




Tackling Infectious Disease Threats

Prevent, Detect, Respond with a One Health Approach

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We all know that healthcare today is faced with ever greater challenges. While advances in research and innovations may open new possibilities for better health and improved care, they do not always reach those who need them, for economic, organizational, ethical or other reasons.

Uppsala Health Summit is an international arena for frank and challenging dialogue, exploring possibilities and dilemmas associated with advancement in medicine. Uppsala Health Summit stimulates dialogue from various perspectives, such as medical, economic and ethical.

We are an enabler for change, and an arena laying the foundation for long-term relationships and insights that can help you in your work to improve long-term health outcome in your part of the world.

Uppsala Health Summit is arranged in Uppsala, Sweden, by partners with long experience of developing health and healthcare from different perspectives, and who see the potential for improving health and healthcare globally.

The effort is run as a collaboration between Uppsala University, the Swedish University of Agricultural Sciences, Uppsala Region, the City of Uppsala, the Swedish Medical Products Agency, The National Food Administration, The National Veterinary Institute, Uppsala Monitoring Centre, the Swedish Research Council for Health, Working Life and Welfare, and the network World Class Uppsala.



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Preface

As the threats to our climate and ecosystems are rising, so are the threats from infectious disease. Zika has now arrived in India, there is a fresh wave of avian influenza in China, and a new outbreak of Ebola. These are strong reminders of the many new and reemerging infectious diseases that countries all over the world are grappling with.

Not only do these diseases claim lives, they also break the social fabric of communities and destroy local economies. Some of them, such as malaria and tuberculosis are constant burdens to society, others emerge as urgent crisis, attracting world-wide attention, like the outbreaks of Zika and Ebola we have recently experienced.

The heaviest burden of infectious diseases is however the one generated by the endemic, often neglected, infectious diseases.

As the destruction of fragile ecosystems and climate change continues, along with our growing population and constant movement across the globe, the threats are growing. And with antibiotic resistance added to the mix, we are in dire straits.

Infectious diseases are complex and demand an equally complex response. Preparedness and multi-stakeholder collaboration is key. We need to capitalize on partnerships and hold institutions accountable for their promises of funding and cooperation.

Much has been learnt on how to prevent and respond, but researchers, practitioners, industry and policy makers need to continue to evaluate, discuss and put new thinking into action.

Uppsala Health Summit was created to bring medical, ethical and economic perspectives together to address challenges and dilemmas in order to improve health outcome in all parts of the world, despite limited resources. The partners behind this effort have come together because we sincerely believe that putting our knowledge into work can make the world better.

I welcome you to take part in this effort and invite you to challenging and rewarding discussions at Uppsala Health Summit!

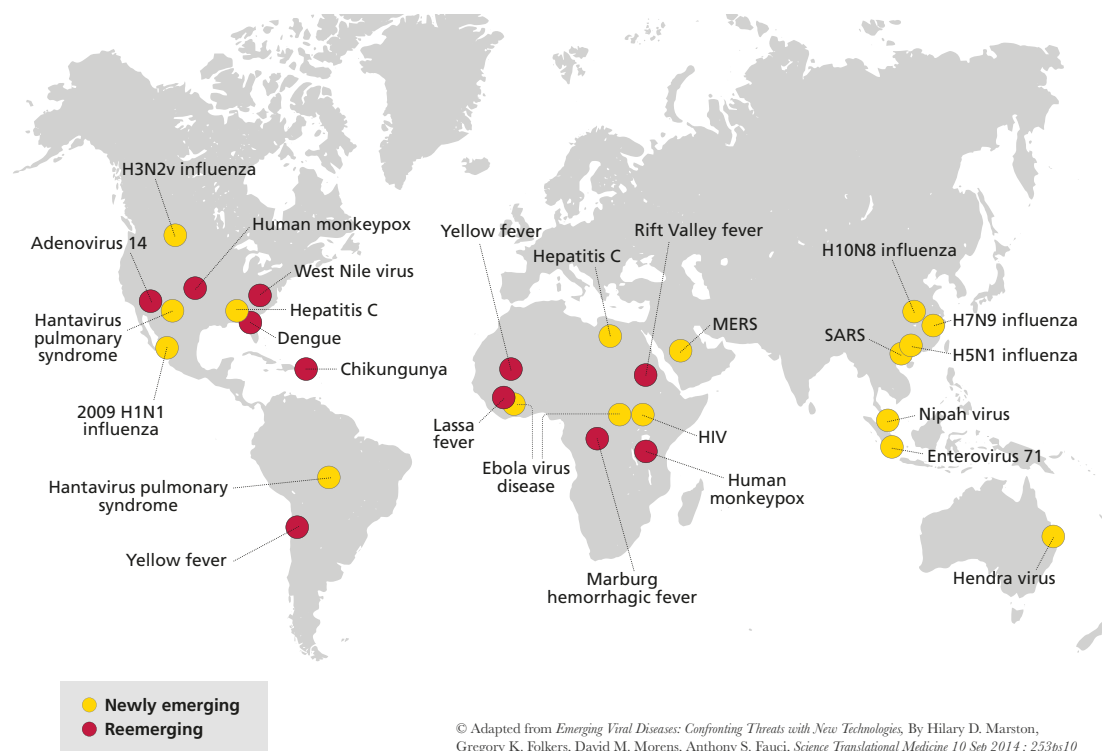


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Tackling Infectious Disease Threats – Preventing, Detecting and Responding with a One Health Approach

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Zoonotic infections, transmitted between humans and animals, are increasing throughout the world. Within their own sector, researchers and practitioners from different fields have a considerable understanding of outbreaks of disease and how to handle them. They also know they must bear in mind how local factors, traditions and politics can determine the outcome. But a disease outbreak causing deaths and disruption is always a complex picture. It requires all actors to gather knowledge from beyond their own field of expertise in order to be fully able to address disease outbreaks efficiently.

Professor Hans Rosling at Gapminder has illustrated how global trends in health and economics have improved during the last century. Life expectancy in China rose from 32 years to 71 between the years 1900 and 2000. In India it rose from 18 to 61 years. Nevertheless, constant vigilance is necessary: transboundary infectious diseases, of which many are zoonotic, are a persistent, major threat to global health.

The increased mobility of people, intensified animal production and climate change, along with the strains put on vulnerable ecosystems around the world, have all provided new pos-



1918, a Spanish influenza ward at Camp Funston, Kansas, US.

sibilities for infectious diseases to strike and become global threats. Our ability to transport people and commodities from one corner of the world to another within a day gives pathogens with an incubation period of 48 hours (the time from being infected to the first signs of disease) a good chance to reach new continents undetected. Climate change has extended the potential habitat for vectors like ticks or mosquitos and slowly but surely they will move a disease into new territories.

Two modern zoonotic outbreaks that made the world take notice

Many zoonotic pathogens have animals as primary hosts. These serve as vectors: bearers of the disease to humans. Vector-borne diseases are carried by birds, mosquitos or mammals. Although infections affecting both man and animals have been known about for centuries, in 1996 the whole world became very aware of them due to the seriousness of “mad cow disease” (BSE, Bovine Spongiform Encephalopathy). It became evident that the prion protein from BSE-infected cattle caused a new variant of the always-fatal Creutzfeldt Jacobs disease in young adults (2).

In 2003–2006, an outbreak of avian influenza, H5N1, also alerted the world to the zoonotic potential of recombination and re-assortment of

the influenza virus and the importance of worldwide surveillance and early detection. It prompted a close collaboration between WHO, FAO and OIE as well as the medical and veterinary professions on country level (3, 4). The human cases of H5N1 had all been in close contact with infected or dead poultry. Although the death toll was comparatively low, it brought back chilling memories of the Spanish flu in 1918. Referred to as “The Mother of all Pandemics”, the Spanish flu killed approximately 50 million people in Europe and 100 million worldwide (5).

Zoonotic threats continue to be a major global health problem

One of the zoonotic infections with the potential to remain a modern problem worldwide is tuberculosis. The host range is wide including both humans and wild and domestic animals. The bovine type (*Mycobacterium bovis*), as well as the human type (*Mycobacterium tuberculosis*), can infect humans and animals irrespective of type (6). Tuberculosis is highly contagious and around a third of the world’s population are carriers of the bacteria although only one in ten will come down with the disease. Tuberculosis kills around 1.5 million people worldwide every year, second only to malaria. The infection is spread mainly by airborne droplets (6, 7) but unpasteurized cow milk can be a significant means of transmission in countries where the disease is endemic.

Vector-borne diseases are estimated to cause more than a million deaths per year but many more individuals are infected and chronically debilitated for the rest of their lives. The global incidence of mosquito-borne dengue has grown dramatically in recent decades. About half of the world's population is at present estimated to be at risk (8).

The global tally of malaria in 2015 was 212 million new cases and 429 000 deaths. Across Africa, millions of people still lack access to the tools they need to prevent and treat the disease. Funding shortfalls and fragile health systems restrict access to life-saving interventions and jeopardize the attainment of global targets. According to the report, fewer than half of the 91 malaria-affected countries and territories are on track to achieve the 2020 milestone of a 40 % reduction in case incidence and mortality (9).

Another important vector of often deadly viruses for man is bats, as evidenced by the Ebola outbreak in West Africa in 2013–2015 which caused the death of 11 000 of the infected 28 000 persons. Analysis of the outbreak in Sierra Leone shows that in time of crisis, it is necessary for different actors, local and international, to join forces, and have preparedness and structure for response before the outbreak occurs (10).

Responses will be effective only when there is shared knowledge

Rapid detection of the serious infectious diseases listed above, and others, in any country is of vital importance to limit the spread and to restrict the number of infected and dead. Zoonotic diseases can have serious consequences for both health systems and food production, jeopardising the livelihood of whole regions. By using modern surveillance systems for both endemic and emerging diseases, a rapid response can be achieved. The taking of further measures in an acute crisis needs to be based on science and good practice and furthermore the use of financial resources in an efficient way. But if there is poor communication and a lack of agreement between the actors involved, this can spark off disagreements leading to panic and despair among the public. Therefore, responses to outbreaks of emerging diseases can only be successful if all involved parties, from politi-

cians to local organizations, know more about each other's area of expertise and have a prior understanding of the benefits of a contingency plan and associated agreements and guidelines. It is of vital importance not only to do the right things, but also to do them in the right order. This may sound simple, but is a daunting task in a crisis situation.

What is One Health?

One Health is a holistic approach that recognizes the connection between the health of humans and the health of animals and the environment. The name may be new but it is a way of thinking that dates back to the Greek physician, Hippocrates, who recognized the importance of a clean environment for public health. The goal of One Health is to encourage a collaborative, multi-disciplinary approach, working on a local, national, and global level, to achieve the best health for people, animals and our environment. As approximately 7 out of every 10 emerging infectious diseases in humans are spread from animals, a One Health approach is more important than ever (11).

One Health is today more of an approach than a new concept. And it is rapidly becoming an international movement based on cross-sectorial collaborations (12).

But for One Health to be more than just a name, it is up to the different disciplines to work together and communicate their knowledge to the relevant politicians to provide a solid foundation. Since one size doesn't fit all, global differences have to be taken into consideration. But for a successful approach to acute crises like a major disease outbreak, there are always certain measures that have to be taken, and, with that in mind, a commonly agreed upon and used "best practice protocol" could be of great value.

