# "Translational Strategies to Combat Antibiotic Resistance: A Call to Action"

## Workshop Report

*A Canada/UK Collaboration between:*
*Canadian Institutes of Health Research,*
*Institute of Infection and Immunity (CIHR-III)*
*UK Health Protection Agency (HPA)*
*Canadian High Commission (CHC)*

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Canada

Written by: Judith Bray, PhD, Assistant Director, III
Creative Design by: Diane Christin, Project Officer, III

Canadian Institutes of Health Research
160 Elgin Street, Room 97
Address Locator 4809A
Ottawa, ON K1A 0W9

CIHR Institute of Infection and Immunity
Centre de recherche du CHU de Québec
CHUL – local TR-62
2705, boul. Laurier
Québec, QC G1V 4G2
Phone: 418-577-4688
Fax: 418-577-4689
www.cihr.gc.ca


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# "Exploring Translational Strategies to Combat Antibiotic Resistance: A Call to Action"

## Workshop Report

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**Workshop Report**

# Executive Summary

## Background

Antibiotic resistance is recognized, internationally, as an emerging health crisis that threatens to undermine our ability to control bacterial infections. The complacency generated by the success of antibiotics has led to their widespread overuse and misuse, accelerating the generation of multi-drug resistance. Antibiotic resistance is increasingly impacting on every aspect of health care, including neonatal care, transplantation, and cancer-care, as well as on international travel and humanitarian missions. There is a real possibility that without global intervention we could return to a pre-antibiotic era in which relatively minor infections become lethal. Concomitant with the rising tide of resistance is the lack of new antibiotics currently in the drug development pipeline. There is an urgent need to incentivize industry and promote the kinds of public-private partnerships necessary to generate new diagnostics and effective therapies.

### International Collaborations

Many countries are now ramping up their strategies to combat antibiotic resistance and international partnerships are emerging to promote value-added collaborations in a multifaceted, multidisciplinary approach to the problem. One example is the Canada/UK partnership on antibiotic resistance that stemmed from a bilateral workshop held in 2008. The UK Medical Research Council (MRC) and the Canadian Institutes of Health Research (CIHR) have joined forces to support two large Canada/UK teams in which UK and Canadian researchers are combining their expertise to focus on translational strategies to combat antibiotic resistance.

In February 2013, the Canadian High Commission hosted a second workshop in partnership with CIHR and the UK Health Protection Agency (now a part of Public Health England), entitled: "Translational Strategies to Combat Antibiotic Resistance: A Call to Action." This workshop brought together UK and Canadian biomedical and public health researchers with industry representatives to promote information exchange and networking. The workshop also provided an opportunity for the generation of joint strategies for collaborative action in tackling antibiotic resistance. The two-day workshop was comprised of a combination of overview presentations, case studies and small breakout discussions focused on:

- ⇨ Antibiotic stewardship
- ⇨ Conventional therapies
- ⇨ New approaches

Participants were tasked with identifying the existing barriers and challenges in addressing antibiotic resistance and proposing recommendations for joint strategies to move the field forward. The participant list and agenda can be found in Appendices 1 and 2.

# Workshop Outcomes and Recommendations

## Increasing awareness

There was broad agreement that one of the major challenges is obtaining a true picture of the real global economic and health burden of antibiotic resistance. There is an urgent need for better surveillance data and an accurate measure of antibiotic use in both the health and agri-food sectors. Currently, antibiotic resistance is under-reported and consequently the seriousness of the problem is under estimated. Participants acknowledged that the research community must do a better job of educating the media, the public, and governments to raise awareness of the true extent and seriousness of the problem. As Canada and the UK already have a history of collaboration in the antibiotic resistance field and share many of the same challenges it was recommended that joint strategies be developed to take advantage of the strengths in both countries and provide an opportunity for the sharing of best practices.

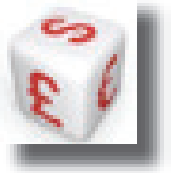
## Supporting Public and Private Sector Partnerships

During the two-day workshop participants learned of many examples of successful public/private partnerships and individual case studies and also gained insight into the interests and needs of industry.

Credit: Angela Wittelsberger, IMI

In many cases, the EU and Canadian programs and initiatives described offer an opportunity for international collaboration and one outcome from the workshop was an increased awareness of existing opportunities open to both Canadian and UK researchers. One strong recommendation was to constitute an inclusive overarching network comprised of industry, government and academia. Such a network would incorporate expertise along the whole translational pipeline fostering connections, innovation and best practices in antibiotic discovery and development.

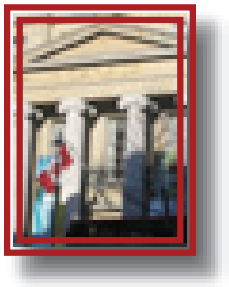
## Increasing Financial Investment



There was strong support for a coordinated approach in developing a business case geared towards obtaining additional “new” funds from UK and Canadian governments to support a bi-lateral network focused on translational strategies. Such a network would serve to bring together researchers from multiple disciplines, public health workers, and all levels of industry (small biotechs, SMEs, large pharma). The network could also serve as a primary conduit for communication and outreach and would facilitate new drug development by increasing key areas for compound discovery, such as validated targets which have industry “pull”, innovation in PK/PD, natural product libraries and clinical trials capacity. This would be a natural progression from the existing Canada/UK partnership in antibiotic resistance but would broaden and extend current collaborations.

## Supporting Collaborative Approaches

The workshop provided a forum for the many different players in the antibiotic resistance field to learn from each other and broaden their perspective. There was genuine interest and enthusiasm for exploring collaborative opportunities and sharing lessons learned. Participants generated many recommendations for shared activities across the full spectrum of research, including antibiotic stewardship, traditional drug development and alternative approaches. Discussion among Canadian and UK funding bodies are continuing with a view to alignment and coordination of effective strategies to combat antibiotic resistance. Ideally, we need cross research council funding models to enable these key activities between academia and industry and to bridge the gap between biology and chemistry in a multidisciplinary approach.



# "Translational Strategies to Combat Antibiotic Resistance: A Call to Action"

# Workshop Report

## Background


Antibiotic resistance is a growing global health threat. The supply of effective antibiotics is rapidly diminishing as bacteria become increasingly resistant to available drugs. Worldwide, we are seeing increased morbidity and mortality as a result of antibiotic resistant infections and few new drugs are in the pipeline.

An internationally coordinated and multi-faceted approach is required to address this emerging health challenge. As an initial step in this direction, the Canadian High Commission hosted a workshop in 2008, jointly organized by the UK Medical Research Council (MRC) and the Canadian Institutes of Health Research (CIHR) to explore potential value-added collaborations between the two countries. The workshop led to the joint support of two large Canada/UK consortia (www.cihr-irsc.gc.ca/e/40453.html). These two teams are combining Canadian and UK research strengths to advance our understanding of antibiotic resistance and facilitate progress along the translational pipeline from biomedical research to clinical practice.

In February 2013, the Canadian High Commission hosted a second workshop in partnership with CIHR and the UK Health Protection Agency (now a part of Public Health England), entitled: "Translational Strategies to Combat Antibiotic Resistance: A Call to Action". The workshop objectives were:

This workshop report summarizes the key points raised during the presentations and breakout sessions. The participant list and agenda are included as Appendices 1 and 2.

# Setting the Scene: UK, Canadian and Global Perspectives

## *David Heymann, UK Health Protection Agency*

Since the discovery of penicillin by Alexander Fleming in 1928, antibiotics have reduced premature mortality caused by infectious disease by more than 48%. However, the generation of drug resistance was forecast by Fleming, himself, as early as 1945 and by the 1990's penicillin was largely ineffective in both hospital and community environments. Although antibiotic resistance is a natural and inevitable phenomenon, resistance has been accelerated by decades of irresponsible antibiotic use, including the widespread and largely indiscriminate use of antibiotics in agriculture and farming. In the US, for example, more than half the antibiotics used are added to animal feed, and antibiotics are in widespread use in salmon farming and to control bacterial infections among fruit trees. Animals can serve as reservoirs for resistant bacteria and farm effluent can contaminate the broader environment, leading to increased resistance in humans.

