

# SUPPORTING THE GENOME MICROBIAL IDENTIFIER AND WHOLE GENOME SEQUENCING IN ADDRESSING FOOD-BORNE DISEASES IN ASEAN

Policy Report  
October 2018

Jose Ma. Luis Montesclaros,  
Mely Caballero-Anthony and  
Joergen Schlundt



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## Executive Summary

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Food-borne diseases (FBDs) have had a significant impact on Southeast Asia's health and quality of life. A significant part of health security concerns relates to diseases caused by dangerous (pathogenic) microorganisms in food. These are exacerbated by the evolution trends of microorganisms, which increase their resistance to antimicrobials<sup>1</sup> used to treat diseases, also known as antimicrobial resistance (AMR). If regulators are unable to keep tabs on FBDs amid these trends, health risks and misdiagnosis could increase and potentially be exacerbated by increasing intraregional integration of food supply chains.

This policy report recommends that ASEAN food safety regulators consider the following actions:

- (1) **Support the development of a global microbial identifier (GMI)**, a global database of genome data on FBD-related microbial isolates, to complement existing ASEAN food safety frameworks.
- (2) **Encourage a shift to whole genome DNA sequencing (WGS) technologies**, a revolutionary technology for diagnostics and prevention, which can help accelerate the development of GMI, and also significantly shorten the response time during disease outbreaks, while giving better foresight on the significant disease burden from both existing and emerging food-borne diseases.
- (3) **Rally support from the private sector to hasten the pace of GMI/WGS development**, including food companies, pharmaceuticals, traders and consumer interest groups, who will benefit from supporting such an endeavour.

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<sup>1</sup>Antimicrobials is a broad term for substances that kill microorganisms. Antimicrobials include antibiotics.

## The Burden of Food-Borne Diseases in Southeast Asia

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As part of a secure and prosperous ASEAN community, ASEAN aims, among others, to promote measures to facilitate the free flow of safe food within the region, ensure that standards for food safety are upheld across the region, and reduce disparities in health outcomes across member states. Despite these measures, meeting the goal of reducing FBDs to zero across all diseases remains a very significant challenge.<sup>2</sup>

Food-borne diseases (FBDs) have had a significant impact on Southeast Asia's health and quality of life. For instance, close to two out of five diarrhoeal disease infections are attributed to food.<sup>3</sup> The burden of FBDs varies across countries at different levels of development. It also reflects variances in geographical elements such as temperature and humidity, in food production practices in source countries, and in handling, transportation, storage and preparation practices in countries where the food is consumed.

Higher income countries may think they are less vulnerable to FBDs. After all, Enteropathogenic *E. coli*, a diarrhoeal pathogen known for infecting children, caused an average of 4 food-borne disability adjusted life years (DALYs)<sup>4</sup> for every 100,000 persons in Brunei and Singapore. This is small compared to the 67–380 DALYs in the rest of the region but it is no less significant (See Figure 1).

Thus, income level is not the only factor that explains FBDs. For instance, Non-Typhoidal Salmonella Enterica, which can cause severe diarrhoeal effects, especially in elderly and child patients, has taken 50 DALYs from the Bruneians and Singaporeans, twice as much as from Cambodians, Laotians, Malaysians, Filipinos and Vietnamese, at 25 DALYs (Figure 1). Reporting standards do vary across ASEAN member states, so higher figures do not necessarily reflect bigger problems, but better reporting. Nonetheless, the burden of top FBDs was generally higher in the poorer countries than in their richer counterparts.

