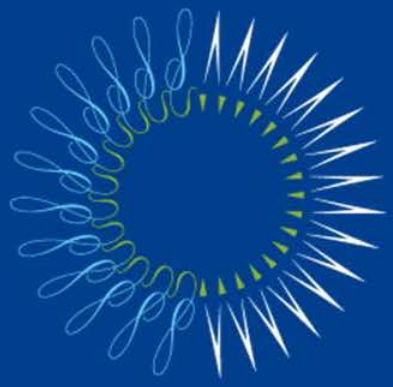

THE PEW CHARITABLE TRUSTS

Developing New Animal Pharma Products – Relevance to antibiotic stewardship in animal agriculture

Karin Hoelzer, DVM, Ph.D.

September 7, 2018

Overview: Structure of today's presentation

- The role of antibiotic alternatives in stewardship
- Examples of alternatives reducing need for antibiotics
- Challenges & opportunities of current alternatives
- Summary & take-home messages

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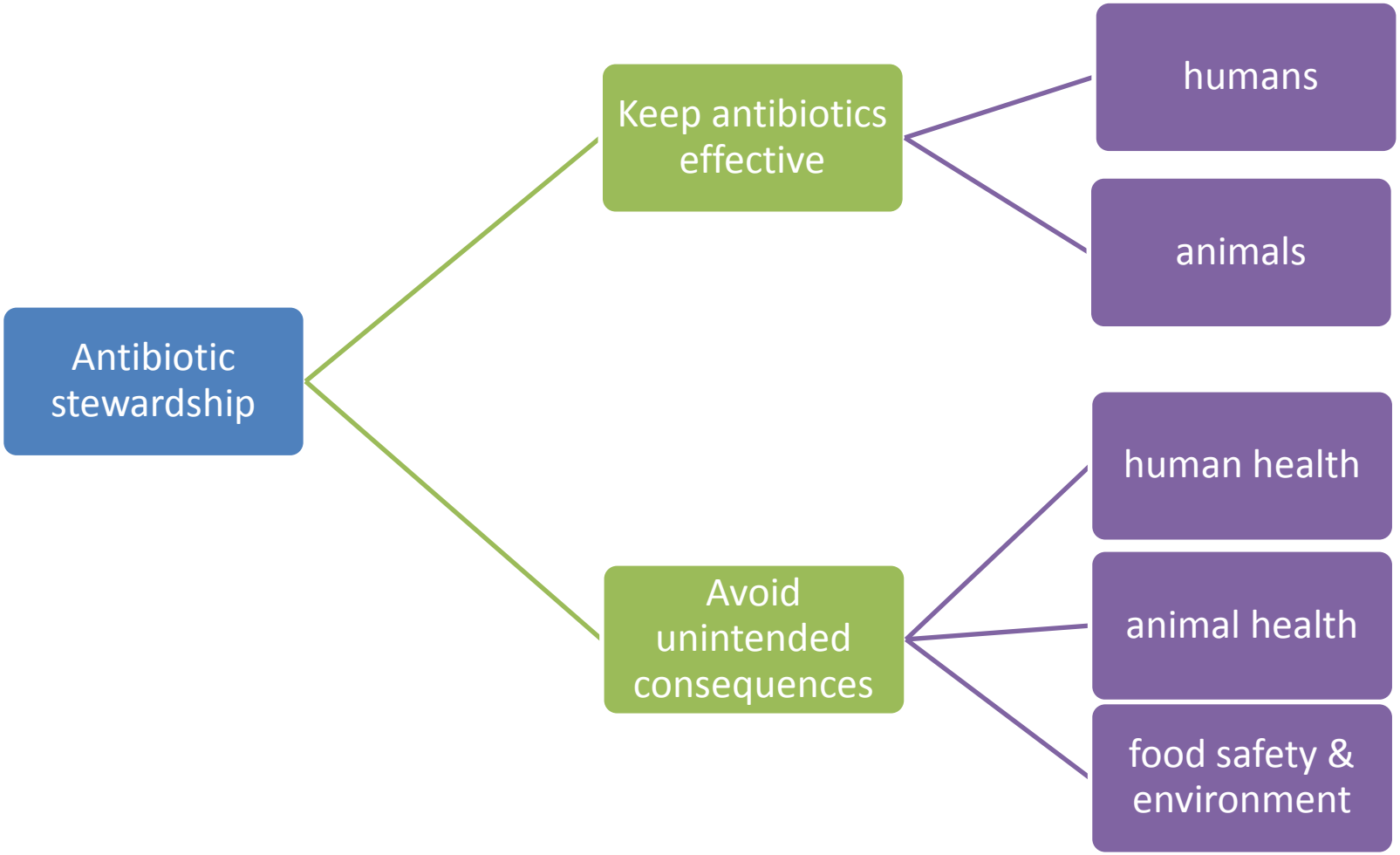
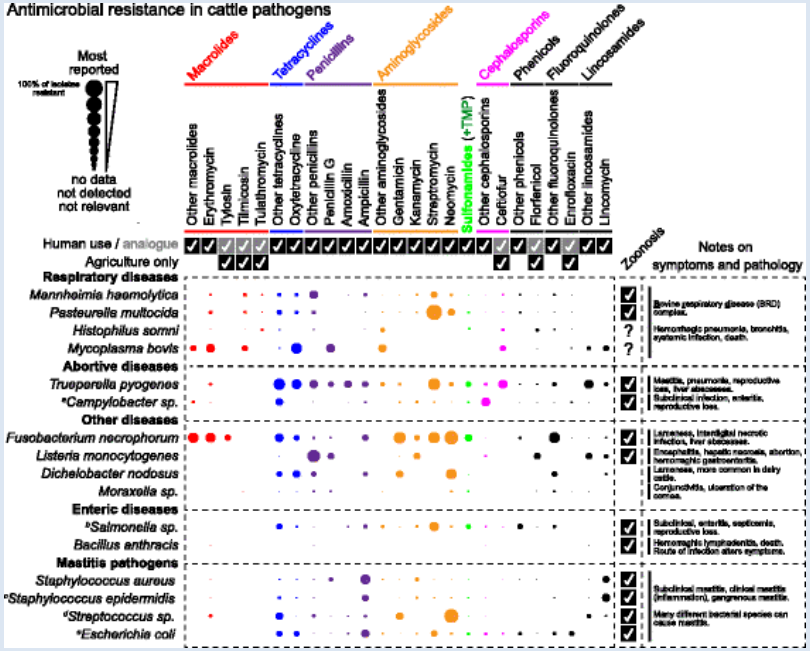
Animal pharma products are important stewardship tools