Which problems hinder the application of a One Health Approach?

The tripartite collaboration agreed between WHO, OIE and FAO has this vision: "A world capable of preventing, detecting, containing, eliminating, and responding to animal and public health risks attributable to zoonoses and animal diseases with an impact on food security through multi-sectoral cooperation and strong partnerships." (13)

While frameworks have been established at international level, policy implementation at the country level remains difficult. There are, for example, many countries with poor communication between human and animal health surveillance, and little understanding of the mechanisms and circumstances that lead to the spread of pathogens between animals and human beings in the first place. When it comes to coordinating a response, it is often not sufficiently understood that measures are urgently needed to halt the spread of disease in the animal hosts as well as in humans.

What is needed to unlock these implementation challenges?

We need to work across boundaries and towards modified academic and government structures which enhance collaboration. A greater awareness is needed of where expertise can be found covering the different aspects that have to be taken into consideration for an efficient disease prevention, control and outbreak response. We must build robust systems that can support sound decision-making based on science, and avoid being side-tracked by rumours and unscientific agenda-setting.

Why we are talking about this at Uppsala Health Summit?

Via lessons learned from recent disease threats and a better understanding of international settings, we have a unique opportunity at Uppsala Health Summit to widen perspectives and agree on what is essential for an optimum response to an outbreak.

It would be heartening to see the development of a common understanding as to how different disciplines could join forces and to have a common basic agenda for how to deal with contagious diseases worldwide. A kind of toolbox giving priorities as to what needs to be done first for a successful outcome. To not only do the right things, but also to do them in the right order.



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Zoonotic Diseases in Livestock

– Mitigating Risk Behaviour

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The aims of this workshop are to identify human risk behaviours related to zoonoses in low-income countries and consequently to design interventions that will help prevent them in the long term.

Zoonoses in low-income countries

The majority of emerging diseases in humans and many infectious ones are zoonotic. In many cases, they originate from livestock which can serve as a bridge for disease transmission between animals and humans. Thus, controlling zoonotic diseases in livestock is an important means to reduce infectious disease threats to humans. Zoonotic diseases are a threat not only to public health, but also to food production, food safety, animal welfare, and rural livelihood. The most severe infections are also a threat to international trade as outbreaks lead to the imposition of trade restrictions.

The transmission of zoonotic pathogens is more common in low-income countries where people often live in close proximity to their animals, hygienic conditions are likely to be poor and the population may lack knowledge about zoonotic hazards or are unable to

prioritize biosecurity measures. This workshop will therefore focus on the conditions in low-income countries. Obviously, there are several factors influencing the risk of transmission of these pathogens from livestock to humans, some of which derive from human behaviour.

The workshop will focus on the following questions to be able to design interventions that will prevent transmission of zoonotic pathogens:

- What incentives can be provided for farmers to contribute to the public good, for example to vaccinate livestock and to contribute to increased food safety? How can this be made economically sustainable?
- What are the economic incentives for implementing control measures against zoonotic diseases at farm and societal level?
- What is the importance of culture and traditions in livestock keeping for the risk of transmitting zoonotic infections?
- Why do livestock owners continue with certain behaviours even if they know they are linked to the risk of transmitting zoonotic diseases?
- What motivates a change of behaviour and how can such a change be made to last?



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Emerging and endemic zoonoses

Avian influenza caused by the H5N1 virus and SARS are examples of well-known emerging zoonoses. These diseases spread almost all over the world and in 2009, WHO classified the Avian influenza epidemic as a pandemic. National governments often pay these kind of zoonoses a great deal of attention and subsequently take forceful actions – if they have the capacity – such as vaccination campaigns, control of travellers, restrictions of animal movements, *etc.* However, endemic zoonoses, *i.e.* constantly present diseases, do not receive that much attention and action is seldom taken – at least in most low-income countries – to eradicate or control them, despite the fact that they contribute considerably to a country's Disability Adjusted Life Years (DALY) and impair animal production.

Conflict between the private and the public good

Besides the technical challenges, such as appropriate diagnostics and efficient treatment or prophylaxis, there are several non-technical challenges related to controlling zoonotic diseases in livestock.

One challenge is the issue of the private versus the public good as regards the vaccination of livestock. For instance, if a disease is endemic in an area, the disease incidence may be low due to high herd immunity and/or the clinical signs might be mild. In these cases, the incentive for the farmers to spend resources on vaccination of their animals might be low. However, vaccinating livestock may have a very positive effect on public health as it reduces the circulation and transmission of pathogens to humans. So, is it the responsibility of the farmers to vaccinate their livestock for the sake of public health?

Furthermore, knowledge does not translate automatically into changed behaviour. One classic example is smoking: many people continue to smoke despite their awareness of the detrimental effect smoking has on their health. Similar risk behaviours are associated with the spread of zoonotic diseases: knowledge and awareness do not markedly reduce practices associated with increased zoonosis exposure (1). Why is there a knowledge-to-behaviour gap, and what motivates people to change a risk behaviour?



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Woman at greater threat to zoonotic diseases?

There is often a traditional division of labour between men and women when rearing livestock. Generally women are more often responsible for small livestock, such as sheep, goats, pigs and poultry, whereas men have the main responsibility for large livestock such as cattle. Women are also often close to the animals as they are responsible for milking, feeding and watering them, cleaning barns and looking after the young and sick. It has also been established that the revenue from livestock kept by women is used to provide food and run the family (2). Does this close contact with livestock make women more exposed to zoonotic diseases?

Inadequate attention paid to low-profile endemic diseases

Emerging diseases of pandemic potential are prioritised by the international community and

seen as global threats, even if they are of comparatively limited importance to impoverished communities. This may result in an exacerbated neglect of endemic zoonotic diseases that already receive inadequate attention due to lack of quantitative and qualitative data (1). Endemic diseases generally attract little interest from donors, who are more prone to invest in emerging diseases despite the well-known fact that, for example, a lack of clean water and poor sanitation cause lethal child diarrhoea and thus constitute one of the most significant global disease burdens. How can global donors be encouraged to invest more in controlling endemic diseases that create few headlines in the press?

The final challenge that will be highlighted here is how to implement a true One-Health approach. To successfully combat zoonotic diseases, the public health sector and the veterinary sector have to communicate and work together.

The challenges are present on all levels in society, from government and national agencies to local government, as well as within the research community. For example, how can we increase collaboration between experts in social science, economics, human medicine and veterinary medicine? How can we go from talking about One Health to providing more proof of the concept?

Brucella in livestock: our starting point

In the workshop, we will use the case of brucellosis in peri-urban farming in the capital Dushanbe of the Central Asian country, Tajikistan, as an entry point for the discussion. Brucellosis is one of the most widespread zoonotic diseases globally present in livestock and is of substantial public health and economic importance. A high incidence among humans and livestock in Central Asia has been reported by the FAO and WHO.

In Tajikistan, a large proportion of the population earn their livelihood in the livestock sector. However, *Brucella* is widespread among livestock in the urban and peri-urban areas of Dushanbe, and there is a high seroprevalence of the bacterium in cattle, goat and sheep. This constitutes

a serious risk to public health and causes significant economic losses. It has also been shown that poor knowledge, several high-risk behaviours and a willingness to learn more provide the rationale for controlling this disease. Examples of high-risk behaviours were the consumption of unpasteurized dairy products and not wearing protective clothing when handling potentially infectious materials like aborted fetuses and discharges (3).

The workshop discussion will broaden out from this starting point. We will cover the foodborne nature of the bacteria and the incentives that can be offered to farmers to improve food safety. What are the lessons to be learnt from previous international vaccination programmes in the livestock sector?

Some risk behaviours are based on culture and tradition and often have clear gender dimensions. Can these traditions in livestock keeping be modified?

What motivation can be provided to achieve a lasting behaviour change that will reduce the risk of transmitting zoonotic infections?

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Empowered and Resilient Communities

– A Need for New Perspectives

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This workshop will focus on developing a new perspective for both understanding and empowering local communities in the context of an outbreak of infectious disease.

Disadvantaged and vulnerable groups around the world continue to suffer death, disability and major social and economic disruption from emerging infectious diseases. However, in order to effectively counter health threats like zoonotic disease outbreaks and epidemics in poor communities, the local structural determinants of health need to be taken into consideration. On paper, community participation that assigns ownership and empowerment is widely recognized as a means to alter these social determinants of health. All too often however, there is a poor understanding of the dynamics and culture of the local community and interventions are based solely on time-bound success indicators. This prevents true ownership of behavioural change processes from taking hold.

A deeper understanding of those mechanisms which assign social position and cultural influence in a specific community is needed in successful community participation both for slowly emerging threats and epidemic outbreaks. There is a need for new perspectives!

The focus areas of the workshop are:

- How can the capabilities and resources of local communities be harnessed?
- How can such communities be strengthened so that they are better prepared for emerging threats?
- How can our response systems be adapted so that they can make better use of local knowledge beyond epidemiology?
- How can continuity in the process of empowering local communities be achieved?
- How can a balance be reached between the pressures of responding rapidly in a crisis and the time needed for knowledge and behaviour change to take root?
- How realistic is it to apply anthropological understanding under time-pressure?



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The impact of social determinants on health outcomes

Health threats, be they the rise of non-communicable diseases, maternal mortality or emerging infectious diseases, affect the most vulnerable to a larger extent than the better off. This is now well established in the scientific literature and the social determinants of ill health have been thoroughly investigated. The focus on inequity in health during the last ten years has highlighted and given explanatory frameworks for how the mechanisms for this work. Having fewer resources to be able to seek care, to eat healthily, to avoid harmful practices and to pay for adequate care is one explanation. Having the decision-making power that comes with financial resources and education is another. Discrimination and cultural misunderstandings have also been brought up as an explanation for inequity in health outcomes. The Commission on the Determinants of Health (CSDH) has concluded that there is an intricate combination of many things: material, behavioural, psychosocial as well as health system factors, the so called intermediary determinants, that mediates the differences in health outcome between different strata in society (1). The CSDH concludes that this is all driven by the social position assigned to people and groups in society. How we value gender, ethnicity, income, occupations and education

impacts on how these mediating factors play out in relation to health.

To counter emerging health threats like zoonotic disease outbreaks and epidemics the structural determinants of health need to be tackled since it is the most disadvantaged and vulnerable groups that not only are most affected, but also where momentum of the health threats is greatest. This is evident in the HIV and TB epidemics: diseases driven by poverty and aggravated social conditions. To only focus on the intermediary level will be to address the symptoms and not the causes. Therefore a deeper understanding of mechanisms assigning social position and cultural influence is needed.

Successes of the policy-driven, top down approach

One way to overcome the disparate health outcomes in different groups has traditionally been to work on the policy level. Whether it is imminent public health threats like Ebola or Zika virus outbreak or the increasing level of childhood obesity, the problem at hand is most often addressed with a top-down approach. This is needed in order to change our perceptions of social position and to mitigate the ill effects of the intermediary determinants. Human Rights Conventions' International guidelines, govern-

ment policies and regulations, affirmative action policies, health insurance systems and social protection schemes are examples of how perception of social position can be modified and altered. Such vertical approaches have had great successes in improving public health after the second world war with the eradication of smallpox, wide-spread immunization campaigns, distribution of family planning to mention a few. All in all, these top-down interventions in global public health are heavily promoted and used and could be considered the “Gold standard” for achieving sustainable change.