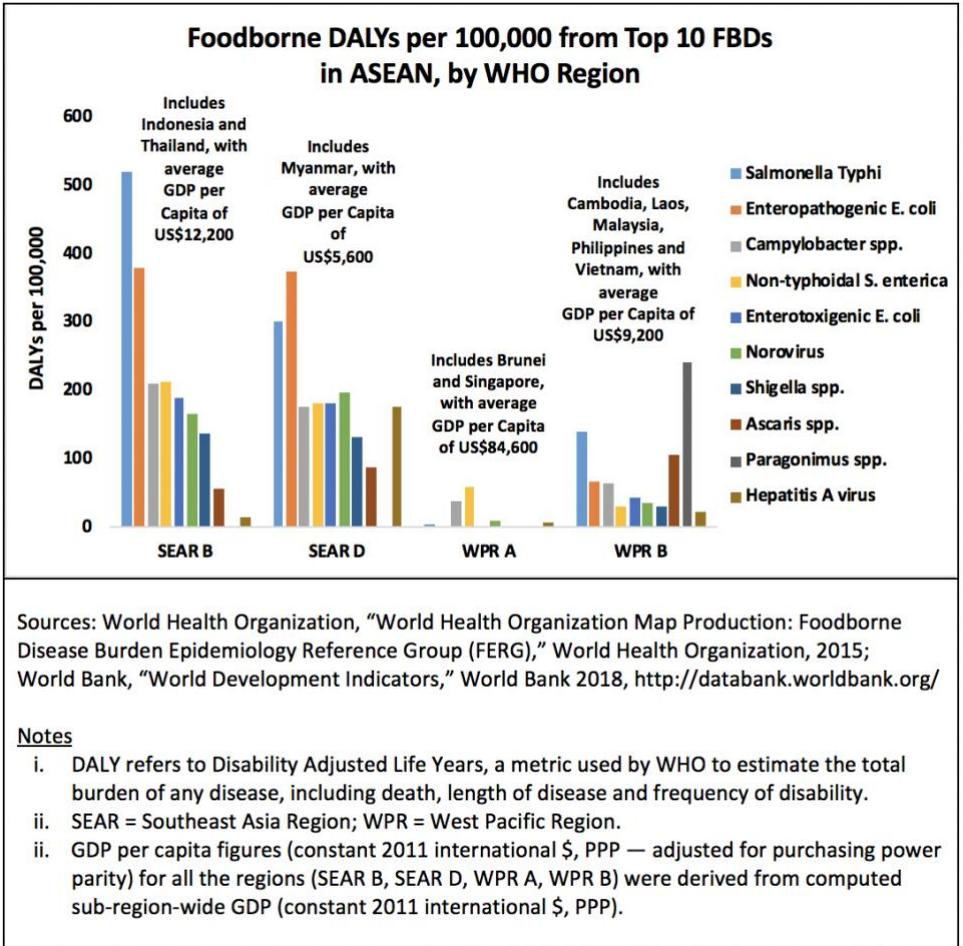
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<sup>2</sup>World Health Organization, "World Health Organization Map Production: Foodborne Disease Burden Epidemiology Reference Group (FERG)," World Health Organization, 2015; See Figure 1.

<sup>3</sup> Ibid.

<sup>4</sup> Disease burden is measured in disability adjusted life years (DALYs), a measurement that includes the burden of deaths, disability and duration of disease; this metric is utilised by WHO for estimations of all types of diseases (infectious and non-infectious).

Figure 1



## Emerging trends of antimicrobial resistance

It is not only the burden of FBDs that poses a serious threat to the health of people in Southeast Asia. A disruptive change is occurring, caused by antimicrobials. Antimicrobials, the very tools used to combat disease-causing pathogens, are turning into catalysts that allow pathogens to evolve and develop into improved versions of themselves. The improved pathogens possess resistance to the antimicrobials intended to treat FBDs in human patients, rendering antimicrobials useless. This phenomenon is referred to as antimicrobial resistance (AMR). Comparable to the Hydra,

the Greek mythological monster which grows two new serpentine heads whenever one is cut off, this looming systemic health hazard has already started to rear its heads globally and in the region.

