Review of evidence on antimicrobial resistance and animal agriculture in development countries

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1

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Introduction

> **Antimicrobials** have become an **integral** part of **human** and **animal medicine**

> In humans they are critical as a frontline defence for a wide range of pathogens

> They are used as a measure to manage and reduce infections caused by surgery

> It is believed that their importance to **surgical procedures** is where there would be the most problems with a growth in antimicrobial resistance

Introduction
- antimicrobial use in animals

> In animals there is widespread **antimicrobial use** in **companion animals** in a **similar** way to **humans**

> The situation in **food animals** is **complicated** by the use of antimicrobials for:

- Growth promotion
- Prophylaxsis
- Metaphylaxsis
- And treatments for disease in general

Introduction
- the range of antimicrobials

> There is a **range of antimicrobials** that have different actions on pathogens and also the hosts

> In countries with **good regulation** and enforcement the antimicrobial use is managed by species with **guarded use** of **antimicrobials** critical for human medicine

> In **poor regulatory environments** the management of use cannot be guaranteed

- Likely that use will be driven by **private interests** and **ignorance**

Introduction
- the actual use of antimicrobials

> The **recording** of the use of antimicrobials by species and production system is **not common**

> OECD countries rely on data from pharmaceutical companies and veterinarians

> It is **rare** that data are generated at **farm-level**, albeit it is becoming an industry standard in the poultry sector and pig sectors are increasingly receptive

Introduction
- *The core issue*

> The range of antimicrobials, different regulatory environments and different levels of use in animals creates **difficulty** and **complexity** in **data collection**

> The recording of these data **hampers** the ability to look at **causality** of **use** to **AMR emergence**

> Some argue that there are weak links in use in animals and AMR and that the problem lies elsewhere, yet **it is important to address this issue scientifically**

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Introduction
- The core issue

> There needs to be **data collection systems** that allow the proper **investigation** of the **link** between antimicrobial **use in animals** and **AMR**

- Does AMR emerge?
- At what usage rates is AMR emergence more likely?
- Where does AMR emerge?
- For which antimicrobials is AMR important?

> Only through such processes will it be possible to define what use is viable and useful to humanity as a whole
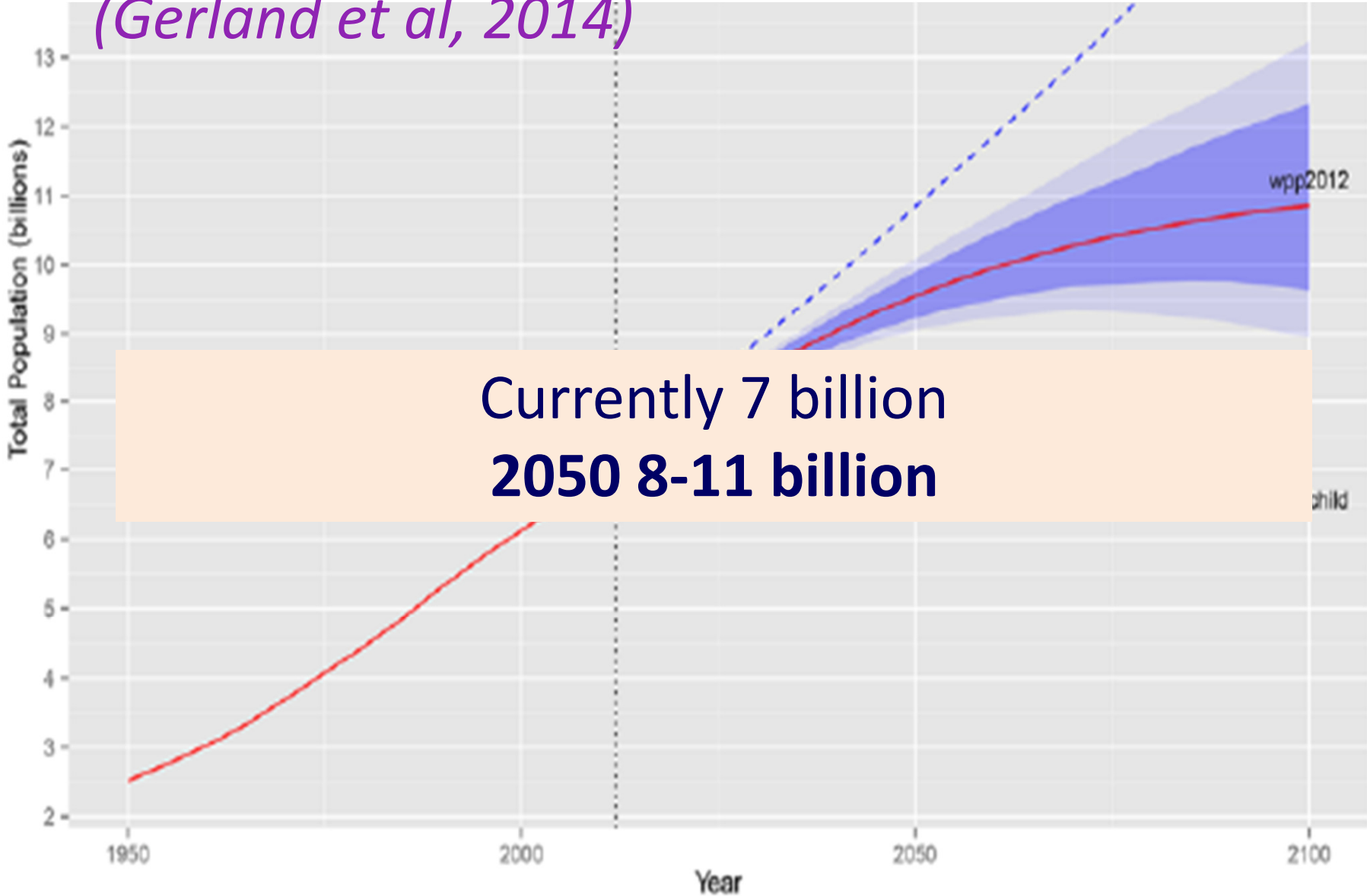
Summary

> I will examine this problem through:

- Looking at the **context** in which animals are kept, raised and used

- Determining what is known about **antimicrobial use** in the main animal systems

- Determining what is known about **resistance** and residues in these systems
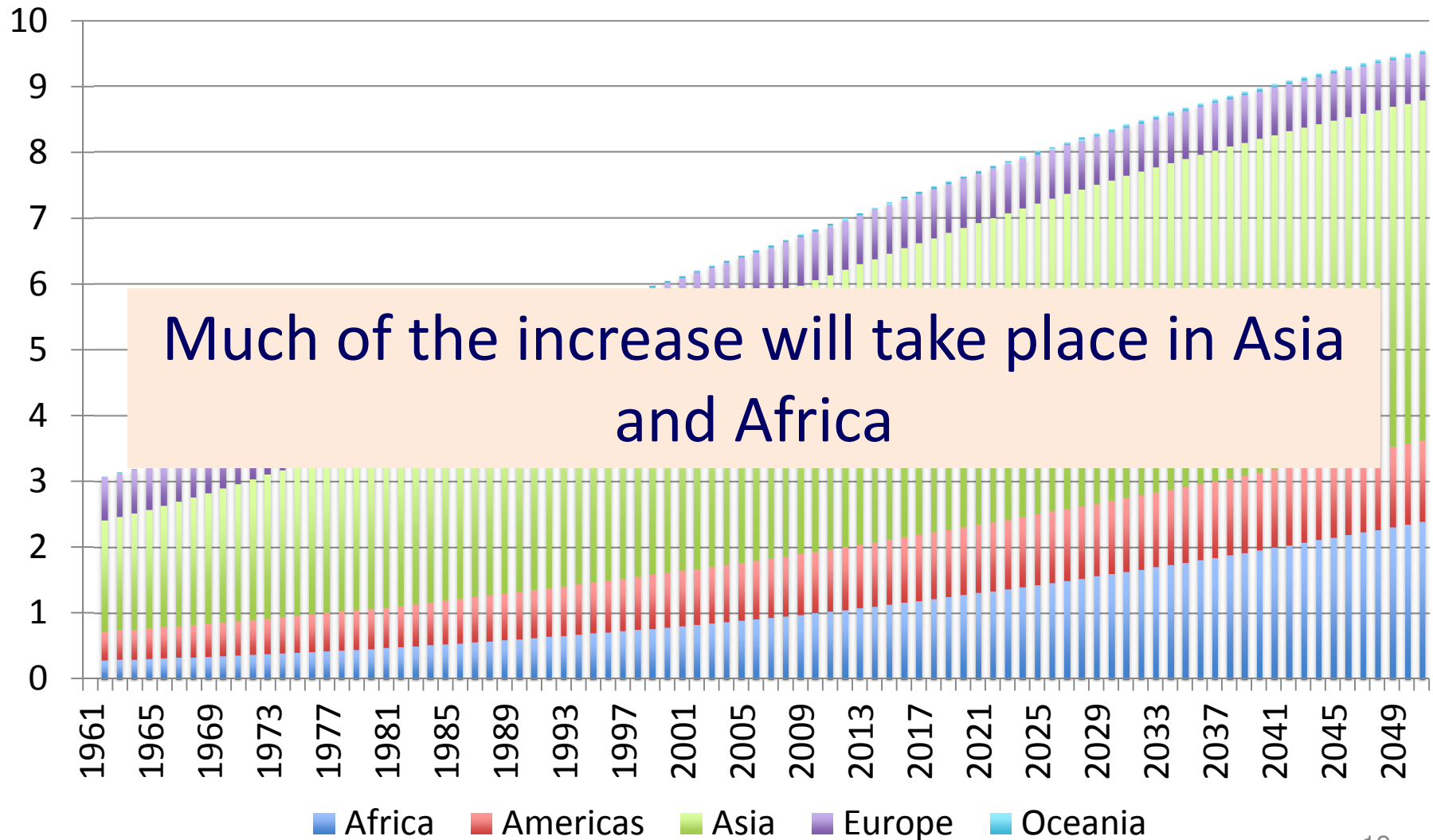
- Some reflections