Community participation: a vital factor for success

At the same time there is a great surge in interest for community-based approaches. The Alma-Ata declaration of Primary Health Care for all in 1978 (2), not only stressed community-based clinics but also emphasized the importance of the Community Health Worker (CHW), a topic which was furthermore mentioned at the health conference in Ouagadougou 2008 (3). To achieve lasting changes on the grassroots level, policies and government regulations are not enough. A more in-depth understanding of how health outcomes are generated at the local level is needed, addressing how the structural determinants of health are formed in each local context. As an acknowledgement of this insight, community participation has been highlighted as a key function in global health, and is currently a standing component of all health intervention initiatives. Major funders expect an account of how this participation has been achieved when reporting, and when applying for funds it is usually obligatory to state how community participation should be promoted. But, just as social position invariably determines the health outcome, there are also distinct preferences when it comes to intervention strategies. Large-scale initiatives applied using a top-down approach, are favoured over local community-based initiatives. In global health research participatory, action-oriented research methods are still under-developed and under-financed, with less impact than epidemiological descriptions and evaluation of vertical interventions. Financial reporting requirements dictate top-down quantitative set-ups and short funding intervals discourage the continuity needed to strengthen communities and behaviour change processes.

Defining community participation

But what does community participation mean? The Ouagadougou declaration urges governments to:

“promote health awareness among the people, particularly adolescents and youth; build the capacity of communities to change behaviours, adopt healthier lifestyles, take ownership of their health and be more involved in health-related activities; and create an environment to empower communities in the governance of health care services in accordance with the Primary Health Care approach (3).”

A community-driven approach to improved health thus includes capacity building, behaviour change, lifestyle adoption, ownership transfer and empowerment. Is this really what the global health actors such as major funding agencies, WHO and governments mean by community participation?

Is the bottom-up approach of involving communities actually a feasible and valued strategy? Or is it just a politically correct opinion and a nuisance requirement from funders? How do we deliver on the good intentions stated in Ouagadougou?

The vital role of people’s science in combatting the Ebola epidemic

The eventual containment of the Ebola outbreak in 2014 demonstrated how essential empowerment and ownership are in outbreak situations. It was not until the community became involved in the needed behaviour changes and devised strategies to handle the threat from within, that the outbreak could be controlled. The inability of the global health actors to recognize the vital role of the local community led to much suffering and unnecessary deaths.

In his book ‘*Ebola – How a People’s Science Helped End an Epidemic*’ Paul Richards explains how this is a striking example of how top-down solutions were favoured by the global community and how little understanding existed of how to harness local capacity among international actors faced with the threat of Ebola (4). Initial responses to the epidemic all bore witness to a generic top-down understanding of what was needed. The health systems were, justly, considered weak, the international interest and investment were accused of being too little too late and the solutions suggested all applied an outsider perspective.

Yet the factors that finally curbed the epidemic were indigenous, starting in the community, and Richards even claims that the top-down strategies actually did harm and sustained the epidemic in the initial phases by being culturally insensitive, spreading information and assigning blame rather than collaborating with the people. It was not until the community perspective was included, as defined by the Ouagadougou declaration, that a “co-production” of the response could start that finally curbed the epidemic. When biomedical knowledge was integrated with local understanding, socially acceptable solutions could be promoted. It was only when “communities learnt to think like epidemiologists and epidemiologists to think like communities” (4) that the response became effective. The initial inability of the global health actors to recognize the existence and importance of people’s science led to much suffering and unnecessary deaths.

Limitations of a top-down strategy when tackling the HIV epidemic

Similarly, the global response to the HIV epidemic that hit southern Africa in the late 1990s and early 2000s was, and still is, to a large extent, driven by a top-down strategy. Much effort has been put into vertical information campaigns, introducing messages of ABC (Abstain – Be faithful – Condomize) that have now more or less been abandoned. Little emphasis was however put on understanding the local circumstances and the cultural dimensions perpetuating the epidemic (5). The challenge has been, and still is, mainly framed within a bio-medical

discourse with a vertical top-down approach (6), and the current, newly introduced, strategy of Test and Treat is basically building on the same perspective. All this, despite the fact that it is well established that the cultural underpinnings of the HIV epidemic need to be addressed. Stigma, culturally harmful practices and destructive gender norms are still left unchallenged: issues that can only be tackled by a bottom-up strategy. Just as in the case of the Ebola epidemic, there is a need for behaviour changes that can only be achieved through locally-based motivation to challenge social and structural determinants (7).

Finding new ways to work that harness community involvement

The case of the Upper West Africa Ebola epidemic in 2013–2015 is maybe an extreme example, generated by an extreme disease, but a similar pattern of action and intervention philosophy can be recognised in slower processes, such as the current HIV/TB epidemic, and more general public health challenges as well. If we are going to be able to decrease inequity in health, which is needed to protect the most vulnerable and thereby create capability and resilience towards emerging health threats, there is a need to find new ways to work with communities. For this to happen, the position and worth given to community knowledge and bottom-up approaches need to change, new structures for financing and accountability are needed and a shift from a medical prescribing perspective to a truly participatory modus operandi is imperative.

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A Roadmap for Effective Diagnostics to Combat Global Infectious Disease

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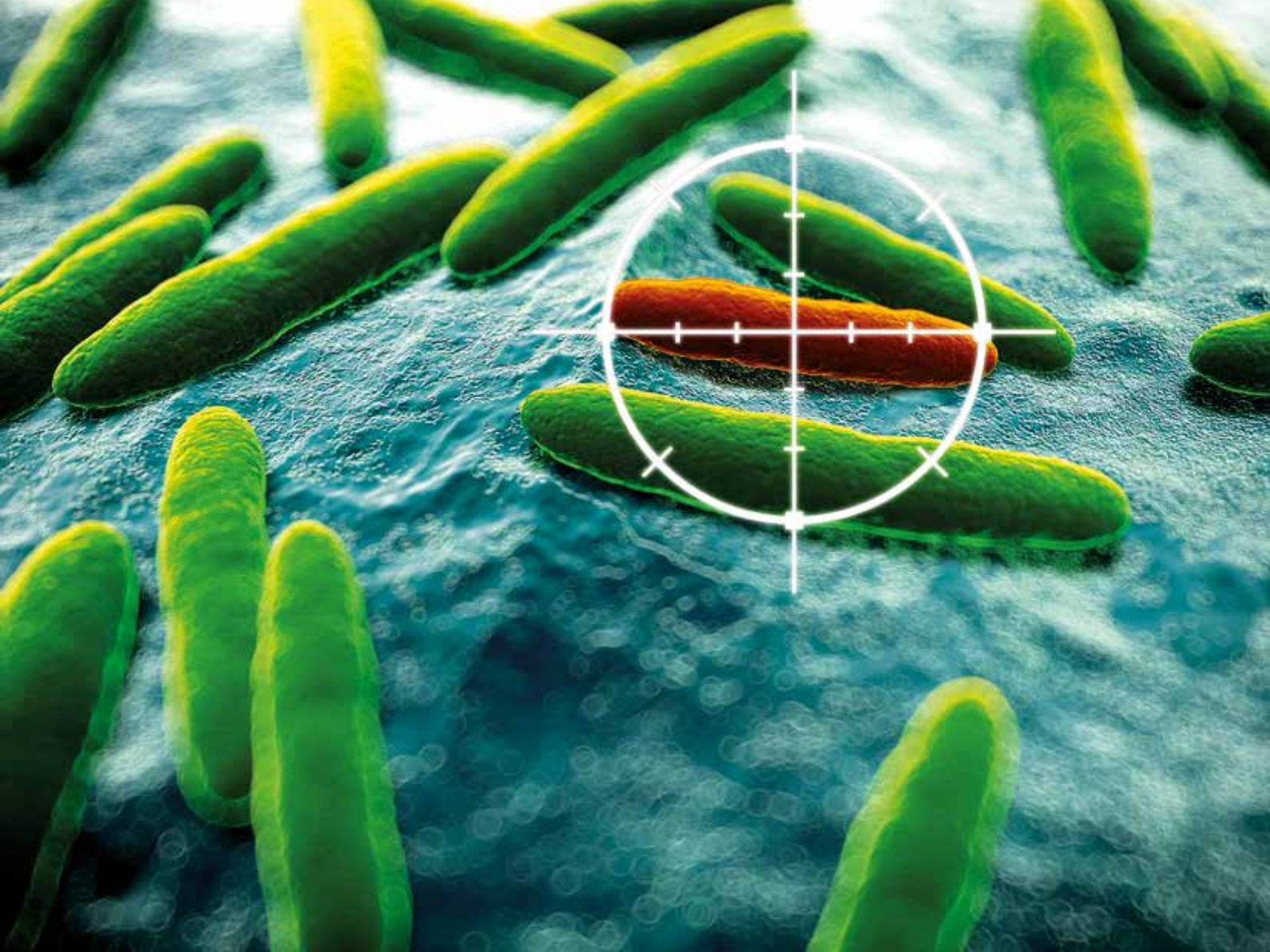
This workshop will deal with the challenges involved in developing and then providing rapid, reliable and affordable point-of-care diagnostic tools for use in low-resource countries at increased risk from infectious disease threats.

Efficient and sustainable management and prevention of infectious disease, particularly in low-income regions/countries, is critically dependent on access to robust, fast and affordable diagnostics. There is great potential for adopting recent technological advances for practical use in diagnostics and infectious disease monitoring, and there can certainly be huge benefits for health, overall life expectancy and quality of living.

However, there are several obstacles to overcome before diagnostics are effectively implemented in healthcare. In this workshop, we will identify major bottlenecks and describe future strategies that we believe will be effective in translating scientific and technological advances into clinical practice.

Questions to be addressed in the workshop are:

- What are the major obstacles to getting rapid, reliable and affordable infection diagnostics on the market and implemented in different healthcare systems?
- How can we accelerate this development to produce emerging diagnostic tools for the future?
- What incentives are there for venture capital and business to invest in this sector and what will be the role of not-for-profit and government-supported stakeholders?
- Who should take responsibility for the different steps to get new infection diagnostics to the market?



A variety of threats demand a variety of solutions

At the global level, infectious disease is one of the leading causes of mortality. As an example, WHO estimates that there were 212 million cases of malaria in 2015 and 429 000 deaths. Respiratory tract infections such as pneumonia, tuberculosis, and viral infections are other examples of infectious diseases which are hard to both control and diagnose and have major negative health impacts. Other infectious diseases of global significance and concern are HIV and sexually transmitted diseases caused by bacteria such as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Symptoms of these communicable diseases vary and are sometimes not present. Their consequences can increase and spread with long-term negative impacts on health and life quality. In many regions of the world, diarrhoeal diseases infect billions every year with millions of fatal cases. These disease symptoms can be caused by fundamentally different infectious agents including bacteria, parasites or viruses. Hence, to control and cure the disease, very different treatments and therapeutic practices may be

necessary. Apart from improved treatment efficiency, reliable diagnostics are also imperative in order to avoid over-prescription of drugs causing resistance development, *e.g.* to antibiotics as well as unnecessary adversary side effects. It is clear that for many of the most globally significant infectious diseases, fast and precise diagnostics will be the first and critically important factor for effective treatment and to limit the spread of the disease.

