REDUCE UNINTENTIONAL EXPOSURE AND THE NEED FOR ANTIMICROBIALS, AND OPTIMIZE THEIR USE

Antibiotic Resistance Coalition Response to the Interagency Coordination Group on Antimicrobial Resistance Public Consultation

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What Next Forum

We commend the IACG for the goal of this paper: to "reduce unintentional exposure and the need for antimicrobials, and optimize their use" across healthcare, food production and the environment. Members of the Antibiotic Resistance Coalition (ARC) convened to develop this joint response to the discussion paper.

A. THEMES TO EXPLORE FURTHER

While the discussion paper lays out a range of challenges and current responses, we would encourage a deeper analysis of the gaps and the high-yield opportunities going forward. Specific themes that we urge be explored further include:

- **Finding synergy across sectors**
- **Prioritizing a Cross-Sectoral Approach**
- **Emphasizing AMR in the SDGs**
- **Identifying policy Levers**
- **Creating an enabling environment for policy and behavior change**
- **Establishing a tiered stewardship approach**
- **Enabling monitoring for accountability**

Synergy across sectors. Healthcare, food production and the environment are just different lenses to the same underlying challenge in reducing the need for antimicrobials and unintentional exposures. More intentional integration of these approaches ought to result in positive synergies, policy coherence and greater success.

The IACG could usefully look for such cross-sectoral opportunities given its frame of analysis. For example, regardless of the sector, surveillance data can serve as a powerful trigger for policy action. A surveillance system that better integrates information from both healthcare and from food production also could have particular value in safeguarding the food supply from drug-resistant pathogens. Point-of-care diagnostic platforms might have dual markets, both in healthcare and in food production. It could be made a priority to identify where economic incentives fail to align with policy goals around AMR -- from the way that healthcare providers might be reimbursed to how veterinarians working for large food producers might be motivated to use antibiotics. Restrictions on antibiotic marketing also need to be implemented both in healthcare delivery and in the food production sectors. Such steps also may require mobilizing greater resources for intergovernmental agencies to carry out these functions.

Prioritizing a Cross-Sectoral Approach. Despite the opportunity for cross-sectoral synergies, the IACG discussion paper is distinctively sectoral in its organization and approach. Each of the seven sections draws most of its analysis in one sector—healthcare delivery, food production,

or the environment. It is true that capacity and assets, governmental and non-governmental stakeholders, regulatory framework, and root causes for AMR differ quite considerably by sectoral context. However, for a government implementing a NAP on AMR, the IACG could recommend the development of a cross-sectoral prioritization framework that better positions a country to make explicit strategic choices as to where limited resources might be invested to address AMR. For example:

- What guidance could be provided to a country as to whether to invest in "clean water, sanitation and hygiene" as opposed to "prevention and control of human infection"?
- Even across efforts just to prevent and control human infection, are vaccines a better investment than antimicrobial stewardship measures to ensure better rational use of antibiotics? If universally administered, pneumococcal conjugate vaccine could potentially prevent 11.4 million days of antibiotic use in children younger than 5, thereby averting nearly half of antibiotic treatment courses in these children.[1] With a global pneumococcal vaccine coverage of below 50%,[2] there is much room for improvement.
- If one were focused on prevention and control of animal infection, under what circumstances would veterinary oversight, curbing the use of medicated feed, or improving animal husbandry practices be the most cost-effective point of intervention?

AMR in the Sustainable Development Goals. Mainstreaming AMR into the SDGs is essential. Tackling AMR is a priority that can and should be addressed in SDG2, but also in SDG12, thereby considering reduction of food waste and changes in the food production model. For example, over 30% of food can go to waste within industrial production.[3] Meat and dairy farms are also the largest greenhouse gas emitters,[4] so increasing industrial food production will both facilitate the spread of AMR and contribute to climate change. This will require moving beyond business as usual. The pressure to increase animal density and growth rate in raising livestock and aquaculture will inevitably require more antibiotic use. Unless this production model is changed and a commitment to a more circular economy or virtuous cycle of production is made, this upward spiral in use of antibiotic use will never be broken, and stewardship efforts will make marginal improvements, not reversing root causes.

Policy Levers. Some of the most significant policy levers for tackling AMR extend beyond the bounds of the current approaches currently described in this paper. Specifically:

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[1] Laxminarayan R, Matsoso P, Pant S, Brower C, Røttingen J, Klugman K, Davies S, Access to effective antimicrobials: A worldwide challenge, Antimicrobials: access and sustainable effectiveness, *Lancet* 2016, 387: 168–75.

