Royal Society of Chemistry Response to the House of Commons Science and Technology Committee "Call For Evidence: Antimicrobial Resistance"

The Royal Society of Chemistry is the world's leading chemistry community, advancing excellence in the chemical sciences. With 48,000 members and a knowledge business that spans the globe, we are the UK's professional body for chemical scientists; a not-for-profit organisation with over 170 years of history and an international vision of the future. We promote, support and celebrate chemistry. We work to shape the future of the chemical sciences – for the benefit of science and humanity.

The Royal Society of Chemistry welcomes the opportunity to respond to the House of Commons Science and Technology Select Committee 'Call for Evidence: Antimicrobial Resistance'. We have chosen to comment on those areas that we feel are of particular relevance to the chemical sciences, and have therefore chosen not to comment on aspects relating to public health trends, behaviour and antimicrobial administration practices.

Key Recommendations

- Addressing antimicrobial resistance (AMR) requires a strategy that involves long-term investment and support for fundamental research across a range of disciplines. Chemistry expertise will be vital for: (1) improving drug discovery, (2) developing a better molecular understanding of infectious diseases, and (3) breakthroughs in diagnostics. Only by developing new drugs and diagnostics will we be able to overcome antimicrobial resistance in the long term.

- There is a need to incentivise academics, SMEs and pharmaceutical companies to engage in antimicrobial research. This could be achieved by providing funding which allows risk-sharing between public and private enterprises, and supporting cross-sector collaboration. Public Private Partnerships (PPPs) are one example of a mechanism to facilitate this as well as a *Therapeutic Centres of Excellence* model.

- Drug discovery expertise within the UK must be integrated within research groups focused on developing new antimicrobials, innovative diagnostics and novel therapies. The importance of co-locating fundamental research with clinical knowledge will ensure that new and effective antimicrobials can be developed efficiently.

- Collaboration and global coordination are crucial for ensuring success in tackling antimicrobial resistance, particularly within research. Governments and professional bodies must encourage collaboration and open data sharing so that research can be more efficient and effective.

Q1. How has antimicrobial resistance developed in the past decade?

No comment

Q2. What are the gaps in our knowledge about antimicrobial resistance?

1. A deeper understanding of the molecular basis of resistance mechanisms in bacteria and other microbes is needed. Gram negative bacteria pose a particular threat due to their heightened resistance to many existing antibiotics. Uniquely, chemistry has the potential to provide a better molecular-level understanding of the biology of bacterial infection and resistance; this is essential for identifying and validating new antibacterial drugs. We also need to develop new tools to allow us to investigate these biological mechanisms. We need to move beyond simply identifying the structure of biological molecules towards gaining a fuller understanding of mechanisms of action and the molecular pathways of infection and disease.

2. We also require new diagnostic tools, including "point of care" diagnostics, to detect disease earlier and more accurately. This is central to tackling AMR, since the use of broad-spectrum antibiotics due to uncertainty in diagnosis has led to increased resistance. The role of chemical scientists - for example, in identifying unique biomarkers and molecular imaging techniques - is pivotal to developing these new tools for diagnosis. Better diagnostics will also allow for more effective clinical trials by ensuring trials are targeted at the correct patient groups.

3. We need to improve biological target validation and screening techniques to ensure fewer drug candidates fail in development. We also need to take novel approaches to fighting AMR, such as developing drugs which inhibit specific resistance mechanisms. In addition, emerging areas such as nanotechnology and colloid chemistry could provide promising new approaches to tackling resistant microbes. Chemistry expertise is central to all of these programmes.

4. Addressing the gaps in our knowledge about AMR will require a multidisciplinary landscape of researchers including, but not limited to, chemists, microbiologists, biochemists, pharmacologists and clinicians. Chemistry has a vital role to play, which has been described in detail in *Chemistry for Better Health*, a white paper from the Chemical Sciences and Society Summit (CS3) 2011[1].

