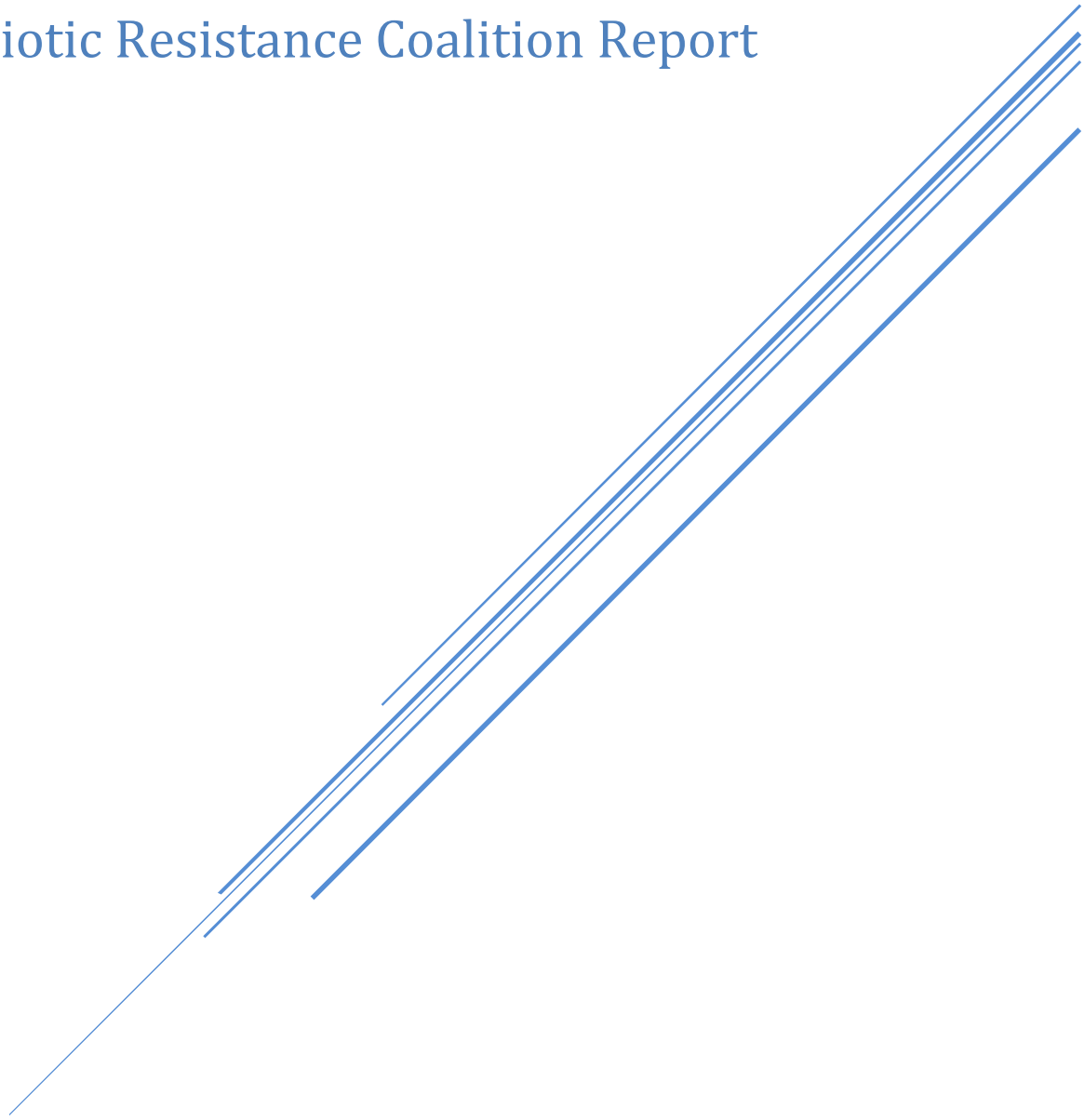
CIVIL SOCIETY CONSULTATION WITH WHO, FAO AND OIE ON THE GLOBAL DEVELOPMENT AND STEWARDSHIP FRAMEWORK