[2] Immunization coverage fact sheet, WHO, January 2018. Available at: http://www.who.int/mediacentre/factsheets/fs378/en/

[3] High Level Panel of Experts on Food Security and Nutrition, Food losses and waste in the context of sustainable food systems, June 2014. Available at: http://www.fao.org/3/a-i3901e.pdf

[4] GRAIN & Institute for Agricultural Trade and Policy, *Emission Impossible*, July 2018. Available at: https://www.iatp.org/sites/default/files/2018-08/Emissions%20impossible%20EN%2012.pdf

1. Behavioral economic approaches to change individual behavior and innovative financing at the institutional level should fall within the scope of potential recommendations.
2. Small-scale producers and resource-limited facilities should be supported technically and financially in making the transition to more sustainable antibiotic use practices.
3. The power of procurement of antibiotics—particularly pooled procurement—in shaping not only access, but also stewardship of these life-saving drugs also warrants careful consideration.
4. Procurement is also a significant lever in shaping the behavior of industry, regardless of sector.
5. Antimicrobial stewardship also requires a vibrant research agenda to test and pilot more effective interventions.

Creating an enabling environment for policy and behavior change. The best practices for cultivating, harvesting and disseminating guidelines and behavior change interventions ought to be a focus for IACG review. By drawing upon exemplars from other fields, an enabling policy environment for supporting efforts in addressing AMR might be created through the recommendations of the IACG. A few examples include:

- Decades of experience in the implementation of the Integrated Management of Neonatal and Childhood Illness;
- Peer-to-peer network approaches like the Institute for Healthcare Improvement's Breakthrough Collaboratives;
- Insurer use of financial and non-financial incentives; and
- Collective action by professional societies and credentialing organizations, including the "Choosing Wisely" initiative of the American Board of Internal Medicine Foundation.

A Tiered Stewardship Approach. Work also must continue to develop a system for implementing stewardship practices, tiered to the level of resources in those settings. Where there are insufficient prescribers or no laboratory facilities, triage, treatment and referral approaches are still needed. What is the governance structure that would enable those tackling AMR the means to position such strategies for country governments and other key stakeholders to adopt? Similar considerations apply in the agricultural sector, where the experience of extension services and the role played by the Consultative Group on International Agricultural Research might be factored into a recommendation.

Monitoring for Accountability. There should be mandates on governments to collect and share data on antibiotic use in both human and animal sectors. Data collection and sharing are the foundation for ensuring effective monitoring of progress toward meeting targets, and therefore accountability. While the Tripartite efforts to put together a Monitoring & Evaluation

Framework are a useful start, the IACG should make a recommendation that ensures an effective framework across Member States for reporting such information. Civil society can also use data, which must be made transparent, to benchmark stakeholder performance against targets and create comparison scorecards. Another way to ensure that such data become actionable is to support the development of tools that empower them to take measure of effects of AMR in healthcare delivery, food production and the environment. Collectively, such efforts could serve as a Global Watch on AMR.

B. RECOMMENDATIONS FOR THE HUMAN, ANIMAL AND ENVIRONMENTAL HEALTH SECTORS

1. The concerns over antimicrobial stewardship in healthcare delivery span both prevention and control of human infection and optimizing use in humans.

1.1 Though plenty of studies document approaches that reduce unnecessary antibiotic use, a Cochrane review suggests that "we do need more research to understand why the most effective behavior change techniques are not more widely adopted within hospital settings. Future research should instead focus on targeting treatment and assessing other measures of patient safety, and different interventions that explore the barriers and facilitators to implementation."[5] By comparison, however, to the recognition and research dollars going into developing new antibiotics, global funding to invest into research on implementation of changes in practice also needs to be bolstered.

1.2 The connection and complementarity between AMR-sensitive interventions and AMR-specific interventions are key to explore. Conditions of clean water, sanitation and hygiene influence the burden of disease faced by the healthcare delivery system. WASH activities can focus on the potable water supply for communities or the need for sourcing water in health facilities. The IACG might consider how WASH efforts might amplify the response to AMR and what country-level guidance in targeting such initiatives might be offered.