The creation of AMR is significantly affected by excessive use of antimicrobials for growth promotion and disease prevention in animals, especially in cases of mass medication of animals. Given the lack of stewardship across food producers and the lack of national policies in ASEAN restricting indiscriminate antimicrobial use, these trends could present a critical systemic health risk to the region. If current trends continue unchanged, it is estimated that the annual number of deaths globally from AMR will reach 10 million, higher than the current number of cancer deaths (7 million).<sup>5</sup>

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<sup>5</sup> O'Neill J., "The Review on Antimicrobial Resistance," UK Government Report, December 2014.

# Understanding the Challenges of FBDs

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## Intractability of diseases from fragmented food networks

ASEAN has already adopted an ASEAN Food Safety Regulation Framework (AFSRF), which seeks to ensure protection of consumer health and to facilitate the free flow of safe food within the region. Among other things, this agreement provides for harmonising sanitary and phytosanitary measures and standards for food; minimising technical barriers to intra-ASEAN trade in food; and reducing discrepancies of national food control systems among individual ASEAN member states. It should be noted that most initiatives within this framework are recent and developing at a modest pace.<sup>6</sup>

Food safety regulators are commonly seen as protectors of the public against menacing FBDs and implementers of the AFSRF. A mounting challenge these regulators face is the *intractability of FBDs*, which can emerge in any part of the food supply chain, from production to transport, storage, and cooking/consumption. In the past decades, this challenge had already multiplied many times over, as *supply chains became increasingly fragmented, with their segments dispersed across multiple locations and networks*.

The result is that there is an immensely large number of nooks and crannies where FBDs might be hiding. Many of them pass regulators unnoticed within seemingly safe food products. Thus, regulators end up allowing unsafe products to enter their jurisdictions and sometimes mistakenly banning safe products. Such errors have already received attention in other regions.

In Europe, for instance, German regulators in 2011 erroneously quarantined Spanish organic cucumber as the source of an E. coli outbreak;<sup>7</sup> its source was later found to be sprouts from imported fenugreek seeds. The time taken before this mistake was uncovered was approximately five days, but the first lab results came out only after close to a month of analysis.<sup>8</sup> By the time the appropriate product was banned, almost 4,000 people had already fallen ill, of whom close to 400 were seriously ill and 53 died.

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<sup>6</sup> "ASEAN Food Safety Developments: Continued Harmonization Efforts," EU-ASEAN Forum on Food Safety, White Paper 2016, <http://www.eu-aseanforum.com/images/ASEAN-Food-Safety-Developments-white-paper-2016.pdf>

<sup>7</sup> Huld S., and K. Kelland, "Spanish cucumbers may be E.coli source, Germans say," *Reuters*, May 26, 2011, <https://www.reuters.com/article/us-germany-ecoli/germans-pin-e-coli-outbreak-on-spanish-cucumbers-idUSTRE74P3ND20110526>

<sup>8</sup> Frank C., M. S. Faber, M. Askar, H. Bernard, et al, "Large and ongoing outbreak of haemolytic uraemic syndrome", *Eurosurveillance* Vol. 16, No. 21, May 2011, <https://www.eurosurveillance.org/content/10.2807/ese.16.21.19878-en>

The repercussions of FBDs extend to jobs and industries, too. FBDs cost Spain's agricultural industry over €200 million in revenues per week as other countries banned its products and orders were cancelled by its markets, which in turn led to the laying off of farm workers.<sup>9</sup> Until the time regulators finally keep pace with the increasing complexity of food production networks, we should not be surprised if similar economically and socially costly blunders are repeated.

Apart from misidentification of diseases, the other problem is that after a disease strikes there is a time delay before regulators can advise the public on necessary measures to adopt, including banning the sale of food from identified affected farms. This time lag can cost lives as illnesses/deaths from FBDs are highest after a disease outbreak occurs and before action is taken.