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The Context
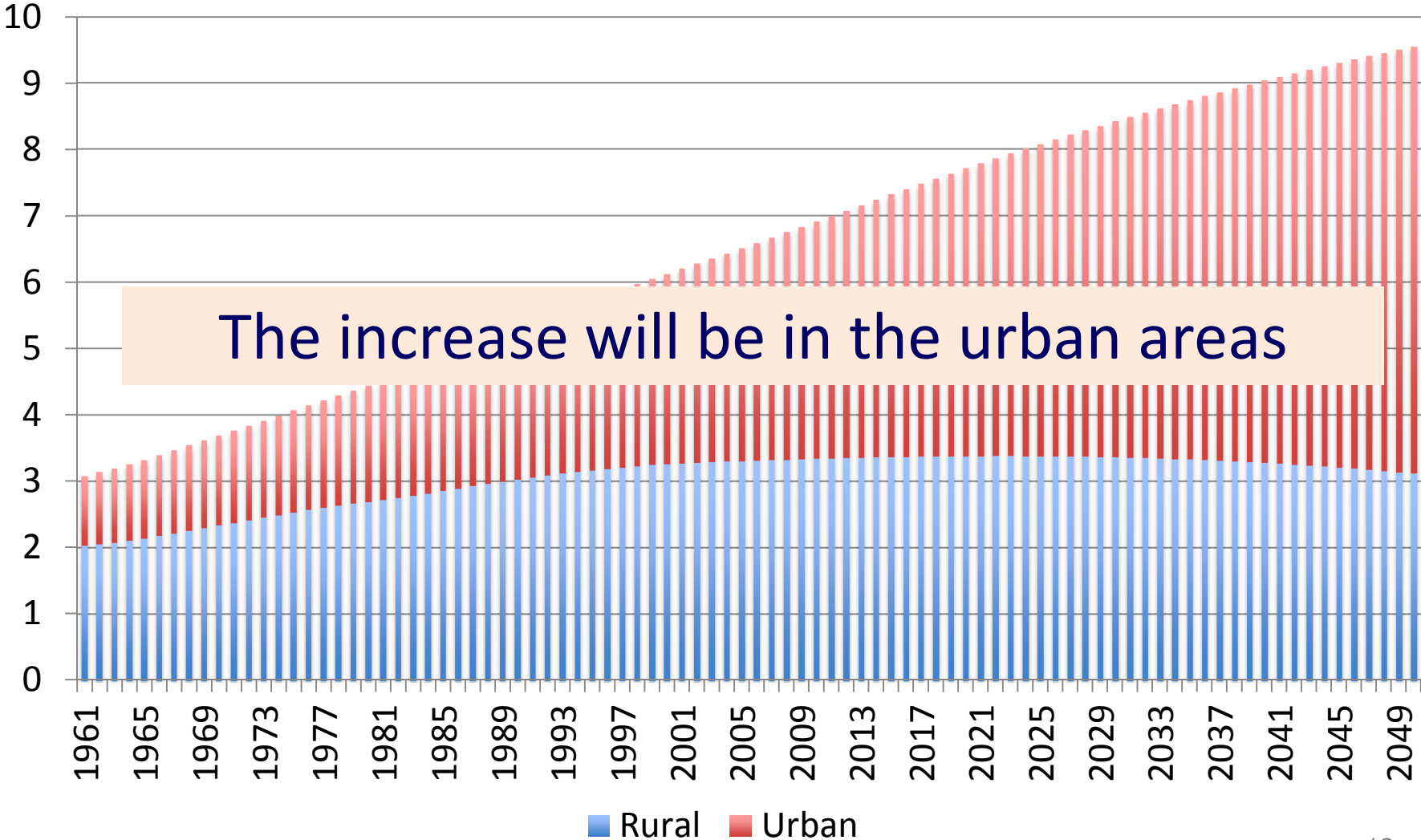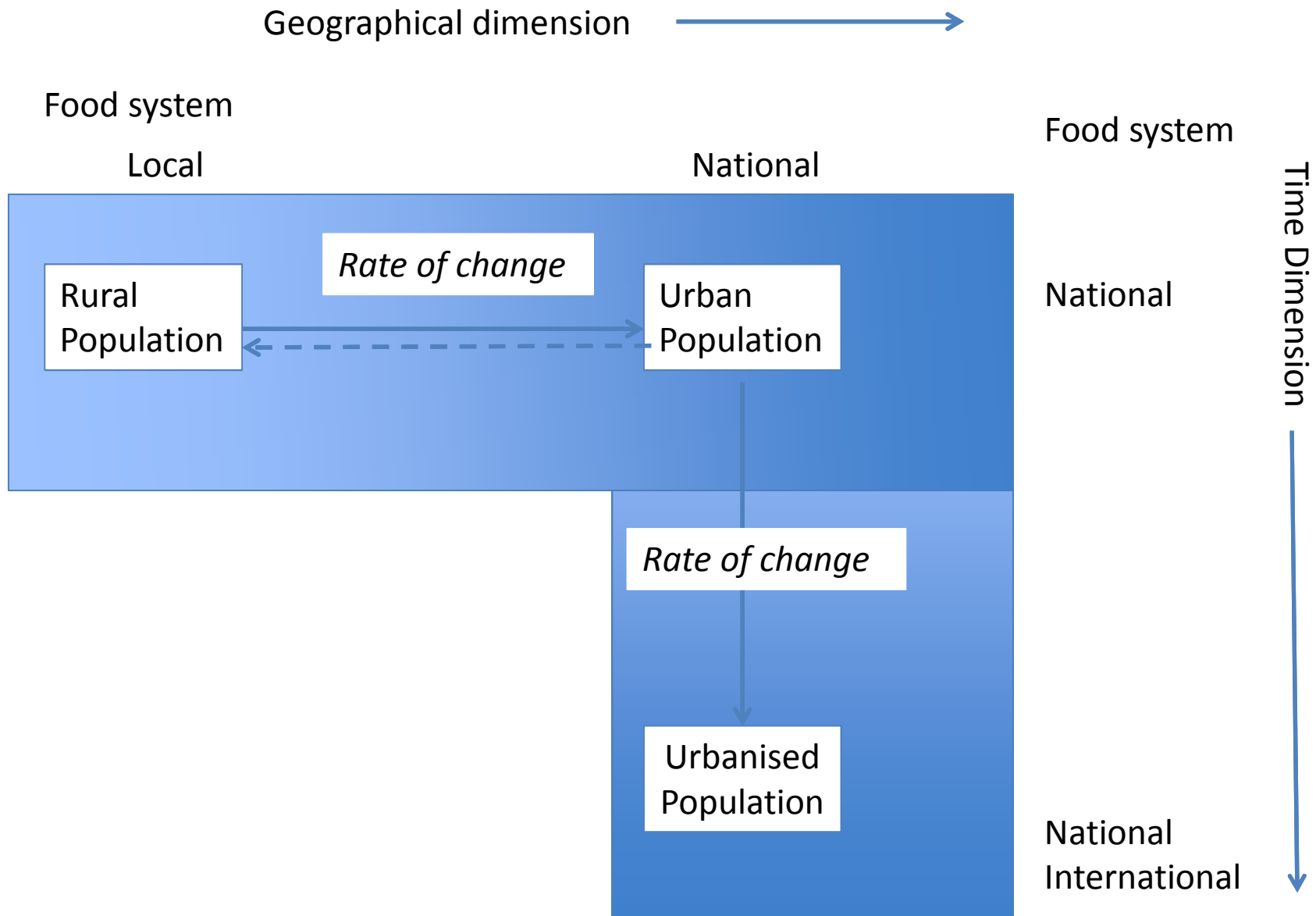
Human world population projection
(Gerland et al, 2014)

