Antibiotics and their Alternatives
Fixing and feeding the Pipeline
Joint Workshop

Brussels, 4 April 2014

Report

Background

The urgent need to develop new antibiotics is driving a new form of cooperation among European researchers. Only two new classes of these life-saving medicines have reached the market in the last three decades, while many older ones are losing their effectiveness in the face of growing drug-resistance. The science is becoming increasingly challenging, and soaring development costs often exceed the potential returns, leading most pharma firms to disengage from the field.

It is in response to this "antibiotic crisis" that leading researchers are now exploring how they can cooperate more in filling the gaps in the development pipeline and countering resistance. At a meeting in Brussels on 4 April 2014, representatives of academia, industry and the European Commission came together to explore how their work could benefit from closer collaboration, and how they can speed their own research by learning from one another's successes – and failures. Ruxandra Draghia-Akli of the European Commission's Directorate General for Research and Innovation urged the participants "to help us fix and feed the pipeline".

The meeting examined the results of recently completed projects on novel targets and drugs against Gram-negative bacteria funded under the 7th EU Framework Programmes for Research (FP7). It looked at the development and discovery platforms within the Innovative Medicines Initiative public-private partnership (IMI). And it offered a showcase for smaller firms running collaborative research projects on new drugs, vaccines and alternative methods also funded under FP7. The meeting was jointly organised by the Health Directorate in DG RTD of the European Commission, the Joint Programming Initiative on Antimicrobial Resistance, IMI and EFPIA. Many projects illustrated new scientific approaches to drug and target discovery, offering ways round the expensive and often unsuccessful methods of large-scale screening of the past.

Session 1

Ruxandra Draghia-Akli of the European Commission's Directorate General for Research and Innovation and Marco Cavaleri of the European Medicines Agency moderated a session on recently completed FP7 projects that aimed to develop novel targets and drugs against Gram negative bacteria. Presentations included "Identification, characterisation and exploitation of novel Gram-negative drug targets – AEROPATH outcome and uptake of results" by Bill Hunter of the University of Dundee in the UK.; "Identification and validation of novel drug targets in Gram-negative bacteria by global search: a trans-system approach – AntiPathoGN outcome and uptake of results", by Xavier Daura of the Universitat Autònoma de Barcelona in Spain; "Exploiting Gram-negative cell division targets in the test tube to obtain antimicrobial compounds - DIVINOCELL outcome and uptake of results", by Miguel Vicente of the Agencia Estatal Consejo Superior de Investigaciones Científicas of Spain, and "Novel approaches to bacterial target identification validation and inhibition (NABATIVI) - outcome and uptake of results", by Alessandra Bragonzi of the San Raffaele Scientific Institute of Italy.

The subsequent discussion centred largely on the characteristics of current research that might give it a better chance of success than was enjoyed by major screening projects conducted by big pharma (such as SKB's Manhattan) decades ago. The answers that were volunteered suggested that critical factors were more extensive collaboration among companies and academia that is filling gaps left by big pharma, a more selective identification of targets and a more focused search for properties of candidates, access to more data and to newer technologies.

Summaries of Projects Presented:

*"Identification, characterisation and exploitation of novel Gram-negative drug targets - **AEROPATH** outcome and uptake of results" by Bill Hunter of the University of Dundee in the UK.* http://www.aeropath.eu/project

New ideas, targets and drugs are urgently sought to combat the rise of bacterial infections, in particular to deal with superbug Gram-negative bacteria. Researchers from the Universities of Dundee and St Andrews, the Karolinska Institutet and two SMEs (LIONEX and mfd Diagnostics GmbH) formed the AEROPATH consortium to identify and assess new drug targets in Pseudomonas aeruginosa. This bacterium infects humans with compromised immunity, particularly those undergoing chemotherapy or with conditions such as cystic fibrosis.