1.3 In optimizing the use in humans, underuse as well as overuse must be addressed. Monitoring for effective stewardship, but not for access to life-saving antibiotics would set back antimicrobial stewardship efforts. Local populations would consider a focus on the former, without the latter, evidence that committing to tackling AMR was not to save their lives, but those of others who already had access to antibiotics. Today, global lack of access to essential antibiotics causes more deaths than resistance. Approximately half of the

[5] Cochrane. "Support for health professionals reduces unnecessary use of antibiotics in hospitals." Available at: https://www.cochrane.org/news/support-health-professionals-reduces-unnecessary-use-antibiotics-hospitals

900,000 children under 5 that die from pneumonia every year could be saved by providing access to correct antibiotics.[6]

1.4 Beyond the various prizes established for bringing a new point-of-care diagnostic forward for AMR, there needs to be greater attention to enhancing the innovation of novel diagnostics suited for resource-limited settings. It is, however, not enough to develop new diagnostics. A strategy for their implementation should be considered and coupled with improvements in care or antibiotic stewardship.[7] The development of a rapid diagnostic test for bacterial pneumonia suited for use where there is minimal infrastructure could save more than 405,000 lives each year, much of it by reducing overtreatment with antibiotics.[8] A test for acute lower respiratory infections could save more than 400,000 lives each year[9].The development of and affordable access to diagnostics suitable for use in developing countries and improved laboratory capacity in LMICs is therefore a top priority.

2. Antimicrobial stewardship must also include the food production system (optimizing use in animals and plants, prevention and control of animal infection, and food safety and food production).

2.1 The need to increase food production from animals is not fully in accordance with SDG2, as ensuring food security is not limited to food animal production. The more animals are raised, the more plant food they will need to consume. Currently over 65% of grains are consumed by livestock in the U.S.,[10] and over 60% are in Europe.[11] The paper calls for increased meat and dairy production for growing populations to align with SDG 2, when in countries with the most intensive agriculture, most of the produce is destined to feed animals, not humans. Therefore, in considering strategies to feed the world more efficiently, using more plant products to feed humans alongside meat and dairy production must be considered.

2.2 Meeting the food security goals of SDG 2 also does not necessarily imply increasing production of all food system models. SDG2 mentions increasing production by small-scale

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[6] Laxminarayan, R. et al. Access to effective antimicrobials: a worldwide challenge. *Lancet* 2016; 387: 168–175.
[7] Wellcome Trust. Four diagnostic strategies for better-targeted antibiotic use. 2016. Available at: https://wellcome.ac.uk/sites/default/files/diagnostic-strategies-for-better-targeted-antibiotic-use-wellcome-jul15.pdf
[8] RAND Research Highlights. Estimating the Global Health Impact of Improved Diagnostic Tools for the Developing World.Santa Monica, California: RAND Corporation, 2007.
[9] Lim, YW et al. Reducing the global burden of acute lower respiratory infections in children: the contribution of new diagnostics. Nature 2006 Nov 23; 444 Suppl 1:9-18.
[10] Cassidy, E. S., West, P. C., Gerber, J. S., & Foley, J. A. (2013). Redefining agricultural yields: from tonnes to people nourished per hectare. *Environmental Research Letters*, *8*(3), 034015.
[11] Virginia W. Mason and Jason Treat, NGM Staff. Source: Global Landscapes Initiative, Institute on the Environment, University of Minnesota. Available at: https://www.splendidtable.org/story/solving-the-worlds-food-dilemma-in-5-steps

producers in a *sustainable way*, but increasing industrial farming for animal production is not sustainable.[12] Thus, sustainable intensification of industrial production does not exist. The agricultural model must take this into account when calling for increased food production. Already, nearly 80% of agricultural land is dedicated to pasture and feed production.[13,14] Intensification of more industrialized production will only add to that figure. In contrast, smaller scale models of food animal production are less likely to rely on the use of feed grains to raise livestock, as opposed to forage.

2.3 In addition to feed grains, more industrialized models of food animal production also tend to use more antimicrobials than less intense production models, making intensive production models to be more significantly driving antimicrobial resistance than less intense food animal production.[15] Intensification would mean increasing the density of animal production, in which case antibiotics would become increasingly necessary. Instead, local growth must be promoted over global intensification. More sustainable food production practices are the solution, not the challenge, to achieving adequate food security and concurrently lowering antimicrobial use in this sector.

2.4 The IACG discussion paper does not adequately address key approaches to tackling antibiotic overuse in animals. In discussing optimizing antibiotic use in animals and plants, the discussion paper fails to refer to the WHO guidelines on the use of medically important antibiotics in food-producing animals, which call for a ban on the use of these antibiotics for growth promotion and disease prevention. In doing so, the paper downplays the relevance of the issue of using antibiotics routinely for disease prevention and growth promotion.