In medicine, antibiotics are still used inappropriately to treat viral infections, or mild infections that would resolve without intervention and although improved infection control measures, in combination with more diligent prescribing practices, have resulted in improvements in many EU countries, much more needs to be done. Antibiotic misuse is particularly prevalent in low and middle income countries, where it is often more cost effective to treat infections with antibiotics, based on syndrome and symptoms. In these countries the introduction of regulatory guidelines can be complicated and difficult to implement.

A further challenge is that antibiotic resistance is not seen as an urgent health care crisis as there is a perception that infectious diseases are no longer a major threat. This situation is compounded by the fact that deaths resulting from antibiotic resistant infections are generally under-reported. In order to galvanize international action, the economic and health costs of antibiotic resistance need to be brought to the attention of the public and governments.

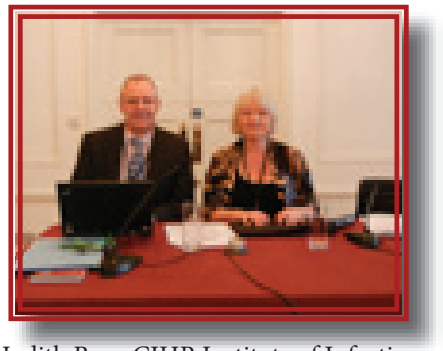
Although many countries, including Canada and the UK, are developing long-term antibiotic resistance strategies, there would be advantages to a coordinated and synergistic approach. Workshops, such as this one, facilitate the sharing of best practices and the development of collaborations and strategies to attract increased investment from governments and industry.

## *Howard Njoo, Public Health Agency of Canada (PHAC)*

Created in the wake of the 2003 SARS outbreak, PHAC has a similar mandate to the UK Health Protection Agency. In Canada, health care is a shared responsibility between federal and provincial governments. PHAC is responsible for surveillance; antibiotic resistance in humans and along the food chain; and the development of national infection control guidelines. However, the provincial and territorial governments deliver health care and public health services and regulate how antibiotics are used in agriculture and veterinary medicines, as well as which antibiotics are covered under their respective drug formularies.

This complexity has created challenges in the development of a coherent approach to antibiotic resistance. Recently, PHAC has taken the lead in developing a Canadian strategy for antibiotic resistance based on a framework spanning the three domains of humans, animals and the environment, across the three areas of: surveillance; research; and knowledge translation. This strategy

will bridge the gap between federal, provincial and territorial activities to provide a national perspective; raise public awareness; and attract federal funding of a scale commensurate with the magnitude of the problem.



Moderators: Dr. Judith Bray, CIHR Institute of Infection and Immunity, and
Professor Nigel Silman, UK Health Protection Agency

## *Breakout Sessions*

Workshop participants were assigned to one of three multi-disciplinary, multi-sector groups for a series of three breakout sessions each focused on a different aspect of antibiotic resistance. Specific questions posed can be found in the Agenda, Appendix 2.

## Breakout Session 1 – Antibiotic Stewardship

### Summary of Report Back and Plenary Discussion

#### Surveillance and Data Collection

All three groups highlighted the need for improved surveillance and prescribing data to better quantify the antibiotic resistance problem and assess the true economic burden. Current surveillance measures are largely inadequate, with a big gap in South-east Asia, Africa and India. A more consistent, integrated approach was recommended in which countries such as the UK and Canada could help underdeveloped countries generate more effective surveillance systems.

One major challenge identified was the need to engage the veterinary and agriculture communities in a harmonized and standardized approach to tackling antibiotic resistance in humans. A first step would be the collection of reliable prescribing data for antibiotics used in the agri-food sector.

#### Antibiotic Use

Participants highlighted the need for improved prescribing practices in both hospital and community health care settings. It was noted that the development of point-of-care rapid diagnostics would be of great benefit in this regard. It was also suggested that restricting the use of new antibiotics might be an avenue to consider although there was some controversy about the appropriateness of this strategy, with some participants feeling that this was an issue best resolved between patient and clinician on an individual basis. There was discussion about the role of vaccines as a potential replacement for traditional antibiotics as well as the value of non-traditional therapies, perhaps in combination with antibiotics.

## Communication and Education

The importance of engaging the public as advocates and identifying champions in government who can generate the political will to move things forward was emphasized. It was noted that the true magnitude of the problem is not fully appreciated and that the research community must do a better job of educating the public and the media to bring the issue of antibiotic resistance to the attention of governments.

Similarly, although infection control measures such as hand-washing and stringent housekeeping play an important role in controlling antibiotic resistance, such programs can be hard to implement and sustain in the absence of consistent control and audit. The overarching recommendation was that improved education is needed at every level: patients, health care workers, public, media, and governments.

# Breakout Session 2 – Conventional Therapies

### Summary of Report Back and Plenary Discussion

## Drug development

All three groups agreed that the current level of financial investment is inadequate to support the academic/industry partnerships needed to bring new molecules and innovative ideas to the clinic. Antibiotics do not represent an attractive proposition for industry when compared to drugs for chronic diseases, such as dementia and cancer. Compared to these drugs, antibiotics are expensive to produce, have a low market value (and therefore low return on investment), are only used for a few days or weeks, and generate resistance almost immediately. Protecting new antibiotics for use only in extreme cases reduces their economic value even further.

It was noted that the high throughput technology revolution of the last decade has created exciting opportunities for the identification of new targets, assays and pathways that might lend themselves to innovative antibiotic discovery, as well as suggesting new ways to inhibit traditional targets. Many potential antibiotics are sitting, untested, in chemical libraries and many more exist in natural products and the environment. This represents a potentially fruitful area of research that is historically difficult to support through traditional funding sources.

Participants agreed that the academic/industry landscape has recently begun to show signs of positive change, with many new initiatives geared towards incentivizing industry. Examples include the Quebec Consortium for Drug Discovery (CQDM) and the Centre for Drug Research and Development (CDRD) in Canada, and the Innovative Medicines Initiative (IMI) in the EU. IMI includes both the new Drugs For Bad Bugs (ND4BB) program and the recently launched European Lead Factory – a 30-partner consortium of industry and academic

partners established to provide a pan-European platform for drug discovery. Developments such as these will enhance our capacity to do infectious disease trials and overcome the challenges of finding health care facilities and clinicians willing and able to enroll sufficient patients for statistically powered trials.

### Diagnostics

A key requirement for successful clinical trials is access to rapid, point-of care diagnostics that are sufficiently reliable and cost effective to be used on a routine clinical basis. It was noted that new technologies, such as nanotechnology, are opening the door to the development of a new generation of easy to use diagnostics with the potential to be adopted in any health care setting. It was suggested that this is one key area in which harmonization between the UK and Canada could be very effective - by increasing datasets and enhancing clinical trials capacity. Success would be predicated on the development of formal collaborative mechanisms uniting industry and academia across the whole research and development spectrum and supported by a secretariat to organize the trials and integrate diagnostics.

## Breakout Session 3 – New Approaches

### Summary of Report Back and Plenary Discussion

### Treatment Combinations

It was noted that that many non-conventional therapies work best when used in conjunction with traditional antibiotics as an adjunct treatment - for example in biofilm disruption, where phage treatment can “open the door” to antibiotics and enhance the response. Such therapies can augment existing antibiotics or restore function to antibiotics that are no longer effective. Various combinations could be envisaged, such as a non-conventional therapy with an antibiotic to augment effect, combinations of existing antibiotics, or the introduction of new molecules, perhaps derived from natural products, to serve as an adjunct to standard treatments. In some cases, it might be enough to reduce the disease burden to a level where the infection could be cleared by the patient’s own immune system. However, not all participants supported the concept that some of the new approaches, such as immune modulation and phage therapy, demonstrate real promise as alternative therapies, feeling that such strategies are, at best, speculative. Further research may resolve this issue.

Another promising avenue of research is the microbiome. The elimination of bacterial species by antibiotics creates a potential niche area for pathogens that might normally be acquiescent. It is possible that deliberate manipulations of the microbiome may hold the key to the control of many pathogens, especially in combination with other approaches, such as the development of more targeted antibiotics.