The consortium applied new approaches to inform about the potential of specific proteins as drug targets, on chemical data of compounds that hit the targets, and of how drug-like those compounds are. Over 35 proteins were genetically tested to investigate if they might be drug targets using modified P. aeruginosa and a mouse model of lung infection. Over 100 new protein crystal structures were determined. A new algorithm to predict “druggability” was developed and applied to over 5000 structures of all P. aeruginosa proteins and homologues. Key targets in fatty acid, folate and sugar biosynthesis progressed through target validation, structure determination, and were exposed to compound libraries in screening campaigns after the development of novel assay methods. In complementary fashion in silico compound screening and molecular design methods were applied to exploit selected structures. These approaches served to prioritise the targets and to identify chemical matter to support further development. The application of modern approaches to several old targets generated understanding of structure-activity relationships and, in the case of penicillin-binding protein 3, indicated how novel drugs might now be assembled.

"*Identification and validation of novel drug targets in Gram-negative bacteria by global search: a trans-system approach – **AntiPathoGN** outcome and uptake of results", by Xavier Daura of the Universitat Autònoma de Barcelona in Spain*

http://www.antipathogn.eu/default.asp

The increasing emergence and spread of multidrug-resistant (MDR) pathogens, particularly among the gram-negative (GN) group, constitutes one of the major threats to public health worldwide. In this context, AntiPathoGN was set to discover new targets and modes of action, less propitious to the evolution of resistance, for the development of drugs against GN bacteria. To this end, the consortium developed a strategy based on a comparative, system-level analysis of proteins and protein-interaction networks of a set of high-priority MDR pathogens such as P. aeruginosa and E. coli, focusing on factors involved in pathogenesis, virulence, drug resistance and cell division/growth. In addition to the identification and validation of new drug targets, AntiPathoGN pursued the discovery of novel antibacterial compounds acting against these targets by screening purpose-specific libraries of products derived from natural sources and from synthetic compounds.

At formal closing, the consortium has identified and validated phenotypically eighteen potential antimicrobial targets in Gram-negative bacteria, and has found hit compounds against two of them. Two of the targets are essential for bacterial growth, while the other sixteen are involved in various mechanisms related to virulence or resistance. Cell-based screens have also identified 33 natural products with antimicrobial activity, including three novel compounds. Further studies will be needed to confirm the potential of these targets and compounds for antimicrobial drug development. The experimental interactome data and bioinformatic databases and tools generated by the consortium constitute a fundamental contribution of AntiPathoGN to the research community, within and beyond the field of antimicrobial-drug discovery.

*"Exploiting Gram-negative cell division targets in the test tube to obtain antimicrobial compounds - **DIVINOCELL** outcome and uptake of results", by Miguel Vicente of the Agencia Estatal Consejo Superior de Investigaciones Científicas of Spain.*

http://www.cnb.csic.es/~divinocell/

To obtain new antibiotics, DIVINOCELL exploited existing understanding and obtained new knowledge on the molecular biology of the cell division machinery (the divisome) of Gram-negative bacteria. Using the divisome, essential for bacterial survival, as a source of inhibitable targets we identified eight new compounds to block the proliferation of Gram-negative pathogens. We also generated new technology to facilitate the validation and the improvement of the properties of antibiotic hits and to help in discovering new antimicrobials. Gram-negative bacteria are encased in a complex envelope formed by two flexible membranes sandwiching a rigid peptidoglycan support layer that together maintain the integrity and the shape of the cell. Due to this complexity they are less susceptible to antibiotics than bacteria that do not contain a second membrane covering the peptidoglycan layer. For most of our work we used Escherichia coli as a model because it is by far the best understood Gram-negative bacterium and we have powerful techniques to study and handle it. Moreover, some strains of E. coli are pathogenic and cause deadly disease outbreaks. The novel DIVINOCELL antimicrobials are designed to block the function of divisome proteins, such as FtsZ, FtsA or ZipA. They should be effective to counteract infections and be largely innocuous to humans and animals because their cells do not contain these proteins. DIVINOCELL participants have published over 63 papers in top ranking scientific journals, have defended 4 doctoral thesis and have participated in over 80 dissemination activities directed to the general public.