Antimicrobial resistance threatens the efficacy of antibiotics

AMR is a threat to human health, veterinary medicine & animal agriculture

- At least 2 million antibiotic resistant infections & 23,000 resulting deaths / year (CDC estimates)
- Emergence of AMR in companion animal pathogens after antibiotic treatments (e.g., tertiary teaching hospitals) well-documented
- Studies have demonstrated emergence of AMR in pathogens from livestock species (although data availability more limited)



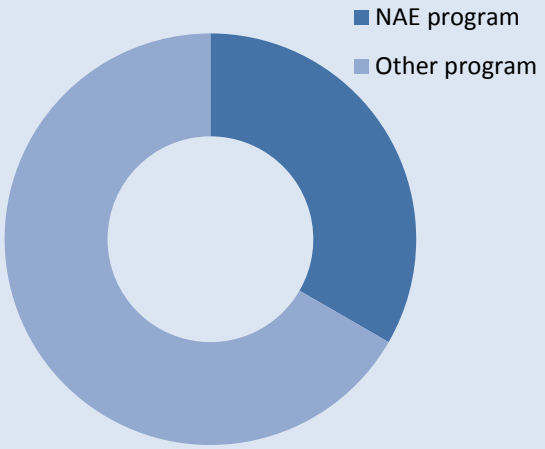
Source:
Cameron, A., McAllister, T.A., 2016. Antimicrobial usage and resistance in beef production. *Journal of Animal Science and Biotechnology* 7, 68.

