Strategic and Technical Advisory Group on Antimicrobial Resistance (STAG-AMR)

Report of the first meeting
Geneva, 19-20 September 2013
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INTRODUCTION

Background to meeting

Since the 1940s, antimicrobial agents have substantially reduced mortality from infectious diseases and have provided a critical margin of safety for many modern medical practices. However, the extensive use, misuse and overuse of antimicrobials in both the human and animal sectors\(^1\) have increasingly raised antimicrobial resistance (AMR) levels worldwide among a wide range of pathogens (bacteria, viruses, parasites). Increasing levels and spread of AMR (exacerbated by travel and food trade), coupled with insufficient infection prevention and control measures in many locations, and the emergence of new multi-resistant pathogens, have created an urgent need for global action. The Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE) both regard AMR as an issue of major importance and a priority for joint action with WHO.

The full scope of AMR is not known, but the picture is already compelling. AMR threatens the long-term sustainability of the public health control of major communicable diseases. This is an issue, in part, because alternative antimicrobial medicines are considerably more expensive than first-line treatment options.

New resistance mechanisms are emerging, which make it difficult or impossible to treat certain infections. Examples include hospital-acquired and community-acquired infections, such as those affecting children (e.g. blood stream infections, pneumonia and meningitis) and sexually transmitted infections (e.g. gonorrhoea). Infections caused by drug-resistant pathogens increase mortality across all settings, and can lead to prolonged stays in hospital and increased risk of admission to intensive care units. Hospital-acquired infections by multidrug-resistant bacteria already cause around 80 000 deaths annually in China, 30 000 in Thailand, at least 25 000 across the European Union and at least 23 000 in the United States of America. The annual cost due to antibiotic-resistant infections has been estimated to be 1.5 billion euros in the European Union (EU)\(^2\) and US$2.0 billion in Thailand.\(^3\) In January 2013, the World Economic Forum warned that AMR is one of the major global health security risks which the world needs to address and called attention to GDP losses from AMR ranging from 0.4 to 1.6 %.\(^4\)

In 2011, there were an estimated 630 000 cases of multidrug-resistant tuberculosis among the world’s 12 million prevalent cases of tuberculosis. Nearly 4% of new cases and about 20% of previously treated cases are multidrug-resistant. Only 50% of multidrug-resistant cases are reported by countries as being successfully treated. On average, the cost of treating one case of multidrug-resistant tuberculosis is equivalent to the cost of treating 100 susceptible

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tuberculosis cases. An even more severe form of resistance, extensively drug-resistant tuberculosis, has been identified in 84 countries.5

The prevalence of HIV drug resistance among people starting antiretroviral therapy in 12 low-income and middle-income countries, rose from nearly 5% in 2007 to nearly 7% in 2010. Levels of HIV drug resistance can reach 10% to 17% in high-income countries. In south-east Asia, artemisinin is the medicine of last resort for treatment of falciparum malaria and resistance to it is threatening malaria control.

Since the publication of WHO’s global strategy for containment of antimicrobial resistance in 2001, several World Health Assembly resolutions on the subject have been adopted (the latest being WHA60.16 concerning the rational use of medicine and WHA62.15 on prevention and control of multidrug-resistant tuberculosis and extensively drug-resistant tuberculosis). Various initiatives have been launched, at all WHO levels, including in 2011 a call for action on World Health Day, with a policy package for stakeholders. Most recently, the Director-General convened a WHO Strategic and Technical Advisory Group on Antimicrobial Resistance which held its first meeting in Geneva, 19-20 September 2013.

Role of the Strategic and Technical Advisory Group for Antimicrobial Resistance

The Strategic and Technical Advisory Group for Antimicrobial Resistance (STAG-AMR) has been convened by the Director-General to be the principal technical advisory group to WHO on antimicrobial resistance (AMR). It will advise the WHO Director-General on: WHO’s strategic plan and priority activities to tackle AMR consistent with WHO’s mandate and considering the comparative advantages and the respective roles of partner organizations, and with special focus on aspects that cover different pathogens; the major issues and challenges to be addressed by WHO with respect to achieving the strategic goals for AMR; the engagement of partners and outreach efforts to tackle AMR. The Terms of Reference for the STAG-AMR were provided to all members and are included as an Annex to this report.

The purpose of this first meeting was to identify the key issues and options so that WHO can develop a global strategy to tackle antimicrobial resistance.

Format and working methodology of the meeting

The STAG-AMR held its first meeting from 19 to 20 September 2013. On the first day, Advisory Group members were joined by representatives and observers from other organizations, providing an opportunity for open discussion on a wide range of concerns and considerations related to AMR. In addition, staff from WHO Headquarters and regional offices were present and able to contribute. A summary of the presentations and the issues raised in discussions is provided below.