A disproportionate global health burden

Infectious disease is a global area of concern, but the negative effects of infectious disease on human health, wellbeing and life expectancy (*i.e.* disease burden) is not equally distributed across the global human population. Poor sanitary conditions, overall low education levels, failing infrastructure and limited resources for treating disease conditions make developing countries and low-income regions particularly at risk and exposed to infectious disease threats. There is also a demographic component with young children and infants being disproportionately affected. All diseases discussed above are an especially



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heavy healthcare burden in developing countries, and most of them take their primary death toll in children under five.

Rapid technological advances in infectious disease diagnostics

The field of infectious disease diagnostics has experienced a rapid transition and technological change over the past few years. Scientific advances in developing molecular recognition tools, finding and validating biomarkers of disease and provision of affordable and fast-sequencing technologies have opened exciting new opportunities for diagnostics that are considerably faster, more precise and informative compared to the traditional microscopy or cultivation-based methods that have been the golden standard since the birth of infection biology as a research field. The benefits could be major and a pertinent example is tuberculosis where microscopic examination of sputum is cheap, fast and unspecific, and cultures are resource-demanding and may require up to 6 weeks to get the first results and highly specific. Using nucleic acid

amplification methods, results can be obtained within a day along with information on drug resistance and sensitivity that may guide further treatments and measures to prevent further spread of the disease.

Inadequate infrastructure and high costs restrict use in developing countries

So this is very good news, at least for some parts of the world. Developing countries and low-income regions invariably cannot provide the infrastructure required to take advantage of most of these technological advances, nor can they afford to invest in the costly instrumentation or diagnostic kits that are often needed. Sequencing and PCR-based diagnostics are already in use for detecting and describing infectious disease agents and finding the appropriate treatment to most efficiently control and cure the disease, but such technologies rely on moderately to very expensive instrumentation such as thermocyclers and DNA sequencers with ancillary equipment. Even if such investments can be made, stable electricity for instrument

performance and distribution networks and refrigeration for storage of reagents, along with considerable training, are required to make it work. It would be unrealistic to expect such diagnostics to be broadly adopted across resource-poor regions around the world. Inadequate infrastructure will probably also prevent broader centralized use of core facilities to serve a country or a region. How should samples be transported to the laboratories? Will it be possible or even desirable that sick individuals travel for diagnostics at a central hospital or core facility? How will the patient then be informed of the result from the diagnostic test and how long will this entire process take?

Advantages of point-of-care approaches in resource-poor settings

Point-of-care approaches have been identified as a more promising strategy for infectious disease diagnostics, management and control in the developing world. Such strategies could open the possibility to meet the patient in their local area or perhaps even in their home and offer simple and robust diagnostic tests that produce rapid results, enabling near immediate action to be taken to avoid spreading the disease, to cure it or to treat the symptoms. Appropriate point-of-care diagnostic tests should ideally adhere to the ASSURED criteria developed by the World Health Organization (Box 1). This would rule out both sequencing and essentially also all PCR-based diagnostics for putative point-of-care diagnostics. Instead, affordable and robust miniaturized assays based on affinity-detection of either antigens associated with the infectious

agent or human biomarkers of disease have been the methods of choice.

Lateral flow immunoassays (LFIA) is the most widespread platform for such diagnostics and is based on binding of a specific antibody to an infectious disease antigen and by incorporating a reporter molecule that can be visibly inspected, readout can be done within minutes. The technical requirements and need for training are minimal with the home pregnancy test being the best-known example. There are many examples of such diagnostic tests for microbial infections (HIV, hepatitis, malaria, cryptococcal meningitis, *etc.*) but one potential bottleneck is the need to obtain samples that are reasonably clean and with high concentration of the respective analytes (disease antigens). If testing is done with samples that feature low levels of the analyte, this may result in false negatives, thus violating the ASSURED principles. Because of these and other limitations, there is much ongoing research to develop more sensitive and versatile (with regards to sample type) diagnostic tests. One promising avenue in this regard is the miniaturization of nucleic acid-based assays in microfluidic devices that should be low-cost and able to operate without expensive equipment and stable electrical supply. But who should safeguard and support the continued efforts and work in such research and development endeavours?

“Globally important” pathogens get priority

Although point-of-care diagnostics have received a lot of attention recently, we are still far from a solution to meet the diagnostic challenges in combatting global infectious disease. Development of functional diagnostic tools is typically very resource-demanding and the monetary return on investment is highly uncertain or sometimes even predictably low. This may prevent industry and venture capital from investing in bringing such technologies to market even if the discoveries have been made. Who should fund the early (pre-clinical) development of diagnostics tools and who should take them to market? Some of the more pertinent examples of the successful development and use of diagnostics for infectious disease, also in the developing world, are for malaria, HIV or disease caused by other

Box 1. Characteristics of suitable diagnostic tests for developing countries (ASSURED) developed by the World Health Organization.

- Affordable by those at risk of infection
- Sensitive (few false negatives)
- Specific (few false positives)
- User-friendly (simple also for non-trained persons)
- Rapid to enable treatment at first visit and no need for special storage, and Robust
- Equipment-free (not relying on electricity)
- Deliverable to those who need it (portable)

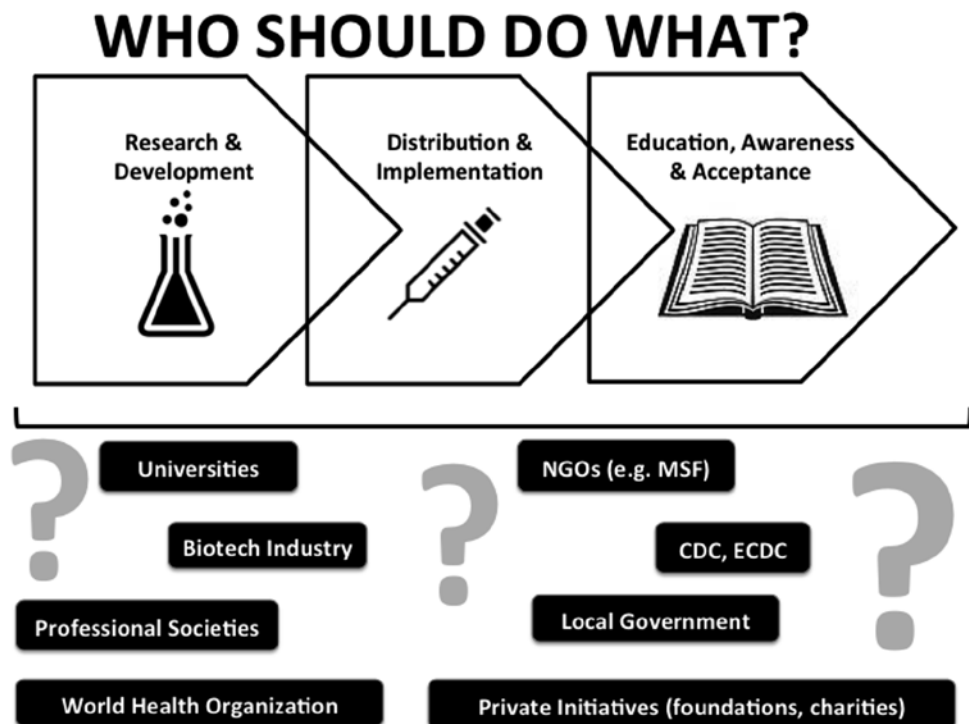
“globally important” pathogens. The worldwide number of infected individuals and the occasional spread and outbreaks in more developed and high-income regions make these diseases relevant targets and accordingly considerable efforts are spent on developing diagnostic tools. There are, however, a large number of lesser known, often regionally limited but still very severe infectious diseases that will not get the same attention, and where prospects of having diagnostic tools developed are less positive. Trypanosomiasis and Leishmaniasis are examples of two such tropical diseases. Who should develop diagnostic tests for infectious diseases where those affected are mainly from poor rural communities? Similar to HIV and malaria, infections of the respiratory and gastrointestinal tracts are global health problems where diagnostics are clearly lagging behind. Such infections cause much suffering and death (particularly among children) in both developing countries and more resource-rich parts of the world. The challenges in providing access to rapid and precise point-of-care infectious disease diagnostics are shared and this may provide a window of opportunity. If we can solve these problems in our own backyard, we can also (in the process) improve the situation for the rest of the world.

Adapting new diagnostic tools to local conditions

Even when a diagnostic tool suitable for point of care according to the ASSURED criteria is available, it may not always be adopted by local health care providers or the population at risk. There could be cultural resistance and conflict with prevailing traditions or beliefs, or there may simply be inertia in adopting new technology. The costs may also be too high and there may be challenges with distribution to the users related to limitations in transport and freight infrastructure. Thus, in addition to the new technologies and methodologies themselves, it is imperative that education, knowledge and information are developed in accordance with the local social and cultural context, in close collaboration with key actors in the target regions.

This begs the question: where does the responsibility lie and who should take action? Training and education is one aspect in this, as is legislation, politics and religion. By discussing and establishing the responsibilities and roles of different stakeholders, we hope that this workshop will pave the way for more efficient infectious disease diagnostics for the benefit of humankind (Figure 1).

Figure 1. Needs for successful implementation of diagnostics for infectious disease management and control with potential stakeholders indicated. During which stage(s) should each stakeholder get involved, how should they collaborate and what should their involvement be for maximum impact on global health and wellbeing?



Identifying the bottlenecks and accelerating progress

The main outcome of the workshop will be the shared experiences, ideas and visions of the participants to stimulate the development of effective and useful diagnostic tools for infectious disease. By participants then bringing the information back to national governments, NGOs, regional health sectors, knowledge-based organizations such as universities and research institutes, funding bodies and industry, we will move beyond the current situation and make a difference. At the end of the workshop, we hope to not only have identified some of the major bottlenecks, but also have solutions for how to accelerate the development and implementation. The obstacles will in part be technical, as well as cultural, legislative and economical. Incentives for investments as well as the role of not-for-profit and governmental organizations will be discussed with a hope of reaching consensus and creative solutions for how to move forward.

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New Medicines and Vaccines

– Monitor Safety in Emergency Situations?

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Emerging infectious diseases disproportionately impact the poorest countries in the world. They typically break out in places where both the healthcare and research infrastructure are limited and inadequate. New medicines and vaccines are being deployed for treatment and prevention efforts in regions where there is a considerable concern about pharmacovigilance resources. Will those countries be able to meet the challenges of monitoring the safety of these medicinal products upon widespread use?

This workshop will discuss whether the current WHO guidelines are sufficient to ensure that new medicines and vaccines used in the treatment and prevention of emerging infectious disease threats in resource-poor settings are adequately monitored for safety. If not, we will define the elements required in the establishment of a “reasonable minimum” pharmacovigilance system for the rational and safe use of medicines in these circumstances.

This workshop will address the following topics:

- Should we reconsider our approach to the monitoring for adverse events? Are resources and efforts best focussed on active surveillance or should we prioritize the support of a passive surveillance infrastructure?
- How can safety problems known at the time a new medicinal product is introduced be more effectively dealt with? How can risk minimization best be carried out on a limited budget?
- Would resources be better allocated to the development of cost-effective ways of identifying individuals known to be at risk of harm from medicines within the context of public health programmes?
- Is there a way to move beyond collecting and analysing adverse event data to ensure that new medicines and vaccines are used in rational and safe ways? How can a culture of drug safety awareness be created and then sustained?
- In what way could better collaboration be established among the multiple stakeholders involved in the development and deployment of new medicines and vaccines in these circumstances? How do we ensure that resources are rationally distributed among stakeholders with different roles?