2.5 While the paper acknowledges the expected 70% increase in antibiotic use in livestock by 2030 with continued intensification, it does not suggest mechanisms for change. For example, the paper does not touch on the use of medicated animal feed.[16,17] Yet data from the European Medicines Agency estimates that the proportion of antibiotics used in food

[12] Committee on World Food Security. *Sustainable agricultural development for food security and nutrition: what roles for livestock? A report by The High Level Panel of Experts on Food Security and Nutrition.* Rome, 2016. Available at: http://www.fao.org/3/a-i5795e.pdf
[13] https://www.globalagriculture.org/report-topics/meat-and-animal-feed.html
[14] Max Roser and Hannah Ritchie (2018). "Yields and Land Use in Agriculture". *Published online at OurWorldInData.org.* Retrieved from: https://ourworldindata.org/yields-and-land-use-in-agriculture
[15] http://www.saveourantibiotics.org/media/1777/asoa-report-real-farming-solutions-to-antibiotic-misues-what-farmers-and-supermarkets-must-do.pdf
[16] Davies, M. & Meesaraganda, R. (January 2018). A game of Chicken: How Indian Poultry Farming is Creating Global Superbugs, *The Bureau of Investigative Journalism.* Accessible at: https://www.thebureauinvestigates.com/stories/2018-01-30/a-game-of-chicken-how-indian-poultry-farming-is-creating-global-superbugs
[17] Paliwal, A. & Singh, J. (March 2018) Hatching Superbugs, Down To Earth. Available at: https://www.downtoearth.org.in/coverage/hatching-superbugs-45547.

animal production for group treatment (including metaphylaxis) varies widely from 90% overall in Europe vs. less than 10% in Sweden.[18] The IACG could address how production practices might be improved to move closer to the antibiotic use levels seen in Sweden and how regional comparisons and targets across countries could be used to identify and motivate the adoption of best practices. For example, standard treatment guidelines could be established for judicious use of antibiotics in animals. Strategies could also include better labelling of feed containing antibiotics, meat raised with antibiotics and antibiotics to increase consumer and purchaser awareness. Finally, better oversight and regulation of imports, online sales and advertising of medicated feed are needed.

2.6 There are good, evidence-based case studies for other countries which, like Sweden, have significantly reduced antimicrobial use in food animal production, by eliminating use of antimicrobials for growth promotion and for routine disease prevention in the absence of disease, as the aforementioned WHO Guidelines recommend. Denmark and the Netherlands, both major food animal producers in Europe, have decreased their use of medically important antimicrobials significantly. Since 2011, overall consumption of those drugs in food animal production has dropped by more than 60% in the Netherlands.[19] And in Denmark, where change happened earlier, antibiotics consumed in pig production fell by more than half from 1992 to 2009, even while productivity increased; the pig sector accounts for 80% of agricultural antibiotic use in Denmark.[20] Profiling of outliers in antimicrobial use, as seen through Denmark's Yellow Card Initiative, among both farming operations and veterinarians, and improvements in animal husbandry, nutrition and vaccination, as seen in Sweden's pig production practices,[21] are useful starting points. However, evaluating such interventions in LMICs requires investment. Barriers to implementing these improvements requires additional study, as does piloting of how best to incentivize changes in behavior and practice in antimicrobial use in a variety of country contexts.

2.7 A "Leapfrog Fund" should be established to help small-scale farmers make the necessary transition to achieve a more sustainable food production approach, to become less reliant on antibiotics, and to abide by efforts to ban medically important antibiotics in farming.

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[18] European Medicines Agency, Sales of Veterinary Antimicrobial Agents in 30 European Countries in 2015. Available at: http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/10/WC500236750.pdf

[19] The Dutch figures are at Netherlands Veterinary Medicines Authority (SDa). 2017. Usage of Antibiotics in Agricultural Livestock in the Netherlands in 2016. Published May 29, 2017. Accessed (Dutch language only) at https://www.rijksoverheid.nl/documenten/rapporten/2017/05/29/het-gebruik-van-antibiotica-bij-landbouwhuisdierenin-2016

[20] Levy, S. (2014). Reduced Antibiotic Use in Livestock: How Denmark Tackled Resistance. Environmental Health Perspectives, 122(6), A160–A165. http://doi.org/10.1289/ehp.122-A160

