Centrient and AMR
Join the fight
About us

We are a leading manufacturer of sustainable antibiotics

Founded in 1869 as the "Nederlandse Gist-en Spiritusfabriek", Dutch Yeast and Spirits Factory.

2700 employees worldwide work together to deliver cutting edge sustainable generics solutions.

Headquartered in The Netherlands, the group has operations in China, Europe, India, the Netherlands, Latin America.

We are owned by Bain Capital and operate at the center of modern healthcare.

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At a glance

• We are a leading manufacturer of beta-lactam antibiotics, and a provider of next generation statins and antifungals
• 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 high-quality products
• Our backward-integrated global manufacturing footprint ensures security of supply
Our global presence

Global mindset Solid support for regional units is provided by our corporate staff. This ensures global coordination, helping us to continually improve our products and services.

Local presence Four regional business units along with one global unit for finished dosage forms (Drug Products) are the cornerstones of our customer and supplier relationships. Together, these units span the entire globe. Individually, they are close and responsive to our valued partners.

Our people Our 2700 employees worldwide work together to deliver cutting edge generics solutions that help to keep customers ahead of the competition.
Our product portfolio – API & Finished Dosage Forms

<table>
<thead>
<tr>
<th>Active Pharmaceutical Ingredients</th>
<th>Finished Dosage Forms</th>
<th>Dosage form</th>
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</thead>
<tbody>
<tr>
<td>Semi-Synthetic Penicillins (SSP)</td>
<td>Amoxicillin</td>
<td>Capsules, hard</td>
</tr>
<tr>
<td>Purimox®</td>
<td></td>
<td>Dispersible tablets (DTA)</td>
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<tr>
<td>Puricillin®</td>
<td></td>
<td>Powder for oral suspension</td>
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<tr>
<td>Amoxicillin + Clavulanic acid</td>
<td></td>
<td>Film-coated tablets</td>
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<tr>
<td></td>
<td></td>
<td>Powder for oral suspension</td>
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<tr>
<td></td>
<td></td>
<td>Powder for oral suspension in sachet</td>
</tr>
<tr>
<td>Statins</td>
<td>Atorvastatin</td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Rosuvastatin</td>
<td></td>
<td>Film-coated tablets</td>
</tr>
<tr>
<td>Anti-Fungals</td>
<td>Nystatin</td>
<td>Powder for concentrate for solution for infusion</td>
</tr>
<tr>
<td></td>
<td>Caspofungin</td>
<td>Powder for concentrate for solution for infusion</td>
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- We manufacture an extensive assortment of generic beta-lactam antibiotics, statins and antifungals
- What sets us apart is our backward integrated manufacturing structure, which gives us complete control of our supply chain
Antimicrobial resistance

At Centrient we believe in creating a sustainable supply chain for pharmaceuticals and keeping antibiotics effective by fighting antimicrobial resistance.
Centrient’s Sustainability Strategy:
AMR as one of our three Pillars

Environment
- Reducing environmental impact

Health & Society
- Improving access to medicines and social impact

AMR
- Combating further spread of AMR (Sustainable Antibiotics)
Antibiotic resistance: Why does industry care?

No effective antibiotics = No modern healthcare

No effective antibiotics = No pharmaceutical industry
AMR is accelerated by the overuse and misuse of antibiotics, and pollution from irresponsible production

“The way that antimicrobials are produced, the by-products which result, and particularly the impact of effluent from factories on AMR, is an issue which has too often been neglected in discussions about AMR”

Source: AMR Review, May 2016

“...concerns are also growing about the impact of antimicrobial resistance on the environment and natural ecosystems due to overuse and discharge of antimicrobials and resistant micro-organisms in manure and waste from health care facilities and pharmaceutical manufacturing, commercial livestock and plant production, and fish and seafood farming”

Source: No Time To Wait: Securing The Future From Drug-resistant Infections, Interagency Coordination Group on AMR, April 2019
Antibiotic pollution associated with manufacturing is a significant cause for concern

“…some concentrations of pharmaceuticals we found in surface water samples were higher than the levels in patients that undergo treatment…”

Joakim Larsson, Professor in Environmental Pharmacology, University of Gothenburg

Irresponsible Manufacturing is contributing to AMR…

- Polluting factories with missing waste management dispose antibiotics into the environment, which can have toxic effects on living organisms and can create resistant bacteria by natural selection pressure.
- Inadequate waste treatment when waste is sent to collective treatment facilities where it is mixed with industrial and household waste, making an ideal breeding ground for Antibiotic Resistance.

…but an issue we can tackle!

Reference indications from the final report of the AMR Review, May 2016

- 30,000 – 70,000 tonnes of waste with antimicrobial activity need appropriate treatment. This does not always happen.
- ~200 antibiotic factories globally. 80-90% are located in China and India.
- Cost of treatment: 0.50 USD/kg API for appropriate waste water treatment.
Our Position: The industry should stop buying, using and selling irresponsibly made antibiotics

Companies to drive higher standards by reviewing their supply chains, and by pushing for mechanisms to improve transparency - via e.g. the PSCI, a ‘Quality Mark’ or serialization – so that environmental criteria for the manufacturing of antibiotics can be included in sourcing mechanisms.

