Consultation on a draft Global action plan to address antimicrobial resistance

The questionnaire is divided into four sections. The questions are broadly framed and intended to give you the opportunity to enter into some depth and explain your organization's viewpoint. While only questions marked with * are mandatory, we would appreciate answers to as many as possible. Where a choice of answer needs to be selected please highlight your answer.

Before answering the questions, please refer to our list of supporting documents.


About you

1. Name of individual respondent*
   (deleted)

2. Email address* (preference for official email addresses)
   (deleted)

3. Are you authorised to represent your organization or interest group?* Y

4. Organization Name*
   Society for Applied Microbiology

5. Address of the organization*
   Bedford Heights, Brickhill Drive, Bedford, MK41 7PH

6. Organization website (if available)
   www.sfam.org.uk

7. Country*
   UK

8. Type of Organization*
   • Other (please specify)
     Learned society

9. Main sector of interest
   • Human health
   • Animal health
   • Finance/economics
   • Agriculture or food
   • Environment
• Communication, education and community
• Other (please specify)
  All of the above

10. Would you like to be added to our mailing list to receive updates on the development of the global action plan?* Y

General questions

1. From the perspective of your organization, what are the most important areas of concern in AMR?

• Rise in resistant infections in humans and animals

  More patients are presenting with antibiotic-resistant infections and there are now several common infections that are resistant to multiple drugs (tuberculosis, gonorrhoea, Staphylococcus, Enterobacteriaceae, enterococcus). The incidence of sepsis associated with drug-resistant organisms, particularly members of the Enterobacteriaceae is on the rise, also, which in the UK kills more people than lung cancer, and about double the number that die from bowel cancer. Without effective antibiotics and measures for infection prevention and control, this will continue to rise. Furthermore, treatment of AMR infections necessitates prolonged hospital stay increasing costs, reducing available beds and increases risks of nosocomial infections.

  From a veterinary perspective, this could also result in untreatable infections which may result in welfare issues, reduced yield, and increased culling. All of these would have a serious economic impact on the farming sector.

• Sustained absence of new drug development

  There has been no new class of antibiotics for over 20 years and our current armoury is weakening, as evidenced by:

  o Widespread emergence of resistance to third-and fourth-generation cephalosporins in both pathogens and non-pathogens, resulting in community outbreaks of Escherichia coli exhibiting resistance to such antibiotics, with numerous fatalities.
  o Emergence of resistance to carbapenem antibiotics in already multiple drug-resistant pathogenic bacteria, predominantly in countries in the Indian sub-continent, thus making infections with such strains almost untreatable.
  o Recent appearance of resistance to carbapenem antibiotics in Acinetobacter spp, Salmonella enterica and E. coli in food animals in some European countries and among wildlife.
  o Emergence of extensively drug resistant tuberculosis (XDR-TB).
  o Detection of MRSA strains with varying levels of resistance to vancomycin (from vancomycin intermediate to vancomycin resistant).
  o Increase in essentially untreatable gonorrhoea.
• Lack of scientific data to provide an understanding of the impact on resistance of the release of antibiotic residues into the environment.
  
  o This can be an unavoidable result of legitimate treatment but there is little understanding of its importance in maintaining or creating resistant populations.

2. Is your organization currently involved in work related to AMR? Y

If Yes, How?

Members of our Society are engaged in research and development relating to AMR, as well as clinical/veterinary microbiology, surveillance, and policy development at both national and European level.

We are also part of a policy working group comprising several UK learned societies. This group is working closely with the UK funders’ forum on AMR and planning complementary work, including a workshop for early career researchers, in early 2015.

Questions about the draft global action plan outline document

Before the WHA resolution was adopted, two WHO AMR Strategic Technical Advisory Group (STAG) meetings were held in anticipation, which included members plus a large number of representatives from other organizations. These meetings identified key issues, concerns and led to the development of a draft outline.

As this consultation progresses and stakeholder meetings are held, the secretariat will harvest and incorporate the input into the draft global action plan.

1. How would you rate your understanding of WHO’s intention in the development of a global action plan to address AMR?

  Fair

  Additional comments

  The principles are fairly clear, but the intention for action is not. Similarly, new initiatives do not seem to have been highlighted or given prominence.