Currently 7 billion
2050 8-11 billion

Where are these people? Where will they be?
(FAOSTAT population 1961 to 2050 in billions)

Much of the increase will take place in Asia and Africa

Legend: ■ Africa ■ Americas ■ Asia ■ Europe ■ Oceania

Global population – rural and urban estimates 1961 to 2050 (FAOSTAT, 2015)

The increase will be in the urban areas

Rural   Urban

13

People and the food system

Geographical dimension →

Food system

Food system

Local

National

National

Rate of change

Rural Population ⟷ Urban Population

Rate of change

Urbanised Population

National

National
International

Time Dimension ↓

Our grazing species

Simple food chain

Family or household

Purchased Inputs → Inputs → Production

Product · Residues · Fresh Produce · Labour

Processing ← Product

Processed Product

Consumption

Labour

$ ← (from Purchased Inputs)

Fresh product → Products sold to consumers with low demands on quality certification and who process the food in their homes

Processed Product →

$ ←

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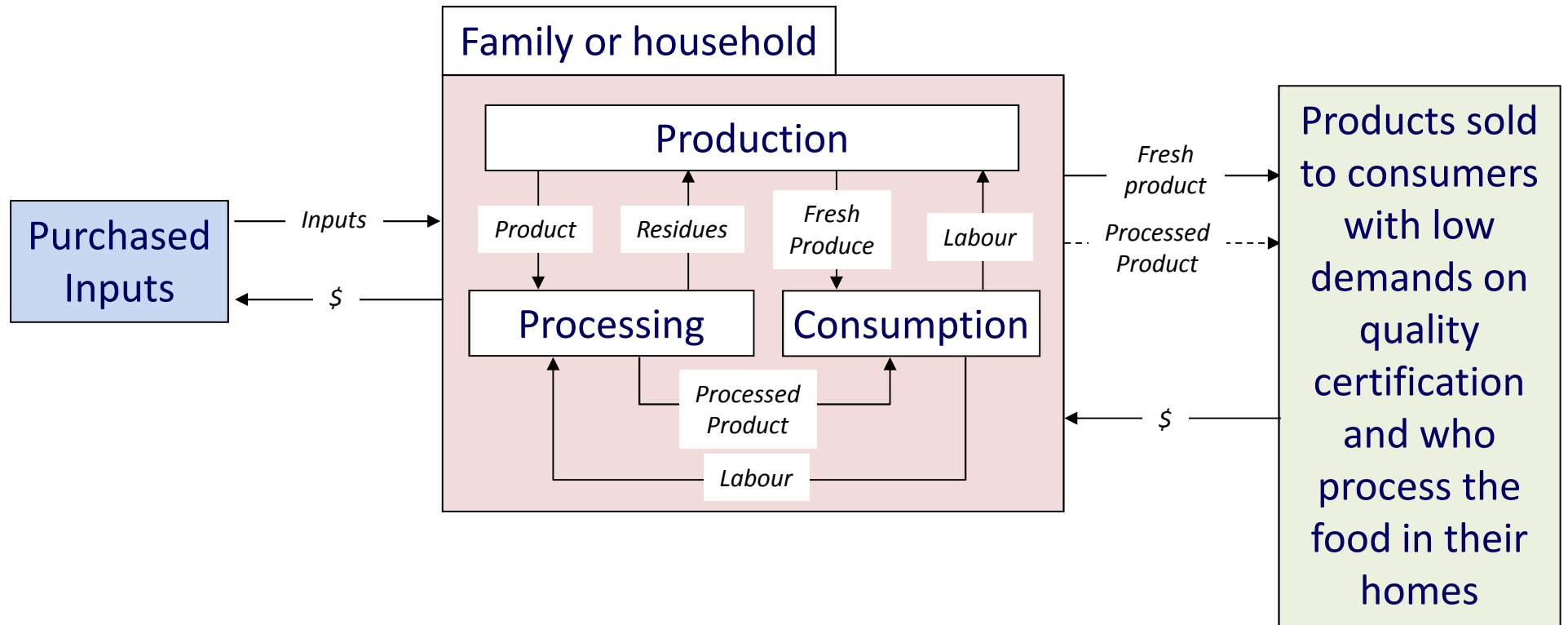
Our scavenging species

The context

> Human populations are increasing

> The increases are predicted to be in:

- Africa and Asia
- Urban areas

> This will have an impact on the types of livestock food systems we can anticipate

> And the types of production systems we are increasingly reliant on

Food Systems

> From simple to complex in a generation in the OECD countries

> From simple to complex in a decade in Asia

> From simple to complex in five years in Africa?

Complex food chain
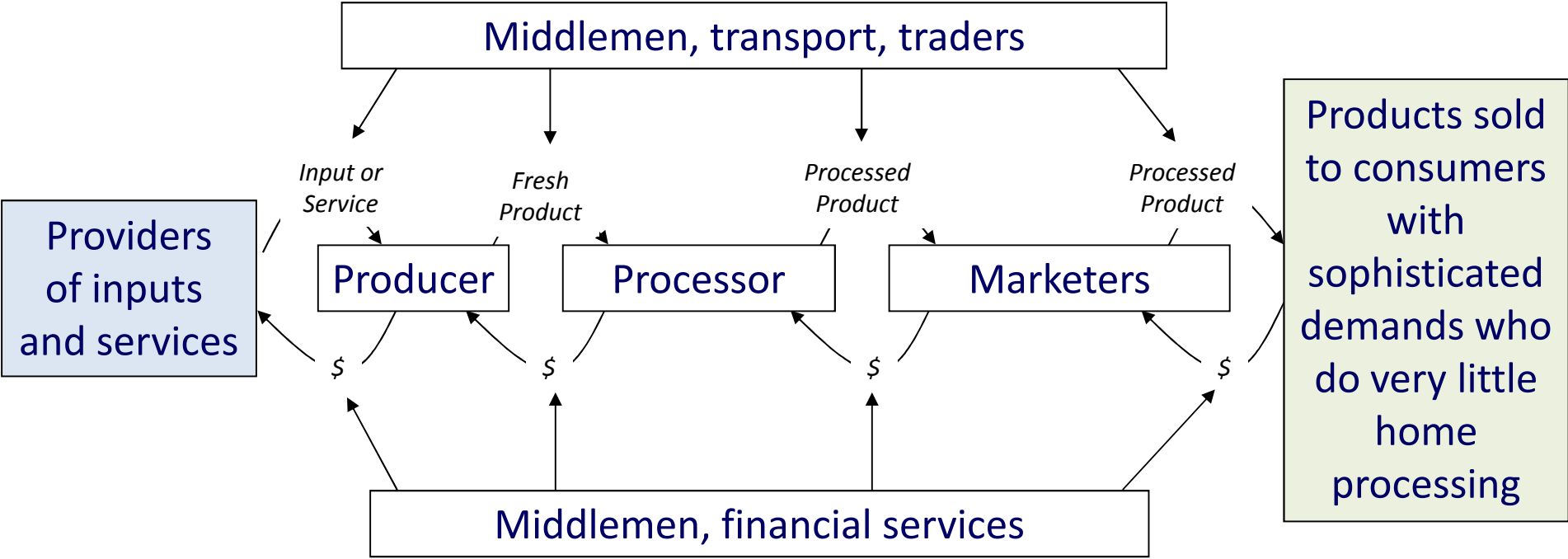
Duck breeding flock
 - Egypt