On the second day, Advisory Group members met without the presence of observers and other representatives, to consider and reach agreement on the specific advice and recommendations for the WHO Director-General.

5 New data now available in WHO Global Tuberculosis Report 2013
Roles and responsibilities of STAG-AMR

Members of the STAG-AMR were briefed on the principal role of the Group, that of an advisory group to the WHO Director-General (see Terms of Reference). Members had been selected and appointed by the Director-General on the basis of their technical expertise and scientific and public health experience. They serve in an individual capacity and not as representatives of their organizations or countries. In the selection of the members, consideration had been given to attaining an adequate technical distribution of expertise, geographical representation and gender balance.

Declarations of Interest

All members completed the standard WHO form for declaration of interests and these were reviewed by the WHO Secretariat, against the purpose and agenda, in advance of the meeting. In the interest of public disclosure and to ensure all members are aware of each other’s relevant interests before the start of the meeting, a summary of relevant interests was presented to the members.

The following interests were reported. Dr Visanu Thamlikitkul, through his employer Mahidol University, had received research grants from public sources for work on AMR. In addition, Dr Visanu’s employer, Mahidol University, had received research support for antimicrobial resistance in the period 2009 to 2013, from three pharmaceutical companies producing antibiotics. Furthermore, Dr Visanu has personally received speaker fees and travel support relating to antimicrobial resistance from five pharmaceutical companies over the same period. Dr Line Matthiessen declared having presented the view of the European Commission at several antimicrobial resistance meetings as part of her official duties.

The declarations of interest were presented to the members for information. There were no comments from any of the members. It was concluded that none of these members’ interests presented any conflict in relation to the objectives of the meeting and their role on the STAG–AMR and as such did not warrant the exclusion of any members from any part of the meeting, including those sessions leading to formulation of recommendations or advice.
STAG-AMR: 19 September 2013

Opening comments by WHO Director-General, Dr Margaret Chan

Dr Margaret Chan, the Director-General of the World Health Organization, opened the meeting and began by presenting the context that had led to the creation of the STAG-AMR. She conveyed to participants the levels of concern that are now being expressed by Member States and their calls for WHO to take the lead in responding to this crisis. She invited members of the STAG-AMR and other representatives present to share their wealth of experience and perspectives and requested that the STAG-AMR develop a series of recommendations for the Organization that will help to shape a global strategy and plan of action to reverse the trend of increasing AMR. Dr Chan underlined the need to view this crisis as not only an acute emergency in need of an immediate response, but also as one that would require a long-term effort to prevent a re-emergence in the future. She urged participants to keep in mind that if the world loses antimicrobials, modern medicine as it is currently understood, will also be lost.

Introduction to the specific objectives of the meeting, WHO Assistant Director-General for Health Security and Environment, Dr Keiji Fukuda

Dr Keiji Fukuda set out the specific objectives for the meeting. He provided participants with an overview of WHO’s recent work, the organizational perspective on AMR and some examples of the health impact of the crisis.

Dr Fukuda expressed his belief that 2013/14 presented the prime opportunity to move ahead from discussion and into action. He noted that awareness levels beyond the health sector had now risen sufficiently to be able to engage political leaders and drew attention to a series of events scheduled over the coming months that would build momentum towards the 67th World Health Assembly in 2014.

He further noted that the problem of AMR was too broad for WHO to address on its own and that the drivers of AMR reach far beyond the health sector and implicate a wide range of stakeholders, many with differing agenda. He proposed that alignment is urgently needed to harness the current energy and to accomplish change across multiple sectors.

Chair

Professor Dame Sally Davis was nominated to be the Chair of the STAG-AMR by Dr Keiji Fukuda. This was confirmed by the Members present.

SESSION I: Knowledge about AMR and its evolution

Presentation: Professor Otto Cars, ReAct, Sweden

Professor Cars presented an overview of the direct impact of AMR on the burden of disease. Although resistance has developed in all antimicrobial agents, Professor Cars focused his presentation on resistance to antibiotics in particular and highlighted the two parallel trends – the rise in resistance to existing antibiotics and the slow-down in development of new antibiotics. No new class of antibiotics has been developed since 1987. The inherent
incompatibility of these two trends is creating a crisis of which the consequences on human health are becoming increasingly apparent.

In both the community and in hospital settings, treatment of infection is totally dependent upon effective antibiotics. Modern health systems, be they weak or strong, have been built in the era of available antibiotics, and rely on these in order to function and to carry out standard procedures safely. Our inability to treat some strains of gonorrhea is compelling evidence that modern medicine is now entering the post-antibiotic era.

