The Rise of Antibiotic Resistance

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AVIVAGEN FORWARD-LOOKING STATEMENTS

This presentation includes certain **forward-looking statements** that are based upon current expectations of management, which involve risks and uncertainties associated with the business of **Avivagen Inc.** and the environment in which the business operates. Any statements contained herein that are not statements of historical facts may be deemed to be forward-looking, including those identified by the expressions ***"anticipate", "believe", "can", "estimate", "prospective***", ***"further", "targeting",*** "***would***" and similar expressions.

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ANTIBIOTIC USE IN LIVESTOCK

Antibiotic uses in livestock include:

- Treatment of sick animals – **treatment dose**
- Promotion of growth (AGP) and to prevent disease – **growth promotion dose**

According to the FDA, in the U.S. alone 15,358,210 kg of antibiotics were given to livestock in 2014.

- The majority of this was used for **growth promotion and disease prevention**

Use of sub-therapeutic doses creates an ideal environment for bacteria to evolve resistance.

Many bacteria are becoming resistant to antibiotic treatments.

Antibiotic growth promoters added to livestock feeds are a key contributor to the development of resistance.

Reference source - https://www.fda.gov

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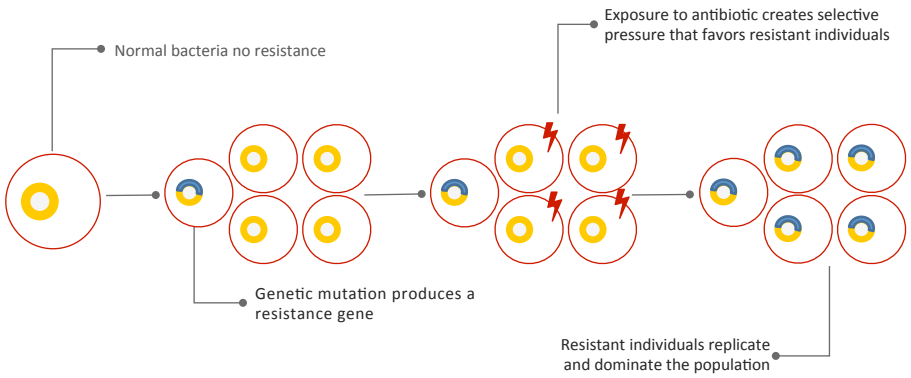
DEVELOPMENT OF ANTIBIOTIC RESISTANCE

Horizontal Transfer



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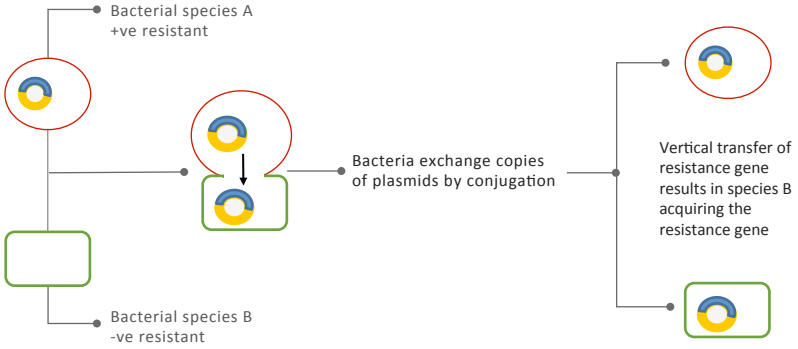
DEVELOPMENT OF ANTIBIOTIC RESISTANCE

Vertical Transfer



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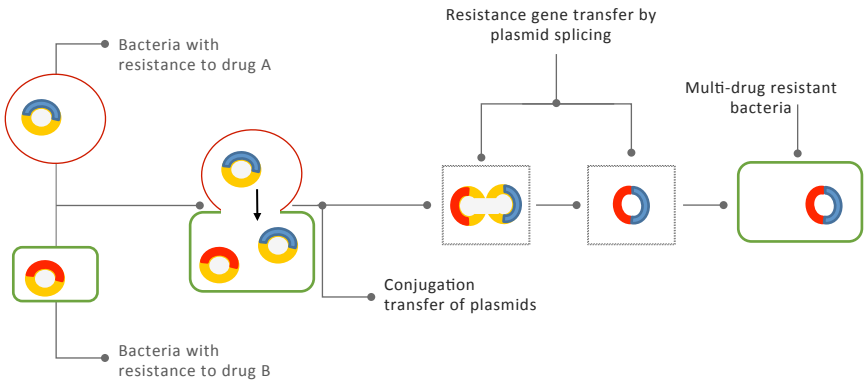
THE RISE OF MULTI DRUG RESISTANT SUPER BUGS