[21] Federation of Swedish Farmers (November 2015). Swedish pig production. Available at: https://www.lrf.se/globalassets/dokument/om-lrf/branscher/lrf-kott/grisnaringen/swedish_pig_production_2015.pdf

The support required would involve both technical and financial aspects in making the transition to more sustainable antibiotic use practices. In certain cases, the continued use of antibiotics can harm farm production, pointing to the need for transition support. For example, feeding certain Gram-positive or broad-spectrum antibiotics orally to farm animals can increase shedding of Salmonella or Escherichia coli, with implications for food safety and human health.[22,23,24,25]

2.8 The IACG discussion paper notes that economic and population growth will fuel greater demand for meat products, and that this could be an important driver of greater antimicrobial use as well. The trade of food animal products is concentrated into the hands of a few countries, both on the export and on the import sides. The impact of AMR-related trade restrictions by importing countries on the adoption of more sustainable food production deserves further analysis. The WTO allows its Member States to establish trade restrictive measures to protect human health or the environment and encourages them to base these on international standards, guidelines or recommendations.[26] In 2017, the WHO established guidelines calling for restrictions on the use of medically important antibiotics in animals. While a harmonized approach to regulation is useful, countries should not be limited by minimal global trade standards but instead have the liberty to establish higher standards based on such guidelines.

2.9 R&D investment into bringing new vaccines and diagnostics that improve food animal production is also needed. Where there are market failures to bring forward such technologies, the IACG might consider borrowing lessons from the product development partnerships and public-private partnerships that have addressed such challenges in the R&D for treatments of neglected diseases. The technologies for achieving these aims among small-scale producers may differ from what might be used in large-scale production, and these must be targeted.

2.10 Antibiotic use for the treatment of small animals and pet treatment should be better regulated. In many countries, the number of pets is higher than number of livestock

[22] Barrow, PA. Further observations on the effect of feeding diets containing avoparcin on the excretion of salmonellas by experimentally infected chickens. Epidemiol Infect. 1989 Apr;102(2):239-52.
[23] Delsol, AA et al., The effect of chlortetracycline treatment and its subsequent withdrawal on multi-resistant Salmonella enterica serovar Typhimurium DT104 and commensal Escherichia coli in the pig. J Appl Microbiol. 2003;95(6):1226-34.
[24] Evans, MC et al., Antimicrobial growth promoters and Salmonella spp., Campylobacter spp. in poultry and swine, Denmark. Emerg Infect Dis. 2003 Apr;9(4):489-92.
[25] Looft, T et al., In-feed antibiotic effects on the swine intestinal microbiome. Proc Natl Acad Sci U S A. 2012 Jan 31;109(5):1691-6. doi: 10.1073/pnas.1120238109.
[26] WHO, WIPO, WTO. Antimicrobial resistance – a global epidemic. Available at: https://www.wto.org/english/news_e/news16_e/heal_29aug16_e.pdf

animals, excluding poultry, yet medication of pets is often under the radar. Data collection and transparency around what small animal veterinarians are prescribing and for what purposes are needed.

3. Both the healthcare delivery and food production systems generate antibiotic pollution into the environment (environmental contamination).

3.1 Antimicrobial contamination of the environment occurs across the value chain. Targets and standards must be set for all contributors, notably not just pharmaceutical production plants,[27] but also farms,[28,29] sewage treatment plants and hospitals. Benchmarks to lower antibiotic pollution can be (a) set through Good Manufacturing Practice (GMP) standards, (b) incorporated into the National Action Plan, and (c) entered into criteria set by procurement and credentialing agencies.

3.2 UNEP, along with Tripartite agencies, must extend the Monitoring & Evaluation Framework on which the Tripartite agencies have started to include data to be collected on antibiotic pollution and evidence of drug resistance in the environment. In addition, concerns are emerging that antibiotic use may have other environmental effects. Research efforts should focus on environmental risk assessments that can serve as a basis for evidence-based regulations.[30] The following examples have been illuminated by new research and underscore the need to evaluate more closely the impact of:

- antimicrobials on potential disruption of ecosystem services provided by dung beetles; antimicrobials on possible increase of methane gas emissions of livestock cattle;[31]
- biocides and metals on the co-selection and promotion of antibiotic resistance;[32,33]

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[27] Sinha, R. (May 2017) Bitter Medicine, *Down To Earth*. Available at: http://cdn.cseindia.org/attachments/0.94770800_1529997685_bitter-medicine.pdf