Chicken broiler flock
 - Tanzania

Beef cattle
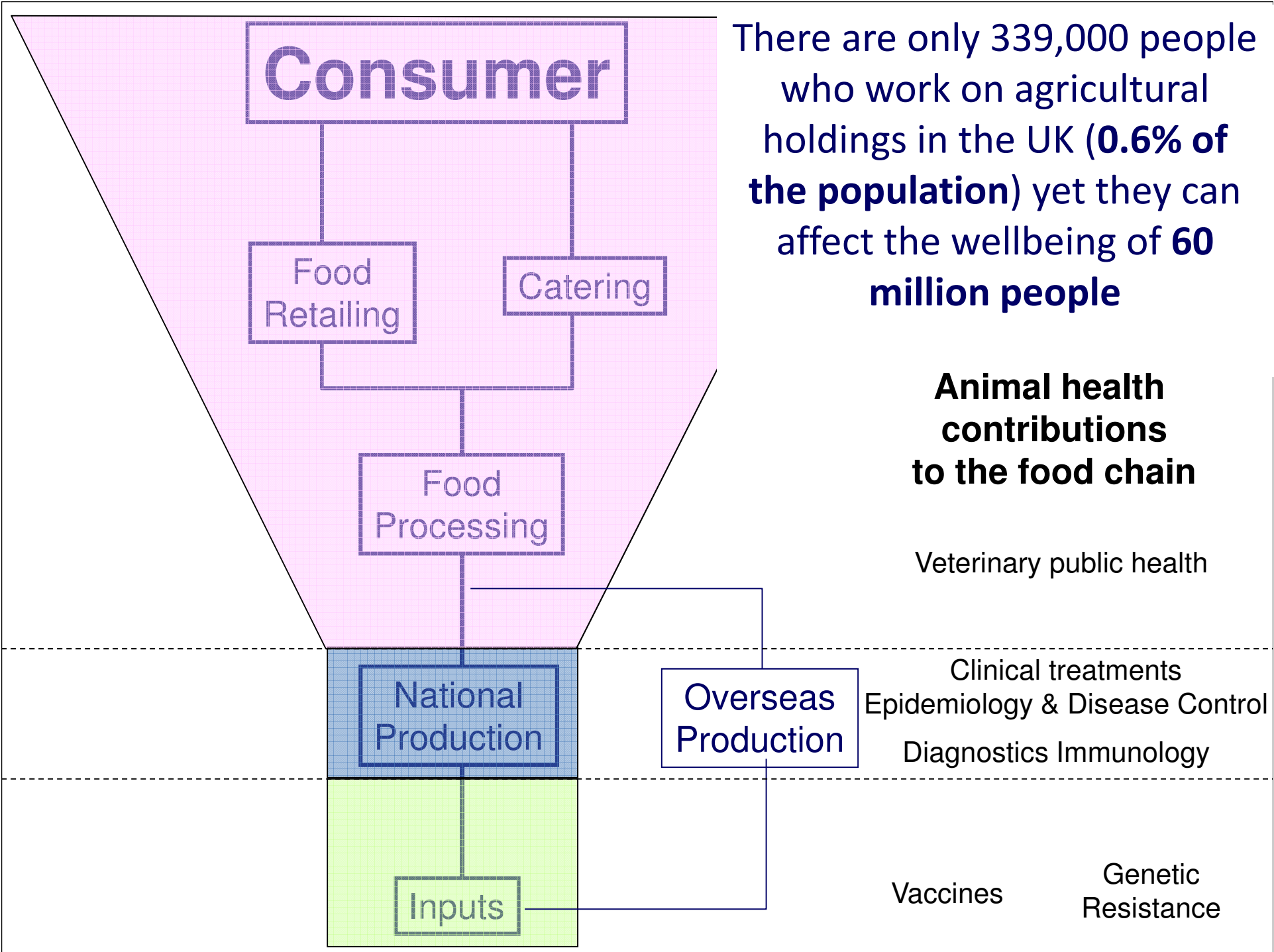 – Northern Ireland

Dairy system –
Nairobi, Kenya

Sheep
 – NSW, Australia

Outdoor pigs
 – East Anglia, UK

Consumer

Food Retailing

Catering

Food Processing

National Production

Overseas Production

Inputs

There are only 339,000 people who work on agricultural holdings in the UK (**0.6% of the population**) yet they can affect the wellbeing of **60 million people**

Animal health contributions to the food chain

Veterinary public health

Clinical treatments
Epidemiology & Disease Control

Diagnostics Immunology

Vaccines

Genetic Resistance

Summary of the animal role changes

> These **changes** in the **role of animals** have been dramatic in the last two decades

The role of animals is constantly evolving
Some of these changes are demand driven
Others relate to supply process changes

While **livestock** are increasingly confined, raised, slaughtered and processed in **large groups**

Antimicrobial use in animals

What to measure?

> Level of use

> Type of product used

> Use versus number of animals

> Or use versus product produced

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Where to measure

> At pharmaceutical production and sale

> At the import/export level

> With veterinary prescriptions

> In the feedmills

> Through farm-level data collection

What do we know on use?

> Globally more antimicrobials are used to treat healthy animals than unhealthy humans

> Country level use will vary with the systems in which animals are kept

- In the US it is estimatd that of the antimicrobials sold for both humans and animals, almost 80% were reserved for livestock and poultry

- In 2012 Denmark used 103 tonnes of antibiotics in animals and 50 tons in humans, reflecting that this country has a large livestock population relative to the human population
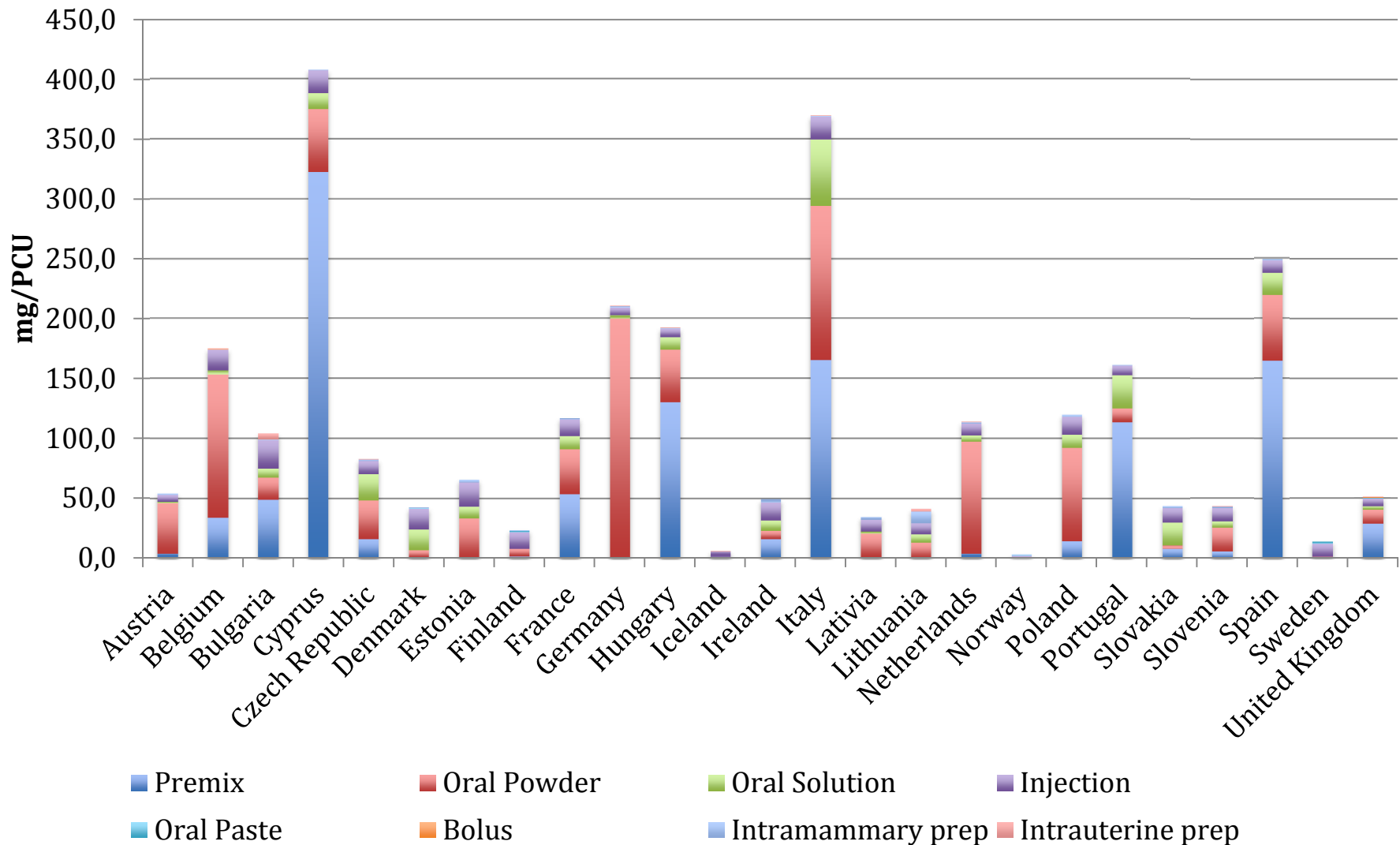
What do we know on use?