The delay is often due to the time needed to gather information, which is not also readily available. (Relative to this, the implementation of the policy response, i.e., banning a product from markets, is rather straightforward, with quick dissemination of information upon approval). Furthermore, the problems of misdiagnosis of diseases, and insufficiently focused recommendations on how to address them, are likely to occur more frequently as a result of the evolution of bacteria, so that even the most efficient regulators cannot claim to have full-proof mechanisms for ensuring food safety. The AMR problem is linked to a serious lack of AMR data both on human and food microorganisms in ASEAN (as in many parts of the world).

## Policy Recommendations

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Accelerated trade integration in the region can increase the risk of FBDs if food safety regulators cannot keep track of FBDs and their evolution. This could also restrict ASEAN's access to the trillion-dollar global food industry, with over US\$1.35 trillion worth of food exported (2016), and a global value US\$8.1 trillion (2017) for the whole of the food and agriculture industry.<sup>10</sup> Given that there is less control over how agricultural industries use antimicrobials in their business processes, the alternative is to improve strategic monitoring of food, from farm to fork. Three interrelated recommendations are pertinent to this.

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<sup>9</sup> Tremlett G., and H. Pidd, "Germany admits Spanish cucumbers are not to blame for E coli outbreak," *The Guardian*, May 31, 2011, <https://www.theguardian.com/uk/2011/may/31/e-coli-deaths-16-germany-sweden>

<sup>10</sup> Plunkett Research Ltd, "Global Food Industry Statistics and Market Size Overview," 2018, <https://www.plunkettresearch.com/statistics/Industry-Statistics-Global-Food-Industry-Statistics-and-Market-Size-Overview/>

## **(1) Support the development of a GMI for better disease tracking at the regional level**

In spite of existing ASEAN frameworks related to food safety, policies will not be effective if there is insufficient capacity on the part of regulators to identify and profile the source of contamination, in particular, the microorganism causing a particular disease, the segment in the supply chain from which it emerges, and the countries where it is more likely to emerge.

A new international initiative, developed by an international consortium of more than 250 scientists, suggests creating an open network of actors sharing information on microorganisms, food and FBDs across borders through a global database, the Global Microbial Identifier (GMI).<sup>11</sup> This will help keep up with the increasingly fragmented and networked nature of food supply chains, and the rapid evolution of disease-causing pathogens, which make diseases almost intractable.

Yet, today, only a few geographical areas have supported this with their own initiatives, such as the open database (“Genometrakr”) adopted by the United States Food and Drug Administration (USFDA), which already contains full genome data on more than 200,000 FBD-related microbial isolates from food and humans.<sup>12</sup>

ASEAN, as a regional body, may thus explore developing its own database for more mutually beneficial exchanges of information at the same level of resolution (i.e., microbial genome data) with other regulators globally. Doing so would also feed better data when complemented with analytics technologies arising from the Fourth Industrial Revolution (e.g., blockchain) for automated tracing of diseases to their sources.

## **(2) Encourage a shift to WGS technologies for diagnostics and prevention**

While current technologies are allowing for a GMI to emerge, the pace is still slow. Under current processes, typically traditional microbiological identification techniques (isolation and detection on agar plates) is followed by typing and comparison between isolates from food and patients. In industrialised country settings, such typing typically includes a method called

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<sup>11</sup>Wielinga, P.R., et al, “Global Microbial Identifier,” in *Applied Genomics of Foodborne Pathogens*, ed. Deng, Xiangyu, den Bakker, C. Henk, Rene S. Hendriksen (Cham: Springer International Publishing, 2016).

<sup>12</sup>USFDA, “Total Number of Sequences in the GenomeTrakr Database,” July 16, 2018, <https://www.fda.gov/downloads/Food/FoodScienceResearch/WholeGenomeSequencingProgram/WGS/UCM422244.pdf>

Pulsed Field Gel Electrophoresis (PFGE), which is utilised in drawing and comparing patterns for microorganisms from clinical patients and suspected foods. The PFGE process could take as long as 4–6 weeks, as shown in a representative timeline in the system used in the United States.