2. From the perspective of your organization, are the major issues relating to AMR outlined in the draft global action plan? Y

If No, what additional issues need to be addressed?

Questions on the ‘Building blocks’ described in the draft outline.
You will notice, the global action plan has been constructed around “building blocks” in recognition that different countries will have different starting points. In this situation, countries can choose building blocks to concentrate upon. Each building block specified has been identified as a key area where specific attention, planning and work are needed to achieve progress in addressing AMR. Through questions in this section, we would like to hear your opinions on these building blocks in more detail.

I. Building block-1: Increasing awareness and understanding about AMR and of the actions and changes needed

a) What do you consider to be the main issues under this priority?

There is a need for clarity of expectation between doctor and patient, particularly in the context of the GP consultation. Recent data suggests that doctors perceive a greater pressure from patients to prescribe than actually exists (http://www.sfam.org.uk/en/news-features/news/index.cfm/only-6-percent-of-patients-admit-pushing-GPs-for-antibiotics-but-they-still-over-prescribe)

There is also a need for evidence-based action in developing measure to combat the overuse of critically important antibiotics for human medicine in food production animals, particularly off-label usage, not only in the UK and Europe, but also world-wide.

b) What are the main actions that needs to be done -- and who are the main actors/stakeholders who need to take action -- to go beyond the status quo?

- In service training for GPs,
- Public education campaigns,
- Revision of AMR and antimicrobial use (AU) in medical/veterinary training programs,
- National surveillance of AMR and AU to improve understanding of drivers and outcomes
- Stakeholders: in the UK, committees such as the Specialist Advisory Committee on Antimicrobial Resistance (SACAR) – predominantly human issues; the Defra Antibiotic Resistance Coordination Group (DARC) – predominantly food animal issues; and the ACMSF Antimicrobial Resistance (AMR) Working Group – food-related issues; all monitor and advise Government on relevant AMR issues (note SFAM members are members of, or contribute to these groups on a regular basis).

- Outwith the UK, key international agencies involved in the monitoring and control of AMR and the development of policies to combat AMR are the European Centre for disease Prevention and Control (ECDC) – human issues, the European Medicines Agency (EMA) – animal and European Food Safety Authority (EFSA) – food. As with the UK committees listed above, SFAM members contribute to AMR-related work undertaken by the above agencies.
c) What steps have already been taken to address this priority? (please provide references where possible)

Considerable efforts have been made in the UK to alert the public about the deleterious consequences of the prescribing of antibiotics by GPs for infections which do not warrant antibiotic treatment—e.g., respiratory tract infections. There are several initiatives underway in the UK to monitor antibiotic usage and the occurrence of antibiotic resistance in both the human and food animal population (described previously).


With regard to antibiotic usage in food production animals, antibiotic consumption in food animals is monitored on an annual basis by the EMA - European Surveillance of Veterinary Antimicrobial Consumption (ESVAC), and their findings are published annually (see ESVAC Report 2013). This report is of considerable value in providing evidence-based figures for action programmes. Regrettably, on a world-wide basis few other geographic groupings produce such figures.

**d) What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)**
• National indicators of AMR and AU and comparison with international indicators, however this approach is challenged by lack of standardisation of measures and methods, and lack of national programs in many instances.

• Development of coordinated national surveillance for AMR and AU

• Production of figures of antibiotic consumption in human and veterinary medicine on a world-wide basis as a means of assessing antibiotic usage in both areas and providing a measure of success of any control measures that may be initiated.

II. Building block-2: Identifying the most important approaches for preventing development of infections and the steps needed to move beyond guidance to more effective implementation of such approaches

a) What do you consider to be the main issues under this priority?

• Informed antimicrobial stewardship in medical and veterinary arenas.

• Many of the antibiotic resistant strains (Gram positive and Gram negative) are isolated from chronic wounds so careful management of these patients are important so they do not become a source of infection. Frequent debridement of the wound using non-invasive techniques (care here because aerosols can be produced) then topical application of antiseptic dressings until bacterial numbers are reduced, is effective. The wound then slowly heals.