Antibiotic Resistance Coalition Report



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Signatories

American Medical Student Association
Alliance to Save Our Antibiotics
Center for Science and Environment
Ecumenical Pharmaceutical Network
Food Animal Concerns Trust
Health Action International
IFARMA
Institute for Agricultural and Trade Policy
Natural Resources Defense Council
People's Health Movement
ReAct – Action on Antibiotic Resistance
ReAct Africa
ReAct Asia Pacific
ReAct Europe
ReAct Latin America
ReAct North America
Society for International Development
Third World Network
Universities Allied for Essential Medicines
What Next Forum

Key points:

Why we need a framework:

- The UN political declaration on AMR provided a mandate for the finalization of the Framework. It is important that there be policy coherence between the IACG process and the current work led by WHO, FAO, OIE and UNEP.
- The Framework provides an overview of the activities and responsibilities of the intergovernmental agencies involved, but it should also lay out responsibilities distributed across Member States, other intergovernmental organizations, professional associations, civil society and other relevant actors.
- The Framework should set targets and establish a transparent evaluation process to enable monitoring for accountability.

What legal form could the framework take?

- It is essential to overcome the institutional fragmentation of the Tri-/Quadripartite structure, including greater engagement of UNICEF, UNDP and other UN and intergovernmental agencies in the Tripartite efforts to tackling the challenge of AMR.
- Future governance arrangements should be firmly grounded on centrality of Member States and rooted in a rights-based approach to ensure that the public's interest is at the center of the AMR agenda, that conflicts of interest are minimized, and that governments can be held accountable.
- Adequate and sustainable financing from the international community is essential for effective global governance. There is a need for attention to the disparate impact on resource-limited settings and for technical and financial transition support.
- The road to future governance should not distract nor detract from the pace of ongoing efforts to resolve the shortfalls in support of building a surveillance system, rational use, innovation of health technologies, or other measures to address AMR.

R&D to foster access:

- The R&D principles are closely aligned with the UN Political Declaration on AMR's key principles of affordability, effectiveness and efficiency, and equity. However, affordability of products, both in LMICs and in high-income countries, remains a concern. Some of the listed financing mechanisms, such as transferable IP exclusivity and priority review vouchers, are not aligned with access goals.
- Public investments should transform the R&D innovation ecosystem rather than just focus on individual bets, drug by drug, and company by company. There should be an increased focus on push incentives, a prioritization of innovation not only of technology but also of practice, and an effort to explore repurposing, combining or finding alternatives to antibiotics.
- A proposal for a unified, holistic and evidence-based prioritization framework, including targets and access indicators, across sectors is needed. The agency roles in the Framework currently remain divided.

Access and stewardship policies:

- The Framework should set standards and plans for country-level implementation for responsible use in human, animal and plant health, and improve national surveillance systems. Exploring ways for integrating some targets as AMR-specific indicators in SDGs would be useful to monitor progress.
- Approaches to antimicrobial stewardship at the global, national, hospital and community level are well acknowledged, but measures are needed to address underuse of antibiotics in the healthcare delivery system.
- To promote prudent use, there is a need to better regulate the private sector and to invest in public healthcare and sanitation facilities.
- Antibiotics are greatly overused in agriculture, and there is need for strong action. Countries should set ambitious targets and promote data transparency for benchmarking. It is critical to support an end to all routine preventative use, in addition to growth promotion and to address the link between intensive farming and high antibiotic use.

Environmental aspects of AMR:

- The Tripartite agencies have an important role in containing antibiotic pollution by eliminating antibiotic misuse in the first place and investing in remediation technologies.
- The UN Environment Programme should take a leadership role in governance over antibiotic pollution, partnering with the Tripartite agencies to manage environmental contamination across the value chain in the human health and agricultural sectors. Strategies could include greater regulatory control over disposal, environmentally preferable purchasing criteria, and greater disclosure by industry, manufacturers and retailers. However, such measures should not put at risk the stable supply of affordable antibiotics in the healthcare delivery system.
- The section on setting targets for AMR and the environment remains thin. Targets and standards must be set for all contributors, notably not just pharmaceutical production plants, but also farms, sewage treatment plants and hospitals.