In contrast, using WGS potentially allows for identifying contaminated food products within roughly a week after the introduction of contaminated food.<sup>13</sup> In disease outbreak situations, WGS offers a 3–5-week advantage over current systems. This represents the time delay before regulatory advisories can be provided to the public under current systems. In addition, WGS outcomes provide a more accurate framework for comparison, avoiding the erroneous outcomes of traditional methods. In fact, based on data from the United States, WGS use has shown to result in a 5–10 fold increase in the number of *Listeria* outbreaks detected and confirmed back to the food source.<sup>14</sup>

At the macro level, more diseases can be prevented as well because WGS upgrades overall research capacity, allowing for foresight on future diseases on an ongoing basis (given the shortened time period for analysis of each bacterium/virus/parasite). Likewise, the outcome of WGS methods will include information about AMR (which is part of the genome), thus broadening significantly the usefulness of WGS.

### **(3) Rally support from the private sector to hasten the pace of GMI/WGS development**

Governments may not be able to make the shift to WGS and develop a GMI in time. As benefits accrue also to other stakeholders, whose business processes to some extent benefit from WGS and the GMI, ASEAN regulators can benefit from reaching out to pharmaceuticals, food companies and traders for support.

Similar to food safety regulators, food companies face the need to characterise microorganisms responsible for FBD outbreaks. Early correct diagnosis of the source points of diseases allows food companies to act in a more timely manner, so these industries require the same information base as that used by regulators. Timely analysis of FBDs also

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<sup>13</sup> Schlundt J., “The next global break-through: the rise of Next Generation Sequencing,” Presentation slides published on website of US Food Safety and Inspection Service, US Department of Agriculture, 2017, <https://www.fsis.usda.gov/wps/wcm/connect/35437429-6e26-4775-b25e-46230b56c8d7/WGS-Slides-Schlundt-102717.pdf?MOD=AJPERES>

<sup>14</sup> Jackson B.R., et al, “Implementation of Nationwide Real-time Whole-genome Sequencing to Enhance *Listeria* Outbreak Detection and Investigation,” *Clinical Infectious Diseases*, Volume 63, Issue 3, August 1, 2016, pp 380–386, <https://doi.org/10.1093/cid/ciw242>

provides guidance to private sector pharmaceutical companies that develop new antimicrobials and vaccines.

Traders may also be roped into supporting this initiative because WGS allows for accurately sifting harmful from unharmed food products. In producing and marketing food one case study of Moroccan exports shows that compliance with sanitary and phytosanitary (SPS) guidelines by the World Trade Organization (WTO) and the standards subsequently defined by the WHO/FAO Codex Alimentarius Commission may cost up to 5 per cent of farm gate costs and 3 per cent of total costs.<sup>15</sup> Yet, the methodologies stipulated by these standards and guidelines may vary as new information on existing diseases is uncovered, increasing the cost of compliance whenever standards are revised.

Finally, consumers benefit. Utilising WGS offers the benefit of a more accurate base of data to develop responsive SPS guidelines and Codex standards, and, in turn, less need for revising SPS standards and lower compliance costs. This can translate to the opportunity to sell food at more competitive (i.e., lower) prices. In turn, consumers will be given access to a greater variety of safe commodities from more sources, at more affordable prices, ultimately leading to better food and health outcomes for all. This is something which consumer interest groups should support as well.