• Understanding the epidemiology of spread of resistant organisms. For example, studies have shown patients leaving hospital to residential aged care facilities who later return to hospital reintroducing resistant organisms from the RACF. Clinical oversight and training of staff in an RACF is likely to be less robust than in hospital, with less attention to infection control measures.

• The prevention of infectious disease through appropriate hygiene and biosecurity, through the use of vaccines where available, and by appropriate nutrition and care of animals and humans, reduces the need for antibiotic use. In animal husbandry the use of alternative measures such as use of probiotics, improved nutrition and phage control are also being examined as alternatives to using antibiotics prophylactically.

• High hygiene standards during slaughter, processing and preparation of animal products (including dairy and eggs) is vital. This means education of food industry workers on compliance with legislation and enforcement where breaches have occurred is effective to reduce the spread of food borne pathogens. Food hygiene campaigns aimed at the general population are also effective to reduce the transmission of bacteria through the food chain.

b) What are the main actions that needs to be done -- and who are the main actors/stakeholders who need to take action -- to go beyond the status quo?

• Global co-ordinated multi-disciplinary approach

• Training and professional development of medical and nursing staff
- Revision of medical curricula by universities and colleges
- Development of appropriate policy framework by governments
- Development of healthcare indicators and inclusion in hospital and general practice accreditation programs to improve antimicrobial stewardship
- Revision of veterinary training programs with respect to the use of antimicrobials
- Work with industry bodies to improve the understanding and use of antimicrobials in animal husbandry
- Funding incentives to prolong the life of current antimicrobials and develop alternative methods to combat microbial infections

c) What significant work has already been done to address this? (please provide references where possible)

- The continued promotion of responsible use of medicines in agriculture, as carried out by the responsible use of Medicines in Agriculture Alliance (RUMA) in the UK, the European Platform for the Responsible use of Medicines in Agriculture (EPRUMA) and the OIE (World Organisation for Animal Health).

- In food animals, the withdrawal of antibiotics as growth promoters in the EU has been a highly effective measure in controlling the appearance and spread of some, mainly gram positive, organisms in food animals and thence their spread to humans through the food chain.

- Similar controls for the prophylactic use of certain antibiotics in food production may have some effect, but such measures need to be balanced against possible effects on animal health and on food production. A typical example is weaner pigs where antibiotic treatment is seen as a crucial preventative measure. This is one area where alternative approaches are being examined by industry eg probiotics. Parallel controls on the use of prophylactic use of antibiotics in humans should also be considered.

- For food animals, EU-wide legislative controls to reduce the occurrence of pathogenic bacteria such as *Salmonella* Enteritidis and *Salmonella* Typhimurium in poultry have been highly effective in reducing the occurrence of such bacteria, including antibiotic-resistant strains of these serovars, as these bacteria are frequently resistant to commonly-used antibiotics as a consequence of antibiotic use in certain food production animals.

- Of fundamental importance in controlling the occurrence and spread of antibiotic-resistant organisms is education. Many medical doctors prescribe antibiotics unnecessarily; veterinarians also often use antibiotics as a substitute for poor husbandry, thereby perpetuating the occurrence of antibiotic-resistant strains in the food chain.

- At the European level a consultation document on possible measures to reduce AMR in food production animals has recently been released for public consultation by a multi-agency ad-hoc expert group (Antimicrobial Advice *ad hoc* Expert Group (AMEG), convened under the auspices of the EMA, with comments to be received by 30th September 2014. A further multi-agency group - Joint Interagency Antimicrobial Consumption and Resistance (JIACRA), has been convened to investigate possible relationships between antibiotic usage and resistance development in both human and veterinary medicine. The first report of this group is scheduled to appear in December 2014.
What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)

- Development and promulgation of healthcare indicators that demonstrate appropriate infection control and management in hospitals and general practice
- Development of programs and measures to demonstrate the incidence of AMR and detect emerging risks in pathogens and commensals in animals and agriculture

III. Building block-3: Optimizing the use of existing antimicrobials for human and animal health and in agriculture

b) What do you consider to be the main issues under this priority?

- Rapid, accurate, bedside diagnosis for appropriate early prescription of the correct drug.
- Behaviour change, especially in the patient-GP relationship (See above)
- Development of appropriate and workable policy frameworks to manage the use of antimicrobials in agriculture
- Promulgation of evidenced based approaches to the use of antimicrobials in agriculture
- Education of agricultural organisations, owners, workers and managers

b) What are the main actions that needs to be done – and who are the main actors/stakeholders who need to take action – to go beyond the status quo?