I. Why we need a framework

It is important to recall that the UN political declaration on AMR provided a mandate for the finalization of the Framework, calling "upon the WHO, together with the FAO and the OIE, to **finalize a global development and stewardship framework**, as requested by the WHA in its resolution 68.7, to support the development, control, distribution and appropriate use of new antimicrobial medicines, diagnostic tools, vaccines and other interventions, while preserving existing antimicrobial medicines, and to promote affordable access to existing and new antimicrobial medicines and diagnostic tools, taking into account the needs of all countries and in line with the global action plan on antimicrobial resistance."

Given this mandate, it is important that there be policy coherence between the IACG process and the current work led by WHO, FAO and OIE along with UN Environment. The Framework provides an overview of the activities and responsibilities of four intergovernmental agencies involved, but it should also lay out responsibilities distributed across Member States, other intergovernmental organizations, professional associations, civil society and other relevant actors, as the Global Action Plan offers as a starting point. There is a need for a clearer mapping of stakeholder engagement, including where healthcare delivery systems and healthcare providers, as well as food producers and intergovernmental organizations, not just "governments, industry, NGOs, academic institutions and the private sector" importantly could contribute. A full assessment of the tables on responsibilities of the Tripartite agencies and UN Environment will have to await filling out this broader picture of how the Global Framework would engage these other parties.

Regarding accountability, the Framework could provide a sense of the timetable and milestones by which the Tripartite agencies plus UNEP would hold themselves accountable to delivering on their commitments. There is a need for more clarity on the link between the needs and the main goals of the framework (Box 1). These goals should also have a link to the setting of targets. The setting of targets to achieve the Framework goals would also be necessary for follow-on monitoring for accountability and prioritization. Effective monitoring and evaluation of progress requires governments to ensure collection and public transparency of relevant data as well as the complementary efforts of civil society to hold key stakeholders accountable. Transparency and openness of the policy process are key for monitoring and accountability in the public's interest. The need for this transparency begins with collecting and making publicly available the data on antibiotic use, drug resistance patterns, price, and measures of access and stewardship. This principle also extends to the policy process. Importantly, there must be mechanisms to ensure that accountability follows from such transparency. We greatly appreciate the opportunity to hold the civil society consultation with WHO, FAO and OIE. However, there is a need to explore how civil society not in official relations with any of the tripartite organizations or UNEP would be able to participate in future Member State consultations that are hosted by, for example, only WHO.

II. What legal form could the framework take?

A. **Building on the Tripartite & UNEP process, it is essential to overcome the institutional fragmentation of the Tri-/Quadripartite structure.**

1. The recent MOU among the Tripartite and that is expected to include UNEP is a good start, but there should be greater engagement of UNICEF, UNDP and other UN and intergovernmental agencies in the Tripartite efforts to tackling the challenge of AMR. It should not remain the province of just the technical agencies steeped in One Health issues.

B. **Future governance arrangements should be firmly grounded on centrality of Member States and rooted in a rights-based approach to ensure that the public's interest is at the center of the AMR agenda, that conflicts of interest are minimized and that governments can be held accountable.**

1. The fragmentation of the governance process for AMR across multiple, intergovernmental agencies (Tripartite or Quadripartite) contributes to policy incoherence. Each of these intergovernmental agencies responds to different Ministries within governments. There is a need for a redesigned governance approach that is Member State-driven and that can address policy incoherence at its roots.
2. Commitments and actions from governments to achieving specific targets at different levels can be stepped up in multiple ways bearing in mind that effective national actions drive global cooperation and commitments.
3. If consensus can be built to work towards an international legal framework for AMR, a new conference or legal space could take form & negotiations can take place in a coherent and holistic manner. The UNGA is a platform where a resolution or mandate could be shaped in leading to an international legal framework down the line (as in the case of climate change). However, the multi-stakeholder approach raised in some fora might create setbacks to confidence building among Member States towards more global commitments.
4. While being Member State-driven, decision-making should still involve inclusive and structured institutional mechanisms of consultation with civil society and other relevant stakeholders with robust safeguards to protect against conflicts of interest. Input into a decision-making process is different than placing non-Member State actors in the policy decision making role, which would risk regulatory capture. Thus, this draws clear distinction between multi-stakeholder input into the policy process as opposed to a multi-stakeholder agreement as the governance process in lieu of a Member State-driven process.
5. Protection against conflicts of interest is related to the integrity of the decision-making process, the trustworthiness of the knowledge generation that supports policy making and the financial integrity of the funding that support the policy and decision-making space. This means that support should primarily be public in nature and delinked from donor-driven approaches.

