial delegation greatly appreciated the opportunity to visit the Netherlands (2016) and Norway (2017) to learn from the practical experiences of these countries in AMR control.

In the outpatient setting, a comprehensive set of prescription guidelines for the most common infections in ambulatory care was issued in early 2018. Physicians’ adherence to

these guidelines should now be promoted and monitored. These guidelines will hopefully have an impact on outpatient consumption, which is being monitored since 2013 and is based on information provided by 65% of all privately run pharmacies in Switzerland.

Financial support for the development of new antibiotics

The NRP 72, with a budget of 20 million Swiss Francs, also aims at discovering novel antimicrobial molecules and developing rapid diagnostic techniques.

Conclusion

Despite all these positive efforts, there is still a great need for action; the global situation shows that isolated measures focusing on individual fields cannot provide a lasting solution to the problem of antibiotic resistance. The Joint External Evaluation of the capacity of Switzerland to prevent, detect and rapidly respond to public health threats, performed in 2017, identified several priority actions (15): 1) Develop screening and outbreak management guidelines for multidrug resistant organisms, and monitor adherence to those guidelines; 2) Enhance surveillance of antimicrobial resistant infections through pilot projects, and implement a national monitoring programme for animal pathogens; 3) Expand and consolidate monitoring of healthcare-associated infections; 4) Foster adherence to outpatient antibiotic prescription guidelines and to the Swiss national plan for stewardship in hospitals (to be released in 2018/19). ■

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References

1. Strategy on Antibiotic Resistance Switzerland <https://www.star.admin.ch/star/en/home/star/strategie-star.html>
2. <https://www.blv.admin.ch/blv/fr/home/das-blv/organisation/kommissionen/unterorgan-one-health.html> (webpage only available in French, German or Italian)
3. Strategy on Antibiotic Resistance 2017 Report https://www.bundespublikationen.admin.ch/cshop_mimes_bbl/8C/8CDCD4590EE41EE7ACCD26E7C74F203B.pdf
4. https://www.antibiotika-richtig-einsetzen.ch/en_GB/home
5. <http://infect.info/>
6. <https://www.nara-antibiotic-resistance.ch/>
7. Decision 2013/652/EU on the monitoring and reporting of AMR in zoonotic and commensal bacteria <https://publications.europa.eu/en/publication-detail/-/publication/83e1934f-4d39-11e3-ae03-01aa75ed71a1/language-en>
8. Swiss Antibiotic Resistance Report 2016 www.bag.admin.ch/bag/de/home/service/publikationen/broschueren/publikationen-uebertragbarekrankheiten/publikation-swiss-antibiotic-resistance-report-2016.html
9. National Research Programme 72 <http://www.nfp72.ch/en/>
10. National Strategy for the Monitoring, Prevention and Control of Healthcare-Associated Infections (NOSO Strategy) <https://www.bag.admin.ch/bag/en/home/service/publikationen/broschueren/publikationen-uebertragbare-krankheiten/publikation-nationale-strategie-noso.html>
11. Prescription of veterinary medicines <https://www.blv.admin.ch/blv/fr/home/tiere/tierarzneimittel/fachgerechter-umgang-mit-tierarzneimitteln/verschreibung--abgabe-und-anwendung.html>
12. Guidance on appropriate antibiotic use in the veterinary sector www.vetpharm.uzh.ch/pdf_data/absouttract.pdf
13. Evaluation of existing and desired antimicrobial stewardship activities and strategies in Swiss hospitals <https://smw.ch/en/article/doi/smw.2017.14512/>
14. Comparative study of various national AMR strategies <https://www.bag.admin.ch/dam/bag/fr/dokumente/int/foph-response-antimicrobial-resistance-threat.download/responsetoheantimicrobialresistancethreat.pdf.foph-response-antimicrobial-resistance-threat>
15. World Health Organization (WHO) International Health Regulations (IHR 2005) JEE tool. <http://apps.who.int/iris/handle/10665/204368>