Professor Cars articulated the importance of viewing the problem from a very broad ecological perspective. Antibiotics, bacteria and resistant genes all travel within different but interlinking contexts; human and veterinary medicine, livestock production, water and sanitation. Overuse and inappropriate distribution and marketing of antibiotics in all sectors and regions are driving resistance and must be addressed, possibly through a code of conduct. Moreover, globalization has facilitated the movement of resistant genes enabling them to become established in many areas of the globe.

A number of good surveillance systems have been put in place in some regions, but many more are needed globally, including early warning systems for the most difficult to treat infections. A lack of effective diagnostic tools has impeded clinicians from being able to target infections with the most effective antibiotic. Better diagnostic tools could offer a solution to the problem of over-prescription.

The burden of the impact of AMR is being felt disproportionately in low-income countries with weak health systems and a lack of effective drugs. Instead, they frequently have to rely on substandard drugs and, when resistance arises, are unable to access newer, more expensive treatment. In many low-income countries, antibiotic resistance is now shown to be a significant risk factor for a fatal outcome in paediatric infections.

Professor Cars concluded by noting that the success of antibiotics in the 20th Century has led to a collective global complacency that these drugs would always be available to us. Also, an overall imbalance has emerged between uncontrolled and excessive use in some areas, and a lack of access in others. In searching for the right measures to address this crisis, Professor Cars stressed that equitable access must be a central principle and that a new financial model is urgently needed to enable the controlled distribution and rational use of antibiotics. Such a model will need incentives from the public sector to avoid volume sales being the main driver for return on investment.

During the discussion, the primary importance of infection prevention and control, and the need for basic hygiene, were frequently stressed. It was noted that in some countries, insurance companies are questioning reimbursement of some hospital-acquired infections leading to standards in prevention being seen as a consumer concern.

Many participants stressed the importance of engaging all stakeholders. In particular, the general public and patient organizations will prove pivotal in raising awareness and changing practice. Health-care workers were also mentioned as an important audience to target education and awareness raising. It was also noted that a dialogue with the private sector, and critically with the pharmaceutical industry, will be essential as there is likely to be tension between efforts to reduce and regulate antibiotic use on the one hand, and the sales and marketing activities of the drug companies on the other.
Improvements in diagnostics, especially point-of-care diagnostics, in order to better target infection with the appropriate antibiotic, were widely recognized as a significant gap. Better understanding of the existing bottlenecks that are impeding development in this area is needed.

Participants were united in stressing the importance of information dissemination as a means to drive action. Some participants raised the need for an early warning mechanism that would enable the rapid identification and reporting of AMR events of serious public health significance. The use of the IHR (2005) as a potential reporting tool was mentioned.

Some participants noted that a ‘code of conduct’, as suggested by Prof Cars, may take many years to put in place but that a defined road map with short- and long-term targets for action was urgently needed.

**SESSION II: Optimal use of antimicrobials**

*Presentation: Dr Elizabeth Erlacher-Vindel, World Organisation for Animal Health (OIE), France*

Dr Erlacher-Vindel outlined the challenge of AMR from the perspective of the animal health and veterinary sector. She highlighted a number of specific challenges that, while not unique to the animal health sector, were of particular concern to OIE. In over 100 countries no controls are in place for the distribution of antimicrobials in the veterinary and farming sectors. In addition, falsified products are in wide circulation and in many countries farmers have unrestricted access to these drugs with no veterinary oversight.

OIE has a long history of collaboration with WHO and FAO and now, under the tripartite agreement, all three organizations are working together closely to address AMR. AMR is a global concern for animal health and welfare, as well as for human health, but food security and the livelihoods of small holders, particularly in developing and transition countries, must also be taken into consideration.

OIE is currently focusing efforts on improving surveillance programmes of resistance in animals, monitoring usage, advocating prudent use of antimicrobials and capacity building among veterinarians at the national level. In addition, with the support of WHO, the organization is providing specific guidance to its Member States on those antimicrobials used in animals and fisheries that are of particular importance to humans. In March 2013, OIE convened a Global Conference on the Responsible and Prudent Use of Antimicrobial Agents for Animals. The organization is currently conducting a survey of all OIE delegates and national focal points to develop a more detailed picture of antimicrobial use among its members.

Dr Erlacher-Vindel stressed that it is the shared responsibility of all sectors – human, animal and agriculture – to work together to prevent and minimize the development of resistance. This calls for a holistic approach, under coordinated management that brings all sectors together, while recognizing their respective differences in ecosystems and geographic locations. Collaborative action is needed to address legislation, good governance, awareness raising, capacity building and risk assessment – particularly in the area of non-priority practices and use of antibiotics for growth promotion. Specifically, OIE has identified the need for support from its Member States and from developing country governments, as well as
as from all its diverse stakeholders, including farmers and small holders and the donor community.