- Training and professional development of medical and nursing staff
- Revision of medical curricula by universities and colleges
- Development of appropriate policy framework by governments
- Development of healthcare indicators and inclusion in hospital and general practice accreditation programs to improve antimicrobial stewardship
- Revision of veterinary training programs with respect to the use of antimicrobials
- Work with industry bodies to improve the understanding and use of antimicrobials in animal husbandry

c) What steps have already been taken to address this priority? (please provide references where possible)

d) What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)

- Development and promulgation of healthcare indicators that promote improved antimicrobial stewardship in hospitals and general practice
• Development of programs and measures to improve antimicrobial stewardship in agriculture

IV. Building block-4: Identifying and closing critical gaps in knowledge needed to address AMR

b) What do you consider to be the main issues under this priority?

• Major gaps in understanding

  o There is a severe lack of understanding of exchange of genes in the wider environment and what drives this.

  It will also be important to understand what resistance reservoir exists in normal human and animal commensal microbiota (even prior to any antibiotic exposure).

  We need to know:

  o What is the composition of resistance genes and/or resistant organisms in gut, skin, oral cavity etc. and how does this contribute to the emergence of resistant pathogens? How does antibiotic exposure alter this in the short and long term?
    • This could tell us the distribution of resistance genes, particularly those encoding resistance to critically-important antibiotics (CIAs), or antibiotics of last resort, in human and food animal ecosystems in non-pathogenic and pathogenic bacteria.

  o Extent of transmission of resistance genes from bacteria from humans (both pathogens and non-pathogens) to animals, and particularly animals bred for food.

  o Extent of transmission of resistance genes from bacteria from animals, particularly food production animals, to bacteria in humans.

  o Contribution of foods imported into the country to the spread of resistant bacteria to humans.

  o Effects of ‘off-label’ use of antibiotics in both human and veterinary medicine in the development and spread of resistance.

  o Can the burden of resistance be reduced by removing the selective pressure (e.g. by reducing prescription of antibiotics or reducing use in animal treatment)? This would require a large scale carefully controlled study.

  o The potential for metal resistance, particularly silver, as used in wound dressings.
    • Resistance in clinical isolates is seldom seen but exposure around silver mines and in other non-clinical settings is documented to confer resistance.
We know that a number of metal resistances are co-transmitted with antibiotic resistances on plasmids/transposons (genetic material) so the use of silver as an antimicrobial treatment in many different environments has the potential to start to select for resistant strains and could indirectly drive antibiotic resistance – this requires further investigation.

- Silver is synergistic with a number of antibiotics and therefore has the potential to be extremely useful if we can understand how to use it appropriately.

b) What are the main actions that need to be done – and who are the main actors/stakeholders who need to take action – to go beyond the status quo?

- Research programs in universities, hospitals, care facility, community and agricultural settings, supported by medical and veterinary colleges
- Translation of research evidence into practice
- Support of governments through policy and funding mechanisms

c) What steps have already been taken to address this priority? (please provide references where possible)

- Research programs in universities, hospitals, care facility, community and agricultural settings, supported by medical and veterinary colleges
- Translation of research evidence into practice
- Support of governments through policy and funding mechanisms

d) What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)

- The number of and level of investment in relevant funded research programs
- Measures of research outcomes
- Measures of research evidence translated into practice

V. Building block-5: Developing an innovative and sustainable approach to develop and distribute critical products and technologies needed to address AMR

a) What do you consider to be the main issues under this priority?

- In the past, pharmaceutical companies have been prepared to invest to find formulations that are both effective antibiotics and also discourage/minimise the evolution of resistance. That isn’t the case at present and there is relatively little R&D going on in this area. The reason appears to be the greater financial rewards available in developing other classes of drugs. This puts the onus on the UK government to fund antimicrobial drug development outside of the pharmaceutical companies and/or incentivise this work within the industry.

