Antibiotic Manufacturing Industry Initiatives and Challenges to Reduce Antibiotic Pollution

August 8, 2022
Outline

• Who we are and Why do we care for AMR?

• AMR – Environment – Manufacturers

• Global Approach and Why Indian Antibiotics Manufacturers need to build sustainability

• Centrient’s Journey

• Pharma Industry Initiatives

• Challenges

• How Policy Makers can help to shape
Centrient Pharmaceuticals at a glance
Global B2B leader in sustainable, enzymatic antibiotics, next-generation statins and anti-fungals.

- We produce and sell intermediates, active pharmaceutical ingredients (APIs) and finished dosage forms (FDFs)
- Quality, Reliability and Sustainability shape how we do things as a company
- Our world-leading proprietary enzymatic technology ensures an unmatched eco-friendly production process for our high-quality products
- Our backward-integrated global manufacturing footprint ensures security of supply
Our purpose is to improve lives through innovative and sustainable manufacturing of medicines.
AMR is Core to Our Sustainability Strategy /ESG

E: Minimising Environmental Impact

- 45% reduction in carbon emissions (2025) and Carbon Neutral by 2030
- All waste repurposed and zero landfill waste by 2030
- 5% reduction in water consumption (2025) and maximized water recycling by 2030
- Sites and suppliers compliant with AMR IA Common Manufacturing Framework and Predicted No-Effect Concentration (PNECs) (2021)
- R&D projects pass Sustainability assessment (2025)

S: Improving Human Health and Social Impact

- Increasing access to our life-saving antibiotics
- 50,000+ lives touched by Centrient global community programs by 2030 – 7X more than today
- High level of employee engagement being in top 10% for our industry (2025)
- 50% gender balance in senior management roles (2025)
- Inclusive Leadership with less than 5% voluntarily attrition
- Certified human and labor rights compliance in our operations (2024)

G: Acting Responsibly

- Corporate Governance (i.e. board diversity and appropriate decision-making authority)
- Ethical Business Practices
- Data Privacy and Cyber-Security
- Stakeholder Engagement & Corporate Affairs
- Transparency and Disclosure (financial/ESG)
- Responsible supply chain
Causes of Antimicrobial Resistance

- Without effective action on AMR it is estimated that **10 million people will die annually by 2050** with a concomitant loss of **$100 Trillion to the global economy**.
- **Two million deaths** are projected to occur in India due to AMR by the year 2050.

Global calls for Action

- Health minister of G7 Countries issued a declaration in June 2021 calling for action: “We will work with G7 Environment Ministers, AMR Industry Alliance and others to agree on standards…and consider privileging the purchase/reimbursement of antibiotics manufactured according to these agreed standards”.

- In March 2022, the Global Leaders Group on Antimicrobial Resistance comprising ministers, experts and business leaders called on manufacturers in all countries to “commit to prevention and management measures to minimize the impacts of manufacturing discharges in the environment”.

- OECD has urged that “environment health needs to be better embedded into the global AMR agenda…by holding producers and factories accountable for taking steps to prevent AMR pathogens from reaching the environment”.

National and State Action Plans to combat AMR in the environment: The journey so far

To curb the various drivers of AMR in the environment, the NAP-AMR advocated for developing **national framework for the monitoring and surveillance of antibiotic residues in the environment**.

Subsequently, the MoEFCC released a draft amendment to the *Environment (Protection) Rules, 1986* where residue limits for **121 antibiotics** were notified. However, the draft was replaced and the standards for antibiotic residues were **removed** from the final notification released in **August 2021**.
Intervention by the National Green Tribunal to curb antibiotic pollution

The Baddi-Barota-Nalagarh pharmaceutical hub located in the Solan district of Himachal Pradesh is one of the largest pharma hubs of the country. Baddi and Nalagarh are located near the Sirsa river.

In July 2020, Veterans Forum for Transparency in Public Life (VFPTL), an NGO of retired armed forces officers brought to the notice of the National Green Tribunal (NGT) the dangerously high concentrations of antibiotics like ciprofloxacin flowing through the waters of the Sirsa river.

During one of the subsequent hearings, the NGT directed the CPCB to formulate mechanism for antibiotic residues in the rivers and waterbodies pan India. Resultant, CPCB released the Guidelines on Monitoring Mechanism for API Residue in January 2022.