As other speakers had noted, Dr Erlacher-Vindel pointed to the lack of data and evidence on the causal factors that are driving AMR, and that these data are urgently needed. She noted that this lack of evidence had allowed a climate of blame to permeate discussions between different sectors which in the past had hindered progress. Dr Erlacher-Vindel advocated for this culture to now be put aside and that instead, all sectors move ahead together, in a coordinated manner, building on a new era of trust and mutual support, in which international collaboration can flourish, as demonstrated by the multisectoral participation in this meeting.

**Presentation: Dr Hiiti Sillo, Food and Drugs Authority, United Republic of Tanzania**

Dr Sillo presented the perspective of a regulatory authority in a low-income country where inappropriate use of medicines is the overriding challenge. He noted that antimicrobials were frequently distributed without prescription, leading to misuse and sometimes a negative outcome for patients. An insufficient number of prescribers and dispensers in both public and private health facilities often leads patients to self-medicate. In these circumstances access to cheap, poor quality or counterfeit antibiotics is often easier than accessing qualified health care. In addition, many patients have a preference for injectable medicines over oral dosage, perceiving these to be more effective.

Regulatory systems in both the human and animal health sectors are too weak to provide the necessary oversight. As a result unqualified sellers are able to operate freely at animal markets.

He concluded by stressing the need to improve access to quality antimicrobials, to establish good surveillance systems to detect resistance and to monitor use, to increase public awareness of the rational use of these medicines and to strengthen regulatory systems that are harmonized with regional and international initiatives such as the East African Community Medicines Regulatory Harmonization Project, launched in March 2012.

Discussions among participants drew on further examples from developing countries and highlighted common problems of inadequate access to qualified prescribers and dispensers and the huge investment that would be needed to increase the number of health professionals in the long term. Resource-limited settings often face difficulties in implementing best practices and achieving optimal antimicrobial use. Limitations in health-care infrastructure and insufficiently controlled drug procurement, distribution and dispensing systems exacerbate these difficulties. The challenge of prevention of infection in facilities with sub-standard basic hygiene was also raised. The question was also raised as to what extent drug donations are circumventing national regulatory systems. The provision of quality universal health coverage was highlighted as key for improving optimal antimicrobial use and is also a common driver for tackling all types of antimicrobial resistance.

The use of antimicrobials for growth promotion was discussed. It was noted that despite the banning of such use in EU countries, phasing out this practice in developing and transition countries remains very challenging. Some countries have introduced a differentiation between those antibiotics that can be given to animals and those which are reserved for human use only, although it was noted that monitoring compliance remains a challenge.
Participants stressed the need for WHO to assist countries in defining the solutions applicable to their context and in implementing them.

**SESSION III: Development of national policies and programmes**

*Presentation: Professor Visanu Thamlikitkul, Mahidol University, Bangkok, Thailand*

Professor Visanu presented his experience of working with the Government of Thailand to develop a national policy and programme on AMR.

The problem of AMR is widely recognized in Thailand. The last decade has seen a dramatic rise in the prevalence of AMR in both the health-care setting and in the community. An increasing number of patients are being admitted to health-care facilities, who are infected with extensively drug-resistant tuberculosis (XDR-TB) gram negative bacteria. With no available antibiotic treatment, mortality among these patients has reached over 80%. Carbapenem resistance has increased from less than 10% a decade ago to over 70%. In the community, the prevalence of extended-spectrum beta-lactamases (ESBL) positive bacteria has risen to over 50% in some provinces.

The country has shown strong commitment at global, national and regional levels to combating AMR. In September 2011, the Minister of Health joined other governments of south-east Asia in signing the Jaipur Declaration on Antimicrobial Resistance. However, what was lacking was effective and coordinated action by the key players.

In January 2012, in collaboration with the Health Systems Research Institute, a committee was established to define the goals for AMR containment and to propose a road map for a three-year period. The Committee is addressing issues of infrastructure, strategy, systems, research, and appropriate implementation measures.

The Committee began by estimating the burden of AMR in Thailand using existing national data on the number of cases and mortality rates. From these data the overall economic burden could be determined and is now estimated to have reached more than US$ 1000 million per year. Specific measures to contain and prevent AMR have been defined as: rational use, surveillance, infection prevention and control, research and development and improved public awareness. Although some initiatives were already underway in many of these areas, activities were being conducted in a vertical, independent and fragmented manner. An overall package was needed that would bring all systems and initiatives together in a holistic manner and address the gaps.

Before the package was finalized, a national workshop and series of public hearings were held to further engage stakeholders. The package, which addresses regulation, education and promotion, incentives and sanctions, and social and behaviour measures has been implemented since March 2013, under the coordination of the Ministry of Health. However, the challenge of coordination has revealed further problems in terms of government bureaucracy and communication gaps between different sections and ministries. Funding has been forthcoming from a number of donors, each with a different but complementary focus.