### Innovative Bio-materials

Participants highlighted the potential of new materials that are resistant to bacterial adhesion. This would be an especially useful approach for post surgical infections caused by contaminated sutures, implants and prosthetics for example. The introduction of bacterial resistant materials could also significantly reduce transmission in health care settings. However, it was noted that despite promising research, there have been few corporate successes in this area to date.

## Vaccines

Participants felt that although vaccines have been highly successful in preventing, infectious diseases they are not ideal as a replacement for antibiotics. One challenge is the difficulty identifying the patient population that should receive the vaccine. Also the target audience is often already in poor health and may be immunosuppressed. In these individuals vaccines may not promote a strong immune response. However, it was noted that reverse vaccinology could be the "new dawn" in this field. Certainly, vaccines offer the advantage of a permanent solution to specific infections, whereas conventional antibiotics will always be only a temporary solution. The key may lie in our ability to identify sub-populations of both infectious agents and patients in order to deliver a more personalized medicine approach.

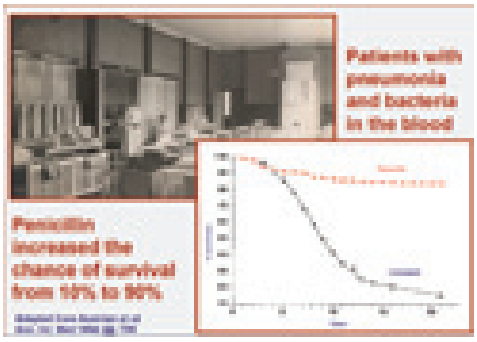
It was generally agreed that in order for non-antibiotic approaches to be widely accepted as a viable and cost-effective alternative, a paradigm shift in philosophy will be required, accompanied by an increased acceptance of non-traditional methods.

# Day 2, February 7th 2013

*Combating Antimicrobial Resistance, Charles Penn, WHO*

It is quite possible that, without intervention, we may return to the pre-antibiotic era in which sepsis and pneumonia killed nine of ten infected people. New multi-drug resistant bacteria, such as NDM-I, have already been responsible for a series of neonatal deaths in India and in countries such as Tanzania, antibiotic resistance is responsible for more deaths than malaria. Antibiotic resistance is impacting on every aspect of health care, including neonatal care, transplantation, cancer-care and also on international travel and humanitarian missions.

The WHO has identified antimicrobial resistance (AMR) as a global priority and is developing regional and national programs spanning surveillance, disease burden, and health economics to obtain a better understanding of the complexity of the situation. It is not as simple as preventing antibiotic use as, in certain parts of the world, there is a health benefit to using antibiotics in malnourished children who do not have infections. An aspect of particular interest to the WHO is quantitating the actual health and economic burden of AMR in order to convince low and middle-income countries that this is a problem that they need to address voluntarily, rather than through enforced controls and regulations.




Credit: Charles Penn, WHO

## Breakout Session 4 - What's working? – Success, failure and lessons learned

Workshop participants chose to participate in an "open mike" session during which they could describe their experiences and lesson learned.

*The Centre for Drug Research and Development (CDRD) - Bob Hancock/ Edie Dullaghan*

CDRD (http://www.cdrd.ca) is a fully-integrated national drug development and commercialization centre, providing expertise and infrastructure to enable researchers from leading health research institutions to advance promising early-stage drug candidates. CDRD is the only centre of its kind in Canada (and one of a handful in the world) with the full expertise and infrastructure to source, evaluate, develop and commercialize both small molecules and biologic innovative technologies in virtually any therapeutic area. To date, CDRD has:

- leveraged public and private sector funding to create a state-of-the-art drug development and commercialization platform with the infrastructure, scientific and business expertise, and professional project management skills to develop innovative health technologies through the pre-clinical stage;
- established Innovation Funds with some of the world's top pharmaceutical companies including Pfizer, Johnson & Johnson, and GlaxoSmithKline (GSK);
- undertaken over 136 research projects representing 99 novel technologies; launched a new start-up company; and out licensed three novel therapies with five additional technologies moving towards the commercial arm; and
- provided project management services based on industry best practices, and rigorous milestone-based project plans.

CDRD is pleased to explore potential collaborations with researchers across Canada and/or the UK; and those interested in accessing its drug development expertise and infrastructure are encouraged to contact Dr. Edie Dullaghan (edullaghan@cdrd.ca) for further information.

*The Innovative Medicines Initiative (IMI) - Angela Wittelsberger*

The Innovative Medicines Initiative (IMI) (http://www.imi.europa.eu/) is Europe's largest public-private partnership initiative designed to advance the development of better and safer medicines for patients. IMI supports collaborative research projects through networks of industrial and academic experts in order to boost pharmaceutical innovation in Europe. IMI is a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations. IMI serves as a neutral broker that:

- fosters large industry collaboration and engagement with the scientific community;
- promotes active involvement of patients, regulators and funders;
- enables innovation via joint effort where singular approaches have so far failed; and
- facilitates Intellectual Property agreements.


Credit: Angela Wittelsberger, IMI

Early IMI projects focused primarily on basic research and non-clinical testing but there has recently been a shift towards societal and public health challenges such as antibiotic resistance. For example, the "New Drugs for Bad Bugs" program is designed to give antibiotic drug development a much-needed boost by advancing novel antibiotic candidates through lead optimization into early clinical stages and by pioneering new ways of designing and implementing efficient clinical trials for novel antibiotics. Going forward, IMI hopes to facilitate the creation of networks that include, for example, vaccine manufacturers and public health agencies, an approach that would be ideal also for antibiotic resistance. IMI program launches encourage international collaborations.

*A Canadian Case Study: "The Canadian Committee on Antibiotic Resistance" - John Conly*

Canada currently lacks a strong coordinated national surveillance program for antimicrobial resistant microbes of epidemiologic significance, especially in the ambulatory setting, and there is no reliable data showing where most antibiotics are used, e.g. human use vs. animal use. Systematic efforts for controlling antibiotic resistance began in 1997 following a national consensus conference held in Montreal entitled "Controlling Antimicrobial Resistance: An Integrated Action Plan for Canadians". The conference, co-sponsored by Health Canada and the Canadian Infectious Disease Society, developed a plan which emphasized 3 core areas: antimicrobial stewardship; surveillance to monitor resistance trends; and infection prevention and control (IPC). The Canadian strategy produced 27 recommendations, one of which was the formation of the Canadian Committee on Antibiotic Resistance (CCAR), a multidisciplinary committee which performed a collating and coordinating role for stakeholder groups across Canada until its dissolution by the Public Health Agency in 2009. In addition to CCAR, several other organizations began working on a national or provincial basis over the ensuing years on one or more of the three identified core areas of the strategy. Data was collected from multiple sources in an effort to evaluate the components of four major AMR programs that were considered national based on their scope or in the delivery of their mandates. Assessment of program components was adapted from the report from the International Forum on Antibiotic Resistance colloquium. Most of the programs used similar tools but only the "Do Bugs Need Drugs Program" (DBND) had components directed towards day cares and schools. Most of the efforts focused on communications to physicians, pharmacists and the general public. Together these programs and additional provincial, regional and local efforts have been temporally associated with a 25.3% decrease in oral antimicrobial prescriptions in Canada between 1995 -2010, mainly due to decreases in β lactams, sulphonamides and tetracyclines. The most comprehensive and sustained nationally focused programs were the CCAR and DBND. Although there has been a decrease in oral antimicrobial prescribing in Canada since 1995, co-ordination of antimicrobial resistance activities at the federal-provincial interface is currently lacking.


Credit: www.dobugsneeddrugs.org

*A Case Study from Industry - David Williams and John Wain, Discuva*

Discuva (www.discuva.com) focuses on the development of new antibiotics using high-throughput transposon mutagenesis approaches. Since January 2012, the group has been studying five gram-negative pathogens that are difficult to manipulate genetically, because of multi-drug resistance. Already the team has screened more than 500,000 small molecules as well as some natural products and described hundreds of new chemotypes with activity against the bacterial pathogens tested. The technology is capable of screening

huge numbers of engineered mutants for over-expression of the target resistance genes in the presence of any antibiotic: experimental or known. Using this method, it is possible to obtain information on every gene involved in resistance as well as defining the molecular target or pathway. Already, the group has had success in identifying two “hit to lead” compounds with many more in development. This technology has huge promise because it can be applied to anything that can be genetically manipulated and so could play an important role in bio-defense, for example.