Antibiotic use in animal agriculture is becoming more limited

Antibiotic use restrictions are on the rise in the U.S. and globally, creating a growing demand for alternatives

- Implementation of FDA policy eliminated growth promotion uses & placed feed and water uses under veterinary oversight
- Market-based antibiotic use restrictions (e.g., 'no antibiotics ever' policies) are on the rise
- Countries such as Brazil & China have limited colistin use in animal agriculture
- The World Health Organization has issued guidelines for the use of antibiotics in animal agriculture

In December 2016, 33 percent of U.S. broiler chicken were in NAE programs



Source:
https://www.wattagnet.com/articles/30116-one-third-of-us-broilers-raised-antibiotic-free

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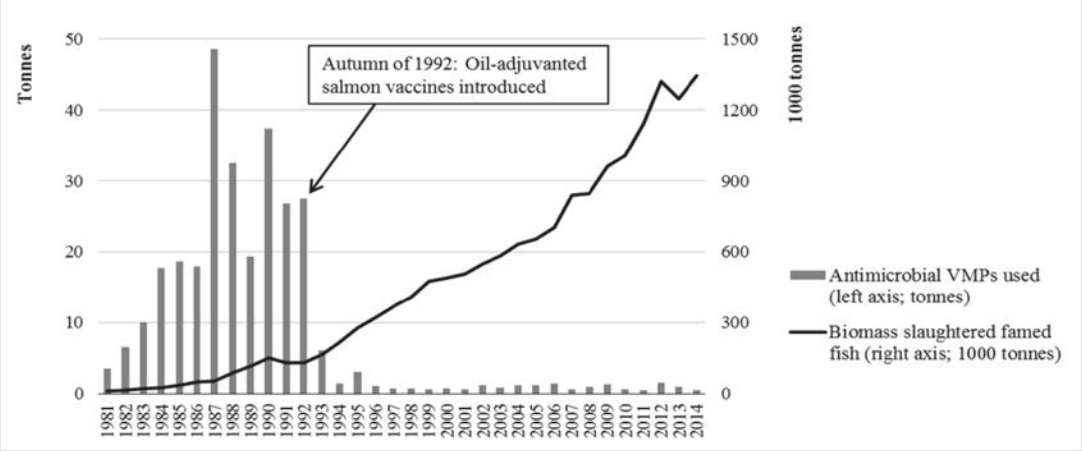
Vaccines effectively reduce antibiotic use & improve productivity

Proof-of-concept studies have demonstrated value of vaccines as antibiotic alternatives

- Experts consider vaccines feasible & effective antibiotic alternatives
- Vaccines can reduced antibiotic use (e.g., in salmon, swine and poultry)
- Studies have demonstrated vaccination can lead to improvements in productivity (e.g., mortality, daily weight gains) and be cost-effective



Source:
https://brage.bibsys.no/xmlui/bitstream/handle/11250/2448746/2015-98_Snorre%20Gulla_%28MatInf%29.pdf?sequence=1