Many challenges remain, particularly in scaling up implementation to achieve nationwide coverage. Nevertheless, good progress is being made, due in many respects to the skill and motivation of a number of key individuals.
The experience of Thailand has demonstrated that developing and implementing a national programme calls for strong leadership backed by high level support and available resources. Bureaucracy and a lack of awareness can both be significant barriers to success and sustaining the current momentum is likely to prove a challenge.

Participants discussed the issues that had been raised by the experience of Thailand and enquired how the Thai authorities were managing the importation of resistance from neighbouring countries that had weaker containment systems. The high level of patients coming to Thailand to seek medical treatment from other countries in the region has highlighted the global nature of the problem and that no one country can solve its national problem alone.

Many health facilities in Thailand are run as private businesses and fall outside of state controls. The prevalence of so many private hospitals and clinics has raised other challenges in controlling AMR. Many private facilities reap financial rewards through the distribution of antimicrobials to their patients. The authorities in Thailand are looking into ways in which accreditation requirements can be used to put pressure on these facilities to decrease their use of antimicrobials, with both incentives for reduction of use and sanctions in cases of over-use.

SESSION IV: Fostering innovation

Presentation: Dr Carmem L. Pessoa da Silva, Pandemic and Epidemic Diseases, Health Security and Environment, WHO

WHO has been engaged with AMR as a matter of global concern for over a decade, but its focus has widened in recent years. In 2001, the Organization launched the WHO Global Strategy with an emphasis on research and development into new drugs and vaccines. A decade later, on the occasion of World Health Day 2011, WHO released a comprehensive policy package. In the area of innovation, the package re-emphasized the need for partnership among all stakeholders, and for new medicines, vaccines and diagnostics, but went further, calling for greater operational research to improve our understanding of the spread of AMR and of the optimal use of existing tools. Specifically, the package highlighted the need for an enabling regulatory system to support the development of new tools.

The importance of innovation for new tools and health technologies has long been recognized as an essential element in tackling AMR. However, it is now recognized that innovation is also needed across many other areas. We need to improve our understanding of the modes of transmission and we need novel approaches towards integrated surveillance, which at present remains largely vertical and is frequently lacking in many parts of the world. We also need a better understanding of how to use, apply and adapt our existing tools to different settings.

At the same time, a vacuum has now appeared in the development of new drugs. In 2010, an independent Consultative Expert Working Group was established by the World Health Assembly to look specifically into the challenges facing research and development. In 2012, the Working Group released its findings on financing for R&D, concluding that: too little investment is being made into research and development for antibiotics; existing business models lack the necessary incentives and; the market is failing, with major consequences for global health.
New business models are needed to stimulate the development of new or improved medicines, diagnostics and prevention measures. New platforms are needed to facilitate information and knowledge sharing. Crucially, low- and middle-income countries must become part of this process and be supported in the implementation and evaluation of new tools.

Participants discussed potential ways in which innovative research could be incentivized. A focus on the academic stream, with financial support from governments, could drive innovation at the research level, with rewards in the form of prizes and academic recognition. Public-private partnerships may also provide opportunities to fund development of new therapeutics.

It was also noted that innovation in vaccines is an underexplored area. New vaccines for specific pathogens, for use in humans and animals, may offer an alternative to antibiotic medicines.

**STAG-AMR: 20 September 2013**

On the second day of the meeting, members of the STAG-AMR reconvened, in the absence of observers. They considered the issues that had been raised by the previous day’s presentations and discussions, and formulated a series of recommendations that would form the basis of their advice to the WHO Director-General.

*Their recommendations were as follows:*

The Advisory Group members were unanimous in calling for urgent action to address the growing public health threat from AMR.

In making this call, the Advisory Group recommended that AMR should be positioned primarily as a health issue, while recognizing that it affects both human and animal health and that it has economic, social, and developmental dimensions.

The Group stressed the importance of recognizing and acknowledging the impact of antimicrobial resistance across all diseases (bacterial, fungal, viral, and parasitic) so that all interested parties are engaged and committed, and that new areas can be included as they arise. The Group also acknowledged that for some specific diseases or pathogens, programmes are already in place that address AMR and concluded therefore, that the most pressing need in the near term was to focus on antimicrobial resistance related to bacteria.

The Advisory Group specifically recommends that WHO should lead in developing a global action plan to address AMR. WHO is urged to work with all stakeholders to build a global action plan to address AMR and to commit to this plan. Within this framework, WHO should also support and guide Member States to develop and implement national action plans and policies for AMR and to put in place appropriate targets and outcome indicators that can be built into national, regional and global plans.