[28] Bhushan, C., Khurana, A. & Sinha, R. (2016). Antibiotic use and waste management in aquaculture: CSE recommendations based on a case study from West Bengal, Centre for Science and Environment, New Delhi. Available at: https://www.cseindia.org/antibiotic-use-and-waste-management-in-aquaculture-7906

[29] Bhushan, C., Khurana, A., Sinha, R., & Nagaraju, M. (2017). Antibiotic Resistance in Poultry Environment: Spread of Resistance from Poultry Farm to Agricultural Field, Centre for Science and Environment, New Delhi. Available at: https://www.cseindia.org/fst-report-antibiotic-resistance-in-poultry-environment-8851

[30] *Strategic and Operational Guidance on Animal and Environmental Aspects: National Action Plans on Antimicrobial Resistance for Developing Countries,* 2017, Centre for Science and Environment, New Delhi. Available at: https://www.cseindia.org/strategic-and-operational-guidance-on-animal-and-environmental-aspects-7858

[31] Hammer TJ, Fierer N, Hardwick B, Simojoki A, Slade E, Taponen J, et al. Treating cattle with antibiotics affects greenhouse gas emissions, and microbiota in dung and dung beetles. *Proceedings of the Royal Society B: Biological Sciences*, 2016; 283(1831): 20160150.

[32] Romero, JL et al., Resistance to Antibiotics, Biocides, Preservatives and Metals in Bacteria Isolated from Seafoods: Co-Selection of Strains Resistant or Tolerant to Different Classes of Compounds. Front Microbiol. 2017 Aug 31;8:1650.

[33] Pal, C et al., Chapter seven – Metal resistance and its association with antibiotic resistance. Adv Microb Phys, 2017 Vol 79: 261-313.

- the use of herbicides such as glyphosate which have been shown to change the response of enteric organisms common to foodborne outbreaks to antibiotics, thereby heightening spontaneous mutation to higher levels of drug resistance and potentially undermining antibiotic therapy.[34]

3.3 Remediation technologies for handling the removal and disposal of antibiotic pollution from the environment need to be developed.

3.4 Procurement and supply chain policies must include environmentally preferable purchasing criteria to guide manufacturers, producers, suppliers, and distributors to be accountable to responsible antimicrobial use and associated pollution. As an example within the healthcare sector, Health Care Without Harm has shown how a virtual global network of hospitals and health systems can work to achieve measurable improvements in greening the practices of these institutions through the "Global Green and Healthy Hospitals" project. Through the EcoQUIP project, Health Care Without Harm and its partners work to support public procurers to secure innovative solutions to "improve the efficiency, quality and environmental sustainability of healthcare." Through the Antimicrobial Stewardship Through Food Animal Toolkit, Health Care Without Harm and its partners guide health professionals in designing a comprehensive, multi-departmental hospital antimicrobial stewardship program that includes food procurement. Industry could also play a bigger role in supporting stewardship by ensuring safe disposal of unused or expired drugs across the supply chain and implementing drug take-back programs.[35]

3.5 Greater disclosure by industry, antibiotic and feed manufacturers, farmers and retailers around the amount of antibiotics sold, procured, used and discharged as effluent would enable better regulation of the flow of antibiotics throughout the environment.

3.6 Another forward-thinking dimension of tackling AMR in the environment is the redesign of health facilities to manage better infection control and prevention. Changing the built environment in hospitals can be as straightforward as ensuring air circulation in operating rooms with windows where negative pressure ventilation is not possible. Research into how to make medical instruments with surfaces resistant to biofilm and bacterial colonization might reduce the reliance on handwashing alone to slow bacterial spread.

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[34] Kurenbach B, Marjoshi D, Amabile-Cuevas CF, Ferguson GC, Godsoe W, Gibson P, et al. Sublethal exposure to commercial formulations of the herbicides Dicamba, 2,4-Dichlorophenoxyacetic acid, and Glyphosate cause changes in antibiotic susceptibility in Escherichia coli and Salmonella enterica serovar Typhimurium. *mbio.asm.org*, 2015; 6(2).

[35] U.S. Food and Drug Administraion, Disposal of Unused Medicines: What You Should Know. Available at: https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/ensuringsafeuseofmedicine/safedisposalofmedicines/ucm186187.htm#take_back

3.7 The best way to mitigate pollution is to avoid antimicrobial use in the first place, both in human medicine and in agriculture. Antibiotic use should only be when necessary, yet much of the use in agriculture and a good portion in human medicine remains unnecessary. Holding practitioners, including physicians and veterinarians, accountable when they prescribe at much higher levels than their peers is important.