*"Novel approaches to bacterial target identification validation and inhibition (**NABATIVI**) - outcome and uptake of results", by Alessandra Bragonzi of the San Raffaele Scientific Institute of Italy* http://www.nabativi.org/

NABATIVI is a network with a strategic objective in the area of antimicrobial drug resistance and infectious diseases research. Nine leading European research teams have combined their expertise and resources in a multi-disciplinary approach through the development of novel antibacterial against the gram-negative bacteria. Focus was on combining basic research on molecular mechanisms of resistance, and host-pathogen interactions with clinical resources towards identification and validation of novel drugs target. NABATIVI has explored two approaches:

A) Discovery Phase Approach A: "From target to lead compound". A combination of advanced genomic approaches followed by validation in a sequential cascade of disease models was applied to Pseudomonas aeruginosa. Essential and virulence genes have been selected as targets candidates and used for inhibition. Several screening processes were used and a number of potential lead compounds identified from both synthetic and natural compound libraries. These compounds will have to be further profiled to assess their therapeutic potential.

B) Discovery Phase Approach B: "From drugs to targets". In this case it was the natural antimicrobial peptide protegrin I which served as starting point to discover a novel class of antibiotics with a novel mode of action. The target gene was identified during the drug discovery process. Hit-to-lead and lead optimisation led the novel compounds POL7001 and POL7080, which are effective against a wide range of clinical strains. Protection against lethal P. aeruginosa infection with potency superior to currently available antibiotics in preclinical studies led to POL7080, which was nominated as a clinical candidate. Phase I clinical trial demonstrated the clinical safety and tolerability of its Pseudomonas specific antibiotic POL7080.

Session 2

Angela Wittelsberger, scientific officer at IMI, and Magda Chlebus moderated the second session, on IMI funded projects of the "New drugs for bad bugs" programme. This covered "Combatting bacterial resistance in Europe - COMBACTE" by Seamus O'Brien of AstraZeneca, "Molecular basis of the bacterial cell wall permeability - TRANSLOCATION" by Mathias Winterhalter of Jacobs University Bremen in Germany, "ENABLE" by Anders Karlén of Uppsala University in Sweden, and "Topic 4 - a new business model" by Judith Hackett of AstraZeneca.

Wittelsberger spoke of the need for public-private partnerships in pooling expertise, knowledge and resources, and in developing incentives to address major unmet needs. A PPP can provide a neutral and trusted platform to align public and private interests. The ensuing discussion highlighted the possibilities of countering the "perfect storm" with greater coordination, and new models for collaborative discovery that are attractive to SMEs and academia as well as big pharma. Among the recipes advanced for further exploration were early discussion with external stakeholders (notably regulators and payers) to generate a real sense of collaboration through a new prism, closer sharing of information and access to libraries, more effective clinical research networks, better understanding of targets, and diagnostic validation. The discussion also clarified IMI's focus that is not restricted to development of new chemical entities (NCEs), but conditioned in its response by the requirement that at least some EFPIA companies wish to commit to a project - and its ability to handle intellectual property issues through innovative approaches making participation attractive both for owners of promising novel molecules as well as for partners contributing to further advance the molecule.

Summaries of Projects Presented:

*"Combatting bacterial resistance in Europe - **COMBACTE**" by Seamus O'Brien of AstraZeneca.*

https://www.combacte.com/

The challenge of developing new treatments and preventative therapy options for serious antibiotic resistant bacterial infections is a societal issue that requires a partnership bringing together leading experts from universities, hospitals, and pharmaceutical companies who are skilled in microbiology, epidemiology, drug development, and clinical trial design. COMBACTE is set to give antibiotic development in Europe a major boost.