The global action plan needs to embrace the following principles:

- AMR prevention practices should be embedded in and integral to all health systems and practice (both human and animal)
• The use of antimicrobials in all sectors should be reduced where appropriate, and optimal and equitable use promoted.
• Emphasis should be placed on hygiene and infection prevention and control
• Extending quality healthcare through universal health coverage, together with increased awareness, are important enabling factors to tackle AMR
• Technical and service innovation in multiple areas is critical and cuts across all aspects of a global action plan
• Engagement with other organizations, systems and stakeholders is a prerequisite to successful implementation.

The Advisory Group also highlighted for inclusion in a global action plan: (i) the need for better data and data sharing; (ii) preservation of antimicrobial effectiveness through optimizing their use; (iii) hygiene measures and prevention of infection; (iv) innovation in both technology development and health services; (v) social mobilization. Specific points for consideration in each of these areas, including tools that could facilitate implementation of action plans, are listed in Annex 1.

The Advisory Group recognized that there will be many challenges in addressing the public health threat from AMR.

These include:
• Establishing focal points and leadership on AMR within Member State governments and other organizations
• Increasing capacities within laboratories and medicines regulation
• Improving transparency and data sharing
• Balancing equitable access with optimal use, and addressing other regulatory issues such as unregulated sales (“over-the-counter” (OTC) and internet) and substandard/spurious/false-labelled/falsified/counterfeit (SSFFC) products
• Addressing the needs of populations that have limited or no access to stable or basic health systems, including to antimicrobial medicines
• Moving away from “business as usual” by introducing innovative thinking across all topics
• Changing some cultural patterns and social norms, particularly in the way in which antimicrobial medicines are used and perceived.

Role of WHO

The Advisory Group recommended that the priorities for WHO, in developing and implementing a global action plan for AMR, should be as follows:

1. **Develop and implement a global action plan for AMR** with Member States, other partners and stakeholders.
2. **Support and guide Member States to develop and implement national action plans and policies** for AMR. Within this, WHO should work with Member States to
develop and put in place appropriate targets and outcome indicators that can be built into national, regional and global plans.

3. **Provide technical support to Member States through the setting of norms and standards** and promoting and monitoring their implementation based on national policies.

4. **Shape the public health research agenda for AMR** to identify needs, gaps and opportunities for technical and service innovation and to stimulate the generation, translation and dissemination of valuable knowledge.

5. **Partner with other organizations** to empower and engage all sectors to contribute to the development and implementation of a global action plan for AMR, including:
   - The economic sector (burden of disease and its economic impact)
   - Life sciences industries, laboratory services, professional groups (diagnostics and other areas of technical innovation, as well as novel antibiotics)
   - Animal/agriculture/environment sectors including FAO, OIE, UNEP (on data, and preservation)
   - Development agencies
   - Regional political (government) and professional groups
   - Research funders
   - Knowledge-based sector including academia, health agencies, major projects and programmes (on knowledge development, application and innovation)

The Advisory Group identified a number of specific recommendations for WHO to consider to support the above five priorities.

1. **Strengthening data and knowledge sharing**
   - As a priority, establish a baseline assessment of capacity, action plans and policies at country and regional levels.
   - Strengthen laboratory capacity by providing reliable data through standard procedures within a quality assured system.
   - Develop norms and standards for collection and reporting of antimicrobial resistance and antimicrobial use in the human and animal sectors. These data should provide the basis for regular global reports to guide policies and action plans, and monitor their effectiveness.
   - Draw on the resources of the planned Global R&D Observatory to assess research relevant to AMR.
   - Strengthen tools and guidance on monitoring of disease burden attributable to AMR (including guidance on application of provisions for AMR within the ICD-11 coding).
   - Education at all levels (professionals and public).

2. **Prevention of infection**
• Give priority to renewed advocacy, awareness and promotion of sanitation, hygiene and infection prevention and control practices.
• Promote best practice and collection of evidence to support implementation of infection prevention strategies (including use of vaccines).

3. **Preservation**

• Work with regulatory and other networks to develop and implement a regulatory framework to ensure optimal use of antimicrobials. This should include an emphasis on use of diagnostics and better diagnosis, removal of unregulated sales (OTC and internet) and may include a special regulatory classification for (some) antimicrobials.
• Work with FAO and OIE to limit antibiotic use and to end antibiotic use for non-therapeutic purposes in livestock and agriculture. Work with other sectors to reduce waste, inappropriate disposal and environmental contamination of antimicrobial medicines.
• Apply the Member State mechanism on substandard /spurious /falsely-labelled /falsified/ counterfeit (SSFFC) medical products to antimicrobial medicines.