In April 2022, the NGT ruled that until the MoEF&CC finalizes standards for antibiotic residues limit, the standards proposed in the draft amendments to Environment (Protection) Rules, 1986 (released in January 2020 and then withdrawn) to be implemented with immediate effect.
Centrient as champion on AMR via Environment
Antibiotic Resistance: Why should the industry care?

**Manufacturing has a direct impact on rising AMR**

Due to the urgent lack of novel antibiotics in the pipeline, it is imperative to **conserve the effectiveness of existing antibiotics.**

**Without effective antibiotics there won’t be:**

- modern healthcare
- pharmaceutical industry

Antibiotics producers should drive **higher standards** through reviewing their supply chains, and the **environmental criteria** on antibiotics manufacturing should become a consideration in the sourcing decisions of buyers, health insurers and governments.
Journey to AMR-Free Manufacturing

Joined Industry Initiative

Joined Pharmaceutical Supply Chain Initiative, AMR Industry Alliance, M4E and RAMP for learning and solution.

Solution development & implementation

Commitment at IA to be PNEC compliant by 2021. Continued CAMF & PNEC assessment. Developed analytical method, biocatalyst to degrade the residual antibiotics.

2017-2020

2018-2020

2016-17
Commitment for solution

2017 onwards
Advocacy to combat AMR

Signed UNGA Industry Roadmap on AMR and signed the Davos Declaration in 2016.

Promotes, advocates responsible mfg, combating AMR, share the best practices across supply chain. DCAT AMR events and represent to regulators.

2019 - 2021
Achieving Full Compliance

Reaching full PNEC compliance across our supply chain i.e., own manufacturing and CMO’s.
Centrient Achieves PNEC Compliance for its Oral Antibiotic Supply Chain

WHERE WOULD WE BE WITHOUT ANTIBIOTICS?
Toansa: WWTP Technology

Centrient’s Toansa facility has a state-of-the-art WWTP equipped with primary, secondary and tertiary treatment. The treatment technology removes antibiotics and other pollutants at each treatment. It meets PNEC targets at the end of pipeline.

**Primary Treatment**
- Mechanical Vapor Recompressor
  - Separation of non-volatile contents

**Secondary Treatment**
- Thin Film Dryer
  - Drying of non-volatile contents
- Biological Treatment Unit
  - COD / BOD & Ammonical nitrogen removal

**Tertiary Treatment**
- Ultra Filtration unit
  - Removal of suspended solids
- Reverse Osmosis unit
  - Removal of dissolved solids

Site was audited by IA member companies in 2019, 2022 as per PSCI and IA. Site successfully passed the audit.

Water management driven by Our Proud and Dedicated team

Treated Water for Recycle & Horticulture
Industry Endeavor Towards Self-Regulation – AMR IA

AMR IA has published Common Antibiotics Manufacturing Framework and PNEC Values in 2018 as part of UNGA commitment. IA expects member companies and their supply chain self-regulate. IA publishes biennial progress report. Some of the outcome of progress report are given below:

**Framework**
- 83% members have assessed all of their own antibiotic sites against the Alliance’s manufacturing framework.
- 82% of owned sites meet the framework’s requirements wholly or in part.

**PNEC**
- 56% of products made at member-owned sites are expected to be made in accordance with discharge targets within the next 3 years.
- 88% within the next 7 years.

**PNEC : Supplier Sites**
- 24% of products at supplier sites are expected to be made as per discharge targets within 3 years and a further.
- 70% of products made at supplier sites are expected to be made in accordance with these targets within 4-7 years.
Industry Endeavor Towards Self-Regulation

AMR IA has published AMR standard in May 2022. IA expects member companies to adopt the standard. IA is developing a certification scheme for antibiotic manufacturing, covering about 30% of the antibiotic supply chain.

Improving global pharma supply chain with a focus on India and China. Principles and audit protocols encompass verification on environment and AMR. PSCI members cover 80% of the pharma supply chain by value. PSCI principles are widely recognized in the industry. PSCI is running a project on AMR in the Musi river catchment area.