The COMBACTE project focuses on addressing the key barriers to the clinical development of antibacterial agents. A key objective of the project is a high quality, pan-European clinical trial network that is capable of recruiting sufficient patients into multinational trials at all stages of development. This network, entitled COMBACTE CLIN-Net, has expanded since the start of the project in January 2013 to include 294 centres and sites in 34 European countries. Alongside this, the project is also establishing a pan-European laboratory network (COMBACTE LAB-Net), which will deliver site level epidemiological information and data from local microbial surveillance work to guide the selection of clinical trial sites and support successful conduct. Crucially, the COMBACTE team aims to generate innovative trial designs to facilitate the registration of novel antibacterial agents. It is also designing and validating tests to support the diagnosis of patients, identify the most appropriate treatments, and monitor the patient's response.

A large part of the project is devoted to the performance of clinical trials of drugs under development in the pharmaceutical companies involved in the project.

*"Molecular basis of the bacterial cell wall permeability - **TRANSLOCATION**" by Mathias Winterhalter of Jacobs University Bremen in Germany*

http://www.imi.europa.eu/content/translocation

The discovery of new agents to treat Gram negative infections relies on developing molecules that can penetrate the cell envelope. This envelope is a selective filter and allows for survival under extreme conditions by harvesting nutrients and protecting against harmful molecules. Translocation is devoted to identify and to quantify the molecular components in the cell envelope limiting the entry of antibiotics. In particular how the composition of this selective filter differs at various infection sites, develop new methods to quantify the uptake and how a molecule should be designed for good uptake. For this, academic and industry experts join forces and share their experience, expertise and knowledge to advance our understanding of efflux mechanisms and penetration barriers in Gram-negative bacteria. The goal is that the results generated from the basic research conducted should translate into new knowledge to inform antibiotic drug design.

The second objective is the creation of an ND4BB Information Centre where antibacterial R&D information and data (including legacy data from pharmaceutical companies) can be shared. Every project under ND4BB is expected to contribute to the Information Centre and explore ways to make use of it. Translocation partners are investigating ways for sharing data and accessing data, with the goal to make as much information as possible accessible not only to ND4BB partners, but ultimately to the scientific community outside ND4BB as well.

"ENABLE" by Anders Karlén of Uppsala University in Sweden

http://www.imi.europa.eu/content/enable

This public-private partnership project represents a unique model of collaboration in the field of drug discovery. Drug discovery and antibiotic R&D experts from the pharmaceutical industry, together with public partners, collaborate with owners of promising new molecules from the academic and SME sectors to jointly advance the most promising programmes towards early clinical stages. In addition, large pharma companies are collaborating on their assets - and bringing these jointly into the consortium.

The project has sufficient funding to develop up to eight hit-to-lead programmes from the academic and SME sector, up to three lead-to-clinical candidate programmes and potentially up to 2 Phase 1 clinical trials.
The ENABLE model of collaboration is based on an unprecedented intellectual property agreement that was tailored to meet the needs of the project. Partners in ENABLE work collaboratively on programs and have found an agreement that makes it attractive both for hit owners and for those who contribute to further progress the molecule to participate in the project.

Importantly, the governance structure of ENABLE ensures that only the best anti-bacterial programmes identified in Europe are developed, and each programme accepted is reviewed by an expert group on a regular basis to ensure timely decisions are made on both progression and closure.

The ENABLE model could prove inspiration for R&D collaborations in other disease areas.

*"**Topic 4** – a new business model" by Judith Hackett of AstraZeneca*

This three-year project is expected to start in October 2014. The project's goal will be to propose options for a new economic model of antibiotic R&D and responsible use of antibiotics. The different building blocks for a new economic model will be investigated, such as new commercial models, a definition of 'responsible use' of antibiotics, quantification of the economic burden of resistance, definition of the clinical impact of emerging multi-drug resistant pathogens, and quantification of the value of a new antibiotic.

