It has been six years since, at the World Health Assembly in Geneva in 2013, the UK Chief Medical Officer, Dame Sally Davies led the call for international action on antimicrobial resistance (AMR). It was a long awaited championing of the pending health crisis posed by AMR and a landmark moment that provided momentum for raising global awareness about the catastrophic threats that AMR poses for human health.

Whilst many know the scale and seriousness of ‘superbug’ infections, there remains much less certainty about what practical action to take next to address AMR globally. There is growing awareness across all sectors that a near unprecedented global response is needed to tackle AMR – a growing conviction aided by several positive developments: from last year’s publication of Jim O’Neill’s AMR Review recommendation, the 2016 United Nations General Assembly’s draft declaration, to the issue being aired again at this year’s meeting of the G20. The topic of AMR has finally fallen firmly under the political spotlight – yet the feeling remains, why aren’t we further down the road with our attempts to transform knowledge and political will into coordinated action?

The ambition for this short publication is to examine opportunities by which to increase momentum by shifting the line of enquiry from, “what is the problem?” to “how are we going to solve it?” The publication looks at how, through combined, co-ordinated and sustained efforts all sectors might work to combine their expertise to tackle antimicrobial resistance in efficient and sustainable ways.

CRITICAL RISK

The world’s most powerful bodies have made AMR a priority alongside the other top threats to our health, wealth, and security (i.e. climate change and terrorism). Unfortunately this is at a time when age-old alliances between the EU, the US, and the UK, are shifting. The effects of Brexit and the US Government’s refusal to sign the Paris Agreement attest to the risk of taking progress for granted and the political spotlight – no matter how bright – will not remain on AMR indefinitely. Failure to act and translate policy and commitments into actions could see progress wasted as political priorities shift and the non-binding nature of global agreements reduce the levers for change.

The past half-decade has produced a range of significant outputs led by politicians and world health policy bodies, figure 1 summarises some of these although the list is not exhaustive; outputs that are a reward of more than two decades of hard work in raising awareness about AMR by scientists and healthcare professionals across the globe. It is imperative that these outputs are distilled, digested, translated from paper to practice, expertise and reduce unnecessary repetition. Practitioners from across the globe, no matter what their economic landscape, will be able to access a range of tried and tested resources that can be adapted for local use.

Creating broad networks and a culture of support and cross collaboration is a key component of the global response to AMR. Such networks will offer opportunities for those within Europe and the northern hemisphere to support low and middle-income countries (LMICs), and in turn for LMICs to offer valuable lessons in how to achieve much from little.

NEW POTENTIAL ENABLERS FOR ACTION

Two emerging outputs if correctly harnessed and supported will greatly enable realisation of policy into practice; these are the Conscience of Antiicrobial Resistance Action (CARA) and World Health Organization’s AMR Community of Practice (AMR CoP). CARA is an independent alliance that seeks to support and monitor implementation of the UN declaration on AMR. Although still in its infancy, CARA is already working with civil society partners across human and animal health and agriculture under the One Health Agenda to look at how progress in implementing the

UN draft declaration can be quantified and measured. Independent accountability will be central to driving and sustaining the change that is needed.

[Whilst the WHO welcomes opportunities to publicise its work and has given permission for inclusion of details of the AMR CoP in this publication it is not an endorsement of any of the parties or associations herein mentioned.] One of the five GAP AMR objectives is to increase awareness and improve understanding of AMR through effective communication, education and training. WHO in 2017 has assembled an expert group on healthcare professional workforce education and training to address this important area. One of the recommendations from this group has been to establish a community of practice for AMR [AMR CoP] housing an AMR knowledge repository/toolkit and providing a facility for dialogue, exchange, sourcing of expertise and networking on AMR education.

AMR CoP is a necessarily bold and ambitious move by the WHO to establish a global community of practice. If successful it will build a pragmatic, dynamic community of practitioners able to share best practice, expertise and reduce unnecessary repetition. Practitioners from across the globe, no matter what their economic landscape, will be able to access a range of tried and tested resources that can be adapted for local use.

