UK ROADMAP TO ADDRESS ANTIMICROBIAL RESISTANCE AND ACHIEVE A SAFE AND SCALED UP SANITATION-AGRICULTURE CIRCULAR ECONOMY

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Background

We are faced with meeting the agricultural demands of a growing population estimated to reach 9.8 billion people by 2050 on soils depleted of essential nutrients, with declining yields and a projected reduction in future rainfall in key agricultural regions. A circular economy between agriculture and organic waste streams can recycle essential resources for farming through the recovery of water, biomass, and nutrients from waste solids, effluents, and livestock manure at scale. Resources can be used for irrigation and as organic fertilisers in arable farming for food and feed production. The benefits are to reduce primary resource demand by creating a closed loop for water and nutrients in farming and food processing. However, there are potential risks and challenges associated with this which need to be fully understood to enable a sanitation-agricultural circular economy to operate in a long-term safe and sustainable manner. One aspect of particular concern is the development of antimicrobial resistance (AMR)[1]. AMR is a global public health crisis that is predicted to result in 10 million deaths per year by 2050[2].

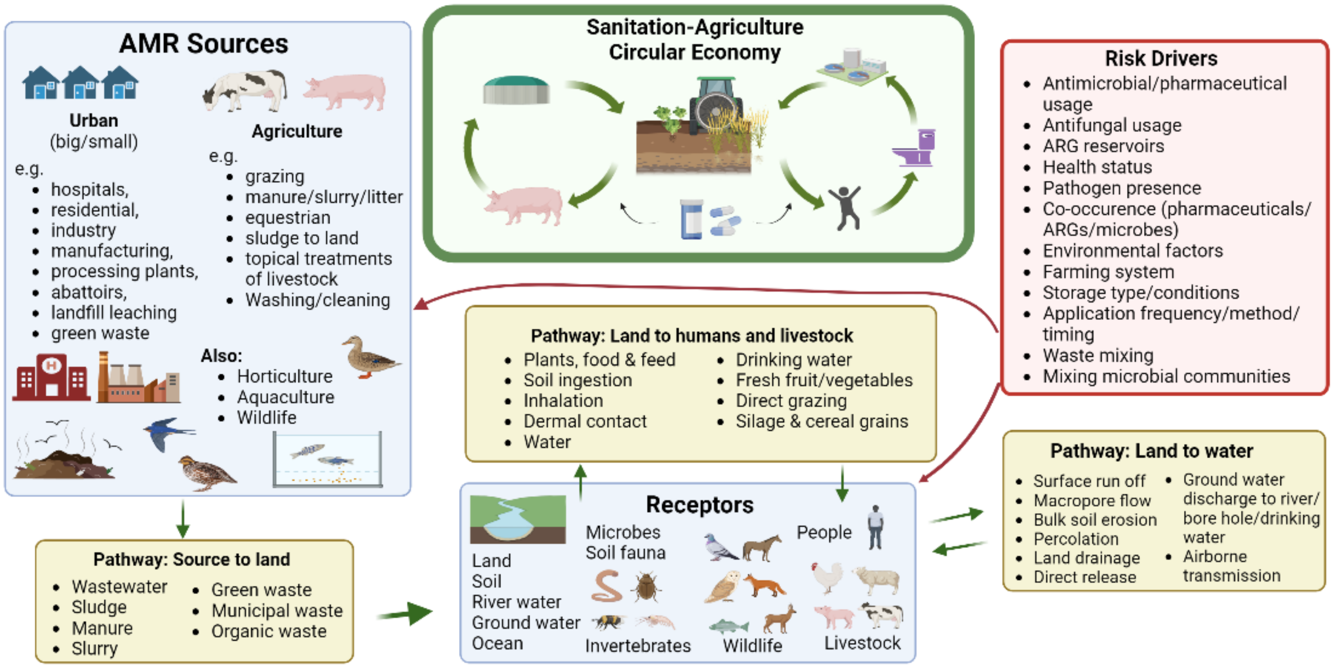

Figure 1: Conceptual model of antimicrobial resistance (AMR) sources, receptors and pathways in a sanitation-agriculture circular economy. Created with BioRender.com