> Interpretation of antimicrobial use in humans and animals should recognise that for every person in the world there are two to three times the numbers of animals when measured in biomass terms.

> For true comparisons the use per population correction unit between humans and animals would be needed.

- In Sweden(2012) it was reported that in humans there was a use of 104mg/kg versus 15 mg/kg to animals.
- The relatively low use in animals relates to investments in animal health systems that reduce the need for antibiotics in animals.

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Production systems and antimicrobial use

> The need for the use of antimicrobials is heavily influenced by husbandry practices and its direct link to animal health.

- UK use of antimicrobials in the intensively farmed pig sector in the UK was 115 times higher than in sheep farming
- In the USA:
  - 16% of all lactating dairy cows receive antibiotic therapy for clinical mastitis each year
  - 15% of beef calves that enter feedlots receive antimicrobials for the treatment of respiratory clinical problems
  - 10% of apparently healthy calves receive the same dose of antimicrobials as a prophylactic measure
  - 42% of beef calves in feedlots are fed tylosin (a veterinary macrolide drug), to prevent liver abscesses that have negative impact on growth;
  - 88% of fattening pigs are treated with growth promoters in their feed (tetracyclines and tylosin).
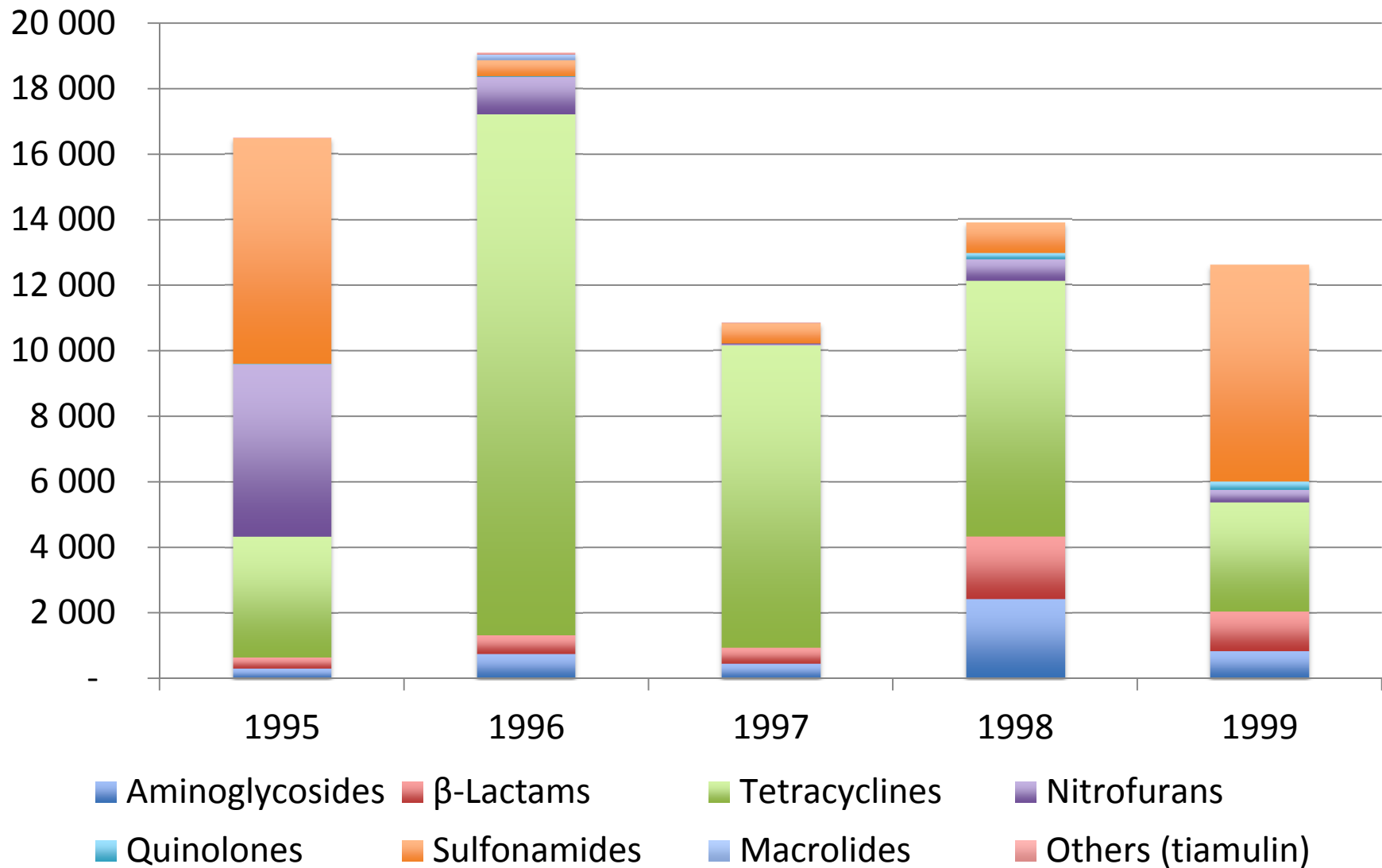
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Estimated antimicrobial use to produce one kilogram of meat in 25 European countries in 2011 (from ESVAC, 2013)

Legend:
- Premix
- Oral Powder
- Oral Solution
- Injection
- Oral Paste
- Bolus
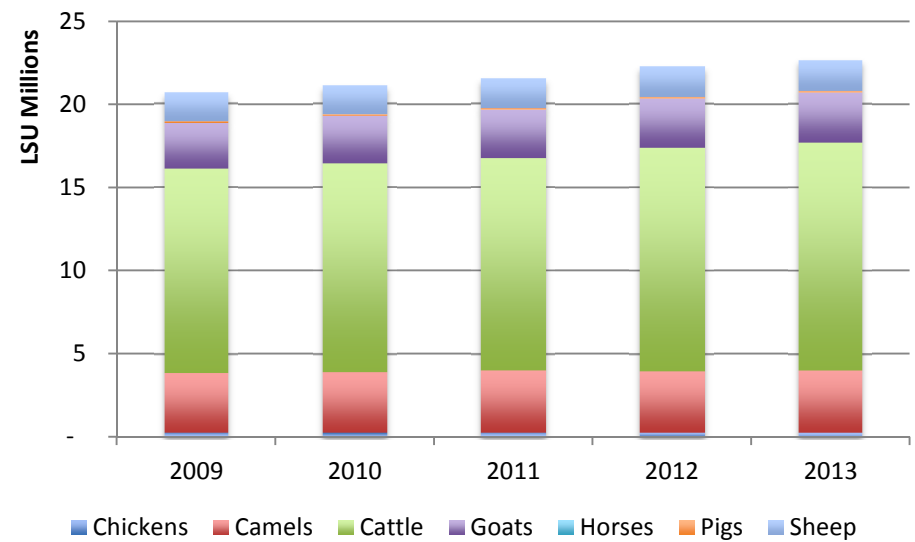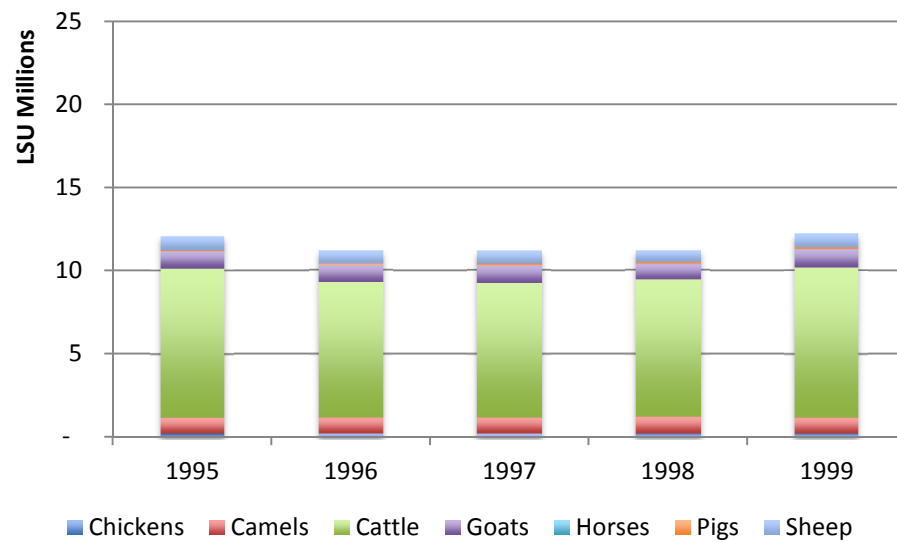- Intramammary prep
- Intrauterine prep