- It is also vital to first understand the drivers selecting for resistance, which may include as yet unknown factors. A quantitative risk assessment of the effects of different control measures in human and animal populations would provide the basis from which to develop new drugs that have the potential for greater longevity. There will always be a degree of selection pressure and as such bacteria remain ‘one step ahead’ but opportunities surely exist to minimise selection pressure and slow the development of resistance.
There is a recent Journal of Antimicrobial Chemotherapy article that provides detailed analysis of the proportion of total infection research spend dedicated to research into antimicrobial resistance ([http://jac.oxfordjournals.org/content/early/2013/09/13/jac.dkt349.full.pdf+html](http://jac.oxfordjournals.org/content/early/2013/09/13/jac.dkt349.full.pdf+html)). The paper also outlines some recommendations for future direction of R&D. In summary: despite the rapid emergence of antimicrobial resistance, the proportion of UK infection-research spend targeting this critical area remains small (3.9%; £102 million of £2.6 billion total spend). Mean annual funding ranged from £1.9 million in 1997 to £22.1 million in 2009. The study concluded that, whilst this is an encouraging indication of increased emphasis and investment in this important area of research, the UK government must continue to fund antimicrobial resistance research in a sustained, targeted manner.

In October 2012 a conference entitled “Antimicrobial Resistance in Human and Veterinary Medicine – one medicine, one problem?” was held in the UK. The conclusions of the symposium, which was organised by the Royal College of Veterinary Surgeons, the Royal College of Pathologists, and the Royal College of Physicians in association with the Health Protection Agency and the Veterinary Medicines Directorate, were as follows:

- Veterinary and medical professionals must work together under the banner of ‘One Health, One Medicine’ to tackle antimicrobial resistance in a social context
- The issue of acquisition, evolution and transmission of AMR is complex and involves human and domestic animal populations (both food animal species and non-food companion animal species), but also wildlife and the environment. It is important to understand how these factors interact, particularly with increasing international movement of people, food and animals.
- In an increasingly connected world, it is evident that any measures need to tackle global use. The probability that selection for resistance will occur where antimicrobial usage is highest and least controlled, coupled with unprecedented mobility of humans, means that, whether AMR originates from animal use or human use, the threats in Britain and in Europe will often emanate from outside.

b) What are the main actions that needs to be done – and who are the main actors/stakeholders who need to take action – to go beyond the status quo?

- Development of drivers to promote research and development (in the context of commercial market failure)
- Development by governments of policy frameworks, and potentially funding, to drive development
- Exploration of the potential for altruistic benefactors and organisations to contribute to development

e) What steps have already been taken to address this priority? (please provide references where possible)

f) What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)
Level of investment in the development of new antimicrobials and technologies

VI. Building block-6: Assessing the long term economic, developmental and social costs and implications of AMR as a basis for sustainable investment and action

a) What do you consider to be the main issues under this priority?
   - A sound research design for cost assessments that links to priorities and drivers for industry and government

b) What are the main actions that needs to be done -- and who are the main actors/stakeholders who need to take action -- to go beyond the status quo?
   - This potentially needs a ‘round table’ approach involving industry, governments, academics and medical and veterinary professionals to develop models that are meaningful to a range of stakeholders

c) What steps have already been taken to address this priority? (please provide references where possible)

d) What are concrete and measurable indicators of progress for this priority? (Including, for example, global and national goals to be achieved within 2, 5 and 10 years)
   - Establishment of working group(s) to develop and evaluate cost models

Concluding questions

3. What contribution would your organization be able to make in implementing the global action plan?
   - Act as a conduit between the WHO, governments, learned societies and professionals at the national and EU level
   - Provision of professional development and training opportunities
   - Assist in the development and/or review of strategies and measures

4. Additional input that you feel would be facilitate development of the GAP.
   - Of paramount importance is controlling antibiotic usage in countries in the Far East. Antibiotics are used freely in these countries in both human and veterinary medicine, often with formulations that have not been subject to proper regulatory controls. This usage has undoubtedly contributed to the appearance of, and subsequent worldwide spread of organisms resistant to CIAs and last-resort antibiotics.
   - Environment pollution around factories producing antibiotics has been reported – see *Environmental Toxicology and Chemistry*, Vol.28, No.12, pp. 2522-2527. Global regulation and compliance with respect to groundwater and drinking water is essential.