C. **Adequate and sustainable financing from the international community is essential for effective global governance.**
    1. There is a need for attention to the disparate impact on resource-limited settings and on those who will face difficulty transitioning to ensure access and meet stewardship standards when domestic resources are not sufficient.
    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 Framework should address the need for funding coordination in a mixed financing model. Table 1 in Annex 1 on selected financing mechanisms shows that public financing remains central.

D. **Regardless of the legal form pursued, the road to future governance should not distract or detract from the pace of ongoing efforts to resolve the shortfalls in support of building a surveillance system, rational use, innovation of health technologies, or other measures to address AMR**.

III. Research and development to foster access

A. **The principles of Chapter 3 are closely aligned with the principles of the UN Political Declaration on AMR's key principles of affordability, effectiveness and efficiency, and equity.**
    1. The Tripartite should continue to insist that Member States sustain their support for these important principles in all current and future relevant initiatives, including in the recent TB High Level Political Declaration and in the establishment of R&D Hub by the G20.
    2. Affordability of products, both in LMICs and in high-income countries, remains a concern. Drug prices too often go well beyond marginal cost plus a reasonable return. Safeguards against high pricing might include ensuring multiple generic suppliers in the procurement scheme and benchmarking against what a product development partnership might be able to do to bring the drug to market. Fulfilling the goals of sustainable innovation and access requires transparency about R&D costs, clinical trial data, and prices, fair return on public investment, and R&D that takes an end-to-end approach, by which upstream incentives are coupled with access and stewardship measures downstream. Target product profiles can be an effective mechanism to help ensure affordability of end products.
    3. Some of the listed financing mechanisms and incentives of Annex 1 are concerning. For example, transferable IP exclusivity places higher drug prices on patients being treated with medicines, subject to the extended monopoly pricing, and this can result in delayed or foregone treatment for these patients. Priority review vouchers risk distorting the regulatory review process, but also do little to

change the way by which such products are brought to market. The value of priority review vouchers also diminishes as the number of such vouchers on the marketplace increases. The table should include an assessment of the degree to which these mechanisms respond to the 'guiding principles' listed both in the annex and under '3.2 Basic principles for needs-driven R&D that fosters access to new products.'

B. Public investments should transform the R&D innovation ecosystem rather than focus on individual bets, drug by drug, and company by company. Such approaches are not represented alongside the financing mechanisms in Annex 1.

1. In the short term, there should be an increased focus on push incentives. With an empty pipeline in AMR-related research for now, the major challenge and opportunity lies within innovation and research rather than the development and production phase. Pooling the building blocks for enabling R&D into health technologies is another key investment approach to transforming the innovation ecosystem.
2. To have the greatest impact on One Health, one must better prioritize innovation of both technologies and of practice in the food production sector and the environment.
3. Going beyond the development of new chemical entities, innovation should encompass the repurposing existing compounds and the exploration of combination therapies and antibiotic alternatives.
4. WHO's continued support of GARDP is welcome. This product development partnership model is one that might be emulated for innovation of diagnostics and vaccines in the animal health sector.

C. A proposal for a unified and holistic prioritization framework across sectors should be developed. The mapped R&D related responsibilities for the Tripartite and UN Environment Programme include R&D prioritization (Table 2; 3.4.2), but the agency roles in prioritization remain divided.

1. Setting targets, including access indicators, enables the international community to set objectives, drive change and measure progress.
2. Target product profiles set by the public sector can play an important role in better channeling R&D funding, ensuring that technology products reflect concerns of affordability and adaptation to resource-limited settings, and coordinating R&D efforts globally.
3. The prioritization should be clearly linked to potential funding mechanisms to ensure that the prioritization is informing the allocation of funding. This needs to extend importantly beyond the Tripartite Agencies and UN Environment to funding agencies supporting this work.
4. Prioritization should be evidence-based, and the responsibilities related to this should be further spelled out. The Global AMR R&D Hub aims to coordinate global R&D activities, but the role of the Hub as a whole and its interpretative role on the data it collects must be clarified. The Hub should promote the meaningful

involvement of and buy-in from low- and middle- income countries, conduct a quality assessment of product pipelines (complementing ongoing work, such as that being undertaken by WHO), and ensure transparency of its process and analyses.