*Quebec Consortium for Drug Discovery (CQDM) - Diane Gosselin*

CQDM (www.cqdm.org/en/index.php) is an innovative not-for-profit Canadian public-private partnership that aims to accelerate the drug discovery process and develop safer and more effective drugs. The model facilitates partnerships between the academic and hospital milieus in the public sector, and the pharmaceutical and biotechnology industries in the private sector. CQDM receives funding from the Quebec government, the Canadian federal government and seven pharmaceutical companies. Since 2008, CQDM has raised more than $60 million in public and private funding and established a pre-competitive research network of 360 researchers. CQDM has a suite of funding programs to support: short term, high-risk research; innovative technologies likely to have immediate impact on drug discovery and development; and national and international collaborations.

A unique feature of CQDM is its mentorship program. Funded projects are assigned one mentor from each pharma member supporting the project. Regular meetings throughout the project promote close interactions and present opportunities to re-align the research to fit the needs of industry, as well as an early and privileged access to the research results for pharma members.

Credit: Diane Gosselin, CQDM

CQDM and CDRD are synergistic in their goals, with CQDM focusing primarily on the development of new tools and technologies whereas CDRD has a stronger focus on producing new molecules and therapies. Both organizations are anxious to establish national and international collaborations with UK researchers.

*A Case Study on Health Economics - Elizabeth Bryce, Vancouver Coastal Health*

In one successful case study, the British Columbia Health Authority hired a health economist to collect and study surveillance data in an attempt to demonstrate the impact of a hospital hand-washing program over a four-year period. The study adjusted the data, determined the main drivers, calculated the cost of the handwashing program, and pulled out the infection control arm. It also calculated the amount of money saved over the four-year period to calculate the return on investment. The results were used to prepare a successful business plan that generated an additional $500,000 in funding. The outcome was widely promoted and the program is now going province-wide. The moral in the story: an in-house health economist is an invaluable asset. Unfortunately they are in short supply in Canada and so capacity building in the area is a pressing need.

# The Pharma Perspective - Priorities and Mechanisms for Collaboration

Three representatives of the industry sector gave very brief overviews of their respective interests in AMR and the challenges and opportunities for new drug development. The panel discussion was chaired by David Rhodes, HPA

*GlaxoSmithKline - Richard Jarvest*

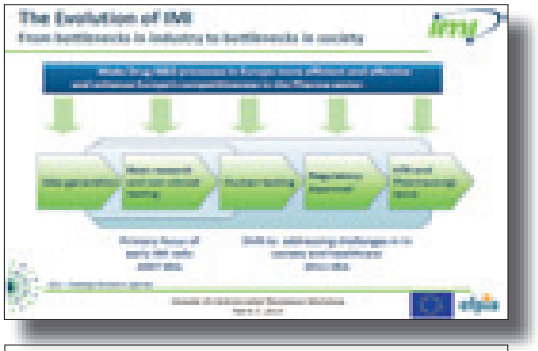
GSK has a commitment to infectious disease research both within an Infectious Disease division covering HIV, other anti-virals and anti-bacterials, as well as a Diseases of the Developing World unit that focuses on diseases such as tuberculosis (TB) and malaria. GSK also has a strong vaccine division. For anti-bacterials, the challenges revolve around scientific challenges for gram negative agents, simplification of the regulatory environment, and creating an innovative commercial model that improves the level and predictability of reward for innovation for the developer by delinking it from reliance on the volume of product used. Most of the current antibacterial research is focused on both broad-spectrum and single pathogen antibiotics for gram-negative bacteria. The GSK philosophy is to work collaboratively with other groups such as the TB Alliance and IMI and to explore partnerships with biotechnology companies to access new technologies and work together to apply them. In the antibiotic resistance field, GSK is always open to potential new collaborations with programs in the Gram negative arena. The IMI program is a good model for broad based industry-biotech-academic collaborations.

*AstraZeneca (AZ) - Seamus O'Brien*

AZ is also moving towards a collaborative work model, especially in the clinical trials space. Collaborators are increasingly required to share the cost and build the capacity to conduct clinical trials in hospital settings. This is particularly true in the developing world where there is a lack of professionalism and expertise in areas where AMR is most prevalent. AZ recognizes the need to collaborate with European economists to develop successful business models. Key areas of interest include clinical trials delivery; obtaining patient data to register compounds; combining new drugs with rapid point-of-care diagnostics; developing effective collaborative business plans; and supporting strong science.

*Innovative Medicines Initiative (IMI) - Angela Wittelsberger*

Both GSK and AZ are supporters of IMI programs. Initially a new topic is identified by industry and then IMI tailors the call to their requirements and manages the evaluation of potential projects. The process signals a change in mindset for pharma involved in public/private partnerships. It is important that, from the outset, there is a shared understanding that the focus of the submission and the quality of the science are paramount and that both the challenges and solutions in discovery and development need to be shared. A strong management structure helps to solve problems quickly and fairly should disagreements arise. For drug development collaborations, the primary challenge is to ensure that the focus is on the regulatory submission and that the pharma company has responsibility for that aspect. In the case of "failed" products pharma generally has no problem, in principle, in sharing these compounds with academia as long as there are no serious safety issues.



Credit: Angela Wittelsberger, IMI

# Breakout Session 5 – Opportunities for Collaborative Action

Workshop participants chose one of the following three broad areas for discussion:

- Partnerships
- Funding mechanisms
- Antibiotic stewardship

## Summary of the report back from the three groups and the plenary discussion

### Partnerships

The need for collaboration was a recurring theme throughout the two-day workshop. Many examples were given of successful public/private partnerships in Canada (CDRD, CQDM) and in Europe (IMI). Many countries now have antibiotic resistance strategies (PHAC matrix model) or action plans (UK Department of Health "Call for Action") that are centred on collaborations among different groups, sectors and countries. Increasingly the divide is narrowing between industry and academia and there are many examples of joint activities under development. Best practices for public-private partnerships are to: define the problem; outline how it can be addressed from an industry perspective; identify areas where researchers can contribute expertise; and then develop an appropriate funding mechanism. This same strategy can be applied equally to partnerships with public health professionals.

Partnerships are not only required between industry and academia, but also within academia, between disciplines, such as microbiology and medicinal chemistry, and between the health and agriculture sectors. The solution to antibiotic resistance will require coordinated action on a number of fronts, including: restricting antibiotic use in agriculture; controlling prescribing practices; improving infection control; and developing new anti-microbial strategies, including the development of new, targeted antibiotics.

Another recurring theme during the workshop was the need to raise public and political awareness about the urgency of tackling antibiotic resistance, and the impending health and economic consequences of failing to act. One potential area for partnership would be international coordination of messaging between public health bodies and industry, perhaps taking advantage of the growing number of social media and social marketing tools.

### Funding Mechanisms

There was discussion about successful strategies used in other areas such as HIV/AIDS to generate significant long-term financial investment. Currently, the funds available for antibiotic resistance research represent little more than seed funding. However, seed funding could be used to support collaborations and networks, paving the way for a coordinated request for substantial funding targeted on antibiotic resistance.

This group took the funding challenge one step further by proposing a bold scheme to build on existing

Canada/UK collaborations to make the case for substantial investment (in the range of $200M) to support a bi-lateral network focused on antibiotic resistance. Such a network would link multiple organizations in each country through a common platform of core infrastructures. The focus would be on translational research and the network would be comprised of researchers, public health representatives and small and large pharmaceutical and biotech companies. The network would also serve as a primary conduit for communication and outreach, and would have a strong training component.

The justification for a bi-lateral, Canada/UK network is based on the enthusiasm of both current Prime Ministers for collaborative science and the creation of strong links between the two countries. We already have the two Canada/UK teams that are jointly funded by CIHR and UK MRC and appear to be working successfully together.