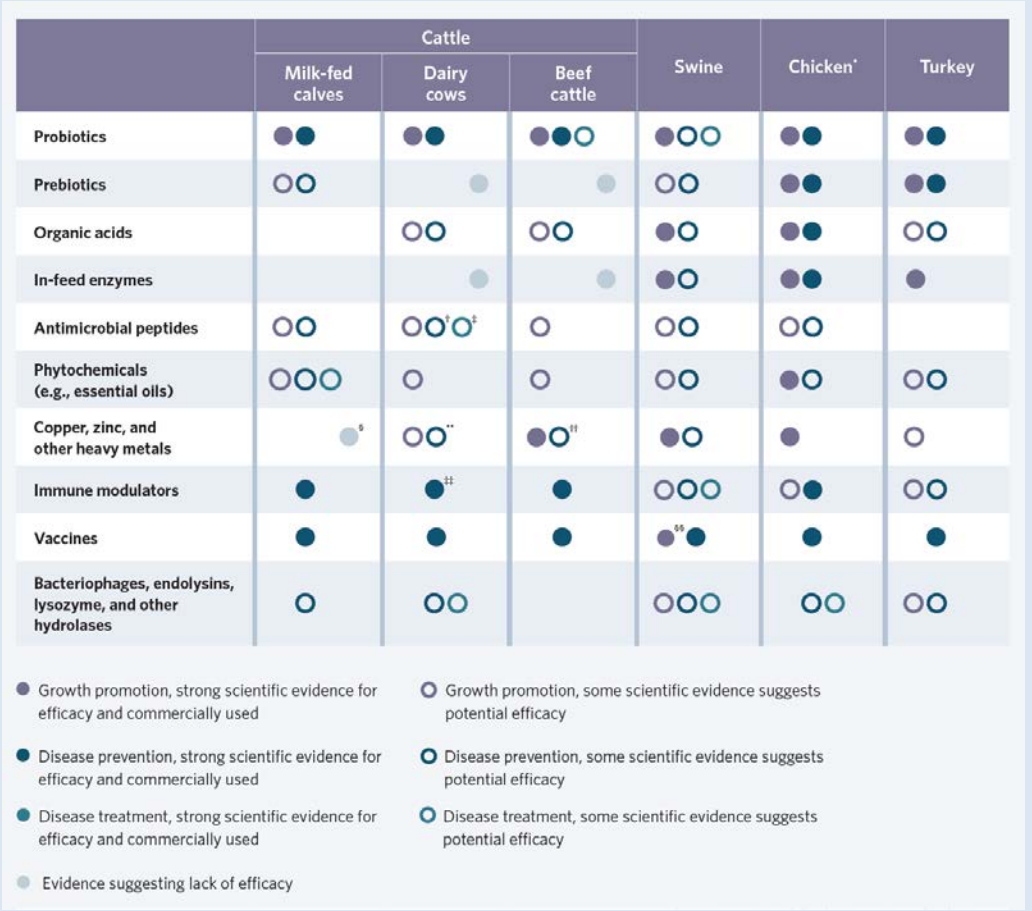
Source:
Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet Res*. 2018: 49:64; **and** Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet. Res*. 2018 49:70.

Several other alternatives besides vaccines also hold promise

Growth promotion & disease prevention alternatives

- More products have shown efficacy for growth promotion & disease prevention than for treatment
- Currently more products exist with proven efficacy for chicken than for other species
- Alternatives often have a narrower spectrum of action & lower efficacy than traditional antibiotics
- Efficacy often varies across trials for largely unknown reasons