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[1] Carter et al., 2024 Mitigating Contaminant-Driven Risks for the Safe Expansion of the Agricultural–Sanitation Circular Economy in an Urbanizing World https://doi.org/10.1021/acsestwater.3c00803

[2] O'Neill 2016 O'Neill J. Tackling drug-resistant infections globally: Final report and recommendations. https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

Manure and sewage are environmental sources of veterinary and medical antimicrobials, and where antimicrobials, antibiotic resistant genes (ARGs) and microbes meet, this results in the selection of resistant ARGs and their subsequent release into the agricultural environment (**Figure 1**). Secondly, livestock and human gut microbiomes are a direct source of both zoonotic pathogens and ARGs to the environment and agricultural food chain. Concentrations of AMR-drivers such as biocides, heavy metals and antimicrobials have been quantified in environmental matrices such as soil and livestock slurry alongside the characterisation of the abundance and diversity of ARGs in the environment. Livestock and the wider farm environment are therefore recognised as reservoirs of AMR and implicated in the dissemination of ARGs; however the impact is variable and not fully understood[3]. An assessment of the human and animal health risks from the potential exposure to antimicrobial selective compounds and ARGs following the consumption of produce (e.g. crops) is thus central to fully realising the potential benefits of a sanitation-agriculture circular economy.

The potential benefits of a circular sanitation-agriculture economy address multiple strategic UK policy goals of urgent national priority, evidenced by the range of industry and government stakeholder partners in this project. These policy goals include green growth and achieving net zero carbon emissions by 2050, the Defra 25-year plan which seeks to reverse historical and ongoing degradation of water and soil quality, and the National Food Strategy that aims to achieve safer and more nutritious food, in part through improved farming practices that reduce environmental and dietary health risks. These policy goals align with commercial drivers for improved environmental outcomes in the food and farming sector to add brand value to food products and retail operations.

To achieve these policy goals, a roadmap to deliver a safe circular economy between agriculture and organic waste streams, that accounts for potential AMR risks to human health, has been devised uniting perspectives from research, industry and regulatory sectors in the UK following a programme of stakeholder workshops. The roadmap consists of four themes which been broken down to short (1-3 years), medium (4-9 years) and longer term (10+ years) goals:

1) Occurrence and monitoring

2) Transmission and exposure

3) Treatment and mitigation

4) Policy and regulation

[3] Woolhouse et al., 2015 Antimicrobial resistance in humans, livestock and the wider environment https://pubmed.ncbi.nlm.nih.gov/25918441/

1. Occurrence and monitoring

Current situation

- Wastewater treatment plants – limited chemical monitoring (e.g. Chemicals Investigation Programme, Water Framework Directive), some biological monitoring but not linked to AMR
- No widespread chemical occurrence data for farms
- Emerging capacity for monitoring AMR in the farm environment; e.g. the Pathogen Surveillance in Agriculture, Food and Environment Programme (PATH-SAFE) is piloting the development of a national surveillance network, using the latest DNA-sequencing technology and environmental sampling, to improve the detection and tracking of foodborne human pathogens and associated AMR through the whole agri-food system from farm-to-fork

Priority actions

Short term 1-3 years

- Comprehensive spatio-temporal monitoring campaign of resources destined for reuse (manure, wastewater, biosolids) to better understand exposure and hotspots of AMR drivers (e.g. antimicrobials, metals, biocides) and genetic signatures (e.g. ARGs)
- Comprehensive spatio-temporal monitoring campaign in the receiving farm environment (e.g. soil, crops) to better understand exposure and hotspots of AMR drivers (e.g. antimicrobials, metals, biocides) and genetic signatures (e.g. ARGs)
- Use existing datasets to identify resistances of concern (e.g. identification of CXTM-15 pig isolates to tie in with national AMR surveillance networks)
- Create a centralised surveillance system that collates existing environmental monitoring data into an open access resource and align to existing monitoring programmes to avoid duplication of effort