Q3. Is there sufficient research and investment into new antibiotics or other treatments and methods to ensure continued protection against infection? If not, how could this be rectified?

5. We must commit to a long term global strategy for developing new antimicrobials. We cannot safeguard against infection without long-term commitments to funding research into new antimicrobials, diagnostics and novel approaches to tackling infectious diseases. The inherent need to fight infection with antimicrobial drugs leads to resistance and this is unavoidable. Therefore there will always be a need for new therapies to ensure we do not return to a "pre-antibiotic" era in healthcare.

6. Large scale, ring-fenced funding must be provided in order to tackle AMR effectively. Due to several factors, discovering and inventing new antimicrobials, and in particular antibiotics, is a challenging and lengthy process which provides little incentive for

[1] Chemistry for Better Health: a white paper from the Chemical Sciences and Society Summit (CS3) 2011

researchers to pursue antimicrobial drug discovery programmes. These include: (i) a low return on investment, (ii) regulatory hurdles, (iii) a high attrition rate during development, (iv) a lack of new leads for novel families of antibiotics, and (v) most antibiotics will be reserved for small subgroups of patients.

7. Many individual pharmaceutical companies have moved away from antibiotics development over the past decade. Though academic groups and SMEs are beginning to move into the field, there is insufficient research to ensure we are able to combat emerging resistance through the development of new antimicrobial drugs.

8. Long-term investment and support for fundamental research across a range of disciplines is required. There is a role for strategic cross-council research funding here that reflects the multidisciplinary nature of antimicrobial research.

9. Investment is required in the exploration of natural products from plants, fungi and bacteria as potentially valuable sources of novel antimicrobials. Currently, natural product research is under-funded and has been significantly scaled-down in recent years. Earlier this year, anthracimycin, which has been shown to be effective against methicillin-resistant *Staphylococcus aureus* (MRSA) in mice, was discovered in a Streptomyces species found living in the waters off the coast of California.[2] This example demonstrates the potential impact that natural-product-related research could have on the future discovery and development of new antimicrobial compounds.

10. Commercialisation is a significant challenge. The Royal Society of Chemistry outlined how the difficulties in bridging the "valley of death" could be addressed in our recent response to the House of Commons Science and Technology Select Committee Inquiry, 2012.[3] Many of the recommendations made are relevant to antimicrobials research. In addition, bespoke, targeted funding sources which actively encourage collaboration and knowledge sharing across disciplines could help to ensure that promising fundamental research is translated into effective therapeutics and diagnostics.

11. The public and private sectors must take a joint approach to funding antimicrobials research, for example via Public Private Partnerships (PPPs). PPPs can provide an effective financial risk-sharing mechanism to encourage involvement in R&D, and could transform the way new drugs are discovered and developed. There are already examples of PPPs in the UK: the Structural Genomics Consortium (SGC) at the University of Oxford supports research towards the discovery of new medicines through open access research. It is supported by several private investors and public funders including, amongst others, GlaxoSmithKline (GSK), Janssen, Takeda, Pfizer, the Wellcome Trust and the Canadian Institutes for Health Research. The Biomedical Catalyst Fund, a joint initiative run by the Technology Strategy Board and the Medical Research Council, provides support to SMEs and researchers to develop solutions to

[2] Jang, K. H., Nam, S.-J., Locke, J. B., Kauffman, C. A., Beatty, D. S., Paul, L. A. and Fenical, W. Angew. Chem. Int. Ed., (2013) 52: 7822–7824

[3] Bridging the "Valley of Death": Improving the commercialisation of research, RSC, House of Commons Science and Technology Select Committee inquiry 2012

healthcare challenges including the investigation of new approaches to antimicrobial resistance. This initiative endeavours to bring together life science companies to foster a culture of open innovation.