Source:
http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf



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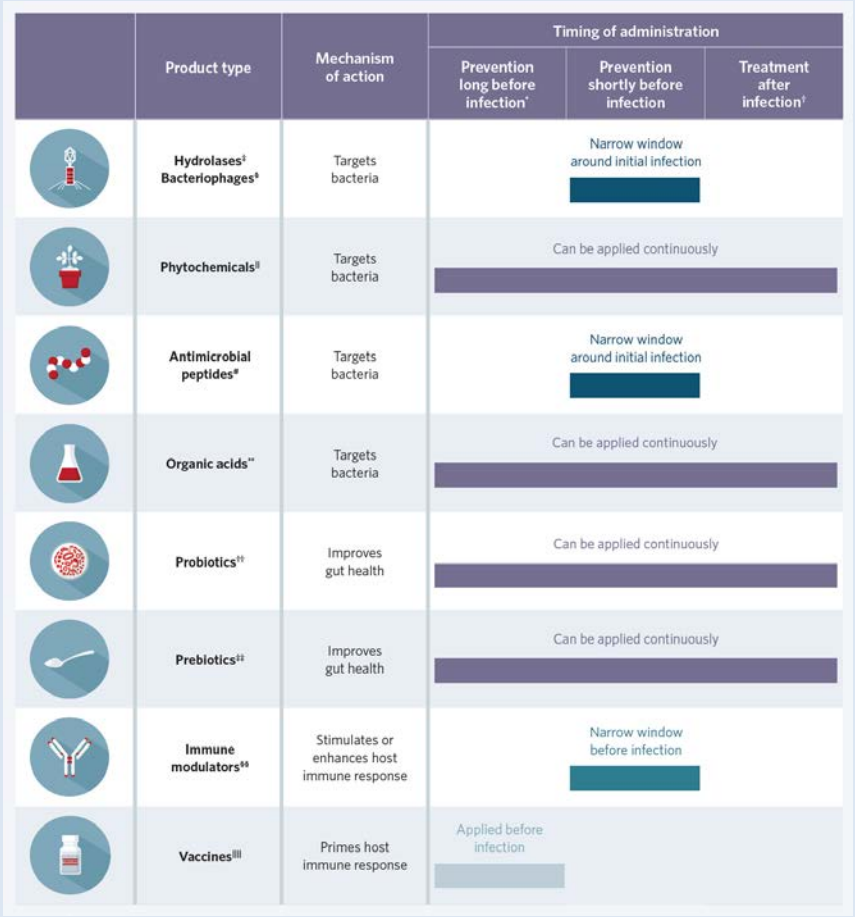
Developing antibiotic alternatives has unique challenges

Alternatives are diverse & often more complex than antibiotics

- Promising antibiotic alternatives are a heterogeneous group of products
- Many alternative products consist of large molecules or complex mixtures of living organisms
- The mechanism of action varies across products & is in several cases poorly understood
- Producers will likely use multiple products together, with largely unknown & hard-to-predict results

Source:
http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf



The need for antibiotic alternatives is not adequately met

Finding alternatives for priority diseases is of key importance

- A few priority diseases drive the majority of antibiotic use
- Commercial vaccines are available for many priority diseases
- Many current, commercially-available vaccines have severe limitations
- Other promising alternative approaches exist but often require further research

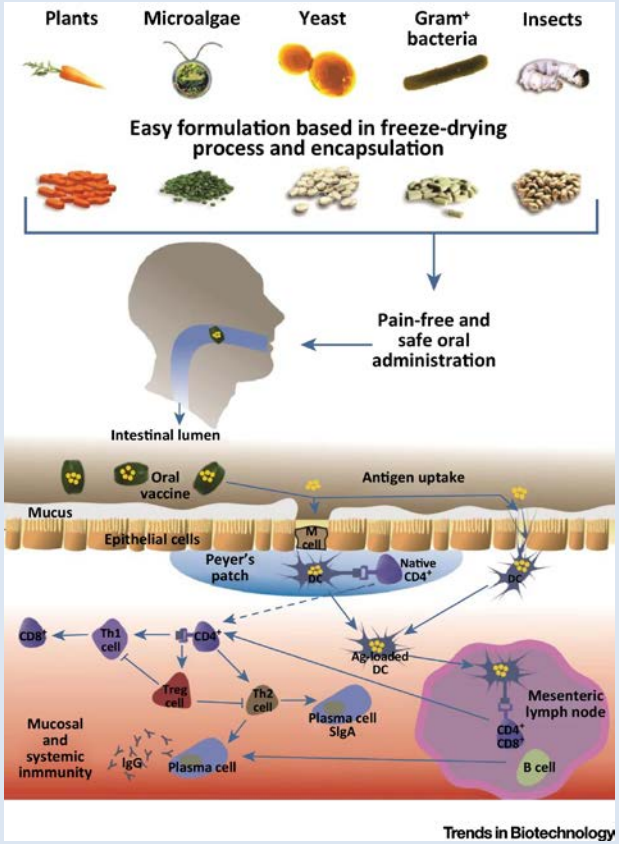
	Priority diseases for broiler chickens*			Disease-specific vaccines†			Other promising alternative approaches requiring more research‡
	Disease	Agent	Antibiotic use	Commercial availability	Major constraints	R&D priority	
Enteric diseases	Necrotic enteritis	Bacterial toxin	High	Yes	• Short-lasting and limited immunity • Application inconvenient, no mass application	High	• Phytochemicals • Prebiotics and probiotics • Immune modulators (e.g., egg yolk antibodies) • Antimicrobial peptides • Substances that bind the bacterial toxin (e.g., clays) • Bacteriophages
	Coccidiosis	Parasite, antibiotic use for secondary bacterial infection	High	Yes	• No cross-protection across strains • Current vaccines can cause disease	High	• Essential oils • Other phytochemicals (e.g., saponins)
	Infectious bronchitis	Virus, antibiotic use for secondary bacterial infection	Medium	Yes	• Protection across strains suboptimal • Virus mutates rapidly	Medium	
Generalized infection	*Escherichia coli*	Bacterium, infection possibly secondary to other diseases (e.g., yolk sac infection)	High	Yes	• Protection across strains suboptimal • No vaccine for some primary conditions that predispose for secondary *Escherichia coli*	High	