And use in the developing countries?

> Otte *et al.* (2012) reported estimates that suggest the Asia and Pacific region to be much more important regarding the use of antimicrobials in livestock production than other regions, but they do not make a specific estimate.

- This region has well over half the world's pig population and a very high proportion of its poultry and the majority of the ducks.
- Many of these animals are reared in intensive or semi-intensive systems where the use of concentrate feed and high population densities require health management that involves antibiotic usage.

> Otte *et al.* estimate that this region has nearly half of the global antimicrobial market, with total 2011 sales in the region of about US$ 1.8billion

Antimicrobial use in Kenya in kg (Mitema et al, 2001)

Legend:
- Aminoglycosides
- β-Lactams
- Tetracyclines
- Nitrofurans
- Quinolones
- Sulfonamides
- Macrolides
- Others (tiamulin)

Kenya livestock population 1995-1999 and 2009-2013 livestock units (FAOSTAT)

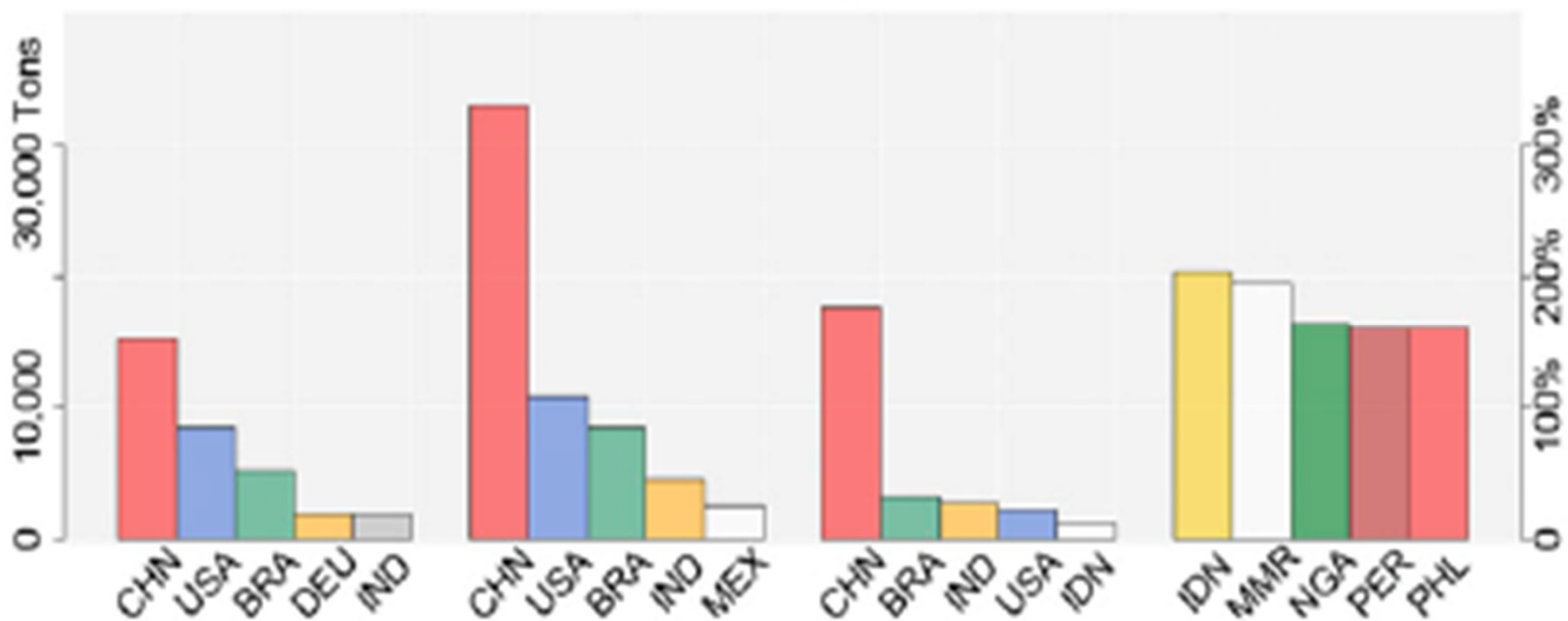# Projections of antimicrobial use (van Boeckel et al, 2015)

Fig. 1. (A) Largest five consumers of antimicrobials in livestock in 2010. (B) Largest five consumers of antimicrobials in livestock in 2030 (projected). (C) Largest Increase in antimicrobial consumption between 2010 and 2030. (D) Largest relative increase in antimicrobial consumption between 2010 and 2030. CHN, China; USA, United States; BRA, Brazil; DEU, Germany; IND, India; MEX, Mexico; IDN, Indonesia; MMR, Myanmar; NGA, Nigeria; PER, Peru; PHL, Philippines.

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And the use in the developing countries?

> However, only very limited information is available from most of the developing countries, with Kenya

There are not enough data collection mechanisms to capture use of antimicrobials globally and this problem is greatest in the developing countries

currently inadequately recorded and represents a key obstacle to risk assessment

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Antimicrobial resistance

Resistance – what and how to measure?

> Where do we need to measure AMR?
- Resistance in the environment
- Resistance in species
- Do we have a baseline

> How do we measure resistance?
- Plating
- Gene detection
- Whole genome sequencing

> What is the overall importance of AMR to human health?