The different concepts will then be assembled into options for a new economic model, and these options will be tested against several requirements for success such as the legal, political and regulatory feasibility, geographical reach and differences, the impact of evolving medical practice, and the impact on real-life antibiotics in development by innovator companies.

Key for success will be the engagement of stakeholders (patients, clinical societies, SME's, large pharmaceutical companies, healthcare payers, public health officials, government officials) as well as dissemination of information to policy makers and the wider public community

Session 3

Line Matthiessen, Head of Unit Fighting infectious diseases and global epidemics, Directorate General for Research and Innovation and Titta Rosvall-Puplett of European Biopharmaceutical Enterprises moderated the third session, on novel SME-driven projects on the development of new drugs, vaccines and alternative methods.

This covered "New anti-bacterials with inhibitory activity on aminoacyl-tRNA Synthetases (NABARSI)", by Lluís Ribas de Pouplana of Omnia Molecular of Spain; "Development of Group B Streptococcal vaccine to alleviate emerging antibiotic resistance through elimination of current prophylactic antibiotic strategies in GBS prevention: NEOSTREP", by Per Fischer of Minervax of Denmark, "Combining cellular and humoral immune responses as a vaccine strategy against staphylococcus aureus pathogen (BELLEROPHON)", by Alexandre Le Vert of Imaxio of France; "Oral vaccination against Clostridium Difficile infection (CD-VAX)", by Jonathan Kearsey of Leads To Development of France; and "Phage therapy for the treatment of burn wound Infection (PHAGOBURN)", by Jérôme Gabard of Pherecydes Pharma of France.

The following discussion noted the high proportion of new products that come from small biotechs –and the corresponding importance of providing them with adequate support, not just in terms of funding but also in terms of opportunities and frameworks for collaboration, and went into further detail of the support that the EU has made available specifically for SMEs in this field.

Antoine Mialhe of the Directorate General for Research and Innovation provided an overview of the instruments and facilities that are available under Horizon 2020 and other EU funding opportunities.

Summaries of Projects Presented:

*"New anti-bacterials with inhibitory activity on aminoacyl-tRNA Synthetases (**NABARSI**)", by Lluís Ribas de Pouplana of Omnia Molecular of Spain* http://www.nabarsi.eu/

The NABARSI consortium will develop a cutting-edge drug discovery project to increase the antibacterial pipeline. The main goal of NABARSI is to find new chemical entities (NCEs) with antibacterial efficacy in animal models of multi-drug resistant (MDR) bacterial infection and to exploit the results through obtaining a co-development with industry. The NABARSI consortium consists of 5 partners: Omnia Molecular (Omnia, SME; Spain). InhibOx (SME, UK). Latvian Institute of Organic Synthesis (LIOS, Latvia), Leeds University (Leeds, UK) and Erasmus Medical Centre (ErasmusMC, The Netherlands - Coordinator).

Antibacterial activity will be achieved through inhibition of essential aminoacyl-tRNA synthetases (aaRS). Individual aaRS are highly conserved across bacteria, enabling the discovery of broad-spectrum antibacterials. To reduce the likelihood of resistance, NABARSI will look for NCEs with inhibitory activity against multiple aaRS enzymes. InhibOx and LIOS will design NCEs by rational and fragment based drug discovery methods followed by synthetic structure optimization. To increase chemical diversity, virtual screening of large (>100 M) compound libraries available at InhibOx will be performed. Limitations of previous aaRS inhibitors will be overcome by novel approaches such as the In Omnia assay: activity of the compounds on pathogenic aaRS enzyme is measured inside a human cell, allowing rejection of compounds acting through human aaRS and identifying compounds that cross biological membranes. The expertise of Leeds in mode of action studies will be used at an early stage. Activity of the NCEs on clinical isolates of MDR strains available at ErasmusMC will be assessed. Resistance appearance frequency and mechanisms will also be assessed early by selection and characterization of resistant mutants by ErasmusMC and Leeds. A co-development agreement with pharmaceutical companies will be intensively sought with the aim of exploiting the NCEs upon finalisation of NABARSI.