12. PPPs have the additional benefit of facilitating interdisciplinary education and mobility of researchers. The current changes in the UK pharmaceutical industry provide an opportunity to ensure that world-leading drug discovery capability is embedded within research centres, and PPPs should play a major role in achieving this. With this in mind, the Royal Society of Chemistry is championing a *Therapeutic Centres of Excellence* model. This model aims to bring fundamental and clinical research closer together, by embedding drug discovery groups within existing centres of clinical excellence.

13. SMEs are playing an increasingly important role in antimicrobials research. Funding must reflect the needs of these groups, so that there are adequate incentives and support for SMEs to engage with antibiotics research. The inclusive nature of PPPs should have an impact on SMEs by reducing the risk involved in taking part in antimicrobials R&D.

14. The Royal Society of Chemistry welcomes several new initiatives that will support research relating to antimicrobial resistance, some of which take novel approaches to addressing the current issues (mentioned above) which are inhibiting the development of new treatments. Examples of these are:

    a. the **Innovative Medicines Initiative (IMI) call for proposals entitled "Combating Antibiotic Resistance: New Drugs for Bad Bugs" (ND4BB)**[4] which will support academia-industry networks, increase data exchange and improve the design of laboratory tests and clinical trials. It aims to create cross-sector networks of researchers at universities, institutes, SMEs and large pharmaceutical companies throughout Europe. The Royal Society of Chemistry has previously identified this approach as crucial for improving drug discovery success rates. While we welcome this initiative, it is not clear how drug discovery expertise will be integrated within the academic groups involved. It is also important that the wider antibiotics research community that does not have access to valuable outcomes from ND4BB will benefit from outcomes of the initiative.

    b. GSK has recently joined forces with the US Government's Biomedical Advanced Research and Development Authority, in a **$200 million project over 5 years with the aim of developing new drugs to combat antibiotic resistance**. Crucially, the project is not focused on a single candidate compound but instead will allow resources to be reallocated to support the most successful leads identified during the discovery process.

    c. **Pharmasea** is a large-scale, four-year project backed by more than €9.5 million of EU funding which brings together a broad international,

[4] http://www.imi.europa.eu/content/8th-call-2012

interdisciplinary team of academics, industry researchers and specialists focused on marine biodiscovery[5]. The project includes 24 partners from across industry, academia and non-profit organisations in 14 countries. The project aims to identify marine microbial strains from extreme environments and assess their potential as drug leads, including as antibiotics.

15. While these funding initiatives are welcomed, further commitment is needed to ensure the future of antimicrobials research in the UK. Investment and support for antibiotics discovery must be long-term in order to allow continuity and flexibility within programmes. Providing funding for a portfolio of projects over longer time periods, rather than single, short-term projects, has the potential to lead to both better distribution of available funding and the successful development of an antimicrobial drug pipeline. The initiatives mentioned above are relatively short term (the IMI call ND4BB lasts for 6 years from 2012) which may mean that these projects are terminated before they are able to deliver a significant impact. To begin with, antimicrobials must form an important part of Innovative Medicines Initiative 2 (IMI 2), but there is no current guarantee that they will.

Q4. What measures (including behavioural change) have been most effective in controlling the spread of resistant pathogens, and could such measures be used to control other pathogens?

No comment

Q5. What global coordination and action is required to fight antimicrobial resistance and is the UK contributing enough towards cross-border initiatives?

16. An open source approach to antimicrobial research will ensure efficiency and avoid redundancy and duplication of research efforts. It is important that the drug discovery environment supports open sharing of data and knowledge within the global research community. There are examples in areas of Neglected Tropical Disease (NTD) such as Medicines for Malaria Venture (MMV), Drugs for Neglected Disease initiative (DNDi) and the Council of Scientific and Industrial Research Open Source Drug Discovery (OSDD) initiative. A worthwhile exercise would be to reflect on lessons learned from NTD programmes, using both negative and positive outcomes, to shape our approach to an antimicrobial resistance strategy. At the same time, work on NTDs would greatly benefit from the results of an effective AMR Strategy.