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EXAMPLES OF KEY POLICY AND LEGISLATIVE OUTPUTS IN RELATION TO AMR 2012-2017

2012

• Generating Antibiotics Incentives (GAIN) Act signed into law by US President

2013 - 2014

• World Health Assembly in Geneva - call for international action on AMR

• World Health Organization Strategic Action Plan on AMR published and supported by no less than 14 global, regional and national strategies across all continents

• Publication of national actions plans to tackle AMR commences – e.g. The UK S – Year AMR Strategy; The Chennai Declaration (India)

• AMR placed on Global Risk Register alongside terrorism and climate change

• The Review on Antimicrobial Resistance (AMR) commissioned by the UK Prime Minister. First report projects 50 million deaths pa from antibiotic resistance infections by 2050 – one death every 3 seconds

• Indian government amends the Drugs and Cosmetics Act 1940 to prohibit the direct sale of antibiotics to the public

2015

• World Antibiotic Awareness Week established to increase awareness of global antibiotic resistance and to encourage best practices among the general public, health workers and policy makers

• WHO Action Plan on antimicrobial resistance [GAP-AMR]

2016

• World Economic Forum event launch of the Declaration by the Pharmaceutical, Biotechnology and Diagnostic Industries on Combating Anti microbial Resistance (Davos agreement)

• The Review on AMR publishes final recommendations with 10 areas for action

• The UN General Assembly draft declaration on AMR – only the 3rd time in its 70 year history that a health topic was addressed

• Conscience of Antimicrobial Resistance Action (CARA): An Alliance to Support the U.N. Resolution on Antimicrobial Resistance established

2017

• World Health Organisation launch an AMR community of practice (AMR CoP) with a sub-community on Health Workforce AMR Education and Training

• G20 Summit, Hamburg Germany – AMR and incentivising antibiotic R&D high on health agenda

FIGURE 1
This global collaborative approach has been identified as a key success factor in implementing the global response to antimicrobial stewardship: [a global call from five countries to collaborate in antibiotic stewardship: united we succeed, divided we might fail. Goff D et al Lancet ID, Volume 17, No. 2, e56–e63, February 2017] This approach is increasingly getting traction supported by the routine and innovative use of social media, such as that described by Debra Goff et al in the Lancet Infectious Diseases in 2016 article Use of Twitter to educate and Engage Surgeons in Infectious Diseases and Antimicrobial Stewardship". [Infectious Diseases in Clinical Practice: November 2016 - Volume 24 - Issue 6 - p 324–327 doi: 10.1097/IPC.0000000000000440]. Critical levers for success will be simplicity of engagement, ease of access to information and resources and securing the engagement and belief of healthcare communities globally.

An example of the emerging value and impact of rapid news dissemination networks is the Centre for Infectious Disease Research and Policy (CIDRAP) [http://www.cidrap.umn.edu/], an organisation dedicated to providing advice, information and analysis on the prevention, control and treatment of targeted infectious diseases, antimicrobial stewardship and public health preparedness.

Engagements such as these offer opportunity to hold policy makers to account and ensure declarations do not remain empty promises. When the UN returns to the subject of AMR in 2018 and beyond, health professionals, journalists, and campaigners, should be able to check progress of against the UN declaration by using indicators that both WHO and CARA are currently seeking to develop. These indicators should identify the commitments made by nations, while measuring the activities that fulfill these commitments. For example, have all governments introduced laws and funding to support the fulfillment of their commitments? Have they tasked a ministry to work on AMR? Have they adopted a plan for antimicrobial stewardship (AMS), or the ITC infrastructure needed to support it? These questions need answers and the answers need monitoring – both of which are part of WHO and CARA ambitions respectively.

Such global initiatives are to be applauded and supported, but they should not be used as a reason to stall local actions. Nations should continue to work on the development and implementation of evidence-based plans that can be adopted and adapted locally, and learning can be ultimately shared in the AMR CoP described above. Inertia is as much a threat to progress as ignorance or a lack of investment. As such, we need to remind ourselves – and most importantly others – of the scale and urgency of the threat we face. In line with Jim O'Neill’s top recommendation, we should use existing opportunities such as World Antibiotic Awareness Week to launch a coordinated global public awareness campaign through which to communicate key critical facts about the human, financial and consequential costs of AMR:

- **AMR IS RESPONSIBLE FOR 700,000 DEATHS PER YEAR CURRENTLY**
- **IF WE DO NOT ACT NOW, AMR WILL BE RESPONSIBLE FOR 10 MILLION DEATHS PER YEAR AND $100 TRILLION OF LOST GLOBAL PRODUCTION BY 2050**
- **$40 BILLION IS NEEDED OVER 10-YEARS TO TAKE GLOBAL ACTION – THIS REPRESENTS ABOUT 0.05 PER CENT OF WHAT G20 COUNTRIES SPEND ON HEALTHCARE CURRENTLY**
- **AMR REDUCES THE EFFECTIVENESS OF ANTIBIOTICS. WITHOUT ANTIBIOTICS THERE CAN BE NO TREATMENTS FOR SIMPLE AND COMPLICATED INFECTIONS, CHEMOTHERAPY FOR CANCER, CYSTIC FIBROSIS, HEART TRANSPLANTS, JOINT REPLACEMENT SURGERY**

A global campaign will offer opportunity to adapt and develop messages for local use across all stakeholder groups – professional, political, economic, and public. However none of what we have talked about so far can bring about success unless words are combined with funds. Those investing in human health, animal health and agriculture will need to prioritise and fund the multifactorial solutions to AMR advocated by the recommendations of the AMR Review (Figure 2) for funding on par with other local, regional or global health priorities.

### NEGLECTED PRIORITIES

Whilst new coalitions, initiatives, actions and funds are important, it is of equal importance that we look at current and past practice and ensure we do not neglect existing priorities. The recent paper by Pulcini et al, *Ensuring universal access to old antibiotics: a critical but neglected priority* addresses the need to ensure steps are taken to ensure equitable and universal access to old antibiotics. The paper offers 6 key recommendations (figure 3), the first of which was realised this summer when the WHO updated the antibiotics section of its Essential Medicines List for the first time in the list’s 40-year history. It is a promising start but we need to follow up on the remaining recommendations.

### FILLING THE IMPLEMENTATION GAP – COLLABORATION, COLLABORATION, COLLABORATION

The biggest challenge lies in translating policy into sustainable practices that lead to improvements in all aspects of AMR from drug research and development, infection prevention and control practices, antibiotic prescribing practices and professional and public education and understanding. The UN declaration offers a 2-year window in which nations must report back on their action plans.

The declaration doesn’t reduce the challenge but it does offer a high profile arena in which all stakeholders can demonstrate their collective commitment and capabilities. The global alliances reference earlier will support and monitor such progress but they will note directly enable the necessary actions, and such is the size of the task that it cannot be achieved by any one organisation alone – governmental, scientific, medical or otherwise. Countries and continents must harness the resources already at their disposal and bring together the efforts and offerings of all stakeholders to deliver against targets and achieve change.
UNLOCKING EXISTING RESOURCE

One available resource across the globe is the professional medical charity sector, using learned societies such as the British Society for Antimicrobial Chemotherapy (BSAC) as critical friends and contributors. This sector’s activities are trained on local, national, regional, and global collaboration. Taking BSAC as an example, our rigorous approach, built on the foundation of evidence-base or professional consensus and apolitical, allows us to act as an honest broker between policymakers, practitioners, industry, and the public. This role is instrumental, because central guidance and local action must be at the heart of all attempts to combat AMR. The BSAC is one of many likewise organisations globally working towards fulfilment of the one health approach to AMR (defined as the collaborative efforts of multiple disciplines - working locally, nationally and globally – to attain optimal health for people, animals and environment). Through such societies there is a wealth of resources and opportunity to tackle the problem of AMR and improve patient care and outcomes.