*"Development of Group B Streptococcal vaccine to alleviate emerging antibiotic resistance through elimination of current prophylactic antibiotic strategies in GBS prevention: **NEOSTREP**", by Per Fischer of Minervax of Denmark.* http://www.neostrep.eu/

The NeoStrep project will develop a novel vaccine against Group B Streptococcal (GBS) infections, responsible for 50% of life-threatening infections in newborns. The aim is to provide a safe and effective alternative to current generally implemented antibiotic prophylaxis. Emergence of clinical isolates of GBS with reduced susceptibility to penicillin (the preferred prophylactic antibiotic) and pattern of genetic mutations in penicillin binding proteins of GBS is identical to that observed in Streptococcus pneumoniae prior to the breakthrough of true widespread penicillin resistance in that pathogen. Combined with already existing resistance to a wide range of other antibiotics, this indicates current GBS antibiotic prophylaxis is highly vulnerable to antibiotic resistance. Emergence of widespread antibiotic resistance threatens to return the incidence of GBS disease to pre-prophylaxis levels with the associated significant increases in health cost and morbidity/mortality caused by infections with resistant GBS.
The NeoStrep project aims to eliminate the use of prophylactic antibiotics in GBS prevention and hence the problem of emerging antibiotic resistance in GBS through the development of a GBS vaccine.

No approved vaccine currently exists, and one currently in development only covers a subset of clinical serotypes. The NeoStrep vaccine, which is based on a novel fusion protein approach, has a wider serotype coverage (95%) and is much cheaper to manufacture than the other GBS vaccine candidate in development. The vaccine is extensively

validated in animal models, and a simple production method has been developed.

The objective of the project is therefore to advance the vaccine through cGMP production, tox studies and into clinical trials, with the aim of generating proof of concept in humans by means of immunogenicity, response rate, durability and effect on spontaneous vaginal colonisation.

*"Combining cellular and humoral immune responses as a vaccine strategy against staphylococcus aureus pathogen (**BELLEROPHON**)", by Alexandre Le Vert of Imaxio of France* http://www.bellerophon-project.eu/

The bacterium S. aureus causes a range of serious infections in humans. It is responsible for approximately 16,000 deaths annually in Europe and 19,000 in the US. Additional studies suggest at least EUR 380 million annual European costs attributable to S. aureus, as well as several billion USD per annum in the US . The emergence of highly antibiotic resistant S. aureus strains, such as MRSA (Methicillin-resistant S. aureus), is creating a serious public health threat around the world, and an increasing economic burden. As recent vaccine candidates have not proven effective in large human clinical studies, there continues to be a high unmet medical need.

The pan-European BELLEROPHON Project is comprised of four European institutions involved in vaccine development, each contributing specialist expertise and technology. It includes Imaxio, a French biotech company focused in immunology and which has coordinated the grant application, and the Jenner Institute at Oxford University, UK, an academic institution with key expertise on S. aureus antigens and viral vector delivery systems and which will coordinate the overall project.

The European Vaccine Initiative is the third partner, assisting with the project management tasks and advising on production and clinical aspects of the project. The fourth member is Preclin Biosystems, a Swiss contract research organization that has a strong expertise in preclinical efficacy models for infectious diseases.

*"Oral vaccination against Clostridium Difficile infection (**CD-VAX**)", by Jonathan Kearsey of Leads To Development of France.* http://cdvax.org/

Clostridium difficile is a spore forming anaerobic Gram-positive bacterium that is normally present in the intestine but that can overgrow as a result of antibiotic use causing a disturbance of the bacterial flora resulting in severe diarrhoea and acute colitis. It poses a major threat to public health in the industrialised world, particularly in the hospital setting. In many EU countries C. difficile hospital acquired infection mortality now eclipses that of Methicillin resistant S. aureus (MRSA) by a factor of four. Furthermore, C. difficile is resistant to a wide range of antibiotics with hypervirulent and multiple drug resistant strains now emerging.