5. Section 3.2 under the 'basic principles for needs-driven R&D that fosters access to new products' states that "uptake of vaccines that have the potential to reduce the use of antimicrobials should be explored." Given the strong evidence base supporting the use of vaccines to reduce the burden of infections and thereby decrease the use of antimicrobials, increasing affordable access to vaccines should be a high priority within the global AMR response.

IV. Access and stewardship policies

A. **The Framework would need to provide further information of how standards for the implementation of responsible and prudent use standards in human health, animal health and in plant production would look like and how the Tripartite and UN Environment will be assisting country level implementation of these standards.**

1. In the case of surveillance, and given the shared needs across sectors for AMR laboratory capacity, it would be critical to explain how an integrated surveillance system would work and what would this mean in the context of developing countries.
2. Exploring ways in which the Tripartite and UNEP can integrate some of the targets as indicators in the SDGs could be a useful way for monitoring progress.
3. Efforts to improve surveillance of antimicrobial use, prices, resistance patterns, and shortages are critically important in assisting country-level implementation of responsible and prudent use standards. This would be of enormous value in taking stock of the situation, refining and looking at priority settings for national action plans. However, this requires a commitment to public data transparency. Therefore, it would be important to ensure that the Tripartite provides information on what actions they can take to increase transparency

B. **Approaches to antimicrobial stewardship at the global, national, hospital and community level are well acknowledged, particularly in the healthcare delivery system, but not so with corresponding measures for addressing underuse of antibiotics in the healthcare delivery system.**

1. While voluntary certification schemes for antimicrobial stewardship programmes in hospitals are a good proposal, more concrete steps are needed to address the health systems and regulation issues to promote stewardship in the unregulated sector.
2. Development and stewardship to combat AMR cannot rely solely on the use of antibiotics. There is a clear need to increased public health-care expenditure,

adequate sanitation facilities and better regulation of the private health sector, among other factors directly affect AMR. The prudent use of antimicrobials cannot be promoted without regulating the private sector.

C. Scientists estimate that about 73% of all antimicrobials are used in livestock, mostly for growth promotion or routine disease prevention. This suggests that in many countries, antibiotics are greatly overused in agriculture, and there is an urgent need for strong action.

1. Regarding targets, it would be important for countries to set ”individual long-term realistic targets”. But in order to do this, there is a need to support and promote data transparency, which makes benchmarking and the setting of meaningful targets feasible.
2. For livestock production, the targets need to be ambitious. In many countries, there is huge scope for reducing on-farm antibiotic use and throughout the supply chain. Some countries have already achieved large reductions in just a few years. Setting easy-to-achieve targets could slow down progress. So targets must be ambitious.
3. The goal of ending antibiotic use for growth promotion and plant protection is very important, but not enough. Experience shows that when growth promoters are banned, blanket use for disease prevention often increases. This is why the European Union is planning on banning preventative group treatments in about three years' time. WHO guidelines have also called for an end to routine antibiotic disease prevention. It would be critical to support the end to all routine preventative antibiotic use, including all preventative group treatments, and proposals for such a ban should be included in the framework. There is need to clarify the qualification on phasing out of antimicrobials as growth promoters “in the absence of risk assessment.”
4. The Framework's goal of limiting the use of fluoroquinolones, modern cephalosporins and colistin in animals is welcome, but the recommendations need to go further. Colistin is a **last-resort** antibiotic in human medicine and should be **banned completely** from use in animals. The use of fluoroquinolones and modern cephalosporins should be restricted to use in individual sick animals, in cases where other antibiotics don't work. They should not be used for prevention or group treatments. Use in companion animals should also be restricted.
5. The link between intensive farming and high antibiotic use needs to be emphasized. According to a European Food Safety Authority and European Medicines Agency 2017 report, “The stress associated with intensive, indoor, large scale production may lead to an increased risk of livestock contracting disease”. The report says that the high pathogenic load and rapid spread of disease in intensive farming can lead to high levels of antibiotic group treatments. It says that “Farming systems with heavy antimicrobial use should be critically reviewed, to determine whether or how such systems could sustainably reduce the use of on-farm antimicrobials. If a sustainable reduction in the use of on-farm

antimicrobials is not achievable, these systems should ideally be phased out." The global framework should similarly be recommending a move away from intensive-farming systems that are unable to reduce their antibiotic use to much lower levels.