17. There are already several initiatives aiming to provide open chemical data which are important for tackling AMR. It is important that initiatives such as these are fully supported and that researchers are encouraged and incentivised to engage with them. Examples of these programmes are:
    a. Open PHACTS, a European Consortium of 28 partners resulting from a partnership between IMI and the European Federation of Pharmaceutical Industries and Associations (EFPIA), provides an integrated platform of

[5] http://www.pharma-sea.eu/

publicly available pharmacological and physicochemical data, and is available to SMEs as well as large pharmaceutical companies and academics[6].

b. The National Chemical Database (NCD) provides a suite of commercial databases of a range of different chemical compounds, all of which are available to all UK academic institutions[7]. The Royal Society of Chemistry is developing the NCD to provide a repository for chemistry data and provide tools and services to increase the value and availability of research data.
c. ChemSpider is a chemical database containing both structures and reactions, which is available for free online, and is a valuable resource to drug discovery programmes[8]. For example, ChemSpider provides much of the physiochemical information within the Open PHACTS Discovery Platform and for the PharmaSea project.

18. No single government can address the threat of antimicrobial resistance, so a global strategy, coupled with widespread collaboration, will be crucial to success. Current joint initiatives such as the EU/US Task Force on antimicrobial resistance are welcomed and we feel the UK Government has been exemplary in leading discussions so far. However, senior government interest from other countries is vital so that achievements are not compromised by lack of engagement from other countries. The UK is in an excellent position to engage in, and influence, high level discussions to explore how a truly global, coordinated, concerted effort can be made to develop new therapies. This could be facilitated through an umbrella group such as Antibiotic Action[9].

19. Learned societies and professional bodies have an important role to play in facilitating collaboration and supporting networks of researchers across the wide range of sectors involved in antimicrobials research. For example, the Royal Society of Chemistry has organised and delivered several pre-competitive workshops, in collaboration with other Learned Societies, to facilitate productive discussion of key issues of relevance to antimicrobial research, such as improving target validation, the utilisation of computer aided drug design and facilitating collaborations in the area of diagnostics.

Q6. What are the strengths and weaknesses of the Government's 2013-2018 strategy for tackling antimicrobial resistance? What changes might be made to further strengthen the Government's action plan?

20. A major strength of the Government's strategy is that it recognises the broad scope and interdisciplinary nature of both the problems facing us and the solutions that are required. In particular the Royal Society of Chemistry welcomes:

    a. The identification of such a wide range of relevant scientific research, including drug discovery, diagnostics, genomics, epidemiology, transmission

[6] http://www.openphacts.org/about-open-phacts
[7] http://cds.rsc.org/
[8] http://www.chemspider.com/About.aspx?
[9] http://antibiotic-action.com/

pathways, combination therapy and novel approaches such as pre- and probiotics. The Royal Society of Chemistry must reiterate that chemistry is critically central to tackling AMR and must be at the heart of a scientific strategy.

b. The recognition of the need for data-sharing, international industry-academia collaboration and improved incentives and regulatory regimes to address commercial viability. These are all factors which the Royal Society of Chemistry has identified previously as key for improving antimicrobial drug discovery success rates.

c. The identification of an important role for professional bodies and learned societies in facilitating collaboration and communicating important messages surrounding antimicrobial resistance. The Royal Society of Chemistry is committed to advancing the chemical sciences for the benefit of society and humanity.

21. We welcome the Government's strategy to tackle AMR but a longer term, global approach is needed for research and innovation (see responses to questions 3 and 5).

22. Monitoring of antimicrobial R&D is vital to identifying the most promising new technologies and ensuring funds are invested wisely, as well as to identify potential future issues within the drug R&D sector. The Government strategy suggests several detailed outcomes which will be monitored by expert Advisory Committees over the next five years. Appropriate monitoring of the R&D landscape should be included in this activity.