Hazard Identification: AMR in Aquaculture

Professor Jason Weeks

Director, IEH Consulting Ltd.

Disclaimer:
I attend this conference as an individual expert, and do not represent the CVMP/EMA/ ERAWP/WHO. The views expressed here are my personal views, and may not be understood or quoted as being made on behalf of the CVMP/EMA/ ERAWP/WHO or reflecting the position of the CVMP/EMA/ERAWP/WHO.

IEHConsulting
The integrated environment and health consultancy

Hazard and Risk of AMR?

HAZARD

?

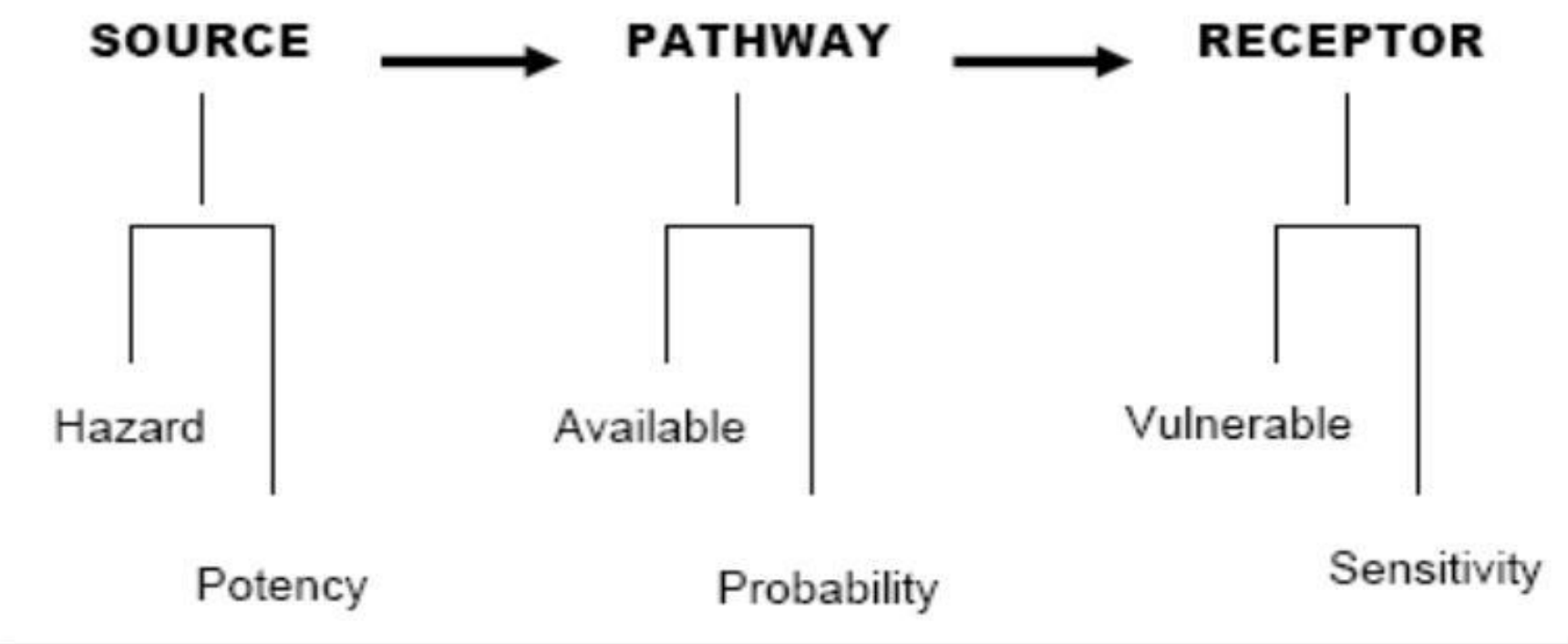
RISK

?