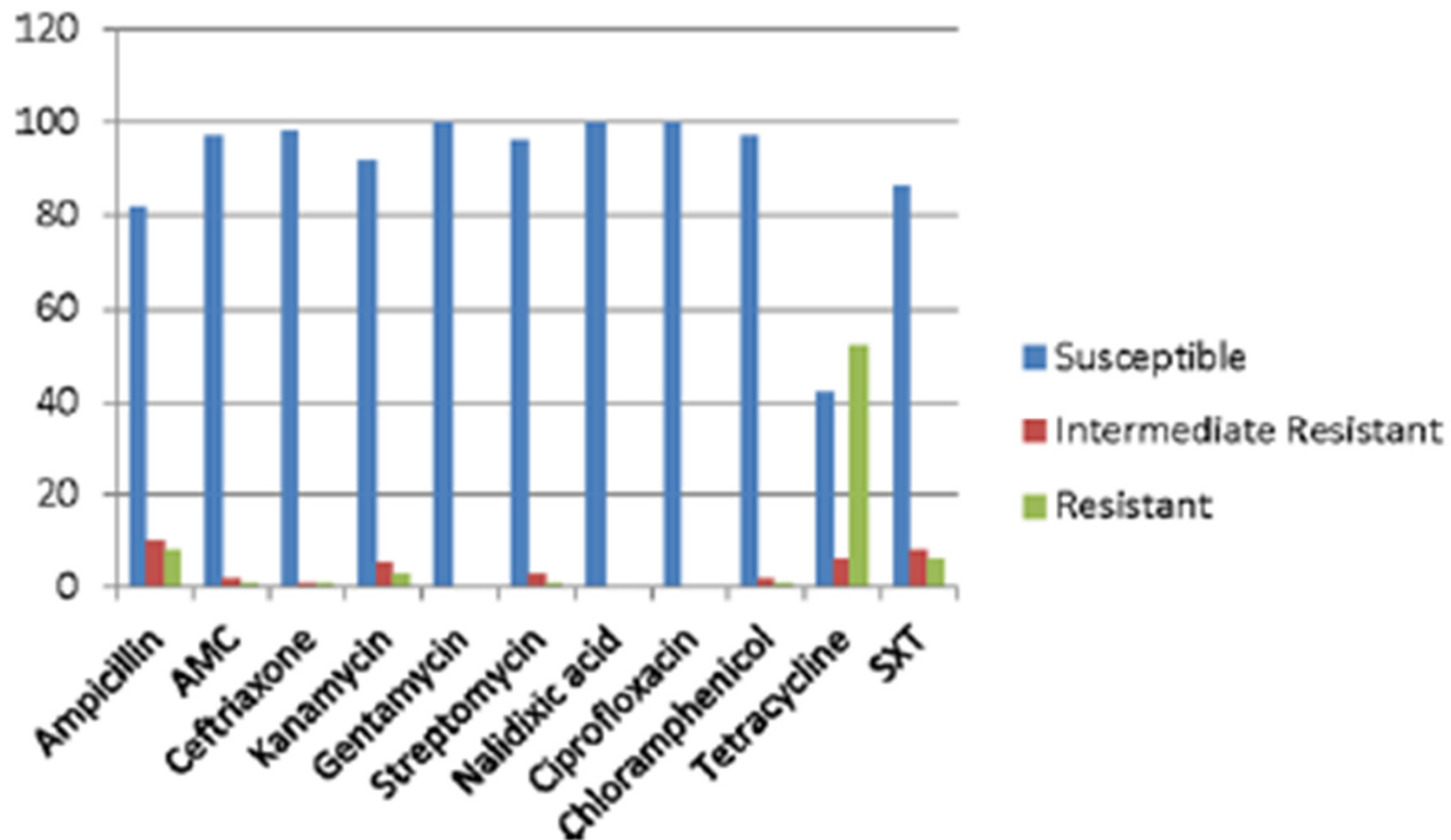# Antimicrobial suspectability patterns in beef carcasses in Nairobi, Kenya (Kariuki & Dougan, 2014)

Figure 3. Antibiotic susceptibility patterns among *E. coli* isolates from beef carcasses at three abattoirs in Nairobi, Kenya ($n = 188$). AMC, amoxycillin/clavulanic acid; SXT, trimethoprim/sulphamethoxazole.

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Antimicrobial suspectability patterns in poultry in small-scale farms in Thika, Kenya (Kariuki & Dougan, 2014)
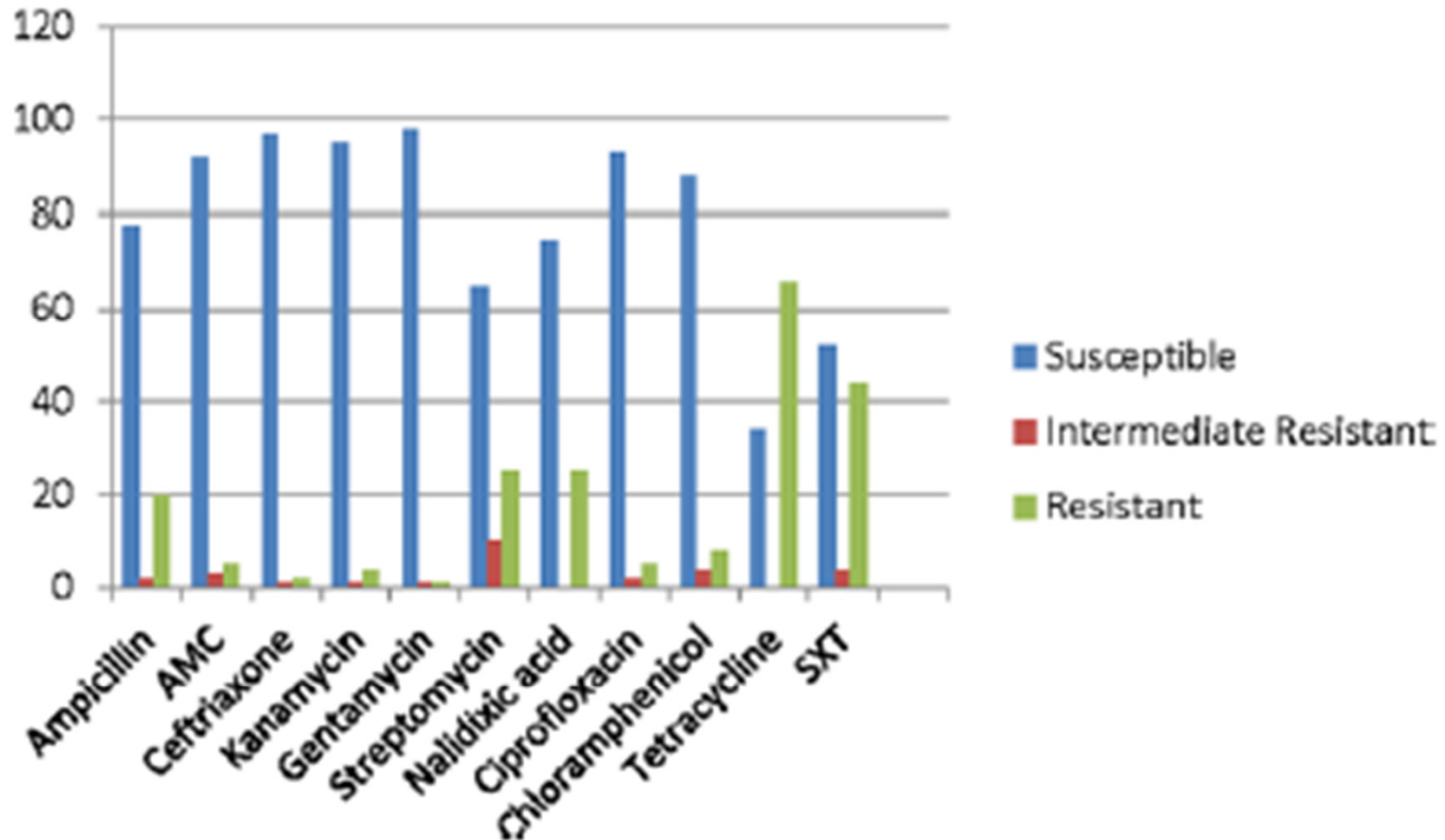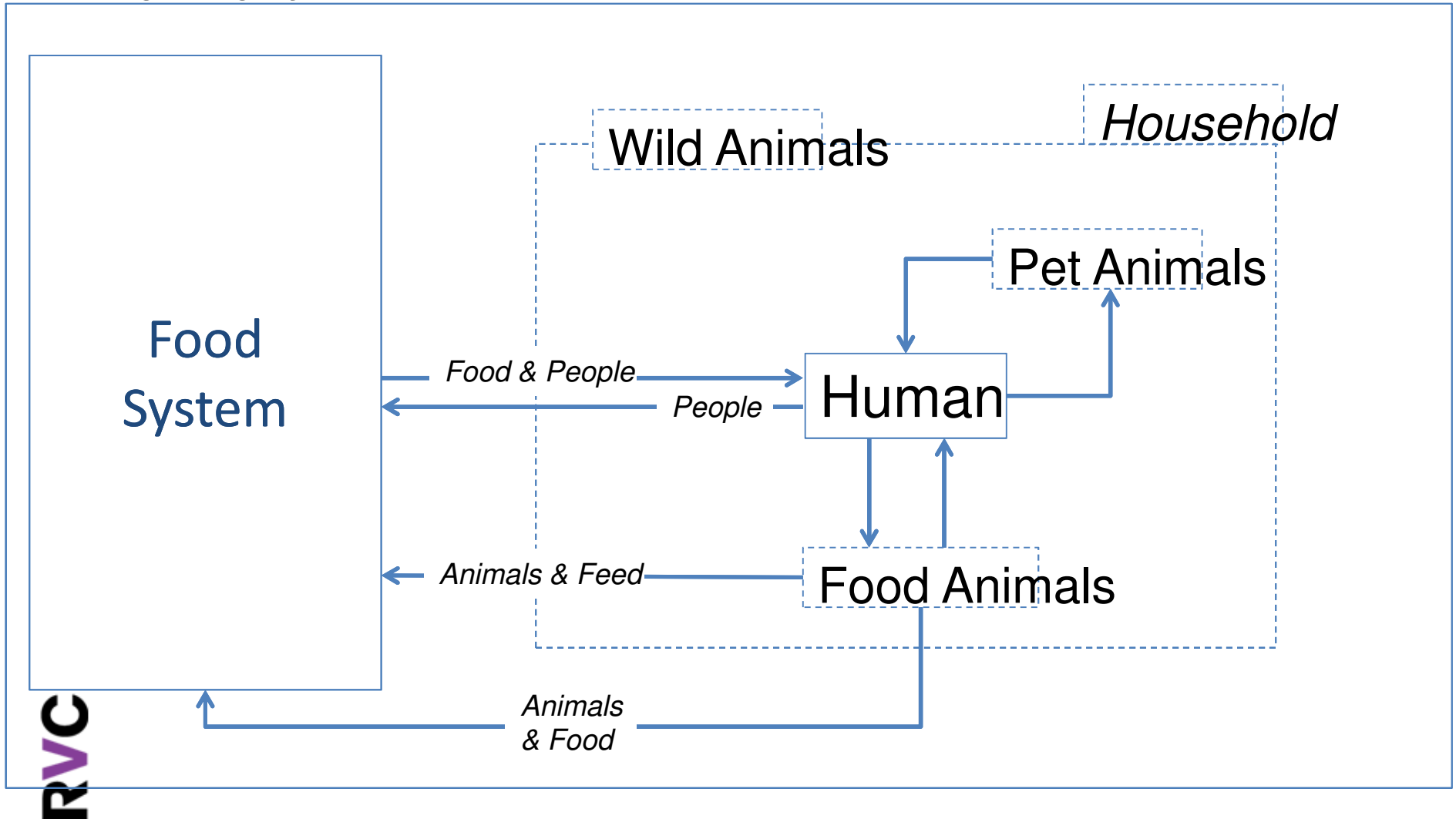