There was strong support for this proposal among workshop participants.

## Antibiotic Stewardship

This group proposed a consolidated effort to change prescribing practices; improve rapid diagnsotics; manage patient expectations; and also control antibiotic use outside the health sector. A dialogue between representatives of the agriculture and health sectors was strongly encouraged. The importance of considering the environment, ecosystems, and the one-health concept when tackling antibiotic stewardship was also noted.

Canada and the UK could better coordinate their public campaigns to raise awareness and consolidate environmental data collection and monitoring as well as evidence of economic impact. In Canada, the public health network is trying to bring the provinces together and align policy across the country and the chief veterinary and medical officers are working together to try and educate both sides on the implications and correct usage of antibiotics. Similar endeavors are underway in the UK, creating an opportunity to share best practices.

It was suggested that a first step might be to create a joint document that compares and contrasts antibiotic stewardship practices in Canada and the UK to explore possibilities for collaboration and sharing of best practices.

# *Closing comments*

Many participants commented that the workshop had provided an excellent networking venue and many had made new contacts and learned of new initiatives that they were hoping to pursue with a view to collaboration. Some expressed the view that the discussions at the workshop had been an “eye opener” for them in that they had not realized the difficulty that exists in quantifying the antibiotic resistance problem and generating the surveillance and economic data necessary to build a case for increased investment.

In terms of moving forward with the development of new initiatives, neither the UK MRC nor CIHR-III currently have the available funds to support the kind of bilateral network proposed and endorsed by many of those at the workshop, but both organizations strongly support a collaborative approach.

Many felt that the time is right to approach governments and other funding sources with an ambitious proposition, as there is no doubt that antibiotic resistance is gaining visibility in the public and political arenas. Hopefully one of the outcomes of this workshop will be to seed sustainable collaborations working towards a common goal.

# APPENDIX 1 - Participants

## Translational Strategies to Combat Antibiotic Resistance:
## *"A Call to Action"*
## February 6-7, 2013
**Canada House, London, UK**

## Participants List

| | Name and Organization | Background |
|---|---|---|
|  | **Danny Altmann**<br>Head of Pathogens, Immunology and Population Health<br>The Wellcome Trust<br>d.altmann@wellcome.ac.uk<br><br>6th Feb only | **Expertise:**<br>➢ Basic HLA, T cell receptor and NK cell immunology<br>➢ Virology research including herpes viruses and HIV and emphasis on the development of transgenic disease models<br>➢ Immunology of bacterial sepsis and the immunopathogenesis of multiple sclerosis |
|  | **Keith Barker**<br>Medical Director, Infectious Diseases Therapy Area Unit, GlaxoSmithKline<br>Keith.f.barker@gsk.com | **Expertise:**<br>➢ Anti-infective late-stage drug development<br>➢ Current focus is with novel mode of action antibiotics<br>➢ Currently clinical lead for GSK in the IMI ND4BB project<br>➢ Previously worked in fields of malaria and chronic hepatitis B & C<br>➢ Before GSK worked with the UK HPA and MHRA |
|  | **Judy Bray**<br>Assistant Director<br>CIHR Institute of Infection and Immunity<br>Canadian Institutes of Health Research, Ottawa, Canada<br>judith.bray@cihr-irsc.gc.ca | **Workshop Organizing Committee** |
|  | **Eric Brown**<br>Chair, Department of Biochemistry and Biomedical Sciences<br>McMaster University, Hamilton, Ontario<br>ebrown@mcmaster.ca | **Expertise:**<br>➢ Complex and poorly understood aspects of biology in bacteria using molecular genetic and biochemical approaches<br>➢ Cell wall and ribosome biogenesis<br>➢ Chemical genomics aimed at mapping and understanding the interaction of drug-like small molecules with bacterial cell systems |
|  | **Elizabeth Bryce**<br>Clinical professor and Regional Medical Director for Infection Control at Vancouver Coastal Health<br>elizabeth.bryce@vch.ca | **Expertise:**<br>➢ Antimicrobial resistance and its Infection Control Aspects<br>➢ Sterilization and Disinfection<br>➢ Infectious Diseases and emerging Infectious Diseases<br>➢ Infection Control Education<br>➢ Infection Control Workplace Assessment and Program Development Surveillance |

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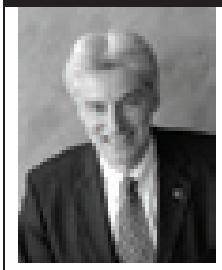
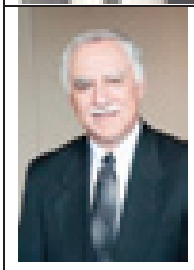
|  | **Anthony Clarke**<br>Professor, Assistant VP (Graduate Studies & Program Quality Assurance)<br>University of Guelph, Guelph, Ontario<br>a.clarke@exec.uoguelph.ca | **Expertise:**<br>➢ Structure and function relationship of enzymes involved in the metabolism of the bacterial cell wall polymer peptidoglycan, and the biodegradation of cellulose<br>➢ Identifying new potential targets for antibiotic development<br>*Anthony is the Co-PI of one of the teams funded under the Canada/UK partnership on AMR |
|  | **Anthony Coates**<br>Prof. of Medical Microbiology, St George's University, London; Founder of Helperby Therapeutics<br>acoates@sgul.ac.uk | **Expertise:**<br>➢ Tuberculosis<br>➢ Non-multiplying bacteria, dormant bacteria stationary phase bacteria<br>➢ Latent infection<br>➢ Antibiotics<br>➢ Chaperonins |
|  | **John Conly**<br>Professor of Medicine, Microbiology, Immunology and Infectious Diseases,<br>Centre for Antimicrobial Resistance,<br>Co-Director, Synder Institute for Chronic Diseases, University of Calgary<br>John.Conly@AlbertaHealthServices.Ca | **Expertise:**<br>➢ Antimicrobial resistance<br>➢ Prevention of hospital infections<br>➢ Optimal antimicrobial utilization<br>➢ Policy development in the area of antimicrobial stewardship<br>➢ Development of innovative tools in healthcare delivery<br><br>Founder, Ward of the 21st Century |
|  | **Lloyd Czaplewski**<br>Director, Chemical Biology Ventures; Founder & Director, Abgentis Ltd & Member, MRC Infection and Immunity Board<br>lloyd.czaplewski@virgin.net | **Expertise:**<br>➢ 20-years biotech R&D experience "Concept to Clinic"<br>➢ DNA Supercoiling inhibitors (GyrB/ParE)<br>➢ Fundraising (>£22m to date)<br>➢ Business development (Deals worth >$100m in upfront, milestones & royalties)<br>➢ Chemical Biology Ventures Ltd: life sciences translational R&D Consultancy<br>➢ Abgentis Limited: Re-engineering novobiocin to create a broad-spectrum IV/Oral antibiotic to treat skin and skin structure infections, community-acquired bacterial pneumonia and sexually transmitted bacterial diseases |