Medium term 4-9 years

- Standardise and validate detection methodologies
- Continue spatio-temporal monitoring campaigns to assess longer term exposure
- Prioritise chemicals of concern (AMR drivers target panel) and AMR genetic signatures based on data from the spatio-temporal monitoring campaigns in years 1-3
- Operational national surveillance system to monitor prioritised chemicals of concern and genetic signatures and inform interventions. Efforts need to be appropriately resourced and align to existing monitoring programmes to avoid duplication of effort and informed by transmission data (priority area #2) to define frequency and timing for sample collection
- Collect associated environmental monitoring data (e.g. soil properties, application timings (meta-data))
- Collate chemical and genetic signature monitoring data to expand the open access repository, including datasets emerging from the national surveillance campaign

Long term 10 + years

- Horizon scanning for novel AMR elements of concern and chemicals to ensure detections are current and applicable
- Real time monitoring of environment, development of sensing detection technologies to feed into open access repository

2. Transmission and exposure

Current situation

- We need to better understand how exposure and transmission in the environment results in a potential risk to human health and the health of animals within the farming system
- No tailored assessment of human and/or animal health risks following exposure in agricultural environment
- Limited knowledge about the movement of AMR constituents (e.g. antimicrobials, resistant bacteria and ARGs) in agricultural systems, including the potential for widespread transmission to other compartments following land application of manure and biosolids (e.g. water, air)

Priority actions

Short term 1-3 years

- Quantify risk to humans and livestock following the consumption of contaminated crops using *in silico* and *in vitro* approaches
- Understand the contribution of different sources (e.g. manure, biosolids, wastewater) to environmental exposure
- Understand the contribution of co-contaminants present in the environment in terms of AMR transmission and exposure (e.g. microplastics as hubs as well as effective carriers of microbial pathogens and ARGs)

Medium term 4-9 years

- Pilot biomonitoring campaign to assess potential risk (*in vivo*) following consumption of crops contaminated with AMR constituents
- Investigate the relationship between chemicals (individual and combination) as drivers of AMR (e.g. development and persistence of AMR) accounting for bioavailability in the natural environment (e.g. sorption)
- Develop metrics to determine risk and underpin regulatory thresholds (e.g. predicted no effect concentrations (PNEC) specific to agricultural environments)
- Understand potential for transmission of AMR constituents between different environmental compartments (e.g. soil-groundwater; soil-air)
- Modelling using *in vitro* and *in silico* techniques to consider how future scenarios may affect transmission and exposure e.g. increased temperatures

Long term 10 + years

- Wider risks of resistance development for animal (wildlife and livestock) and plant health
- Understand potential for fungal resistance development
- Horizon scanning for novel transmission routes, including global commerce

3. Treatment and mitigation

Current situation

- Technologies do exist to reduce chemical and microbial loads in human and animal waste streams (e.g. domestic wastewater treatment)
- During wastewater treatment, secondary treatment technologies can remove >90% of sewage derived faecal bacteria, however substantial loads of antibiotic resistant bacteria, ARGs and chemicals of concern (e.g. antimicrobials) remain.
- Tertiary treatment processes (e.g. ozonation) effectively remove remaining AMR constituents but are expensive to install and maintain and therefore not suitable for rural areas or settings with limited wastewater infrastructure.
- The efficacy of low cost nature-based platforms (constructed floating wetlands, stabilisation reservoirs) to reduce AMR constituents from wastewater remain largely unknown
- Research has started to emerge on the fate of resistant bacteria, ARGs and antimicrobials during on farm manure storage and treatment (e.g. composting)
- Limited information on available treatment options once contamination enters the farm environment following the reuse of waste streams (i.e. how can we clean up soils / create a barrier for potential crop uptake)