IEHConsulting

The integrated environment and health consultancy

The Risk Model; S - P - R



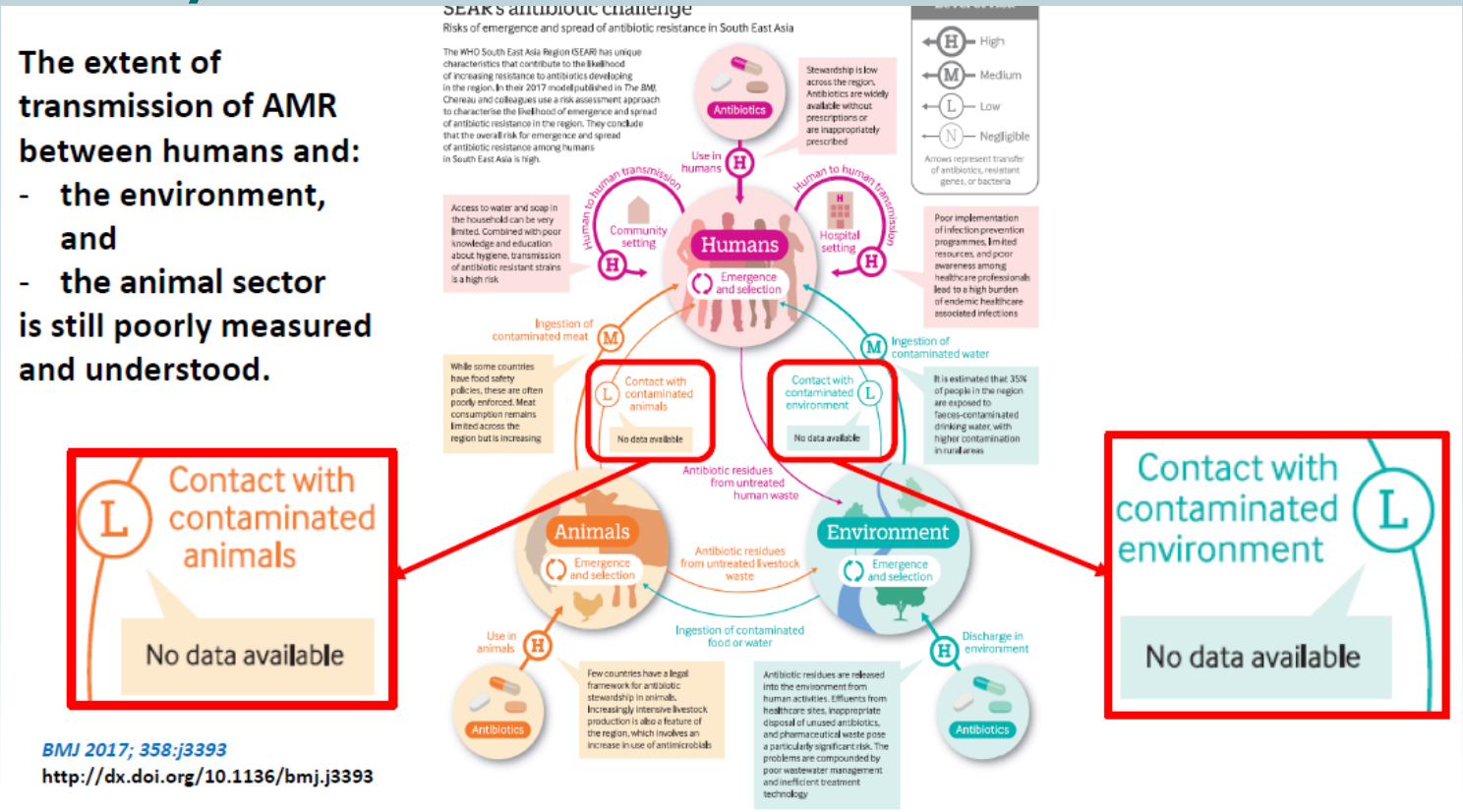
IEHConsulting
The integrated environment and health consultancy

Lack of understanding of transmission pathways

The extent of transmission of AMR between humans and:

- **the environment, and**
- **the animal sector**

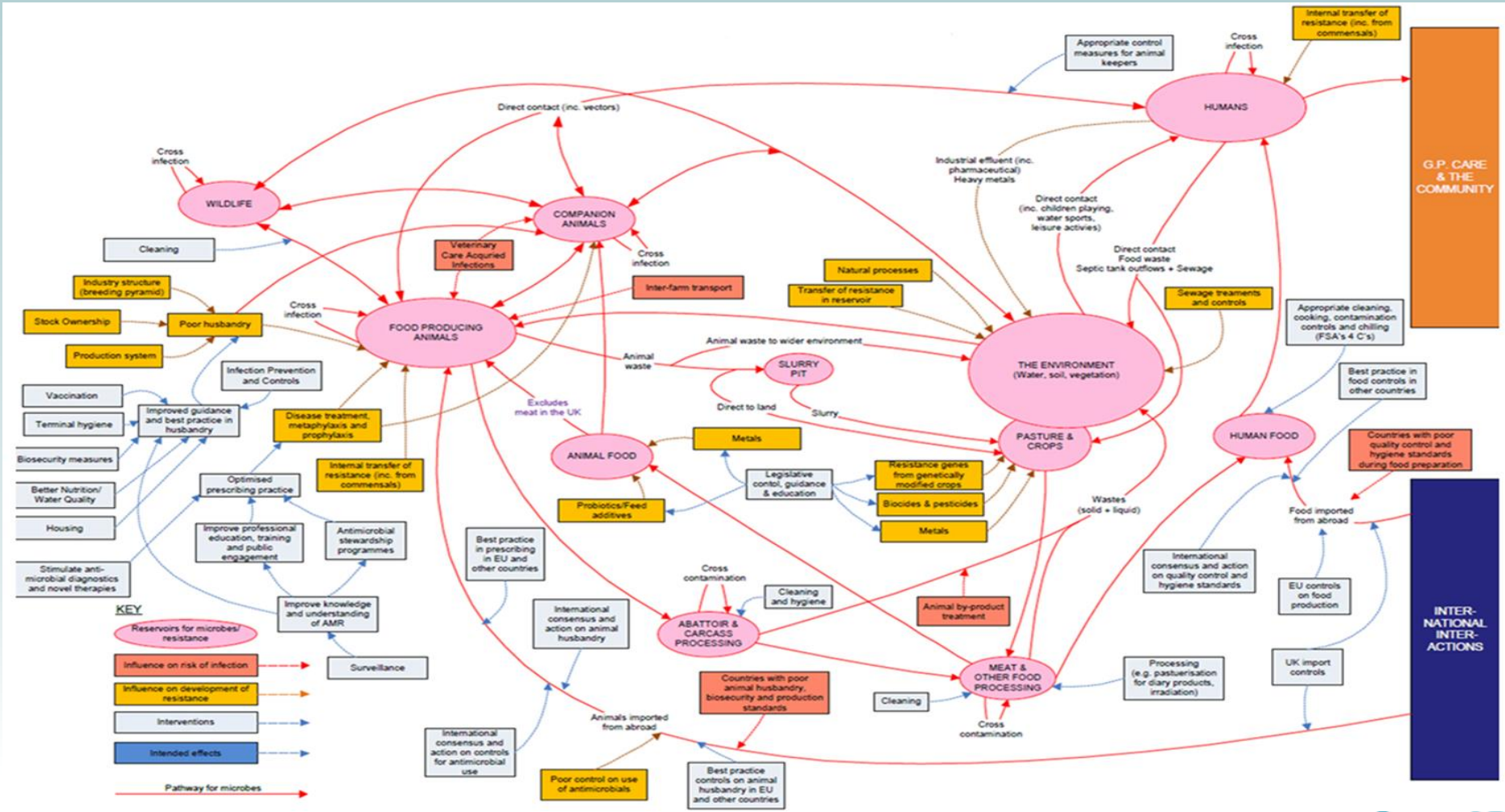
is still poorly measured and understood.