Plasmid Recombination



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EXAMPLE: THE COLISTIN SULFATE STORY

- In 2013 a CDC report identified multi-drug resistant strains of *P. aeruginosa*, *K. pneumoniae and Acinetobacter sp.* among urgent threats to public health
  - Colistin sulfate was identified as a last line of defense against these bacteria
- Colistin sulfate was developed in the 1950s but was not widely used in human medicine due to renal toxicity
  - Was widely used for livestock in Europe and Asia as an AGP and for disease prevention
  - Never approved for livestock use in North America
- As resistance to alternative drugs increased, Colistin sulfate became a last resort option for humans
  - It is now "the drug of last-resort" for treating multi-drug resistant strains of *P. aeruginosa*, *K. pneumoniae and Acinetoibacter sp*
- In 2011 researchers discovered a Colistin sulfate resistance gene (mcr-1) in *E. coli* collected from pigs in China (published in 2015).
  - Subsequently they discovered the mcr-1 gene, in samples from retail foods and patients hospitalized with infection in China
- **Bacteria carrying the mcr-1 gene have now been found in patient samples in the Vietnam, EU, and US**

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Reference source - https://www.cdc.gov/drugresistance/threat-report-2013

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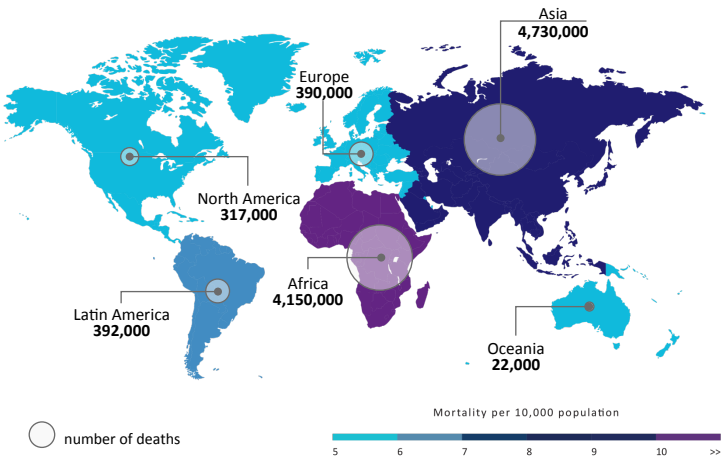
A PROBLEM OF GLOBAL SCALE

Deaths attributable to antimicrobial resistance every year by 2050



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Reference source - https://www.weforum.org/agenda

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OUR RESOLUTION: OxC-beta™ LIVESTOCK

PROBLEM:

- **Antibiotic resistance** is an important, global, human health concern, with massive negative economic impacts.
- Many **food producers depend on in-feed antibiotics** to reliably prevent disease and boost growth in livestock.

RESOLUTION:

- A means to **reliably and economically protect** livestock
- Protect **multiple species from multiple pathogens**
- **Must NOT contribute to the development of "superbugs"**
- Avivagen has a solution: **a unique and validated technology enabling discontinuation of the use of antibiotics for growth promotion and disease prevention.**

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THE OxC-beta™ LIVESTOCK ADVANTAGE

A First-In-Class technology and product, a rarity in the feed additive market
Old technologies and generic products are common
Proven Modes of Action (non-antibiotic)
Published in peer-reviewed scientific literature
Consistent Efficacy
Supported by results of 13 trials
Economically Advantageous
Productivity gains offer producers return on their investment
Excellent Handling Properties
Remains active during feed production, stable long-term storage
Utility Across Multiple Species
Innate immunity is found in all animal species
Defined Manufacturing Processes
Consistent composition and concentration of active
Extensive IP Protection
High value for potential commercialization/distribution partners