BSAC offers a powerful example of what is already developed and available to use in progressing solutions to the AMR agenda. Through a broad portfolio of activities the society has funded over £4.1m (~€4.8m) in research, operates national programmes to measure antibiotic resistance, and has developed software to measure how many antibiotics are prescribed and the quality of the prescription so as to help improve prescribing and patient outcomes. Through Antibiotic Action, a low-cost, high-impact initiative, BSAC has been able to stimulate interest and efforts in antimicrobial drug discovery research and development through a global network of Antibiotic Action champions and ensured the topic of AMR is high on the UK political agenda by helping secure the establishment of the All Parliamentary Group on Antibiotics (APPG). One of the main focuses of BSAC’s current activity is multi-professional education on antimicrobial prescribing and stewardship. This activity has a local, national and international focus and aims to use innovative and cost-effective e-learning methods to complement traditional educational methods with the underlying ethos of high-quality, peer-reviewed, up-to-date and globally relevant educational resources that are free at the point of access. An example of this includes BSAC’s partnership with Scotland’s University of Dundee and FutureLearn to deliver the first open access global educational course on antimicrobial stewardship, the Massive Open Online Course on Antimicrobial Stewardship (MOOC-AS), providing access to free education on prescribing to global health economies. In 18 months the course has attracted almost 40,000 learners (Figure 4) adding to the work the society is doing via the British High Commission Science and Innovation Office to local colleagues in India, Russia and Africa to develop educational frameworks for multi-professional antimicrobial stewardship education. Translations of the MOOC-AS are available in Mandarin, with translations to Spanish and Russian planned by spring 2018, increasing opportunity for global reach and impact.

To support a more interactive forum for learning, these educational initiatives will be embedded into a modern, innovative virtual learning platform dedicated to AMR education [http://bsac-vle.com]. Further BSAC is working to ensure its high quality, pragmatic evidence based guidelines are implemented more effectively in healthcare settings and is working at the forefront of embracing the use of improvement and social science in the context of AMR. A prime example is publication of the Cochrane Systematic Review Interventions to improve antibiotic prescribing practices for hospital inpatients published February 2017 and already highly valued and cited [https://www.cochranelibrary.com/crl/review/16158632]. BSAC’s journal, JAC, has always provided a forum for articles highlighting AMR which was one of the main motivations for starting it in 1975. Indeed about 1 in 4 articles has the word “resistant” or “resistance” in the title. Moreover, the first article with “stewardship” in the title or abstract was published in 2007 [Nathwani & Christie The Journal of Antimicrobial Chemotherapy 2007; 60 Suppl 1: i69-71] and finally published (18 (22%) which is line with the current 1 in 5 acceptance rate. One of these articles described the contribution of JAC to antimicrobial stewardship. Johnson, The Journal of antimicrobial chemotherapy 2016; 71: 3001-7. and most of the articles were about increasing awareness, education and training. However 5 articles reported the outcomes of studies and is hoped that more such articles will be offered in the future to help build a much needed evidence base. Lastly, BSAC actively supports the CIDRAP mentioned earlier in this article in its ambition of making current information widely available to educate and inform healthcare providers, public health professionals, business leaders, students, opinion leaders, policy makers, the media, and other national and international stakeholders.

The opportunities that BSAC’s activities afford in meeting the UK 5-year strategy on AMR are considerable (Figure 5) – imagine if governments were able to harness, consolidate and use the connected resources
of all learned and likewise societies working in the AMR arena; the implementation of policy into practice gap would narrow considerably.

DEEDS NOT WORDS – TOGETHER NOT ALONE

Governments, and society as a whole, must harness the resources they have, and work with those already active to start turning the tide on resistance. As demonstrated, one such resource is the professional medical charity sector that through the expertise and dedication of their professional members are able to offer significant contributions and solutions to tackling AMR. This remains a seriously under-used option. Governments and federal organisations must find ways to engage learned societies and likewise organisations, to join forces with them and identify the mechanisms by which they must work together.

Professional or learned bodies work alone, in partnership with others and collectively. They are a fundamental part of the research, policy, service and education development landscapes. They provide substantial intellectual, public and reputational good at minimal cost to the public purse. The majority, if not all, have a charitable or a recognised status within their country and are committed to expending their time and resources on activities that are driven by philanthropic objectives and are free from the need to meet financial or shareholder targets and expectations.

Learned societies can also be more agile in the way they work, operating under unrestricted educational grants from industry, philanthropic contributions or directly sponsored activities where the benefit to both or all parties is declared. BSAC is one of many learned societies in the infection world. We are all working tirelessly to meet the same goals and agenda.

Risk can be transformed into opportunity by those who work deftly and collaboratively. AMR presents us with a once-in-a-lifetime challenge – because what we choose to do (or not do) now is going to make a difference, one way or the other, to millions of people across the world.

BSAC believes that we will only meet this once-in-a-lifetime challenge by successfully aligning the work of professional organisations with health administrations, governments and industry.