BMJ 2017; 358:j3393
http://dx.doi.org/10.1136/bmj.j3393

IEHConsulting
The integrated environment and health consultancy

A complex web of connectivity



IEHConsulting

The integrated environment and health consultancy

Three major pathways for AMR to the environment

1. Municipal and industrial wastewater;
2. Land spreading of animal manure and sewage sludge, and;
3. Aquaculture

IEHConsulting

The integrated environment and health consultancy

The value chain

Community?

Disease?

Feed in?

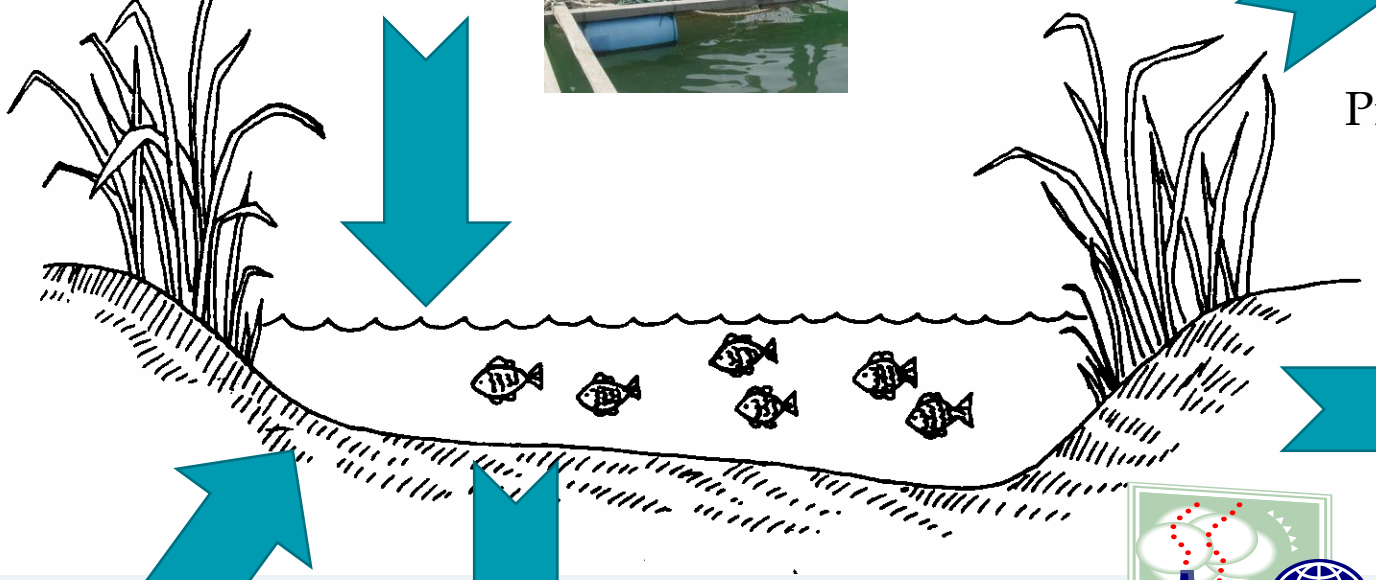
Ethics?

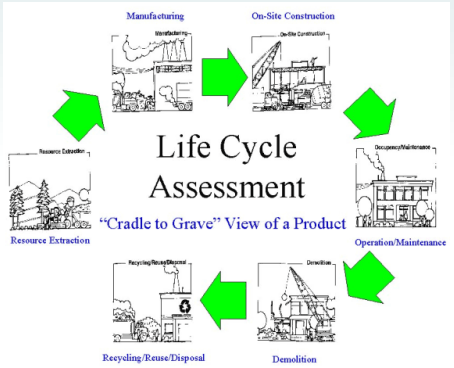
Welfare?

Product quality?

Chemicals in?

Chemicals out?

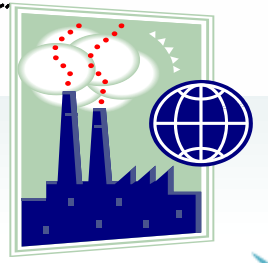




Nutrients in?

Nutrients out?

Processing?