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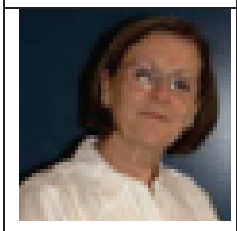
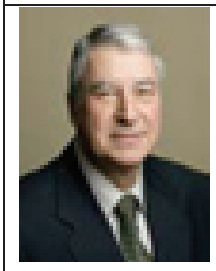
| | Name and Organization | Background |
|---|---|---|
|  | **Chris Dowson**<br>Professor of Microbiology<br>University of Warwick<br>C.G.Dowson@warwick.ac.uk | **Expertise:**<br>➢ Characterization of key biochemical pathways present across a diverse range of human and animal pathogens<br>➢ Re-exploration of peptidoglycan biosynthesis – the structural polymer of bacterial cell walls - for drug discovery<br><br>*Chris is the Co-PI of one of the teams funded under the Canada/UK partnership on AMR. |
|  | **Edie Dullaghan**<br>Head, Target validation<br>Centre for Drug Research and Development (CDRD)<br>Vancouver, British Columbia<br>edullaghan@cdrd.ca | The Centre for Drug Research and Development (CDRD) is Canada's fully-integrated national drug development and commercialization centre, providing expertise and infrastructure to enable researchers from leading health research institutions to advance promising early-stage drug candidates. Its mandate is to de-risk discoveries stemming from publicly-funded health research and transform them into viable investment opportunities for the private sector. Canada's Networks of Centres of Excellence Program has recognized CDRD as a Centre of Excellence for Commercialization and Research (CECR) www.cdrd.ca. |
|  | **Rainer Engelhardt**<br>Assistant Deputy Minister<br>Infectious Disease Prevention and Control<br>Public Health Agency of Canada<br>Ottawa, Canada<br>rainer.engelhardt@phac-aspc.gc.ca | **Expertise:**<br>➢ Development of federal legislation and environmental regulation<br>➢ Management of large-scale national and international industry-government science and technology programs in Canada and the United States<br>➢ Biomedical physiology<br>➢ Prevention and control of infectious diseases, including antimicrobial resistance and development of biopharmaceutical products alternative to antibiotics |
|  | **Diane Gosselin**<br>President and CEO<br>The Québec Consortium for Drug Discovery (CQDM)<br>dgosselin@cqdm.org | CQDM is a non-profit organization whose mission is to identify, fund and support research projects conducted jointly by university teams and groups from the private sector in biopharmaceutical research. Projects funded by CQDM target the development of innovative tools and technologies that accelerate the drug discovery process. CQDM intends to expand Quebec's leadership in biopharmaceutical research and open new research avenues that will have a strong impact on the industry. |

**Translational Strategies to Combat Antibiotic Resistance:**
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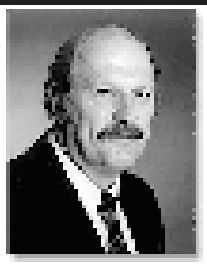
|  | **Robert(Bob) Hancock**<br>Professor<br>Department of Microbiology and Immunology<br>University of British Columbia<br>bob@hancocklab.com | **Expertise:**<br>➢ Mechanism of action of cationic host defence (antimicrobial) peptides and their role as modulators of innate immunity (including basic functional genomic studies to define the innate immunity network)<br>➢ Novel therapeutics based on the immunomodulatory and antibiotic activities of host defence peptides<br>➢ Functional genomics of the nosocomial pathogen, *Pseudomonas aeruginosa*, with reference to antibiotic resistance and the regulation of resistance and virulence |
|  | **David Harper**<br>Chief Scientific Officer<br>AmpliPhi Biosciences<br>drh@ampliphibio.com<br><br>6th Feb only | **Expertise:**<br>➢ Antibacterial solutions to improve human health through the application of its proprietary bacteriophage platform<br>➢ Gram negative bacterial infections that are often resistant to existing antibiotic treatments<br>➢ Product development opportunities to combine bacteriophage-based therapeutics with conventional antibiotics and develop multi-target, indication-specific therapeutics through the application of its bacteriophage technology and its established and expanding phage bank applicable to a range of bacterial targets |
|  | **David Heymann**<br>Chairman<br>UK Health Protection Agency<br>david.heymann@hpa.org.uk<br><br>6th Feb only | **Expertise:**<br>➢ Development of a global framework for the control of antimicrobial resistance,<br>➢ Emerging and other Communicable Diseases<br>➢ Medical epidemiology<br>➢ Public health<br>➢ Global health<br>➢ Malaria and other tropical infections |

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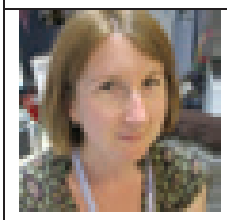
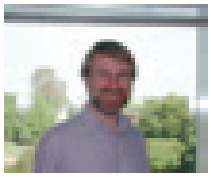
| | Name and Organization | Background |
|---|---|---|
|  | **Rebecca Hodges**<br>Programme Manager, Infections and Immunity<br>Medical Research Council<br>rebecca.hodges@headoffice.mrc.ac.uk | Dr Rebecca Hodges is the programme manager for general infections at the UK Medical Research Council. Rebecca manages the MRC's portfolio of research on infectious disease and strategic investments in the area, including AMR. |
|  | **Katie Hopkins**<br>Clinical Scientist, Antimicrobial Resistance and Healthcare Associated Infections Reference Unit (AMRHAI),<br>Health Protection Agency, Colindale<br>katie.hopkins@hpa.org.uk | **Expertise:**<br>➢ Molecular mechanisms and epidemiology of antimicrobial resistant organisms<br>➢ Application of novel genotypic and phenotypic methods for the rapid detection of AMR |
|  | **Richard Jarvest**<br>Senior Scientific Director, Infectious Diseases and Diseases of the Developing World Business Development<br>GlaxoSmithKline<br>richard.l.jarvest@gsk.com | **Expertise:**<br>➢ Anti-infective drug discovery from target to candidate<br>➢ Targets and chemical classes for antibacterial agents against antibiotic-resistant bacteria<br>➢ Establishing and managing GSK-biotech drug discovery collaborations in infectious diseases |
|  | **Malcolm Kendall**<br>CEO and Director<br>Indel Therapeutics Inc.<br>Vancouver, British Columbia<br>mkendall@indelrx.com | Indel Therapeutics Inc. is a biopharmaceutical company dedicated to developing new drugs to address the global health crisis caused by antibiotic resistance. The Company has a growing pipeline of novel antibiotic drug discovery programs that focus on curing difficult-to-treat and hospital-acquired infections. These programs are based on Indel's paradigm-changing antimicrobial drug discovery platform, a patented technology that has opened a rich, new area of drug targets for the treatment of bacterial and parasitic infections and, potentially, fungal and viral infections. |
|  | **Debbie Laubach**<br>Operations Manager<br>MediWales<br>debbie.laubach@mediwales.com | Debbie oversees all research, events organisation, and advisory groups within MediWales. Debbie has spent the past five years forming professional relationships with clinical, academic and industry stakeholders and assisting collaboration between them. |

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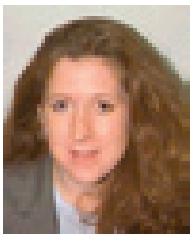
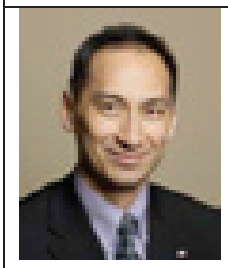
|  | **Caroline Martin**<br>Manager, Science & Innovation Programme<br>High Commission of Canada, London, UK<br>caroline.martin@international.gc.ca | **Workshop Organizing Committee** |
|  | **David McIntosh**<br>Global Scientific Affairs Expert, Novartis Vaccines & Diagnsotics & Honorary Clinical Senior Lecturer, Department of Medicine, Imperial College<br>e.mcintosh@imperial.ac.uk<br><br>6th Feb only | **Expertise:**<br>➢ Pediatrics<br>➢ Vaccines<br>➢ Infectious diseases |
|  | **Howard Njoo**<br>Director General of the Centre for Communicable Diseases and Infection Control<br>Public Health Agency of Canada<br><br>Howard.Njoo@phac-aspc.gc.ca | **Expertise:**<br>➢ Public Health<br>➢ Risk Assessment<br>➢ Risk Management for the Prevention and Control of Tuberculosis<br>➢ Antimicrobial resistance<br>➢ Infection control |
|  | **Seamus O'Brien**<br>TA Clinical Director, Global Clinical Infection<br>AstraZeneca<br>seamus.o'brien@astrazeneca.com | **Expertise:**<br>➢ Therapeutic Area Clinical Director and Operations and Strategy lead for AZ's Infection Global Medicines Unit<br>➢ Antibiotics and biologics for the treatment and prevention of serious bacterial infections<br>➢ Clinical development of antibiotics for the prevention & treatment of resistant bacterial infections |
|  | **Marc Ouellette**<br>Scientific Director<br>CIHR Institute of Infection and Immunity<br>Université Laval<br>Québec City<br>Marc.Ouellette@crchul.ulaval.ca | **Expertise:**<br>➢ Antimicrobial resistance<br>➢ Mechanisms of resistance in the parasite, Leishmania and the bacteria Streptococcus pneumoniae<br>➢ Development of new tools to diagnose resistance and novel targets for new drugs; novel pathways; potential therapeutic and diagnostic targets; phage therapy; whole genome analysis |