And so we stand at a crossroads. We know what we need to do – but we need to decide how we are going to do it. Boiled down, our options might best be expressed by this African proverb: “If you want to go fast, go alone. If you want to go far, go together”. The lengths we have to go to means we have no choice. We must go together – and soon.

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xi  Africa: http://ican-ams.com

As past president, president and president-elect of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID), which has been at the forefront of the fight against antimicrobial resistance for more than 30 years, we welcome the fact that this topic moved to the top of the global agenda in September when the United Nations General Assembly called a high level meeting to address this complex problem.

We are deeply concerned about the ten million annual deaths antimicrobial resistance is projected to cause by the year 2050. Over the past years we have been observing the speed with which pathogens develop new resistance in every country within and outside the European continent. As no new antibiotic classes have been discovered over the last three decades, and due to globalisation allowing resistant bacteria to spread more easily between countries and continents, we today face a situation demanding immediate and decisive actions from governments.

Drug-resistant infections are now recognised as such a big threat to humanity that we believe that only a concerted effort by the international community is able to tackle it. After efforts on HIV, Ebola and non-communicable diseases, it was only the fourth time in the organisation’s 70-year history that the UN decided to act on a health issue. The 193 member states on 21 September committed to curbing this growing challenge, which is not only directly threatening human health but also, indirectly, food production and the environment – and ultimately the success of the UN’s growth and development targets.

It was recognised that the keys to tackling antimicrobial resistance are avoiding overuse of antibiotics and the prevention and control of infections in humans and animals within the framework of a one health approach, a comprehensive collaboration of human, animal and environmental health experts. Concrete measures include immunisation programmes, improved structures for the monitoring and surveillance of antimicrobial resistance, as well as investments in strong health systems and research and development of new therapies, rapid diagnostic tests and technologies.

Since its foundation in 1983 ESCMID has been promoting research and training to improve the diagnosis, treatment and prevention of infection-related diseases. Antimicrobial resistance has been at the core of our activities – at our study groups, committees, courses and conferences over the past years. Our experts have been committed to developing hands-on solutions by supporting and promoting research and training to tackle the problem around the world.

The society offers professional training and programmes on antibiotic stewardship, infection control and surveillance resistance. It develops medical guidelines, policies for antimicrobial use, and initiatives to promote novel diagnostics, vaccines and therapies. In line with a one health approach ESCMID brings together physicians, veterinarians and microbiologists specialised in bacterial, viral, fungal and parasitic infections to improve infection control and prevent inappropriate antibiotics use.

In addition, the European Committee on Antimicrobial Susceptibility Testing (EUCAST), a standing committee jointly organised by ESCMID, the European Centre for Disease Prevention and Control (ECDC) and European National Breakpoint Committees, offers expert services on resistance. EUCAST acts as the breakpoint committee on behalf of ECDC and the European Medicines Agency (EMA), for example for the regulatory approval of a new drug. It defines so-called ‘breakpoints’, which are defined by the lowest concentration of a drug needed to inhibit the growth of an organism and thus distinguish between therapeutic success and failure. Its experts need to review and sometimes revise these breakpoints and dosing schemes as new resistance mechanisms develop and new infections or pathogens emerge. One of its main priorities is the harmonisation of these values – first of all in Europe but, as micro-organisms know no borders, also in co-operation with partners across the globe.

Threats

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Priorities

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Actions

In 2014 ESCMID formed the European Committee on Infection Control (EUCIC) to develop and implement infection control and preventive measures, including training programmes, support structures and an effective network to reduce the burden of healthcare-associated infections (HAI). HAI are a leading cause of morbidity and mortality worldwide, affecting around one in 20 patients and leading to thousands of deaths every year. Therapy is becoming evermore difficult because of the increasing rate of antimicrobial resistance among common HAI pathogens.

ESCMID organises the world’s largest and most comprehensive congress in the field of AMR. At ECCMID 12,000 specialists – including physicians, microbiologists, public health specialists, epidemiologists and economists – in the fields of infectious diseases, clinical microbiology and infection control come together to discuss research, solutions and policies to tackle the antimicrobial resistance. The 27th ECCMID will take place in Vienna, Austria, from 22-25 April 2017. From 21-23 September 2016, ESCMID organised an international conference with the American Society of Microbiology that aimed at accelerating drug development to meet the challenge of antimicrobial resistance.