IEHConsulting

The integrated environment and health consultancy

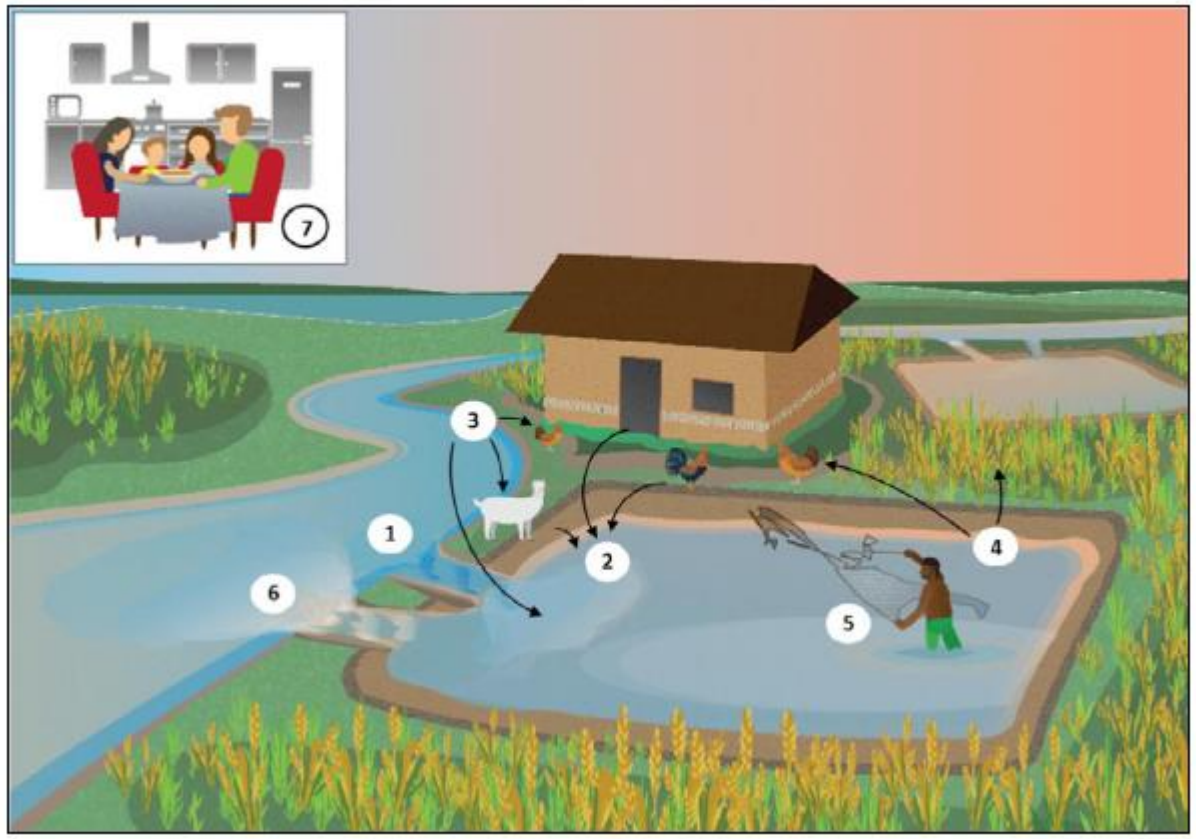
REVIEWS IN Aquaculture

Reviews in Aquaculture, 1–21 doi: 10.1111/raq.12367

Evaluating antimicrobial resistance in the global shrimp industry

Kelly Thornber[1,2], David Verner-Jeffreys[1,3], Steve Hinchliffe[1,4], Muhammad Meezanur Rahman[5], David Bass[1,3] and Charles R. Tyler[1,2]

1 Centre for Sustainable Aquaculture Futures, University of Exeter, Exeter, UK
2 Biosciences, University of Exeter, Exeter, UK
3 Centre for Environment, Fisheries and Aquaculture Science, Weymouth, UK
4 Department of Geography, University of Exeter, Exeter, UK
5 Worldfish Bangladesh, World Fish Bangladesh Office, Dhaka, Bangladesh