The objective of the CDVAX consortium is to develop an oral vaccine based on the use of inactivated spores from the harmless bacterium Bacillus subtilis that have been modified to express recombinant C. difficile antigens on their surface. The oral delivery of this vaccine will ensure its ease of use and will induce both mucosal and systemic immune responses. In vivo proof of concept studies have provided compelling evidence for the vaccine's efficacy. The CDVAX project aims to undertake the preclinical and phase I clinical development of this vaccine.

A consortium has been built that has the expertise to optimise and manufacture the vaccine and to evaluate its safety and immunogenicity in both preclinical and phase I clinical studies. The project will enable a unique oral vaccine against C. difficile to be clinically validated.

*"Phage therapy for the treatment of burn wound Infection (**PHAGOBURN**)", by Jérôme Gabard of Pherecydes Pharma of France.* http://www.phagoburn.eu/

PHAGOBURN is a European collaborative project funded by the 7th Framework Programme for Research and Development (Health Programme). It has been launched on June 1st, 2013. Under the coordination of the French Ministry of Defence (Army Health Service – Percy Military Hospital) collaborating with Pherecydes Pharma (French SME), PHAGOBURN gathers six other international burn treatment centres – including the Royal Military Academy/Queen Astrid Military Hospital (Belgium) and the Lausanne University Hospital (Switzerland) – as well as a second French SME, Clean Cells.

PHAGOBURN aims at evaluating phage therapy (therapeutic use of bacteriophages) to treat skin infections caused by Escherichia coli and Pseudomonas aeruginosa bacteria in burn patients, according to Western criteria. Phage therapy interest is based on natural predators destroying bacteria: bacteriophages. These environmental viruses are found wherever bacteria exist. They account for Earth most important biomass.

Phage therapy efficacy and safety will be evaluated through a phase I/II clinical multicentre study according to Good Clinical Practices. Scientific meeting with France, Belgium and Switzerland drug regulatory agencies helped validating the clinical protocol, as well as, manufacturing control quality. Currently, bioproduction is being carried out according to Good Manufacturing Practices, whereas regulatory filing has been initiated. PHAGOBURN clinical trial is the first of its kind at world scale.

The project has a total budget close to 5 million euros, with a European funding of over 3.8 million euros.

Conclusions and Outcome

More selective identification of targets, a tighter focus on the properties of potential medicines, and wider access to data and to technologies were among the principal recommendations. Incentives would have to be matched more closely to major unmet needs, and intellectual property management should be adapted to a more coordinated approach. Extending collaboration to early dialogue with regulators and the agencies that pay for medicines would be necessary. And the creative contribution of small biotech firms merited support not just in terms of funding but also in opportunities and frameworks for collaboration. Both Line Matthiessen of the European Commission and Magda Chlebus of EFPIA stressed that H2020 including the next stage of IMI could continue to provide support – but for maximum effectiveness in planning and use of funds, "feedback from the research and industry community is essential". Also, collaboration will continue between the different instruments available in the European Commissions' Horizon 2020 collaborative research, Joint Programming Initiative on Antimicrobial Resistance and IMI-2. A joint task force has been established with representatives of these three research funders, in order to ensure coherence and complementarity.

New opportunities were identified for intensive sharing and efficient exploitation of results, and for making the fullest use of available funding from EU and national sources. The immediate outcome was the clear agreement on the need for establishing a research community focused on tackling anti-microbial resistance, in which it is possible not only to perceive projects and ideas as they emerge and develop, but also to afford an overview in which their complementary nature becomes clearer.

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