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Surveillance of new medicines under “normal” circumstances is a long process

Currently, the practice of pharmacovigilance in the setting of the treatment and prevention of emerging infectious diseases has been limited to the monitoring of adverse events from new medicines and vaccines. However, there is evidence to suggest that short-lived programmes of active surveillance may not be adequate to draw strong conclusions on safety and that the level of reporting from public health programmes into passive surveillance systems, most notably the database of the WHO Programme for International Drug Monitoring (PIDM) remains low.

Even under “routine” circumstances, the amount of knowledge about new medicinal products at the time of introduction to public use is limited. Clinical trials, designed to investigate both the efficacy and safety of products, are performed using a relatively small sample of participants, include specific inclusion and exclusion criteria, and have limited participant follow-up times. Spontaneous case reporting is central to the safety surveillance of medicines in the post-marketing period, as it allows for the early detection of rare, unexpected or suspected adverse drug reactions. Risk management plans/

risk evaluation and mitigation strategies are implemented by marketing authorization holders at the time of approval. This is done in order to minimize the risk from known safety concerns, to collect important missing information on populations not included in clinical trials, and to further characterize effectiveness and safety through observational studies.

It is common practice for new medicinal products to be developed and first introduced into high-income countries, allowing drug manufacturers the opportunity to recover the cost of the research and development of their products. Consequently, there are typically several years of post-marketing experience in these countries, which contributes to the knowledge base regarding both effectiveness and safety prior to their introduction in lower- and middle-income countries.

Emerging infectious disease threats, however, typically do not offer the luxury of “routine circumstances”. The knowledge base at the time a new medicine or vaccine is introduced may vary from fully completed clinical trial programmes to only “proof of concept” data. Furthermore, given that such diseases disproportionately affect

lower- and middle-income countries, new medicinal products are directly introduced into countries with limited pharmacovigilance resources and less advanced health care systems.

Are the current approaches to surveillance adequate?

New medicines and vaccines against emerging infectious diseases are typically developed through governmental, academic and industry partnerships. Public health programmes orchestrate the implementation of such campaigns, often with the additional support of international public health and non-governmental organizations. The practice of pharmacovigilance in these situations has been largely limited to the collection of adverse event data, using active surveillance methodologies for limited periods at the initiation of the campaign. Furthermore, pharmacovigilance data from public health programmes is not often shared, and results are not always communicated.

There are examples to suggest that the current approaches to the practice of pharmacovigilance in the treatment and/or prevention of emerging infectious disease threats are not adequate. It is imperative that efforts should focus on the establishment of sustainable pharmacovigilance systems to ensure an overall rational and safe use of medicines. The absence of such a system may not only cause great harm to individual patients but also lead to a detrimental effect on public confidence in the public health campaigns required for the treatment, prevention, and/or control of emerging infectious diseases.

The use of LapDap in malaria treatment

Chlorproguanil-dapsone or “Lapdap” was a new medicine introduced directly into Africa for the treatment of malaria. It was developed in a collaboration between GlaxoSmithKline (GSK) and the UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR). It was approved by the UK national regulatory authority, the MHRA, for the treatment of uncomplicated *Plasmodium falciparum* malaria in children, adolescents and adults in July 2003 based upon a clinical trial database of less than 3000 persons. Within a relatively short amount of time after MHRA approval, the drug was registered in more than 20 African countries.

A known safety concern for Lapdap, which interferes with folate metabolism, is haemolytic anaemia. This well-characterized adverse drug reaction (ADR) is more severe in persons with inherited glucose 6-phosphate dehydrogenase (G6PD) deficiency. Formal clinical trials of LapDap were undertaken in Africa; however, no G6PD testing was done during a key trial. Anaemia was found to be more common in patients given LapDap, which the investigators termed as a “possible” ADR. In the regulatory approval of LapDap, its use was to be contraindicated in patients with G6PD deficiency; however, there were no further recommendations described to minimize this risk (1).

WHO assessment leads to questions about safety of LapDap

Given the known high prevalence of G6PD deficiency in sub-Saharan Africa in addition to the limited availability of screening tests for this condition, WHO undertook a safety assessment of the product in 2004 to provide recommendations on the safe use of LapDap in Africa. The WHO committee determined that there was a lack of sufficient information to substantiate its safe and efficacious administration in the circumstances under which it was to be used in Africa; it therefore provided guidance for use as well as priorities for further research (2).

A retrospective analysis of clinical trial data revealed that 35 % of children in whom there was a notable drop in haemoglobin were G6PD deficient. The number of events that happened outside of controlled trials is unknown.

LapDap remained on the market in many African countries until February 2008, at which time it was withdrawn by GSK because of “significant reductions in haemoglobin levels of patients with G6PD deficiency” (1).

Use of MenAfriVac in Africa’s “meningitis belt”

MenAfriVac is a meningococcal A conjugate vaccine directly introduced into several countries included in Africa’s “meningitis belt”, which stretches from Gambia in the west to Eritrea in the east. The conjugated vaccine, PsA-TT, was developed in a collaboration between the Meningitis Vaccine Project (a partnership between the WHO and the



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non-governmental organization PATH) and the Serum Institute of India and underwent clinical trials in Africa and India in 2005. It was licensed in India in January 2010 and prequalified by the WHO in June 2010.

Upon the recommendation of the WHO Global Advisory Committee on Vaccine Safety, the vaccine introduction began with an initial phased approach to collect additional safety information; this approach was meant also to serve as an opportunity for capacity building in vaccine pharmacovigilance. The vaccine was then initially introduced into three countries (Burkina Faso, Mali, and Niger) and subsequently offered to all countries in the meningitis belt (3).

Problems of adequate surveillance

There are several papers which report on the incidence and types of adverse events following immunization collected from both passive and active forms of surveillance at the time of vaccination campaigns in various African countries (4–7). Two publications have also highlighted the challenges and difficulties in the collection of safety information in both the clinical trial as well as early post-marketing use of MenAfriVac (8, 3). Collection of safety data in the clinical trial setting was complicated by a lack of uniformity in collection methodology and medical practice among clinical study sites, communication challenges, and local endemic diseases which made safety evaluations of vaccinations difficult

(malaria, rotavirus). Challenges in the safety surveillance in the initial phases of the vaccination campaign included limited resources which impacted on the sustainability of data quality and the establishment of national expert committees for investigation and causality assessments of serious Adverse Events Following Immunization, AEFIs; difficulties in the establishment of collaboration and an unequal distribution of resources among healthcare systems, immunization programmes and national regulatory (pharmacovigilance) centres; and an inability of the less sophisticated local healthcare systems to detect, diagnose and register conditions of interest likely to be reported after vaccination.

Conclusions on the safety of the vaccine, especially as it relates to less frequently and/or later occurring adverse effects following immunization therefore remain limited.

WHO guidance and resources

The WHO has issued guidance in various forms intended to promote safe use of specific medicines and vaccines being used in public health programmes.

An overall guide, “The Safety of Medicines in Public Health Programmes: Pharmacovigilance an essential tool”, aims to encourage the integration of pharmacovigilance as an essential component of public health programmes that use medicines. It highlights the importance of collaboration and communication among public health programmes and pharmacovigilance systems/drug regulatory authorities, both locally and internationally (9).

The WHO additionally offers disease-specific guidance in various forms. Examples include a practical handbook on the pharmacovigilance of antimalarial medicines (10), interim guidance on the use of bedaquiline for multi-drug resistant tuberculosis (MDR-TB) (11), and a position paper on dengue vaccine (12).

Specifically available for vaccines is a manual: “Active Vaccine Safety Surveillance” by the Council for International Organizations of Medical Sciences (CIOMS) Working Group on Vaccine Safety. Developed to address objective #8 of the WHO Global Vaccine Safety Initia-

tive, it is intended as a practical approach to aid immunization professionals and decision-makers in determining the best course of action if additional vaccine safety data is needed when a new vaccine is being introduced into lower- and middle-income countries (13).

WHO Programme for International Drug Monitoring and Vigibase

In 1968, after the thalidomide experience, Resolution 16.36, passed during the 16th World Assembly, called for “a systematic collection of information on serious adverse drug reactions during development and particularly after medicines have been made available for public use”. The WHO Programme for International Drug Monitoring (PIDM) was subsequently formed with an initial composition of 10 countries. Today the programme has grown to include 127 countries as full members. In addition, there are 28 associate members who are in the early stages of establishing their pharmacovigilance systems. Many lower- and middle-income countries which have been targets for public health programmes, such as LapDap and MenAfriVac, have joined the programme in recent years.

VigiBase aids reporting of anomalies

A harmonized system of vigilance is found in local and national pharmacovigilance centres, in regional organizations, as well as in the WHO PIDM. Member countries record incidents of medicinal harm suffered by patients and submit them to the WHO global database, VigiBase. Data within VigiBase are recorded in a structured and comprehensive way to allow for the detection of potential medicinal safety hazards.

An integral part of pharmacovigilance is the sharing of data and/or knowledge among relevant stakeholders. Members of the WHO PIDM have access to the data collected within VigiBase so that when an ADR is reported in their country, they are quickly and easily able to see if it has been reported in other countries and to understand their reports in a global context.

Many of the countries in which public health programmes for the treatment and prevention of infectious disease threats are ongoing are members of the WHO programme; however, there remains a relative paucity of reports on the new medicines and vaccines in VigiBase.

Towards a robust pharmacovigilance system

There are many aspects to a sustainable, robust pharmacovigilance system. Far more than simply the collection and analysis of adverse event reports, it also develops and relies upon a public awareness of drug safety and nurtures a culture of reporting suspected adverse drug reactions. In addition, it encourages communication within the local context along with the sharing of safety data on a global scale. The absence of such a system may not only cause great harm to individual patients but also lead to a detrimental effect on public confidence in the public health campaigns required for the treatment, prevention, and/or control of emerging infectious diseases.

Currently, the practice of pharmacovigilance in the setting of the treatment and prevention of emerging infectious diseases has been limited to the monitoring of adverse events from new medicines and vaccines. However, there is evidence to suggest that short-lived programmes of active surveillance may not be adequate to draw strong conclusions on safety and that the level of reporting from public health programmes into passive surveillance systems, most notably the database of the WHO PIDM, remains low. Furthermore, sustainable pharmacovigilance systems do not simply monitor reported adverse events from medicines or vaccines; they also promote an awareness of medicine safety and aim to ensure the rational and safe use of medicines in specific context.

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Innovation and Big Data in Health Surveillance

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This workshop will discuss the priorities and challenges related to building the health surveillance systems of the future.

In an era of ubiquitous electronic collection of data, there is growing opportunity to monitor the health of populations in real-time. This will allow the early detection of signs of disease introduction, natural or man-made, as well as the production of information to support prevention and control. Teaching computers to transform data into actionable information allows us to overcome the challenge of data volume and velocity. This is however conditional on our ability to overcome greater challenges, such as processing a large variety of (noisy) data, interfacing with medical knowledge, and producing valuable outputs for actors in different contexts. Moreover, effective disease prevention and control needs to be operationalized, taking into consideration all the populations that affect and are affected by disease spread.