Source:
http://www.pewtrusts.org/~/media/assets/2017/07/alternatives_to_antibiotics_in_animal_agriculture.pdf

Veterinary vaccines can become effective antibiotic alternatives

Scientific progress in 4 key areas can make vaccines effective antibiotic alternatives

- **Safety improvements** (*e.g.*, vectored vaccines & new adjuvants) to minimize unintended consequences
- **Efficacy improvements** (*e.g.*, combination/ recombinant vaccines & protocol optimization) to generate robust & durable protection against broad range of pathogens (including in very young animals)
- **Easier administration** (*e.g.*, new oral vaccination strategies & increased stability) to permit easy mass vaccination
- **Cost reductions** to make use economically feasible and cost-effective



Source:
Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet Res*. 2018: 49:64; **and** Hoelzer, K., Bielke, L., Blake, D.P., Cox, E., Cutting, S.M., et al. *Vet. Res*. 2018 49:70.

Source:
https://www.cell.com/trends/biotechnology/fulltext/S0167-7799(15)00247-4

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Summary & key take-home messages

- Safe & effective alternatives are central stewardship tools
- Growing demand for safe & effective alternatives
- Vaccines & other alternatives reduce antibiotic need
- There is an unmet need for antibiotic alternatives
- Developing antibiotic alternatives poses challenges
- New research provides strategies for better alternatives

Contact me with questions & to learn more about our research

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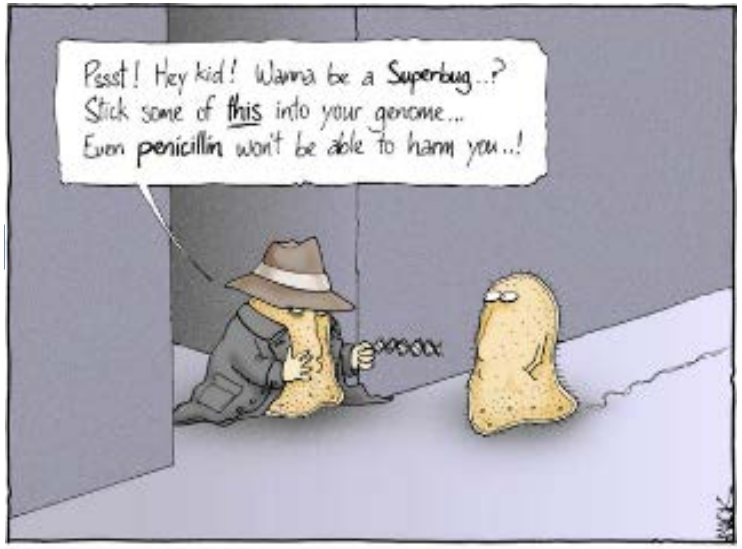

It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

Source: http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.0050112