4. **Technical innovation**

• Work with life science industries, academia and other sectors to facilitate (i) the development, evaluation and application of diagnostics and diagnostic tools and (ii) the development, evaluation and application of new treatment and prevention options, including new business models to encourage investment and controlled distribution and use.

5. **Service innovation**

• Identify and promote best practice and collection of evidence to encourage innovation in service delivery, and social mobilization.
• Work with Member States to identify and foster networks and centres of excellence that can provide technical and service leadership at national, regional and global levels.
• Work with Member States and other partners to identify innovative mechanisms to support capacity development at a country level.

6. **Social mobilization**

• Support Member States to build capacity, and develop continuous health promotion, education and communication programmes that can change culture, understanding and demand for antimicrobial medicines.
Annex 1. Points for consideration in development of a global action plan for AMR.

Improved and available data and knowledge:

- Improvements in the quality, availability and accessibility of data, in particular on the health and economic burden of AMR, are urgently needed in order to support policies and plans and to monitor the effectiveness of interventions.
- Standardization in data collection and reporting is imperative across all relevant sectors, for epidemiological and microbiological data alike, as well as for data on antimicrobial drug use at the country level. Quality assurance and accreditation schemes should be supported.
- An early warning system, based on an internationally agreed mechanism, should be instigated as rapidly as possible, to detect outbreaks/events as well as new mechanisms of resistance.
- Improved understanding of the causal factors surrounding AMR, including medical practice and behaviour/beliefs, among practitioners and the lay public, will lead to more effective interventions.
- Use of information gathered by the Global R&D Observatory to support innovation, research and evaluation, should be explored.
- Outcome and impact indicators are required in order to monitor progress and evaluate the impact of actions/interventions.

Preservation of existing antimicrobials (appropriate use, improving use, responsible use, conservation):

- Promoting the optimal use of existing antimicrobials, while ensuring equitable access to patients who need them, will help to preserve their benefits.
- Inappropriate incentives to prescribe, over the counter sales and internet sales should be eliminated.
- Greater emphasis should be placed on the development, availability and use of rapid diagnostics to enable optimization of treatment and antimicrobial use. A global meeting on diagnostics and diagnosis could be convened to consider the technical/clinical aspects, economic implications, implementation bottlenecks, and public and professional behaviour changes needed in this area.
- The role that governments, professional bodies and businesses could play in the development of a code of conduct should be explored.
- Possible changes in regulation relating to quality (and use of existing mechanisms such as SSFFC), advertising, and promotion of antibiotics should be considered.
Strategic and Technical Advisory Group on Antimicrobial Resistance: Report of first meeting

**Strengthened prevention:**

- Greater emphasis should be placed on prevention, including strengthening hygiene and infection prevention and control measures, improving sanitation and access to clean water, and exploring a more widespread use of vaccines.

**Technical innovation:**

- Technical innovation is needed in all areas, including preservation of existing benefits, drug development, vaccines and rapid diagnostics at point of care and other diagnostic tools. Similarly, innovation in business models and funding/financing mechanisms, such as PPP, for research, and the development and use of new health technologies is needed.

**Service innovation:**

- Innovation in services is required alongside technical innovation, to drive the development and implementation of national policies and plans.
- Other potential service innovations include: AMR indicators as criteria for accreditation of health facilities, institutions and laboratories; incentives; institutional development; capacity building and professional development; training; and staff retention.
- Universal Health Coverage, based on equitable access to quality health care, could provide an opportunity to promote optimal use of antimicrobials and prevent the emergence and spread of AMR.

**Social mobilization:**

- A change in the perception and culture of antimicrobial use is needed, among professionals (from all relevant sectors) and public alike. Education, advocacy and social marketing initiatives should be developed based on the principles of dignity and solidarity. Patient groups will be key stakeholders, in particular in addressing demand management, balancing equitable access with appropriate use.

**Tools (mechanisms) that can be employed:**

A number of new and existing tools and mechanisms were considered, from a variety of different sectors and sources, that could potentially be applied to AMR.

These included:

- A new Code of Conduct to address the supervision of appropriate clinical use of antimicrobials. The Code could potentially be applicable to governments, health professionals and the private sector. Alternatively, existing codes of conduct could be adapted to include AMR.
- Enhanced use of existing surveillance networks.
- New and existing platforms for information exchange and as repositories of tools and best practice, using innovative technologies such as the internet and social media.
- The outreach role of the UN family (along with other IGOs and NGOs), WHO regional/country offices and regulatory authority networks (e.g. ICDRA SSFFC).
• Classification of antimicrobials as a global public good, rather than as simply a commercial commodity, as a means to encourage greater control and better use of antimicrobials.

• The list of “Critically Important Antibiotics” for human use only, that, if adhered to more widely, could help impede the development of resistance associated with husbandry practices.