IEHConsulting
The integrated environment and health consultancy

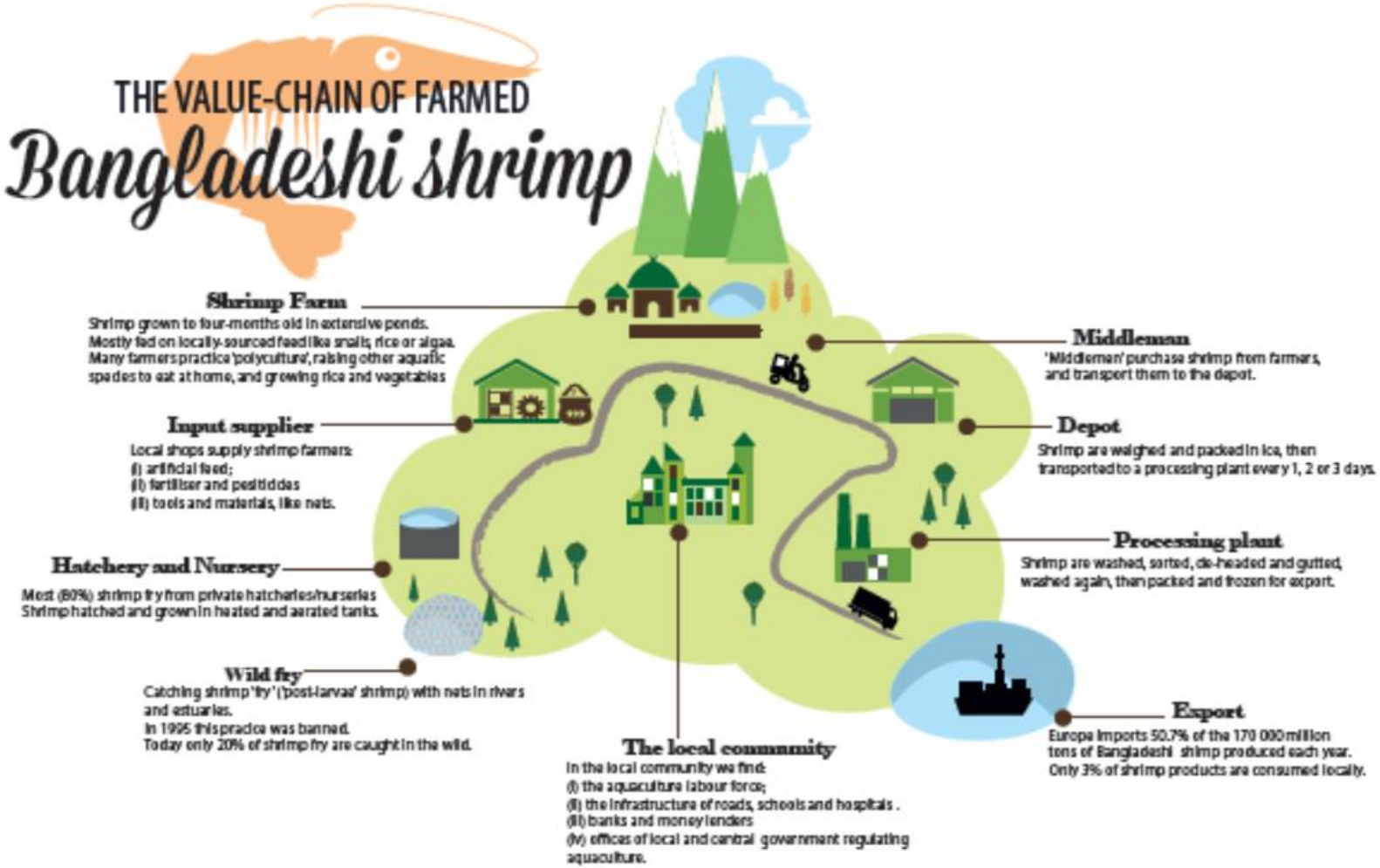


Figure 2: The Bangladeshi shrimp value-chain. Delphi experts were invited to ground their peer review in the Bangladeshi value-chain, but most spoke to their experience with other value-chains.

Sustaining Ethical Aquaculture Trade

EAFI Value Chain Landscape Narrative – Vietnam Striped catfish

Country	Vietnam
Product	

Summary

There are various culture practices in Viet Nam's aquaculture as a result of its ecological diversification. These include integrated aquaculture systems suc
mono-aquaculture such as semi-intensive, i
catfishes and marine finfish and poly-aquac
Hypothalamus) farming in the Mekong Delt
contributing barely 40% of the total produc
based on use of deep ponds and better wat
corresponding to almost 1.8 Billion US$ in 2
seafood value. Since 2001 and significantly
European markets growing strongly whilst t
Europe are Spain, German, Holland, UK and
place via the food service sector via restaur
NGOs and thus *Pangasius* is marketed as a l

Value chain

Inputs

Production

Collection

Processing

Trading

Consumption

Regulatory/ Institutional Aspects

The Ministry of Fisheries is the government
is under the administration of the National
legislation, aquatic resources management,
veterinary services, ministerial inspectors a
There are also unions and associations whic

Future trends

Aquaculture is a key economic sector of Vie
to stimulate further development. Focus ha
assist in the expansion of export markets as
been difficult to regulate, this has in some c

Sustaining Ethical Aquaculture Trade

EAFI Value Chain Landscape Narrative – Bangladesh Shrimp & Prawn

Country	Bangladesh
Product	

Summary

Bangladesh is one of the world's leading inland fisheries producing countries producing 223,000 T of shrimp (70%) and prawn (30%) in 2007-2008. Of this total, 95% was exported as 49,900 T of processed product; representing 2/3rd of all exported frozen seafood product. Although globally only a small producer, shrimp and prawn earns Bangladesh 8% of its export earnings. Shrimp production systems are mainly extensive, with some semi-intensive and in very few cases intensive systems. About 12 million people are associated with the fisheries sector, of which 1.4 million people rely exclusively on fisheries related activities. An estimated 9.5 million people (73 percent) are involved in subsistence fisheries on the country's flood plains, including 0.45 million fry collectors (fish and shrimp) it is estimated that fisheries related activities support more than 7 percent of the country's population. More than 600 000 people are engaged in shrimp farming activities. Shrimp farming is concentrated in saline coastal districts in the SE (Khulna region) and SW (Cox's Bazar). Freshwater prawns are cultured further inland integrated with rice and fruit and vegetable production on pond dykes. Alternating shrimp/ prawn and rice cultures take place in a semi saline transition zone between the shrimp and prawn zones.

Value chain (shrimp and prawn enter the same chain post-harvest)		**Sustainability issues**
Inputs	Most prawn farmers still rely on wild post larvae (around 75% of all sales) and or natural recruitment. Most shrimp farmers use hatchery produced PLs where wild brood stocks sources are used rather than SPF cultured stocks. Shrimp hatcheries are clustered in Cox Bazaar.	Most farmers perceive wild PLs to have a greater survivability than hatchery reared PLs – this perpetuates issues regarding inadequate biosecurity and negative environmental impact of wild sourcing PIs. Poor planning and land use conflicts also attract criticism of NGOs.
Production	Farming systems range from extensive (shrimp) to semi-intensive (shrimp and prawn). Polyculture with carps and other whitefish is the norm. Production is entirely of indigenous species mainly black tiger shrimp and giant freshwater prawn. Juvenile fish and shrimp which enter with the tidal waters are reared extensively without feed or additional husbandry resulting in an average harvestable production of only around 300 kg/ha.	Contaminated feed stocks are a major source of onward quality issues. Semi-intensively farmed prawns in rice fields have a greater risk of having high residues of pesticides and antibiotics. Disease has been a major constraint on intensification and consolidation.
Collection	A large number of people are involved in the fish marketing chain and include farmers, processors, traders, intermediaries, day labourers and transporters. The market chain defined for freshwater prawn from producer to consumer is the field workers, prawn traders, agents and processing companies. The processors are clustered in Chittagong (linked to export infrastructure) and Khulna in the SW.	The fragmented nature of production, supply and post-harvest distribution networks complicate implementation of traceability schemes.
Processing	The value chain is highly fragmented with over 250,000 mainly small (50% < 0.5 ha) family managed farms, similarly small scale supply and distribution chains supply 145 EU registered processors.	Periodic product bans due to product contamination remain a threat to the entire industry. Microbiological and phyto-sanitary contamination risks have been addressed by processors and cold chain intermediaries. Government subsidies contribute to in excess (>80%) of processing capacity, unstable employment conditions mostly female staff.
Trading	Fish markets in Bangladesh are situated in both rural and urban areas, they tend to be unhygienic, unscientific, and dirty and operate using weak management systems.	Most recent export bans mostly linked to presence of anti-biotic residues. Most importers will not buy Bangladeshi products due to food safety concerns