To ensure that big data innovation contributes to population health, it needs to be incorporated into governments' routine decision-making processes, building a framework of data-driven surveillance in a One Health context.

The challenges abound: from technical difficulties related to extracting information from Big Data and privacy and ethical issues, to

governmental and organizational barriers and funding challenges. Who pays when everybody benefits, but nobody profits?

The aims of the workshop

This workshop will identify and prioritize the challenges related to the use of innovation to achieve data-driven decision-making in population health. Workshop participants will have a chance to discuss the challenges, and prioritize them using objective measures, such as opportunities for improvement and impact.

How do we build the surveillance systems of the future? What are the priority challenges to address in order to achieve the following aims:

- Develop systems capable of transforming data into actionable information for One Health Surveillance (*technical challenges*)
- Translate research into practice, and combine new and traditional methods in order to incorporate innovation into the daily practice of disease prevention, detection and control (*operational challenges*)?
- Address cultural and ethical norms and gain public trust to develop data-driven systems (*normative challenges*)
- Deliver innovation to the right actors in public, animal and environmental health, taking into account funding and organizational barriers in the public sector, including legislation (*public good predicament*)?



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Health surveillance in real time

In an era of ubiquitous electronic collection of data, there is growing opportunity to monitor the health of populations in real-time.

The systematic collection of data from a defined population, with the specific aim of taking actions to mitigate risks and improve well-being, is the goal of *health surveillance* (1). Public and animal surveillance are concerned with strategies to improve the health of people and animals respectively. In a One Health context, surveillance is carried out in a holistic framework that involves animals, humans and the environment.

Enabling computers to transform data into actionable information allows us to overcome the challenge of data volume and velocity that characterize today's growing flow of digital data, coined "Big Data", as defined by US NIH's program Big Data to Knowledge, BD2K (6). This will allow early detection of signs of disease introduction, natural or man-made, as well as produce information to support prevention and control.

Big data, however, is not just about volume. Extracting value from the complexity and diversity of the data sources available is condi-

tional on overcoming greater challenges, such as processing a large variety of (noisy) data, interfacing with medical knowledge, and producing valuable outputs for actors in different contexts. Moreover, effective disease prevention and control needs to be operationalized taking into consideration all populations which affect and are affected by disease spread. Developing effective systems to convert single data streams into information is only part of the challenge. To support decision-making and action, the ultimate challenge is combining evidence from multiple sources.

Research and development in the field of Big Data have brought innovation to all stages of the surveillance continuum, from *data collection*, through *data analysis*, to *communication and information sharing*. How do we use this innovation to build the surveillance systems of the future?

Capturing data and producing information for health surveillance is *difficult!*

In going about our daily lives, we leave a great number of digital footprints. Analyzed at the population level, data concerning people's mobility, preferences and actions can give great insights about the distribution of health and disease, and even create a "riskcape – maps of the

distribution of risk in space” (2). But these small pieces of data are usually disconnected, and a large number of them are not directly related to health. Combining these pieces of evidence is, therefore, not a straightforward matter.

Algorithms need to be trained on a wide variety of data, most of which are not collected for surveillance. Relationships and interactions crucial for risk characterization and quantification need to be identified (2), but data are rarely linked and system interoperability remains a big challenge. The technology needed to overcome these issues needs not only to be powerful, but also dynamic (3). The underlying data are constantly changing, as are the goals of surveillance to keep up with evolving populations and pathogens.

Capturing data and producing actionable information for health surveillance is difficult!

Innovation comes fast in big data, and technology is already available to address many of the technical challenges. The issue of access to innovation by governments is discussed below, but incorporation of these solutions into surveillance practice goes beyond technology access.

“Big Data’s strength is in finding associations, not in showing whether these associations have meaning. Finding a signal is only the first step” (4). How do we validate and investigate these signals? Beyond validity, how do we assess utility? What routines need to be established in order to allow the decision-making process to incorporate this information – in order to allow it to trigger action? There seems to be a consensus that modern information systems need to be combined with traditional epidemiological systems, but there is no straightforward recipe for that.

Sustainability is another important issue to consider. Hay *et al.* discussed the need to demonstrate the feasibility and sustainability of audience engagement for Web-based technologies such as HealthMap, www.healthmap.org (5). Sustainability of the tools themselves should also be considered, as they depend on collaborations across many disciplines and sectors.

Capturing data and producing actionable information for health surveillance is controversial!

Moving away from population averages, and developing systems capable of processing personalized information, has great societal benefits in terms of health control (3). However, public perception of whether the benefits outweigh their privacy concerns will, as Heitmueller *et al.* stated, “set boundaries on the usage of big data”. The author describes a ‘crisis of confidence’ in the way that personal information and behaviour data are being used, pointing out that although a very large proportion of customers use store loyalty cards, medical information is a far more sensitive issue, and concluding that “views about personal health information are more complex than views about other data”.

Different levels of access to different types of data may need to be considered. A clear ethical framework needs to be established, with norms that set the data usage boundaries. Communication is also essential, as such a framework will not be enough unless there is public trust in the protection of their data confidentiality.

Capturing data and producing actionable information for health surveillance is expensive!

The data privacy concerns discussed above remind us that data is not always seen as a public good. Monetary and non-monetary incentives are probably needed for individuals and organizations to share data (3).

In discussing the sustainability of big data opportunities for surveillance, Hay *et al.* stated that the “ultimate vision is to democratize the platform by providing the code to all interested authorities”. As we have argued in the operational challenges however, operationalizing a system is more than generating information. To operate data-driven surveillance systems, governments need to employ multi-disciplinary teams capable of using the tools, communicating results to epidemiologists, and supporting them in the process of combining this information with evidence gathered through traditional surveillance methods.

Moreover, to make big data innovation a public good, governments need to balance other population interests. Discussing the development of public policies for the use of big data, Heitmueller *et al.* summarized the issue as two main trade-offs: “The first trade-off concerns the role of government in simultaneously protecting people’s privacy and taking advantage of the benefits of large data sets [...]. The second trade-off is related to the tension between realizing the societal benefits involved in sharing data and safeguarding proprietary rights.”

To add to the complexity of the debate, the solutions will probably need to be tailored to individual countries, as the resources and needs of different nations need to be taken into account. It is beyond the scope of this workshop to debate resource access in countries at different development stages.

All challenges considered, Heitmueller *et al.* suggest that governments should focus on a few main tasks, such as: building support for data sharing; building an evidence base, gathering systematic and robust evidence of how data sharing has resulted in benefits in health care; establishing open data commons of anonymized data; creating demand and capability; and creating trust networks. Legislating wisely to address these tasks, however, is not a straightforward task, as big data evolves fast, and policy makers must deal with great uncertainties regarding the future risks and benefits.

Inter-connecting the perspectives on data-driven surveillance

How do we build the surveillance systems of the future? How can we implement systems capable of transforming data into actionable information for One Health Surveillance?

The workshop aims to connect those facing the problem, mainly governmental surveillance officials, with researchers and developers in academia and the private sector, who are most often the drivers of big data innovation. Different sectors – private, public and academia – may have different perceptions regarding the challenges to achieve data-driven surveillance. They may also have different access to solutions. Engaging actors from these sectors in a joint discussion will allow us to share these solutions, and understand

how they can be combined to address existing challenges.

Considering the areas listed previously – technical, operational, normative, and the public good predicament – participants will, in a first phase of the workshop, brainstorm any further challenges not already listed in this report.

Listing and prioritizing the challenges

In a second phase, participants will have a chance to prioritize all challenges based on two criteria: how easy it is to solve the challenge; how big is the potential impact to improve population health. In the process, we will take notes on discussed solutions. A full characterization of possible solutions may demand specific discussions and studies that are beyond the goal of this workshop. We expect, however, that the workshop will serve as a networking exercise, opening opportunities for collaboration and new research and development ideas.

The outcome of the workshop will be a prioritized list of challenges. This list will be informative to allow the tackling of readily solvable issues, and guide research, development and implementation of new solutions based on likely impact to improve disease prevention, detection and control in a One Health context. The outcome will help public health officials in the adoption of innovation, and in the operationalization of data-driven health surveillance systems.

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Whose Priorities Count?

– Empowering Scientific Capacities for Locally Relevant and Sustainable Solutions

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The purpose of this workshop is to examine how the local conditions for conceptualizing and carrying out research can be modified to further empower local scientists to address local and regional infectious disease priorities.

In a world that is increasingly interconnected through technology and infrastructure, and where private and public actors are investing in research and development of new solutions for infectious disease control, there is great potential for scientific collaborations that address complex health challenges across the globe. Nevertheless, it is still the case that many priority infectious diseases garner less attention than they deserve, at the same time as the scientific capacities that are closest to the sites of the problems are disempowered and under-utilized. Nowhere is this problem more acute than in low- and middle-income countries where neglected infectious disease research is underfunded, and where local scientific communities struggle to overcome complex health challenges. Solutions to this double-bind require new forms of synergies

between local and international science, as well as between science and society. New and renewed engagements amongst governments, private enterprises, science funders, civil society, and scientists themselves can contribute to improved conditions for human health and sustainable development.

The workshop will address, among others, the following topics:

- If biomedical solutions to infectious disease challenges require stronger connections to the places where the problems arise, then how can these be achieved?
- What are the bottlenecks and blind spots that hamper local research priorities from receiving the attention that they deserve?
- How can new synergies be achieved among local, national, regional and international partners in science that combine multiple competencies across more equal positions of power?
- Are there new forms of local, national, regional or international funding that can contribute to these synergies?



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Global drop in funding for neglected infectious diseases

Not all deaths weigh equally heavily when research priorities are determined. Market forces encourage research and development to address health challenges whose solutions can generate significant financial returns on investment for private actors. Even though death and disability attributable to infectious diseases are declining significantly across the globe, infectious disease remains a major day-to-day health issue in less developed parts of the world (1) (2). Neglected infectious diseases cause high rates of mortality and morbidity but receive relatively little investment in relation to the harm they cause. Admittedly the imbalance has improved since the 1990s when only 10 % of global health research funding was directed to the 90 % of preventable mortality that was taking place in developing countries (3). Nevertheless, despite high profile investments by public institutions (e.g. US government and the European Union) and private institutions (e.g. Wellcome Trust and Gates Foundation), the imbalance is far from resolved. Meanwhile, with a few notable exceptions (e.g. Ebola), investments in neglected infectious disease research and treatment are lower today than they have been at any other time since 2007. There is a trend towards less funding

of research on neglected infectious diseases by the large public funders and foundations in high-income countries that is not offset by the modest increases in investments by private enterprises (4). Meanwhile, low- and middle-income countries report that they contribute less than 2 % of all research funding for neglected infectious diseases (4). Continued advances made in reducing the death and disability caused by neglected infectious diseases, in the tropics in particular, are threatened by declines in funding for research on those diseases and the looming threat of antimicrobial resistance. Furthermore, the recent outbreaks of the Ebola and Zika viruses are evidence of the continuing risks posed by newly emergent, often zoonotic, diseases.

Necessity of local research capacity to tackle local problems

However, it is not enough to find more money and resources to tackle low-priority diseases that affect low-priority populations. Investments in institutional and research capacity-building in developing countries by bilateral and multilateral donors have resulted in growing human and infrastructural capacity to identify and address local research priorities. Nevertheless, it is a common experience of scientists and science leaders in developing countries that they are



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hampered from setting and then acting upon local and national research priorities. One cause is weak support and interest for health research amongst their own national governments. Another is the, sometimes unintended, influence of science funders and partners that are based in developed countries and who understand and experience the health challenges of developing countries from a distance.