• Use advocacy tools such as the antibiotic awareness day/week and other health days.

• Regional and global “Declarations” as expressions of long term government and public commitment to change.

• Dissemination of examples of good practices and their impact on AMR.

• Building on the value of academic networks, professional societies, patient associations, nongovernmental organizations and other civil society groups as agents for change.

• The International Health Regulations (2005) as a means to build on core competencies and improve early identification of emerging threats, outbreak response and communication.
ANNEX 2: TERMS OF REFERENCE OF STAG–AMR

Functions
The STAG–AMR is the principal technical advisory group to WHO on antimicrobial resistance (AMR). It will advise the WHO Director-General on:

- WHO's strategic plan and priority activities to tackle AMR consistent with WHO’s mandate and considering the comparative advantages and the respective roles of partner organizations, and with special focus on aspects that cover different pathogens;

- The major issues and challenges to be addressed by WHO with respect to achieving the strategic goals for AMR;

- The engagement of partners and outreach efforts to tackle AMR.

Membership
Members of the STAG–AMR will be selected and appointed by the Director-General on the basis of their technical expertise and scientific and public health experience. In the selection of the members, consideration will be given to attaining an adequate technical distribution of expertise, geographical representation and gender balance.

The STAG–AMR shall have no more than 20 members, including the Chair, who shall serve in their personal capacities to represent the range of disciplines including those relevant to public policy development and implementation for AMR control, monitoring and surveillance, research and development, community and civil society engagement and health systems strengthening necessary to properly advise on all aspects of WHO’s AMR work.

The STAG–AMR Chair will be appointed by the Director-General for an initial period of three years.

The duration of the initial appointment of each member will be three years. All members will be eligible for one reappointment for a duration of one to three years. After the initial three years of the STAG–AMR, one third of the members will be replaced every year; replacements must maintain the equitable representation of the six WHO regions. In the event of resignation or incapacity of a member for any reason, the Director-General will appoint a replacement member with a view to maintaining the equitable representation of the six WHO regions. The replacement will complete the term of the previous member and be eligible for one reappointment.

Members must respect the impartiality and independence required of WHO. In performing their work, they may not seek or accept instructions from any Government or from any authority external to the Organization. They must be free of real, potential or apparent conflict of interest. To this end, proposed members/members will be required to complete a declaration of interest form and their appointment, or continuation of their appointment, will be subject to the evaluation of completed forms by the WHO Secretariat, determining that their participation would not give rise to a real, potential or apparent conflict of interest.
Roles and responsibilities of STAG–AMR Members

Members have a responsibility to provide WHO with high quality, well considered advice and recommendations and to be committed to the development and improvement of public health.

Members play a critical role in ensuring the reputation of STAG–AMR as an internationally recognised advisory group in the field of AMR.

The group has no executive or regulatory functions, it is solely to provide advice and recommendations to the Director-General of WHO.

Operation

The WHO PED Department will serve as the Secretariat to the STAG–AMR.

The STAG–AMR will usually meet at least once per year. WHO shall provide any necessary scientific, technical and other support for the STAG–AMR. WHO may convene additional meetings, including through teleconferences and videoconferences, on an ad hoc basis, as decided by the Director-General.

STAG–AMR Working Groups may be established as agreed upon by WHO and as resources allow, to increase the effectiveness of STAG–AMR. These Working Groups will function for a time limited basis to help address specific questions identified by STAG–AMR.

In addition to the Members, STAG–AMR may recommend that selected experts be invited by the WHO Secretariat to attend STAG–AMR meetings as advisors on specific issues when their technical collaboration is required.

Representatives from major organizations, institutions and other stakeholders involved in AMR activities may be invited by the WHO Secretariat to STAG–AMR meetings as observers.

The report of the STAG–AMR meetings will be submitted to the Director-General. All recommendations from the STAG–AMR are advisory to WHO, who retains full control over any subsequent decisions or actions regarding any proposals, policy issues or other matters considered by the STAG–AMR. WHO also retains full control over the publication of the reports of the STAG–AMR, including whether or not to publish the reports.

Information and documentation to which members may gain access in performing STAG–AMR related activities will be considered as confidential and proprietary to WHO and/or parties collaborating with WHO. STAG–AMR members shall not purport to speak on behalf of, or represent, the STAG–AMR or WHO to any third party. All proposed members will be required to sign an appropriate confidentiality undertaking and provisions on ownership.

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6 A public web page for the STAG-AMR has been established on the WHO website (at http://www.who.int/drugresistance/stag/en/index.html ) on which information on meetings and membership, as well as meeting reports will be published by the Secretariat.
ANNEX 3: LIST OF PARTICIPANTS

Members of STAG–AMR

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