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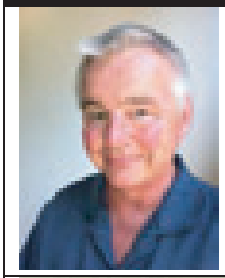
|  | **Thomas Parr**<br>President and CEO<br>Fedora Pharmaceuticals Inc<br>tparr@fedorapharma.com | **Expertise:**<br>➢ Discovery and development of novel antibiotics targeting life-threatening microbial drug resistance<br>➢ β-Lactamase inhibitors with potent activity against highly resistant bacterial strains including the newly emerging metallo-β-lactamase NDM-1 |
|  | **Charles Penn**<br>Coordinator, Pandemic and Epidemic Diseases,<br>World Health Organisation<br>pennc@who.int<br><br>7th Feb only | **Expertise:**<br>➢ Use of antivirals in influenza management<br>➢ Antimicrobial resistance<br>➢ Infection prevention and control<br>➢ Hepatitis and respiratory viruses<br>➢ Vaccine research and development<br>➢ Epidemic and intervention modelling in infectious diseases |
| **N/A** | **Mair Powell**<br>Chair EMA Infectious Disease Working Party<br>MHRA<br>Mair.Powell@mhra.gsi.gov.uk<br><br>7th Feb only | The Medicines and Healthcare products Regulatory Agency (**MHRA**) is the UK government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe. The MHRA is an executive agency of the Department of Health. The European Medicines Agency's (**EMA**) is responsible for the protection and promotion of public and animal health, through the evaluation and supervision of medicines for human and veterinary use. |
|  | **Jennifer Raven**<br>Associate, Strategic Initiatives<br>CIHR Institute of Infection and Immunity<br>Université Laval,<br>Québec City<br>Jennifer.raven@crchul.ulaval.ca | **Workshop Organizing Committee** |
|  | **David Rhodes**<br>Director of Business Development<br>UK Health Protection Agency<br>david.rhodes@hpa.org.uk<br><br>7th Feb only | David Rhodes is Head of Business Development for the Health Protection Agency and a Deputy Director in the Finance and Resource Division of HPA. He is responsible for the external business activities of HPA, where infectious disease, including antimicrobial resistance, forms a key element in the business portfolio. Responsibilities include commercial strategy and policy, intellectual property management, negotiation of R&D and scientific services contracts, and marketing, both in the UK and globally. |

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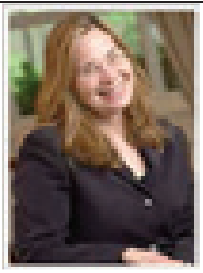
|---|---|---|
|  | **Mitch Rogers**<br>Business Development Manager<br>UK Health Protection Agency<br>mitch.rogers@hpa.org.uk | **Workshop Organizing Committee** |
|  | **David Roper**<br>Associate Professor of Structural Biology, School of Life Sciences<br>University of Warwick<br>david.roper@warwick.ac.uk | **Expertise** :<br>➢ Antibiotic Resistance Mechanisms<br>➢ Bacterial Cell Wall Biosynthesis<br>➢ Bacterial Cell Division<br>➢ Bioremediation and Degradation of Aromatic Chemicals.<br>➢ Antimicrobial Drug Discovery |
|  | **Nigel Silman**<br>Strategic Co-ordinator, Research<br>UK Health Protection Agency;<br>Visiting Professor of Infectious Diseases, University of the West of England<br>nigel.silman@hpa.org.uk | **Workshop Organizing Committee** |
|  | **Natalie Strynadka**<br>Professor, Biochemistry and Molecular Biology, Medicine; and Associate Member, Michael Smith Laboratories<br>natalie@byron.biochem.ubc.ca | **Expertise:**<br>➢ Structural and mechanistic characterization of membrane associated assemblies as targets for antibiotic and vaccine development<br>➢ Structure-based design of novel, therapeutically useful antibiotics and inhibitors of antibiotic-resistance mechanisms<br>➢ x-ray crystallography, NMR, EM, mass spectrometry, molecular modeling, molecular docking and molecular biology<br><br>*Natalie is the Co-PI of one of the teams funded under the Canada/UK partnership on AMR |

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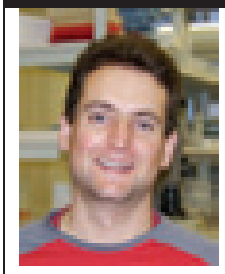
|  | **Jim Spencer**<br>Lecturer in Microbial Pathogenesis, University of Bristol<br>Jim.Spencer@bristol.ac.uk | **Expertise:**<br>➢ Structure-based design of novel antimicrobials, Application of rapid kinetic and crystallographic methods to study of the structure, mechanism and inhibition of both serine and metallo-beta-lactamases<br>➢ Molecular mechanisms by which resistance arises to a number of other antibiotic classes including the quinlones and oxazolidinones (Qnr and Cfr proteins, respectively) |
|  | **Peter Taylor**<br>Professor of Microbiology, University College London, School of Pharmacy<br>peter.taylor@ucl.ac.uk | **Expertise:**<br>➢ New approaches to the treatment of bacterial infections, particularly in relation to reversible modification of the bacterial phenotype<br>➢ Natural products with antibacterial activity<br>➢ Impact of the space environment on the staphylococcal phenotype<br>➢ New DNA-interactive drugs |
|  | **Nick Taylor**<br>Epidemiology and Risk Team Leader<br>UK Centre for Environment Fisheries and Aquaculture Science (Cefas)<br>Weymouth Laboratory<br>nick.taylor@cefas.co.uk | **Expertise**:<br>➢ Epidemiology<br>➢ Population Dynamics<br>➢ Pathogen control<br>➢ Environmental reservoirs of AMR<br>➢ Modelling the acquisition and persistence of AMR<br>➢ Risk assessment of AMR dissemination pathways |
|  | **David Verner-Jeffreys**<br>Senior Microbiologist,<br>UK Centre for Environment Fisheries and Aquaculture Science (Cefas)<br>Cefas Weymouth Laboratory<br>david.verner-jeffreys@cefas.co.uk | **Expertise:**<br>➢ Aquatic animal health<br>➢ Development of sustainable aquaculture<br>➢ Aquatic animal health product development and testing<br>➢ Antibiotic resistance in pathogens of fish and shellfish<br>➢ Monitoring aquatic environmental reservoirs of resistance<br>➢ Member of the UK's Department for Environment Food and Rural affairs (Defra) Antimicrobial Resistance Committee (DARC) |

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|  | **John Wain**<br>Prof in Medical Microbiology, University of East Anglia and CSO, Discuva Ltd<br>j.wain@uea.ac.uk | **Expertise:**<br>➢ Genetic diversity in antibiotic resistant bacteria,<br>➢ Translation of basic science research into public health-relevant tools. |
|  | **Des Walsh**<br>Head, Infections and Immunity, Lead for Stratified Medicine Medical Research Council<br>desmond.walsh@headoffice.mrc.ac.uk<br><br>7th Feb only | Dr Des Walsh is Head of Infections and Immunity and Lead for Stratified Medicine at the UK Medical Research Council. Des is responsible for shaping and developing the Infections and Immunity portfolio, developing and implementing strategy and collaborative activities in the area. |
|  | **Sally Wellsteed**<br>Team Leader Infection Control, Infectious Diseases and Blood Policy Branch<br>UK Department of Health<br>Sally.Wellsteed@dh.gsi.gov.uk | **Expertise:**<br>➢ Healthcare associated infections<br>➢ Antimicrobial resistance |
| **N/A** | **David Williams**<br>CEO, Discuva Ltd<br>david.williams@discuva.com | **Expertise:**<br>➢ Drug discovery in Pharma/Biotech including infectious disease - small molecule antibiotics to any bacteria.<br>➢ Identification of molecular target(s) and any potential resistance mechanisms.<br>➢ Prioritisation of compound series for hit-to-lead chemistry.<br>➢ Rapid point-of-care diagnostics |