The tempting allure of finding global solutions

Recent advances in biomedicine and global communications technologies can lead us to envision cures to diseases that are universally applicable across the globe. We are sometimes enticed by the idea of discovering those magic (medical) bullets which are immune to variations

of geography and politics, or the best practice breakthroughs which are resistant to local configurations of patronage and morality. Nevertheless, as tempting as the prospect of universal solutions may be, experience reminds us time and again that global and universal visions are usually frustrated by the complexities and specificities of health across multitudes of localities (5).

Studies of scientific knowledge production over the past forty years demonstrate that social, cultural, historical and economic factors influence what kinds of biomedical knowledge and technologies are produced by science (6). Similarly, these same factors influence how biomedical knowledge and technologies in turn interact with the health problems that they are meant to solve (7). Put simply, we know that health out-

comes are a product of the co-productive influence of biomedicine with society, history, culture and environment.

Examples of co-productive relationships between science and its social context are many, and well researched. This is evidenced by cultural and economic models that influenced historical and contemporary pathways for antibiotic development, as well as practices of antibiotic use that exacerbate the spread of resistance (8). It is apparent in the cultural, political and economic factors that influence whether research on malaria follows pathways towards the disease eradication or disease management, just as the successful application of bed nets or vaccines will inevitably be subject to a wider range of social factors (9). We also find evidence in the recent Ebola outbreak in West Africa that the epidemic was finally controlled through a synthesis of biomedical, social and cultural knowledge amalgamated through the practices of a mixture of local and international actors (10).

**Importance of the local perspective:
“They have read about it, you have lived it”**

From these examples we learn that, just as biomedical solutions to infectious disease challenges must be tailored to the characteristics of a particular disease, so too must science priorities and research practices be informed by and responsive to local social, historical, and cultural conditions. Health science that is primarily produced in laboratories and libraries far from the sites where it will eventually be applied, primarily by scientists that have little personal experience of the health challenge or the context in which it occurs, are alone unlikely to produce biomedical knowledge that is well-adapted to local health challenges and research priorities. This is evidenced by the continued overrepresentation of infectious disease mortalities and morbidities in countries where science capacities are small or underfunded, much of sub-Saharan Africa being a glaring example (1).

While the underfunded healthcare systems in developing countries provide part of the explanation for this gap, the conditions under which biomedical knowledge is produced and the limited scientific capacity available are also key factors. The scientific capacity gap is illustrated by the fact that high-income countries have approximately 352 times as many health researchers as

do all other countries combined (11). Operating in this context, a Ugandan molecular biologist working in Kampala explains that “It is very difficult for someone that does not live in your home to solve the problem in your home. They have not suffered or truly experienced those problems. The kinds of questions that are posed by that person are different than you who live in your home. They have read about it, you have lived it” (12). In Uganda and elsewhere, the dependency of local science upon foreign funding, foreign primary investigators and global priorities produces a normalized inequality whereby local scientists’ capacity to pursue locally important research priorities are undermined (13).

**A change of emphasis is needed
for research priorities**

Efforts have been made by both development and science funders to identify new models for priority-setting that will take into account local research priorities (14). Nevertheless, the centralization of priority-making mechanisms in global and bilateral institutions may not be sensitive to important local specificities and priorities, especially in low-income countries where both scientists and links between society and science are fewer. Meanwhile, calls for centralization of priority-making and funding allocation risk undermining the ability of existing local researchers to effectively localize the advantages and potential of international collaborations. In these contexts, global research priorities shared by international and local scientists can hide specific differences in perspective and approach regarding the problems at hand. For example, one finds vaccine safety trials carried out by local scientists at the behest of international partners for vaccines intended for viruses (or variants of viruses) and markets in other countries. In such cases, local scientists are diverted from local health priorities to work on international or foreign priorities (15).

**New global initiatives with a larger role
for local scientists**

A number of interesting initiatives and processes are currently taking place that offer fruitful examples to reflect and build upon as we engage with these questions. The WHO Global Observatory on Health Research and Development is a global initiative intended to improve coordination of health research and development, with particular sensitivity for neglected infectious diseases in developing countries. The

European Union's Horizon 2020 programme together with the European & Developing Countries Clinical Trials Partnership (EDCTP) offer additional models of collaboration and engagement. New programmes and projects support and expand scientific leadership and research capacity-building in neglected science communities by making intellectual space in foreign-funded initiatives which allow scientists from developing countries to take meaningful leadership roles. These include examples such as the Alliance for Accelerating Excellence in Africa (AESA) comprising Afrique One-African Science Partnership for Intervention Research Excellence (ASPIRE), Human Heredity and Health in Africa Initiative (H3Africa), Training Health Researchers into Vocational Excellence (THRIVE), Makerere/UVRI Infection and Immunity Centre of Excellence (MUII+). Meanwhile, well established bilateral programmes are of continued importance to support graduate research training that strengthens local science communities, notable amongst these are Nordic models that offer "sandwich PhDs," post-doc programs, and supervisory support (16).

Adjusting the balance between international and national actors

The globally observed epidemiological shift is evidence that infectious disease can be reduced and mitigated as a major cause of death and disability. Nevertheless, the tenacity of infectious disease to cause harm in developing countries reminds us that biomedical knowledge and technology are only successful when they are in tandem with local knowledge of social, cultural, economic and environmental contexts. As such, further successes in mitigating the consequences of heretofore neglected infectious diseases will require further engagement with local scientists and their research environments (17).

Actors from science, government, private enterprise, philanthropy and civil society must take further steps to identify open-ended policy guidelines that support locally-driven research

initiatives on aspects of infectious disease in humans and animals that are otherwise overlooked or neglected due to the specific contexts in which they prevail. There are several questions they must ask themselves. Which innovative new funding and priority-setting tools and policies are available to international, regional, national and local actors in science and science funding? Which incentive structures might further invigorate research practices in local institutions? What scope is available for balancing the power of international and local science partners to conceptualize and implement research agendas? Is it possible to decentralize priority-setting and research conceptualization while continuing to benefit from international collaborations and synergies? To what extent are One Health approaches being utilized to integrate the human and animal sciences?

More local funding can reduce reliance on international donors

Answers to these questions can profitably enrich ongoing local, regional and global discussions of how to further empower science to contribute to the resolution of persistent and neglected health challenges. They can contribute to and inform the ongoing efforts of the WHO to develop a blueprint for research and development preparedness and rapid research response for potentially epidemic diseases (18). They can complement and further nuance calls by global health NGOs for the G20 countries to develop a more effective and far-reaching strategy for addressing future pandemics (19). They can produce new guidelines and evaluation practices for science funders on how to track the degree to which the biomedical research that they fund is well integrated in local research environments and social contexts. Finally, they can assist researchers from these countries when lobbying their national governments to diminish reliance upon international donors. Governments can thus further strengthen their own scientists' contribution to local well-being by providing locally sourced funds.

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Drivers and Constraints in the Use of Modern Typing Tools to Trace Foodborne Disease

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The aim of this workshop is to stimulate different stakeholders and disciplines to realize the benefits of data sharing and the opportunities the new molecular surveillance tool, Whole Genome Sequencing (WGS), is providing in a One Health perspective. What are the national and international drivers and constraints in regard to data sharing, joint analysis and communication in outbreak investigations?

Globally, infectious diseases account for about 22 percent of all human deaths, and are also a major burden on animal health. In addition, they also increase the financial burden on health systems and society at large. The longer it takes before the causative agents are detected, the greater the consequences for the individual or the population. The (often international) epidemiology of foodborne infections can also have significant implications for trade. Therefore, rapid national and

international surveillance systems and methodologies for the exchange and comparison of information on the worldwide spread of foodborne zoonotic pathogens are greatly needed to trace the origin of the source and to investigate complex outbreaks.

The focus areas of the workshop examine the different challenges of data sharing by means of Whole Genome Sequencing:

- What are the legal constraints between both sectors and countries?
- The technical challenges and analysis normalization where different platforms and analysis software are used.
- In the transition from old to new technology, will backward compatibility and thereby the link to historical data be lost?
- What is needed to reach the goal of real-time surveillance?



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New possibilities provided by Whole Genome Sequencing (WGS)

Molecular typing methods for foodborne pathogens are beginning to be routinely applied worldwide for public health protection, *e.g.* investigating foodborne outbreaks, identifying strains of foodborne bacteria with high virulence potential or resistance to antimicrobials. This development stems from continuous advances in the understanding of the molecular characteristics of bacteria and their genetics linked to technological developments. Over time, a range of molecular methods has evolved, such as pulsed field gel electrophoresis (PFGE), multiple locus variable number of tandem repeats analysis (MLVA) and multilocus sequence typing (MLST), which are all commonly applied to foodborne pathogens, with applications in outbreak investigations as well as source attribution. All of these methods have some limitations; *e.g.* they only provide one type of characterization of the genome, older methods are not easily replaced with more modern methods due to a lack of backwards compatibility and they are

not suitable for all purposes due to differences in phylogenetic resolution.

However, the evolution of rapid sequencing technology as well as an increased capacity in bioinformatics has led to bacterial whole genome sequencing (WGS) methods becoming more and more feasible. The potential of WGS is now actively being considered in several areas including: pathogen characterization and typing, outbreak detection and investigation, risk assessment and high-resolution epidemiology. Using WGS will also improve the accuracy and effectiveness of disease surveillance and the evaluation of prevention policies by enhanced assessment of disease and drug resistance transmission dynamics with the final goal to make a difference for public health intervention. WGS data make it possible to assess the molecular diversity and circulation of strains within the food chain and could be useful for source attribution studies when estimating the contribution of different food categories or animal species as sources of human infections.

Inter-agency and inter-lab co-operation assists cluster detection

In the United States, agencies like the Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) have taken initiatives to facilitate a more widespread application of WGS. Building upon existing data sharing networks among laboratories in addition to tighter cooperation between the food and public health sector in regard to data sharing have proven successful in solving an array of different foodborne outbreaks. In Europe, the European Centre for Disease Prevention and Control (ECDC) started a two-year molecular surveillance pilot project in 2012, linking public health reference laboratories across Europe for real-time data sharing from traditional molecular typing techniques for selected foodborne bacterial pathogens. In addition, limited additional information about the isolates (metadata) can be shared, such as country of origin, age and gender, depending on the ability of each country. Today, the European Surveillance System (TESSy)'s molecular surveillance service (MSS) is used by ECDC for routine molecular surveillance. If multi-country clusters are detected, the countries concerned are informed and, when needed, ECDC can also provide support during the outbreak investigations.

A joint database for molecular surveillance in Europe

The European Food Safety Authority (EFSA), whose mission is to improve EU food safety and ensure a high level of consumer protection, recommended at their 10th Anniversary Conference in 2012 the building of a centralized WGS database for foodborne pathogens. Since then, EFSA, together with the European Union Reference Laboratories (EURLs), and ECDC, in partnership with the public health agencies, have successively strengthened their collaboration in the field of molecular surveillance of foodborne diseases. A first step has been to initiate the sharing of data generated using traditional molecular typing tools within the ECDC platform. The purpose of the joint ECDC-EFSA molecular typing database is to share comparable typing data in a common repository so that microbiological data from humans can be linked to similar data from the food chain (1). In other words, at EU level there is a clear need and willingness to foster a multidisciplinary interpretation of the information arising from the

combination of epidemiological and molecular pathogen characterization data to guide public health action.