Sustaining Ethical Aquaculture Trade

EAFI Value Chain Landscape Narrative – Thailand shrimp

Country	Thailand
Product	

Summary

Thailand is the global leader in shrimp production and export (408,000T in 2010). It's a major foreign exchange earner (US$ 3 Billion) Production is mainly intensive culture systems based on white shrimp (*Litopenaeus vannamei*). Production provides jobs and income to a wide variety of stakeholders. In the region there is major compliance with local and global food safety and eco-standards. There are established feed, hatchery and processing sectors. Both corporate and household production is important.

Value chain

Inputs	More than 240 suppliers of PLs, feed and health supplements, chemicals, equipment, technical and professional services. Some with contract agreements.
Production	Greater than 25,000 individual, family or corporate farms, mainly intensive monoculture systems from small to large scale operations.
Collection	Producers and buyers agree on a price before harvesting. Shrimp taken directly to processing plants or sold in auction markets
Processing	More than 200 processing centres and cold storage for basic and value added processing. Raw materials are obtained from farms (with local & global certifications) and auction markets.
Trading	More than 150 processors exporting frozen shrimp to >50 countries. Companies generally have long-term contracts with buyers.
Consumption	Majority (>70%) exported as frozen fresh and value added in various forms. Processed/ value added production was at 26.5 T in 2010.

Regulatory/ Institutional Aspects

The Thai government operates a farm registration scheme and Since 2002, the Department of Fisheries has been strengthening its food safety programme. It set up Aquaculture Development and Certification Centre (ADCC), which offers aquaculture certification and promotes good aquaculture practice. The department is offering an alternative to the complex and expensive nature of certification schemes by offering Thai farmers the GAP TAS, a voluntary standard which promotes good practice shrimp farming. There is also widespread use of Fisheries management documents, feed analysis certification, a chemical substances registry, AQ insurance and club membership. There are contract farming agreements, fisheries movement documents and price standards. At the processors there are registration/ certification schemes, standards/Codex, fisheries movements, health sanitation certification, and importing country and buyer requirements being met. Consumers are protected through industry and supermarket standards and the EU Hygiene package.

Future trends

Aquaculture in Thailand is increasingly in government priority leading to clear, well-formulated, and realistic policies for aquaculture development, based on financial, social and environmental sustainability. Aquaculture in Thailand will continue to be an increasingly vital function in maintaining low-input aquaculture as supplier of protein for domestic consumption. It will also develop into a highly competitive, sustainable aquaculture industry to meet consumer demand for cultivated aquatic foods and products that are of high quality, safe, competitively priced, and nutritious and are produced in an environmentally responsible manner with maximum opportunity for profitability in all sectors of the export industry.

IEHConsulting

The integrated environment and health consultancy

Inflow water is a major source of trout farming contamination with *Salmonella* and multidrug resistant bacteria

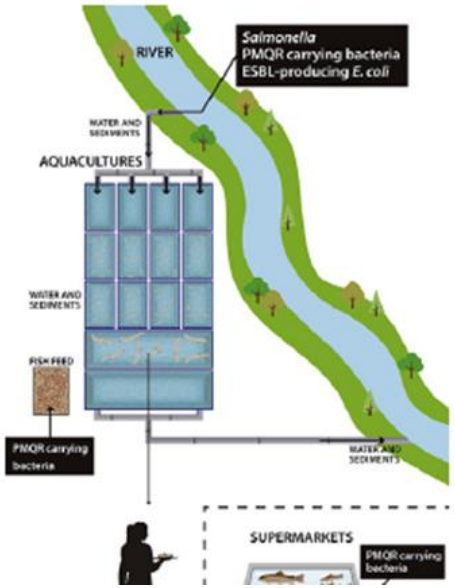
Patrícia Antunes [a,b], Joana Campos [b], Joana Mourão [b], Joana Pereira [a], Carla Novais [b], Luísa Peixe [b,*]

[a] *Faculdade de Ciências da Nutrição e Alimentação, Universidade do Porto, Porto, Portugal*
[b] *UCIBIO/REQUIMTE, Departamento de Ciências Biológicas, Laboratório de Microbiologia, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal*

HIGHLIGHTS

- Occurrence of resistant bacteria and *Salmonella* in trout farms and surroundings.
- Quinolone resistance genes were frequently found in trout farms and environment.
- Trout farms were contaminated with low-level ciprofloxacin resistant Enterobacteria.
- Inflow water in trout farms was a source of SHV-12-producing *E. coli*.
- Inflow water contaminated trout farms with *Salmonella* serotypes of diverse origin.