Priority actions

Short term 1-3 years

- Devise a funding pipeline to support research into mitigation measures and treatment technologies that are appropriate to the setting, available resources and existing treatment capacity, including financial incentives to promote cross sector collaboration
- Scoping of potential of interventions for implementation at source (i.e. in sanitation and farm waste streams) and in the environment/receptors (e.g. soil, crop)
- Pipeline plan for technology development, validation, implementation and maintenance

Medium term 4-9 years

- Use model systems to test interventions at a smaller scale (e.g. *in vitro*, pilot scale)
- Funding for transdisciplinary networks and research and innovation grants to support the expansion and testing of interventions
- Target treatment and mitigation measures to AMR hotspots (guided by monitoring data developed in priority area #1)
- Explore the potential for source control, reduced use of chemicals

Long term 10 + years

- *In situ* (i.e. in field) testing and evaluation of intervention efficacy of developed treatment technologies
- Explore scalability and long-term efficiency of solutions (cost benefit analysis)
- Showcase efficacy and safety to promote use and overcome barriers to reuse

4. Policy and legalisation

Current situation

- Existing policy promotes the reuse of waste streams but does not account for the resulting inadvertent release of AMR constituents or the wider implications of AMR development
- In 2019 the UK published its [20-year vision for AMR] which recognises the need for multi-sectoral data and evidence gathered from human and animal health, agriculture, environment, food and water.
- Published five-year UK AMR national action plans (NAPs) consider past and present contexts to prioritise actions and direct resources to tackle AMR; specifically the [2024-2029 national action plan] calls for action across all sectors including improved diagnostics, treatment and surveillance in agriculture

Priority actions

Short term 1-3 years

- Review understanding of current situation (reviewing data, consideration of existing policies) (e.g. SUiAR, safe and sustainable sludge use, 2024-2029 UK National Action Plan)
- Understand potential alignment to other policy or regulatory initiatives such as Phase II of the National Bioresources strategy; EU drivers are important e.g. integrated sludge management
- Develop appropriate metrics to quantify value of resources and enable appropriate cost benefit analysis to be undertaken to evaluate the effectiveness of potential mitigation strategies
- Promote open dialogue, opportunities for knowledge transfer between sectors

Medium term 4-9 years

- Implement policy and updated risk assessments
- Joined up policy thinking that accounts for 'One Environment, One Health' with input from multiple sectors across the UK (e.g. Veterinary Medicines Directorate, Environment Agency, Defra, water industry)
- Understand requirements for regulatory approval of new technologies for treatment/mitigation
- Policy that advocates for extended producer responsibility (i.e. to encourage removal processes at source where removal efficacy is greater than in highly mixed feed at wastewater treatment works)
- Raise awareness, information dissemination, education across sectors

Long term 10 + years

- Monitor policy implications for farmers / agricultural sector
- Promote safe and sustainable reuse of resources
- Continual review of science-policy developments to ensure regulation is current

Summary statement

In January 2019, the UK published its vision for AMR to be contained and controlled by 2040. The vision recognises that a global problem as significant and complex as AMR requires long-term action, working across sectors, which must strengthen understanding of AMR itself alongside developing measures, and strategies that can best control it. In the most recent UK national action plan (*Confronting antimicrobial resistance 2024 to 2029*) a 'One Health' approach and a shared vision to contain and control AMR is highlighted as a crucial step forward given the close links between humans, human food, animals and the environment (including water, crops and land). It is encouraging to see that agriculture recognised within this context, including the need for improved understanding about what drives resistance in natural environments, with explicit reference to the spread of resistance genes in soil.

In response to this, a UK roadmap to prioritise research and regulatory efforts in agricultural systems is needed to tackle key questions raised in the 5-year national action plan such as '*What are the basic drivers and effects of AMR, and how does it spread?*' and '*How can we prevent AMR from spreading'.* Joined up and coordinated efforts that mobilise multiple sectors, disciplines and communities at varying levels of society will, in the long-term, ensure successful delivery of objectives set out in the 20-year vision for AMR. Only through these efforts can we address the need for clean water and soils, safe and nutritious food, and contribute to sustainable agricultural development.