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<sup>15</sup> Aloui O., and L. Kenny, "The Cost of Compliance with SPS Standards for Moroccan Exports: A Case Study," Agriculture and Rural Development Discussion Paper, World Bank, 2004, [http://siteresources.worldbank.org/INTEXP/COMNET/Resources/Morocco\\_Impact\\_of\\_Standards\\_on\\_Cost.pdf](http://siteresources.worldbank.org/INTEXP/COMNET/Resources/Morocco_Impact_of_Standards_on_Cost.pdf)

## About the Authors

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**Jose Ma. Luis Montesclaros** is Associate Research Fellow at the Centre for Non-Traditional Security Studies (NTS Centre) at the S. Rajaratnam School of International Studies (RSIS), Nanyang Technological University (NTU) Singapore. Louie develops dynamic models of public policy systems for issues such as food security amid changing climates and resource scarcity, and urban agriculture in Singapore, and is First Inventor of UrbanAgInvest, a tool for preliminary commercial assessment of indoor farms. He has managed fieldwork/analysis for a country report on property rights in the Philippines (Center for International Private Enterprise), and has served as World Bank Group consultant on agriculture; small/medium enterprise development; tourism development; and inclusive growth in ASEAN. He holds a Master's Degree in Public Policy from the Lee Kuan Yew School of Public Policy, National University of Singapore (funded by a generous two-year ASEAN Scholarship) and a BS Economics degree from the University of the Philippines, Diliman.

**Mely Caballero-Anthony** is Professor of International Relations and Head of the NTS Centre, RSIS, NTU Singapore. She is currently the Secretary-General of the Consortium on Non-Traditional Security Studies in Asia. From 2013-2017, Prof Anthony was a member of the UN Secretary General's Advisory Board on Disarmament Matters and served at its Chairperson in 2016. She was Director of External Relations at the ASEAN Secretariat from 2011-2012 and was recently a member of the World Economic Forum (WEF) Global Agenda Council on Conflict Prevention. From 2015-2017, she was Vice President-at-large of the Governing Council of the International Studies Association (ISA) and is currently member of the ISA's Global South Task Force. She was also a visiting fellow at the Elliott School of International Affairs, George Washington University in 2015.

**Joergen Schlundt** is the Michael Fam Chair Professor in Food Science and Technology at the School of Chemical and Biomedical Engineering, and works at the NTU Food Technology Centre (NAFTEC), College of Engineering, NTU Singapore. Joergen has participated in the development of food safety Risk Analysis principles and in studies to estimate the global burden of foodborne diseases. In the past, he was Director of the Department of Food Safety and Zoonoses, WHO, Geneva, Director at the National Food Institute, Technical University of Denmark; and Professor at that University. He continues an active, international involvement in major new initiatives based on the generic principle that sound scientific decision support provides the best background for innovative improvements and sensible solutions to

reduce risk in food production systems. He promotes the global use of next generation DNA sequencing for in global open-source systems to identify microorganisms, and heads the Steering Committee of the Global Microbial Identifier (GMI), suggesting the creation of such systems.

## About the Centre for Non-Traditional Security Studies

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The **Centre for Non-Traditional Security Studies (NTS Centre)** conducts research and produces policy-relevant analyses aimed at furthering awareness, and building the capacity to address NTS issues and challenges in the Asia Pacific region and beyond. The centre addresses knowledge gaps, facilitates discussions and analyses, engages policymakers and contributes to building institutional capacity in the following areas: Humanitarian Assistance and Disaster Relief; Climate Security and Migration. The NTS Centre brings together myriad NTS stakeholders in regular workshops and roundtable discussions, as well as provides a networking platform for NTS research institutions in the Asia Pacific through the NTS-Asia Consortium.

More information on NTS Centre and a complete list of available publications, policy briefs and reports can be found here:  
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## About the S. Rajaratnam School of International Studies

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The **S. Rajaratnam School of International Studies (RSIS)** is a think tank and professional graduate school of international affairs at the Nanyang Technological University, Singapore. An autonomous school, RSIS' mission is to be a leading research and graduate teaching institution in strategic and international affairs in the Asia Pacific. With the core functions of research, graduate education and networking, it produces cutting-edge research on Asia Pacific Security, Multilateralism and Regionalism, Conflict Studies, Non-traditional Security, Cybersecurity, Maritime Security and Terrorism Studies.

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