Figure 4. Antibiotic susceptibility patterns for *E. coli* isolated from poultry in small-scale farms in Thika, Kenya (*n* = 350). AMC, amoxycillin/clavulanic acid; SXT, trimethoprim/sulphamethoxazole.

# What do we really understand of the flows through these systems?

Reflections

Set a baseline

> Data can be gathered relatively quickly

- Pharmaceutical companies
- Companies involved in feed production
- Companies involved in the intensive livestock industries

> An initial assessment of these data will provide information of the weaknesses of the regulatory environment

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Strengthening the system

> The animal health system will have weaknesses

> They are likely to be at the level of interactions between animal owners and their animals

> The application of medicines and a poor understanding of withholding times could well influence the presence of antimicrobial residues in livestock products

> This may have impacts on the emergence of resistance and where this takes place
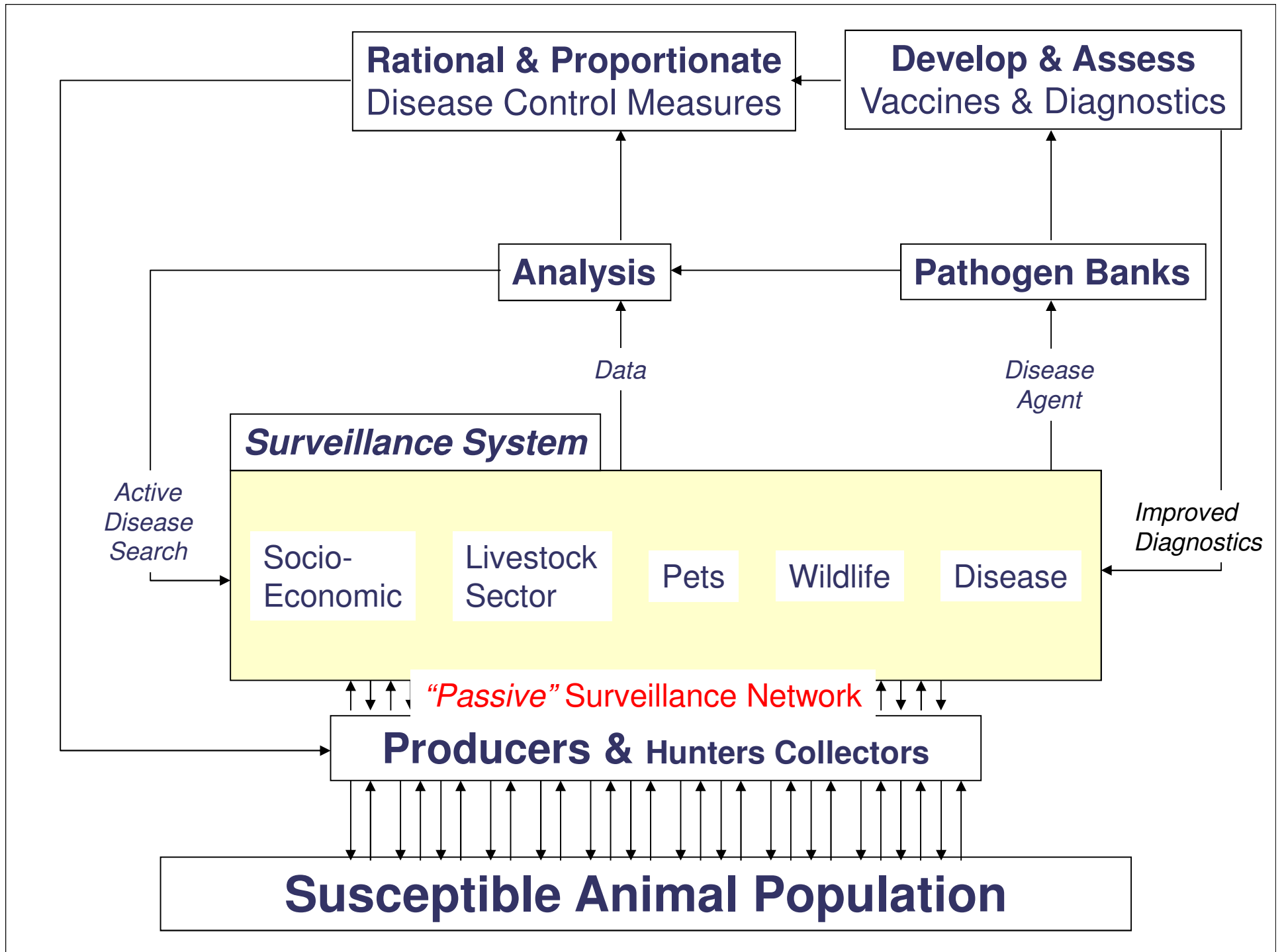
Key messages

> We know that livestock food systems are changing and in the process the use of antimicrobials is

Animal health decision making could be improved by better use of data capture and analysis of antimicrobial use

> Only with better data can will it be possible to understand links between usage and AMR

> And to refine the use of antimicrobials in animals

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Further information

> For more information on NEAT please look at
- www.neat-network.eu

> For information on NEOH please look at
- http://neoh.onehealthglobal.net

> For information on the work we are involved in with agriculture and health please look at
- http://www.lcirah.ac.uk/home

> For courses offered at RVC please look at
- http://www.rvc.ac.uk/Postgraduate/Distance/Index.cfm
- http://www.atp-ilhp.org

References

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> Kariuki, S. & Dougan, G. (2014) Antibacterial resistance in sub-Saharan Africa: an underestimated emergency. Ann N.Y. Acad Sci 1323 pp 43-55

> Mitema ES, Kikuvi GM, Wegener HC, Stohr K. An assessment of antimicrobial consumption in food producing animals in Kenya. *J Vet Pharmacol Ther*. 2001;24(6):385-90. Available at: http://www.ncbi.nlm.nih.gov/pubmed/11903868. Accessed May 5, 2014.

> Rushton, J., J. Pinto Ferreira and K. D. Stärk (2014), "Antimicrobial Resistance: The Use of Antimicrobials in the Livestock Sector", OECD Food, Agriculture and Fisheries Papers, No. 68, OECD Publishing. http://dx.doi.org/10.1787/5jxvl3dwk3f0-en

> Van Boekel et al (2015) Global trends in antimicrobial use in food animals. PNAS Early Edition