ESCMID is urging governments and international organisations to implement policies on evidence-based prevention, infection control, surveillance of resistance, antibiotic stewardship and sanitation to guarantee an optimal use of antimicrobial medicines. This requires investments in resources, capacities and capabilities at health facilities, laboratories and regulatory bodies within individual countries and at a pan-European level. Action plans on antimicrobial resistance already exist in many countries in Europe.
The Netherlands, for example, marked its European Union presidency by inviting ministers of health and ministers of agriculture in all EU/European Economic Area member states to a ministerial conference on antimicrobial resistance in February 2016.

Professional education, training and certification among health, veterinary and agricultural practitioners are also part of the cornerstone. We need to introduce comprehensive training and education programmes for specialists who are currently underrepresented and/or undervalued in many countries. These efforts are complicated by non-uniform legislations and regulations within Europe. Infectious disease experts, for example, are not even recognised as a professional specialty in some countries, including Spain.

Governments need to mobilise adequate, predictable and sustained funding and resources through national, bilateral and multilateral channels to support the development and implementation of national action plans and investment. We require incentives, innovative funding systems, public-private and industry-academia partnerships to promote the development of new medicines, and diagnostics. Finally, we urge governments to run public campaigns to increase awareness of antimicrobial resistance and engage a change of behaviour among health professionals, patients, consumers and the general public.

TARGETS

It is of utmost importance that efforts include binding targets that are measurable and accountable. Measures must include quantitative targets and concrete plans for implementation and enforcement to reduce the inappropriate use of antimicrobial drugs in human medicine and animal farming. We need specific plans to phase out antibiotics as growth promoters in livestock; we need to ensure access to antibiotics to people who really need them; and we acknowledge that countries can only implement and enforce effective surveillance, monitoring and regulatory frameworks if they take the national contexts into account whilst complying with international commitments.

The international community must urgently act on this issue. We have two years until governments and stakeholders will meet again to assess our progress. This is a unique opportunity to make a difference and set the course. As one of the most experienced players in this specialised field, ESCMID is offering the support of its experts to help policy makers develop and implement effective measures to tackle the problem. Not only does the society have more than 7,000 active members on all continents, it also reaches every expert in the field through its extensive global network. We already have many structures and networks in place in Europe to set an example and spearhead an international effort.

At the UN’s high level meeting on antimicrobial resistance, the president of the 71st session, Peter Thomson, impressed upon the gathered delegates the sheer scale that the AMR crisis could reach: “In recent years [...] microbes or ‘superbugs’ have adapted, undermining the effectiveness of antimicrobial medicines. When medicines used to treat many types of infections are no longer effective, it is a warning of great challenges that go beyond our health systems, affecting aspects of our way of life.

“AMR has the capacity to kill millions each year and cost trillions to address,” Thomson explained, adding that the crisis “will impact our environment, the health of our wildlife, our access to sustainable and safe food, and, especially, our means of agriculture production”. The outcome of the meeting was a draft political declaration on antimicrobial resistance which looks to address the emerging crisis in light of achieving the UN’s Sustainable Development Goals. The declaration adopts the World Health Organization’s (WHO) Global Action Plan on Antimicrobial Resistance, which offers a number of objectives to prevent the crisis and advises on the actions that should be taken by national and international bodies.

Dr Margaret Chan, director general of the WHO, was in attendance at the UN meeting and welcomed the declaration, but warned of the need for swift action: “The commitments made today must now be translated into swift, effective, lifesaving actions across the human, animal, and environmental health sectors. We are running out of time.”

Thomson concluded his remarks with a rallying cry: “No one country, sector or organisation can address this global health challenge on its own, and innovative public-private partnerships, funding initiatives and inclusive approaches will be essential. For sustainable development to be achieved for all, it is critical that we safeguard our ability to protect our health, feed ourselves and our families, conserve our environment, and develop our economies. Ultimately, the future of humanity will depend on our ability to respond to the challenge of antimicrobial resistance.”

Professor Mario Poljak
ESCMID President

Professor Jesús Rodríguez Baño
ESCMID President-elect

Professor Murat Akova
ESCMID Past President