RAMP, growing collaborative platform promoted by SIWI, Centrient, SDC, AMR IA, Shawview, GSK, and Sandoz to combat AMR. Centrient committed to provide financial and technical resources. RAMP is deeply interfaced with industry and authorities in Europe & India.
Increasingly Buyers and Regulators Integrate Environmental Criteria in Antibiotic Tenders to Combat AMR

European procurers (e.g. Germany, UK, Norway, etc) are including manufacturing criteria for antibiotics to ensure a responsible supply chain - and more are following suit.
CHALLENGES

- Scientific understanding and knowledge
- Standard and method for risk assessment and measurement.
- Technical training, skill for solution development and application.
- Complex wastewater matrix and stringent PNEC values
- Lab testing capabilities and cost.
- Implementation at suppliers.
- To Think Ahead – Building Sustainable Supply chain
The Solution Calls for Collaboration to Mainstream Standards and Level Playing Field Across the Supply Chain

Working across the supply chain from manufacturers down to procurers to ensure delivery of antibiotics which do not contribute to AMR

Cross-Sector Collaboration  Single, Harmonized Standard  Credible, Rooted in Science
Way forward to curb AMR from Pharma manufacturing: NAP 2.0 and State Action Plans

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<thead>
<tr>
<th>Develop <strong>India-specific guidelines</strong> for monitoring antibiotic residues in the environment related to manufacturing</th>
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<tr>
<td>Establish regional <strong>Centers of Excellence</strong> to promote sustainable antibiotic manufacturing in India</td>
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<td>Incentivize pharma manufacturers for adoption of international standards such as <strong>Good Manufacturing Practices</strong> (GMP)</td>
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<td>Incentivize companies to <strong>incorporate green procurement standards</strong> for the procurement of antibiotics and other pharmaceuticals. Such a practice is already underway in the EU and the UK</td>
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Back Up Slides
Our Processes to Prevent AMR

Combating AMR is a top priority at Centrient. We invested considerable resources in preventing AMR through our processes linked with AMR IA guidelines:

<table>
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<tr>
<th>Dedicated global and local technical teams</th>
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<tr>
<td>Mandatory sustainability requirements (AMR) and awareness campaigns.</td>
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<tr>
<td>Assessment of our sites against AMR IA Common Antibiotic Manufacturing Framework</td>
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<tr>
<td>Validated analytical method to measure antibiotic concentration in treated wastewater.</td>
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<td>SOP to monitor wastewater treatment plants for PNECs</td>
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<td>Periodical assessment of waste streams for potential risks</td>
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<td>Supply chain assessment via AMR survey, CAMF and PNEC</td>
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### PNEC Status - Manufacturing Network

Samples are filled monthly and tested quarterly

<table>
<thead>
<tr>
<th>Site</th>
<th>Product</th>
<th>PNEC Compliance</th>
<th>Compliance Point</th>
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<tbody>
<tr>
<td>Deretil</td>
<td>SSP</td>
<td>Compliant</td>
<td>Mixing Zone</td>
</tr>
<tr>
<td>Mexico</td>
<td>SSP</td>
<td>Compliant</td>
<td>Mixing Zone</td>
</tr>
<tr>
<td>Toansa</td>
<td>SSP</td>
<td>Compliant</td>
<td>End of Pipeline</td>
</tr>
<tr>
<td>Zibo (North &amp; South)</td>
<td>SSC</td>
<td>Compliant</td>
<td>Mixing Zone</td>
</tr>
<tr>
<td>Astral*</td>
<td>SSC &amp;SSP</td>
<td>Work under progress</td>
<td>Mixing Zone</td>
</tr>
<tr>
<td>Yushu</td>
<td># Intermediate</td>
<td>Compliant</td>
<td>Mixing Zone</td>
</tr>
<tr>
<td>Delft</td>
<td># Intermediate</td>
<td>Compliant</td>
<td>Mixing Zone</td>
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**Astral is new acquisition in India. Site is assessed and developing action list to be compliant.

# Intermediates are not considered as part AMR monitoring as per AMR IA guidelines. However, we developed our in-house limits for intermediates and test the samples regularly.
Key Drivers

- Proposed European pharma strategy dialogue.
- Procurement Environment

- Resolution in 2016 to combat AMR
- Davos declaration

- Draft standard & NGT order to CPCB
- Sky Blue & Biosafety
- Proposed environ aspect into GMP

Our Customers

Sustainable Mfg
National and State Action Plans to combat AMR in the environment: The journey so far

- Only 3 states and Delhi have formulated their State Action Plans.
- States having significant pharma footprint like Telangana, Himachal Pradesh, Gujarat etc., are yet to develop SAPs.
- In the absence of a national regulatory framework for monitoring of antibiotic residues, instances of antibiotic pollution are on the rise.

IIT Madras study finds pharmaceutical contaminants in Cauvery river water

Pharma pollution turns hazardous for Yadadri

Pharmaceutical pollution in rivers poses health risk, says study

India had the world’s second highest concentration of anti-diabetic APIs at 21,000 nanogram per litre, after Bolivia’s 25,400