GRAPHICAL ABSTRACT



IEHConsulting
The integrated environment and health consultancy

Science of the Total Environment

journal homepage: www.elsevier.com/locate/scitotenv

Water supply and feed as sources of antimicrobial-resistant *Enterococcus* spp. in aquacultures of rainbow trout (*Oncorhyncus mykiss*), Portugal

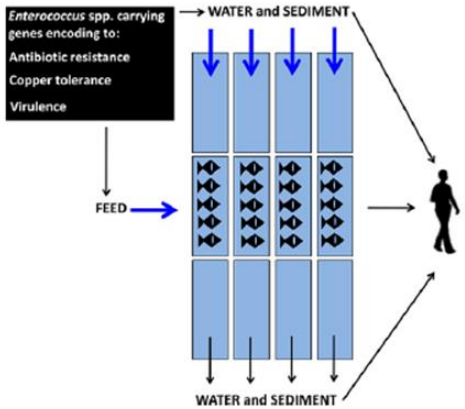
Carla Novais [a], Joana Campos [a], Ana R. Freitas [a], Mariana Barros [a], Eduarda Silveira [a,e], Teresa M. Coque [b,c,f], Patrícia Antunes [a,d], Luísa Peixe [a,*]

[a] UCIBIO/REQUIMTE, Departamento de Ciências Biológicas, Laboratório de Microbiologia, Faculdade de Farmácia da Universidade do Porto, Porto, Portugal
[b] Servicio de Microbiologia, Hospital Universitario Ramón y Cajal and Instituto Ramón and Cajal de Investigación Sanitaria (IRYCIS), Madrid, Spain
[c] Centro de Investigación Biomédica en Red de Epidemiología y Salud Pública (CIBER-ESP), Madrid. Spain
[d] Faculdade de Ciências da Nutrição e Alimentação, Universidade do Porto, Porto, Portugal
[e] Centro de Investigação Vasco da Gama (CIVG), Escola Universitária Vasco da Gama, Coimbra, Portugal
[e] Unidad de Resistencia a Antibióticos y Virulencia Bacteriana asociada al Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

HIGHLIGHTS

- Aquacultural water supply and feed are sources of multidrug-resistant *Enterococcus*.
- Aquacultures are underestimated sources of low-level resistant *Enterococcus*.
- *Enterococcus* with Cu tolerance and virulence genes are spread by water and feed.
- *Enterococcus* lineages of human and non-trout animal origins contaminate aquacultures.
- Antibiotic resistant bacteria search is a requisite for future Water Frame Directive.

GRAPHICAL ABSTRACT



The microbiome and antibiotic resistance in integrated fishfarm water: Implications of environmental public health

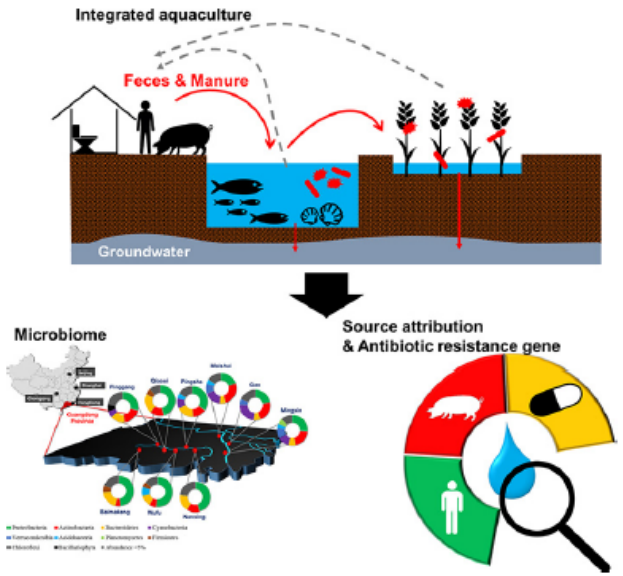
Gary Klase [a,1,2], Seungjun Lee [a,1], Song Liang [b,c], Jinnam Kim [d], Young-Gun Zo [d], Jiyoung Lee [a,e,*]

[a] College of Public Health, Division of Environmental Health Sciences, The Ohio State University, Columbus, OH 43210, USA
[b] Department of Environmental and Global Health, University of Florida, Gainesville, FL 32610, USA
[c] Emerging Pathogens Institute, University of Florida, Gainesville, FL 32610, USA
[d] Department of Biology, Kyungsung University, Busan 48434, South Korea
[e] Department of Food Science and Technology, The Ohio State University, Columbus, OH 43210, USA

HIGHLIGHTS

- Integrated fishfarms in China were tested for microbial threats to public health.
- Pathogens, antibiotic resistant bacteria, and fecal contamination were detected.
- Human fecal contamination was confirmed; shows elevated risk of disease transmission.
- All ponds tested positive for presence of antibiotic resistant bacteria.
- Suggests high risk to pond workers directly exposed; possible risk to consumers

GRAPHICAL ABSTRACT



Contents lists available at ScienceDirect

Aquaculture

journal homepage: www.elsevier.com/locate/aquaculture

Antibiotic use in Vietnamese fish and lobster sea cage farms; implications for coral reefs and human health

N. Hedberg[a,b,*], I. Stenson[b], M. Nitz Pettersson[a], D. Warshan[a], H. Nguyen-Kim[c], M. Tedengren[a], N. Kautsky[a]

[a] Department of Ecology, Environment and Plant sciences, Stockholm University, Sweden
[b] Baltic Sea Centre, Stockholm University, Sweden
[c] Institute of Oceanography (IO), Vietnam Academy of Science and Technology (VAST), Vietnam

ARTICLE INFO

Keywords:
Antibiotics
Bacillus niabensis
Sea cage aquaculture

ABSTRACT

Several papers have reported on the development of antibiotic resistance and implications for human medicine but fewer deal with environmental impacts of antibiotic use. Marine sea cage aquaculture in SE Asia is often established close to coral reef ecosystems. Large amounts of antibiotics are used in the cultivation of fish and lobster and hence released directly into the environment.

This study investigates the antibiotic practices in sea cage farms producing fish and spiny lobster in Vietnam, mainly for the domestic market. There are approximately 3500 sea cage farms in Vietnam and we performed semi-structured interviews with 109 sea cage farmers asking them if they use antibiotics and if so; what sort/when/how often/how much.