The challenges to achieving EU-wide use of WGS

In 2016, ECDC published a strategy, according to which WGS will be the method of choice for typing of bacterial pathogen across the EU by 2021. The role of the EU authorities will be to enable and facilitate the EU-wide use of this universal typing technique. Already today, WGS is the tool used in many international investigations, although it is only used after the outbreak signal has been identified using existing, 'old', typing methodology.

To reach this goal – EU-wide use of WGS in routine surveillance – there are a number of challenges that have to be addressed, such as:

- (i) technical constraints in the laboratories;
- (ii) different national and sectoral legal frameworks;
- (iii) the need for agreement and understanding on sharing data among countries and sectors; and finally,
- (iv) to jointly interpret and communicate the data (WGS and epidemiological).

The agreement about sharing molecular typing data among countries and sectors described above is a large step forward 'politically'. One of the challenges that now lie ahead concerns the sharing of both sequence data, or interpretation thereof, and more specifically epidemiological data that is connected to each and every isolate.

Legal obstacles: the conflict between openness and privacy

Today the epidemiological data shared is either non-existent or very limited. There could be sensitive epidemiological data that will have to remain available only to the competent authorities, so releasing this sensitive data will not easily, or even necessarily, become a routine procedure. There could be several impediments for the free sharing of sequencing data. By contrast, the deposition of the microbial genomic sequence data in databases for public access beyond the control of the owner of the data is common practice. Legal obstacles are to be expected and a careful balance must be struck between desirable complete openness from a food safety point of view and the privacy and related con-

cerns that necessitate confidentiality. A standard for encryption may well need to be developed to allow exchange of data to be limited to authorized parties only. Ignoring these issues is likely to considerably delay the successful large-scale implementation of WGS for public health at international level.

Technical challenges

Currently, there are different commercially available, high-throughput next generation sequencing (NGS) platforms. In addition, there are different bioinformatics pipelines for sequence data analysis, both in-house pipelines as well as commercial and free software. A laboratory for routine WGS application that aims to share data requires the following:

- (i) the adoption of appropriate quality assurance/quality control (QA/QC) measures;
- (ii) the development and harmonization of standard operating procedures, SOPs;
- (iii) the establishment of database infrastructure; and
- (iv) the generation and dissemination of appropriate genomic reference datasets.

Transition from old to new techniques and linkage to historical data

There is a need to link these data to previous isolate characterization schemes and nomenclatures as well as to the phenotypic properties of the isolates from which the genomic data are obtained. A major difference between WGS and the traditional typing methods is that WGS allows all genes to be included in the analysis, instead of a well-defined subset of genes or variable intergenic regions. Therefore, the analysis of WGS data will yield new types of insight. With the sequencing technique in place, this is still a financial limitation for many laboratories due to the high costs of the new technology. The costs for the NGS platforms and the sequencing *per se* are continuously dropping; however the transition from the old typing techniques to WGS will probably take a number of years before most laboratories have reached this goal.

Real-time surveillance

To be able to upload the data in a timely manner, it is important to have a chance to act upon multinational clusters that are identified, break the chain and stop the spread. Usually in outbreak scenarios, the authorities are always one step behind, timewise. After a case has been

exposed to a pathogen, the incubation time can be anything from a few days up to a week before illness onset. Then the pathogen has to be identified and reported to a surveillance system and typed. It is important to upload the information and data to the surveillance system more or less in real time in order not to lose more time before food no longer can be sampled, or other information can be lost and the transmission chain can be a challenge to identify and break. Consequently, reporting systems that are easy to use and that can link isolate data with case data must be in place, which can also be a challenge on a national level.

In conclusion, in order to have an efficient, multi-national molecular surveillance system based on WGS, three major issues must be fulfilled: to be able to legally share the data; to have a common database platform; and to be able to analyse and interpret the molecular typing tool in a normalized way in a timely manner.

The workshop will start with an introduction highlighting the work done on EU level to facilitate cross-border sharing and communication and to trace back investigations. In addition, an illustration will be given of a recent multinational outbreak investigation where WGS was the pathogen typing tool. The workshop participants will work to collectively identify existing barriers that prevent the sharing of molecular and epidemiological data, and then solutions for sharing and tools that will allow the full potential use of WGS will be discussed.

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GE Healthcare is a major sponsor of Uppsala Health Summit 2017. In the run-up to this year's meeting, we caught up with Customer Applications Director, Dr. Mats Lundgren, to gain his insights on emerging infectious disease threats and current trends from a biopharmaceutical manufacturing perspective.

As a biopharmaceutical expert and someone with deep insights into the industry of producing medicines and vaccines, what are some of the issues surrounding the response to emerging infectious disease threats of today?

In recent years, the world has witnessed emerging and re-emerging diseases that demand flexible responses. We don't know which disease we will face next. It could be avian influenza, but then also something completely different as we saw with Ebola. Pandemic preparedness is really a multi-fold issue

that needs to be addressed at many different levels and in different ways. On one hand we have the political climate which influences decisions on prioritization and economic incentives and models for financing and ethical aspects as well. But then we also have the important role of technology and production and this is where we come in. The biopharma and vaccine industry must leave long-established and time-consuming production processes behind and invest in research and operations that make it possible to produce vaccine and medicines fast with so called platform technologies that are efficient, flexible, scalable and applicable to multiple projects at the same time.

Can you give an example of what can be done with this technology?

With these new technologies, vaccines and medicines can be quickly produced with single-use equipment that allows flexibility

and cost-efficient rapid scale-up. As an example, we use disposable bioreactors containing plastic bags for cultivation. Furthermore, GE can also provide modular factories which arrive pre-equipped with modern bioprocessing equipment. This saves a lot of time and money in contrast to traditional facilities based on stainless steel which have long lead time and allow very little flexibility.

We are experiencing a paradigm shift with new vaccines being made by vaccine producers in middle-income countries, for example in India, Brazil, China and Indonesia. What are the challenges here?

Yes we are, and here, I think the ethical aspects come in. In the western world, we tend to focus on what is important to us. Therefore, I think it is really important that poorer countries are supported in their own R&D and the production of vaccines and medicines in the places where they are intended to be used. Also, intellectual property legislation, such as patents, can hinder development of modern vaccines and biopharmaceuticals. The private sector has a responsibility to support this development with know-how and capacity-building. I am personally involved in the Developing Countries Vaccine Manufacturers Network as a resource on production technology.

But for companies like GE Healthcare who supply processing solutions, this also means taking care so that the production is efficient and sustainable. If this is not the case, the overall price of vaccines that may have been developed quite cheaply in the first place will rise significantly. We need to explore cost-effective solutions and work out economic models that allow us to see costs per dose. Making sure that new technology is not more expensive than old technology is also in our interest.

As the vaccine market has evolved, so has the emphasis on high-quality production and safety of vaccines. How can we speed up production while not jeopardizing the safety of the vaccine and medicines that are produced?

Certainly it's not just a question of producing! To ensure that high-quality products are made it is very important to have strong, robust regulatory bodies. So far, there are not many developing countries that have this. Strong gov-



Dr. Mats Lundgren, Customer Applications Director GE Healthcare.

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ernment leadership is important in emerging infectious disease preparedness, also to ensure that the necessary medicines and vaccines are *de facto* being developed and produced so that it's not up to vested private interests solely to decide which ones to focus on. Also, local production may be important if other vaccine-producing countries decide not to share their doses in times of emergency.

What are you most looking forward to at Uppsala Health Summit on the theme Tackling Infectious Disease Threats – Prevent, Detect and Respond with a One Health Approach?

I am really looking forward to the multi-disciplinary discussions. I believe that this is when progress is achieved. Importantly, those discussions need to bring in political, economic and ethical aspects as well. It feels important to set in motion a conversation which can then continue in other places. As a big cooperation we have a responsibility to see where we fit in and how we can help.

Tackling Infectious Disease Threats

Preventing, Detecting and Responding with a One Health Approach

Uppsala Castle, Sweden

Monday 9 October

17:00 Reception at Uppsala Art Museum, in Uppsala Castle

Meet and greet with delegates, speakers and organizers

Tuesday 10 October

8:45 Opening of Uppsala Health Summit 2017

9:00 Emerging Infectious Disease Threats, Their Global Drivers and One Health

Dr. Björn Olsen, Professor, Dept. of Medicine, Uppsala University

Dr. Peter Daszak, Director, Eco Health Alliance

Dr. Maria K. Lapinski, Professor, Department of Communication and Michigan AgBio Research, Michigan State University

10:00 Coffee break with speed-dating

10:45 Workshops in parallel

A. Zoonotic Diseases in Livestock – Mitigating Risk Behaviour

B. Empowered and Resilient Communities – A Need for New Perspectives

C. A Roadmap for Effective Diagnostics to Combat Global Infectious Disease

D. New Vaccines and Medicines – Monitor Safety in Emergency Situations

12:00 Lunch

13:00 Workshops continued

15:00 Coffee break with speed-dating

15:45 Prevent, Detect, Respond: Experience of Policy Implementation

Dr. Eric Fèvre, Professor of Veterinary Infectious Diseases, Institute of Infection and Global Health

Dr. Paul Richards, Emeritus Professor of Technology and Agrarian Development, University of Wageningen

Dr. Christianne Brusckke, Chief Veterinary Officer of the Netherlands

Dr. Beth Ann Griswold Collier, Executive Director, Global Clinical Development, Merck & Co. Inc.

17:00–17:30 Conclusions from workshops

19:00 Dinner at Norrlands Nation, one of Uppsala's traditional student clubs

Wednesday 11 October

8:30 Welcome back

8:45 One Health and Governance

Dr. Pierre Formenty, Team Lead in Vulnerable Settings Unit, Infectious Hazard Management Department, WHO

Dr. Timothy Bouley, Global Health and Environmental Specialist, World Bank

Dr. Johanna Takkinen, Head of Food- and Waterborne Diseases and Zoonoses Programme, European Centre for Disease Prevention and Control, ECDC

Dr. Bassirou Bonfoh, Professor, Director, CSRS, ASPIRE-ONE Afrique Consortium

10:00 Coffee break with speed-dating

10:45 Workshops in parallel

E. Innovation and Big Data in Health Surveillance

F. Which Priorities Count? Empowering Scientific Capacities for Locally-Relevant and Sustainable Solutions

G. Drivers and Constraints in Modern Typing Tools for Detection of Food-Borne Infections

12:00 Lunch

13:00 Workshops continued

15:00 Coffee with speed-dating

15:30 Conclusions from workshops

16:15 Implementing Lessons Learned – Future Priorities

Dr. Hannah Akuffo, Senior Researcher Advisor and Programme Manager, Swedish International Development Agency, SIDA

Dr. Charlie Weller, Head of Vaccine Programme, Wellcome Trust

Dr. Jim Gallarda, Senior Program Officer – Diagnostics, Bill and Melinda Gates Foundation

17:15 Concluding remarks

Programme Committee Chair, **Professor Marianne Elvander**, National Veterinary Institute

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