6. Regarding capacity building. LMICs will need assistance in phasing out antibiotic use and making the transition to improved healthcare and sustainable agricultural models. Such resources should prioritize those at greatest risk and with the least resources, such as small-scale farming operations, to make their own transition to production practices less reliant on the use of antimicrobials. Capacity-building should thus be an important component in the Framework and could be made more explicit.
7. Regulations on the use of antibiotics in pets should also be taken into account.

V. Environmental aspects of AMR

A. The broadening of governance beyond the Tripartite agencies to include the UN Environment Programme is an important step in acknowledging the environmental aspects of AMR.

1. However, UN Environment's presence does not diminish the role and responsibility of the Tripartite (in particular FAO and the OIE) in containing antibiotic pollution. A major part of antibiotic pollution could be best addressed by eliminating antibiotic misuse in the first place, by phasing out mass administration of antibiotics in medicated feed and via aqueous routes for example. Remediation technologies for handling the removal and disposal of antibiotic pollution from the environment need to be developed. Such technologies would find particular use in hospitals.
2. UN Environment should be integrated at the earliest stage possible into the ongoing efforts to combat AMR and take a greater leadership role in advancing efforts on the environmental front. Its role should not be limited to supporting the Tripartite on the responsibilities related to R&D, regulation and waste management and risks.

B. **The 'life cycle approach' for managing environmental contamination of antimicrobials is crucial. Environmental pollution occurs across the value chain in the human health and agricultural sectors.**

1. The Framework should aim to facilitate and push for regulatory control at the national level regarding safe disposal of antibiotics by industry or healthcare facilities, for example, as developing compendia of best practices or guidance will not be sufficient. Similarly, raising awareness will not be sufficient to motivate safe disposal from homes and farms, and therefore take-back programmes must be weaved into extended producer responsibility programmes.

2. 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. 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 for unused and expired antibiotics.
3. Greater disclosure by industry, antibiotic and feed manufacturers, farmers and retailers on the amount of antibiotics sold, procured, used and discharged as effluent would enable better regulation of the flow of antibiotics throughout the environment.
4. The draft Framework focuses on point sources of pollution and waste water treatment plants but does not address non-point sources of pollution. In LMICs for example, a high proportion of human fecal waste (through households or open defecation) does not necessarily undergo treatment at sewage treatment plants (STPs) and can directly enter into non-point sources such as rivers and groundwater. It is important to factor-in such non-point sources in generating evidence on environmental aspects of AMR.
5. Research efforts should focus on environmental risk assessments that can serve as a basis for evidence-based regulations.
6. Standards and guidelines that help harmonize testing methods, analysis and reporting across different sectors, sub-sectors and geographies should be formulated.

C. While the Framework recognizes the importance of setting targets for the emission of resistant microorganisms and active pharmaceutical ingredients into the environment, the section on setting targets for AMR and the environment remains thin.

1. Targets and standards must be set for all contributors, notably not just pharmaceutical production plants, but also farms, sewage treatment plants and hospitals. For example, antibiotic point source pollution from hospitals where antibiotics, particularly those of last resort, might be used needs to be considered.
2. Benchmarks to lower antibiotic pollution can be (a) set through Good Manufacturing Practice standards, (b) incorporated into the National Action Plan, and (c) entered into criteria set by procurement and credentialing agencies.
3. Such efforts to ensure greater environmental stewardship in the supply chain, of course, must be implemented carefully, so as not to compromise the stability of the supply chain for critically important antimicrobials. Underuse of antibiotics claims more lives today than drug resistance from overuse.
4. AMR-centric approach should be adopted and embedded into the environmental regulations across food, veterinary feed, drug and healthcare sectors. For example, presence of antibiotics in industrial waste or effluents such as from the pharmaceutical industry should be considered as a hazardous chemical, and policy changes made accordingly.