We found that the Vietnamese cage farmers are using antibiotics in an unstructured way, which seems to have little or no effect on the survival of the stock, or profit of the farm. The fact that the farmers live at their farm and use the sea next to the cages both for fishing and collecting filter-feeding bivalves for direct consumption, as well as a toilet, poses an additional risk for the spreading of human antibiotic resistant pathogens. Thirteen different antibiotics were found in the study. Eighty-two percentage of the lobster farmers and 28% of the fishfarmers used antibiotics. The average amounts used were over 5 kg per produced ton of lobster and about 0.6 kg per ton of fish, which is much higher than in other studies. Several antibiotic substances listed as "critical" and "highly important" for human medicine by WHO were used prophylactically and routinely with little control and enforcement of regulations.

We tested and detected antibiotic resistance to Tetracycline, Vancomycin and Rifampicin in the coral associated bacteria *Bacillus niabensis* as far as 660 m from fish farms with resistance decreasing with distance from the cage farms. The antibiotics are likely to have negative effects on the coral-symbiont relationship adding further risks to an already stressed environment.

MINIREVIEW

Exploring fish microbial communities to mitigate emerging diseases in aquaculture

Irene de Bruijn[1,†], Yiying Liu[1,*,†], Geert F. Wiegertjes[2] and Jos M Raaijmakers[1,3]

[1]Department of Microbial Ecology, Netherlands Institute of Ecology (NIOO-KNAW), Droevendaalsesteeg 10, Wageningen 6708PB, The Netherlands, [2]Cell Biology and Immunology group, Department of Animal Sciences, Wageningen University & Research, De Elst 1, Wageningen 6708WD, The Netherlands and [3]Institute of Biology (IBL), Leiden University, Sylviusweg 72, Leiden 2333 BE, Leiden, The Netherlands

*Corresponding author: I. de Bruijn, Department of Microbial Ecology, Netherlands Institute of Ecology (NIOO-KNAW), 6708PB Wageningen, The Netherlands. Tel: 0031 317 473496; E-mail: i.debruijn@nioo.knaw.nl

† Shared first authors.

One sentence summary: This review describes insights in the diversity and functions of the fish bacterial communities elucidated with next-generation sequencing and discusses the potential of the microbes to mitigate (re-)emerging diseases in aquaculture.

Editor: Marcus Horn

ABSTRACT

Aquaculture is the fastest growing animal food sector worldwide and expected to further increase to feed the growing human population. However, existing and (re-)emerging diseases are hampering fish and shellfish cultivation and yield. For many diseases, vaccination protocols are not in place and the excessive use of antibiotics and other chemicals is of substantial concern. A more sustainable disease control strategy to protect fish and shellfish from (re-)emerging diseases could be achieved by introduction or augmentation of beneficial microbes. To establish and maintain a 'healthy' fish microbiome, a fundamental understanding of the diversity and temporal-spatial dynamics of fish-associated microbial communities and their impact on growth and health of their aquatic hosts is required. This review describes insights in the diversity and functions of the fish bacterial communities elucidated with next-generation sequencing and discusses the potential of the microbes to mitigate (re-)emerging diseases in aquaculture.

Keywords: aquaculture; fish; emerging diseases; microbiomes; beneficial microbes

Environmental Antibiotic Concentrations

Antibiotic	Effluent conc. µg / L (max)	Surface waters µg / L (max)
Penicillin	0.2	-
Erythromycin	6.0	1.7
Fluoroquinolones (ciprofloxacin, norofloxacin)	0.1	0.1
Sulfamethoxazol	2.0	1.9
Chloramphenicol	0.5	-
Trimethoprim	0.7	0.7

Kummerer 2009

Antimicrobial residues in water bodies downstream of different sources

Location / source	Country	Antibiotic	Levels	
			PNEC *	Recorded
Hospital wastewater	Thailand	Sulfamethoxazole	16,000 ng/L	1,499 ng/L
Pharmaceutical/industrial wastewater	India	Ciprofloxacin	0.064 µg/L	**31 000 µg/L**
Municipal/community wastewater	India	Ampicillin		21 µg/L
STP/WWTP	Thailand	Ciprofloxacin	0.064 µg/L	**.20 µg/L**
	Thailand	Oxytetracycline	0.500 µg/L	**3 µg/L**
		Enrofloxacin		1.6 µg/L
	Thailand	Roxithromycin		Influent – 235 ng/L Effluent – 50 ng/L
Aquaculture	Thailand	Oxytetracycline	500 ng/L	180 ng/L
Water bodies	India	Ciprofloxacin	0.064 µg/L	**6500 µg/L**

- PNEC = predicted no effect environmental concentrations
- Bengtsson-Palme J, Larsson DGJ. Concentrations of antibiotics predicted to select for resistant bacteria: Proposed limits for environmental regulation. *Environ Int* 2016;86:140-9. doi:10.1016/j. envint.2015.10.015

Linus Sandegren. Selection of antibiotic resistance at very low antibiotic concentrations. Upsala Journal of Medical Sciences. 2014; 119: 103–107

- Rate with which resistance mutations (or acquisition of resistance genes through HGT) will arise is expected to be higher at low concentrations of antibiotics. Non-lethal concentrations of antibiotics mean that the bacterial population is not eradicated as with high levels of drug where only pre-existing resistant mutants will survive.

- Low levels of antibiotics have been shown to increase homologous recombination rates, stimulate horizontal gene transfer, and activate integrating genetic elements (29–34).

Next steps….

- Having identified the hazard….
- Linkage to most important sources
- And determining the risk represented to the end receptors
- Risk managers typically prioritise effective mitigation through critical control points.
- But what is the hazard in question – ABR, AMR bacteria, or AMR genes transferred between species/ pathogenic bacteria?
- Lack of evidence to inform dose/ response, source attribution and risk assessment methodologies

Thank you

- Professor Jason Weeks
- jasonweeks@btinternet.com

IEHConsulting
The integrated environment and health consultancy