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| | Name and Organization | Background |
|---|---|---|
|  | **Angela Wittelsberger**<br>Scientific Officer<br>Innovative Medicines Initiative, Brussels, Belgium<br>angela.wittelsberger@imi.europa.eu | The Innovative Medicines Initiative (IMI) is the largest public-private partnership in life sciences. In 2012, IMI launched the New Drugs for Bad Bugs (ND4BB) programme, as a result of the EU *Action plan against the rising threats from Antimicrobial Resistance*. In an unprecedented € 348M effort, IMI's first three projects under the ND4BB programme aim to improve clinical trials for new antibiotics, to increase our understanding of penetration into and efflux out of Gram-negative bacteria, and to push novel antibiotic discovery programmes from the academic and SME sector into clinical development. |
|  | **Gerard (Gerry) Wright**<br>Director of the Michael G. DeGroote Institute for Infectious Disease Research at McMaster; Professor, Department of Biochemistry and Biomedical Sciences; founding director of the McMaster Antimicrobial Research Centre<br>wrightge@mcmaster.ca | **Expertise:**<br>➢ Genomic Enzymology to study antibiotic resistance.<br>➢ Mechanisms of Antibiotic Resistance<br>➢ Reversing Resistance with Small Molecules<br>➢ Origins, Evolution and Sources of Resistance |

# APPENDIX 2 - Agenda

**Translational Strategies to Combat Antibiotic Resistance:**
***"A Call to Action"***

***A Canada/UK Collaboration between:***

**Canadian Institutes of Health Research - Institute of Infection and Immunity (CIHR-III)**
**UK Health Protection Agency (HPA)**
**Canadian High Commission**

**February 6-7, 2013**

**Canada House, London, UK**

**Workshop Objectives:**

- To provide a forum for dialogue among international experts from the academic, industrial and public health sectors.
- To facilitate networking among participants with a view to potential collaboration.
- To promote the development of joint recommendations to combat antibiotic resistance and improve health outcomes at the population level.
- To identify actionable items that could be addressed through a collaborative approach.

## AGENDA

### Day 1 – Wednesday, February 6th

| Time | Agenda Item | Presenter |
|---|---|---|
| 9.30 | **Registration and networking**<br>*Participants will be assigned to specific tables* | |
| 10.00 | Welcome | Caroline Martin, Canadian High Commission |
| 10.05 | Aims and Objectives of the Workshop | Judy Bray, CIHR-III<br>Nigel Silman, UK-HPA |
| 10.15 | Introductory Remarks | Marc Ouellette, Scientific Director, CIHR- III |
| 10.25 | Round table introductions<br>*Participants will have an opportunity to briefly introduce themselves and their area of expertise.* | All |
| 11.15 | An overview of the challenges in AMR<br>➢ The UK/Global Perspective<br>➢ The Canadian Perspective<br>➢ Plenary discussion | <br>David Heymann, HPA<br>Howard Njoo, PHAC<br>All |
| 12.00 | **Networking Lunch** | All |

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| 12.45 | Introduction to Breakout Session 1 | Mitch Rogers, HPA |
| 12.50 | **Breakout Session 1: Antibiotic Stewardship**<br>*Participants will discuss and prioritise the unsolved challenges and barriers in:*<br>➢ The true magnitude of the AMR problem – *burden of disease (national and global), relative health risk, vulnerable populations, current trends, emerging problems*<br>➢ Antibiotic use – *prescribing practices, environmental use (agriculture, animal husbandry), emerging trends*<br>➢ Infection control strategies – *policy development, educational programs*, *infrastructure issues* | All |
| 13.50 | Report back and plenary discussion | All, Chair: Mitch Rogers |
| 14.15 | Introduction to Breakout Session 2 | Nigel Silman, HPA |
| 14.20 | **Breakout Session 2 – Conventional Therapies**<br>*Participants will discuss and prioritise the unsolved challenges and barriers in:*<br>➢ Drug development pipeline<br>➢ Development and uptake of rapid, point of care diagnostics<br>➢ Discovering new antibiotics – *sources, mechanisms of action* | All |
| 15.20 | **Health Break** | |
| 15.35 | Report back and plenary discussion | All, Chair: Nigel Silman |
| 16.00 | Introduction to Breakout Session 3 | Judith Bray, CIHR-III |
| 16.05 | **Breakout Session 3 – New Approaches**<br>*Participants will discuss and prioritise the unsolved challenges and barriers in:*<br>➢ New approaches such as – *vaccines, immunomodulation, therapeutic antibodies, combination therapies, probiotics, phage, etc.*<br>➢ Which are currently the most promising?<br>➢ What is needed to take these new approaches to the clinic? | All |
| 17.05 | Report back and plenary discussion | All, Chair: Judith Bray |
| 17.30 | Workshop close and health break prior to evening event | Light refreshments: High Commissioner's Salon, 1st Floor |

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| **18.00** | **One Nucleus BioWednesday: "An evening with John Carroll"**<br><br>18.00 - Registration with tea/coffee<br>18.30 - Welcome from the Host<br>18.35 - Welcome from the CIHR-III<br>18.45 - Introduction from the Chair<br>18.50 - Guest Speaker: "An Evening with John Carroll"<br>19.20 - Q&A<br>19.35 - Closing remarks from the Chair<br>19.40 - Networking over drinks & canapés | All<br><br><br>Brian Parrott, CHC<br>Marc Ouellette, Scientific Director<br>Harriet Fear, CEO One Nucleus<br>Editor of FierceBiotech |
| **21.00** | Meeting adjourned | |

## Day 2 - Thursday, February 7th

| Time | Agenda Item | Presenter |
|---|---|---|
| 9.00 | **Coffee available on arrival** | |
| 9.15 | Welcome and re-cap of Day 1 | Judy Bray, Nigel Silman |
| 9.30 | Keynote Speaker | Charles Penn, WHO |
| 10.00 | Introduction to Breakout Session 4 | Judy Bray, Nigel Silman |
| 10.15 | **Breakout Session 4: What's working? – Examples of success, failure and lessons learned**<br>*Participants will self-assign to a group to share translational examples of success stories, failures and best practices – e.g. innovative funding programs; translation of research outcomes into practice; development of new therapeutics or diagnostics; examples of successful public/private partnerships, etc. in the following areas:*<br><br>➢ Topic 1 - Antibiotic Stewardship<br>➢ Topic 2 - Conventional therapies<br>➢ Topic 3 – New Approaches<br>➢ Topic 4 – Other ??? | All |
| 11.15 | **Health Break** | |
| 11.30 | Report Back and Plenary Discussion<br>*Each group will select up to three exemplars to present in plenary. Additional examples from the floor will be solicited.* | All, Chair: Chris Dowson |
| 12.15 | **Networking Lunch** | |

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| 13.15 | **"The Pharma Perspective" - Priorities and mechanisms for collaboration** | Richard Jarvest, GSK<br>Seamus O'Brien, AstraZeneca<br>Angela Wittelsberger, IMI<br><br>Chair: David Rhodes |
| 14.00 | Introduction to Breakout Session 5 | Judy Bray, Nigel Silman |
| 14.10 | **Breakout Session 5: Opportunities for collaborative action**<br>*Participants can stay with their group or re-assign themselves to another group. Additional groups may be added if new topics are identified. Participants will be tasked with identifying potential areas for collaborative action. For each action item a 'champion' should be identified to help move the item forward.*<br><br>➢ Antibiotic Stewardship<br>➢ Conventional Therapies<br>➢ New Approaches<br>➢ Other(s) | All |
| 15.10 | Report back and plenary discussion – actionable items<br>*The plenary discussion will include an "open mike" session where any participant can put forward an actionable item that they are prepared to lead.* | All<br>Chair: Marc Ouellette, Nigel Silman |
| 15.45 | Next Steps & Closing Remarks | Judy Bray, Nigel Silman |
| **16. 00** | **Meeting Close** | |

## Notes