Use clean technology available with lowest environmental impact throughout the supply chain

Operate dedicated wastewater treatment plants 24/7/365 at every antibiotic manufacturing site

Apply antimicrobial activity testing to ensure disposed water is clean

Good practice methods must be defined to reduce environmental impact of antibiotics manufacturing. Science-driven and risk based maximum discharge standards must be set and enforced.
AMR Combating Action at Centrient

Centrient has set up a robust and structured program at corporate and site level. It is reviewed, monitored by Board. This program is perfectly backed up by R&D, Operations and sufficient funds are allocated. It forms part of our CAPEX and OPEX proposals.

- **Waste Treatment**: Liquid and solid waste treated under a global synchronized protocol
- **Waste Water Treatment Plant**: Manufacturing sites equipped with WWTP
- **Development of AB Test**: DELVO™ test SP-NT is our in-house patented test for residual antibiotics
- **In House Specifications**: < 50 ppb, our WWTP capable of achieving*
- **Test before release to environment**: Residual AB contents validated, frequently tested, monitored & reviewed globally
- **Supply Chain Evaluation**: AMR assessment of suppliers conducted with AMA in their supply chain.
- **Cleaning of supply chain**: Aim to cleanse by 2020 as per PNEC limits.

<table>
<thead>
<tr>
<th>Our Advocacy Efforts</th>
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<tbody>
<tr>
<td>• Engagement with Government decision makers to create urgency for action</td>
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<tr>
<td>• Technical support and guidance to Government and regulatory bodies for drafting standards</td>
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<tr>
<td>• Working with independent technical experts to create push for research to fill critical gaps</td>
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<tr>
<td>• Media advocacy on impact of pharmaceutical pollution and the need for action</td>
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<td>• Promoting sustainable supply chain and improvement in quality and regulatory compliance through STEM (Sustainability through excellence in Manufacturing) trainings</td>
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<td>• Supporting initiatives such as Sustainable Health in Procurement Project (SHiPP)</td>
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Analytical results from our tests in Annexure
Local Industry Perspective: Challenges Manufacturers Face

- Demand for sustainably manufactured antibiotics needed to stimulate supply – Level playing field
- Major cost pressure exists along supply chains, no incentive to produce responsibly
- Lack of agreed upon standards/MRL for antibiotic residue in effluent
- Additional investment for upgradation and operation of treatment facility to remove AMA
- Need for lower cost testing methodology
- For manufacturers with ZLD, no clarity on whether future standards will apply
- “Where does responsibility end?” – Smaller players may not have ETP/ZLD and discharge effluent into CETPs or STP
Data Available for Research

Manufacturers will need to give consent for collection, analysis of samples and use of the data for research purpose

- Data on antibiotic residue levels from effluent samples (inlet, outlet)
- Information on treatment technology and process used
- Antibiotic residue levels from CETPs
- Antimicrobial activity in CETP and surrounding water bodies
- Resistance levels in water bodies around manufacturing units
- Global studies and agreed upon PNEC values – including evolving standards
- Data from Pollution Control Boards (online monitoring for pharmaceutical companies)
- Currently available testing methods – LCMS, HPCL
How Researchers can Engage/Work with Pharmaceutical Companies in India

- Need for research to support both sustainability in manufacturing and policy making pertaining to pharmaceutical industry to reduce AMR burden
- Antibiotic standards not too far in the future, need for industry to start preparing now to safeguard business and public health interest

| Research Support Needed for | 1. Limits on maximum levels of antimicrobials in the effluents discharged into the environment  
  | - Science based no-effect levels not available yet  
  | - Standards need to be enforceable  
  | - Researchers can support in methodology development, validation and pilot of standards  
| 2. Economic methods to eliminate antimicrobials and antimicrobial resistance genes from waste streams  
| 3. Economic, scalable testing and measurement tools that can be used for a variety of compounds  
  | - Per sample cost of HPCL and LC-MS too high for industrial use  
| 4. Development of newer antimicrobials  

As signatory to **UNGA Industry Roadmap**, committed to work with independent technical experts to establish science driven, risk-based targets for discharge concentrations for antibiotics and good practice methods to reduce environmental impact of manufacturing discharges, by 2020.
At the centre of modern healthcare
Thank you
Suman Sharma
suman.sharma@centrient.com
## Corporate Social Responsibility

<table>
<thead>
<tr>
<th>Themes</th>
<th>Project</th>
<th>Illustrations</th>
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</thead>
<tbody>
<tr>
<td>Health &amp; Sanitation (Swach Bharat Drive)</td>
<td>✓ 230 Bio toilets. 100% households in Toansa.</td>
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<tr>
<td></td>
<td>✓ Gymnasium</td>
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<td></td>
<td>✓ Medical Camps and running dispensary</td>
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<tr>
<td>Drinking Water</td>
<td>✓ Free Drinking water in 2 villages</td>
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<tr>
<td></td>
<td>✓ 69 Water filters</td>
<td></td>
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<tr>
<td></td>
<td>✓ 16 water coolers</td>
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<tr>
<td></td>
<td>✓ 2 Portable water tankers</td>
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</tr>
<tr>
<td>Educations</td>
<td>✓ Renovation of school buildings</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ 1250 Benches</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ 600 School Bags</td>
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<tr>
<td></td>
<td>✓ 10000 Note books</td>
<td></td>
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<tr>
<td>Environment</td>
<td>✓ Solar Lights</td>
<td></td>
</tr>
<tr>
<td></td>
<td>✓ 1200 Tree plantation</td>
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<td></td>
<td>✓ Creating awareness</td>
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**Touching more than 6000 Lives**
Toansa School, 22.04.19
Analytical Results

(A) Treated Water (Permeate from Reverse Osmosis Unit)
• COD : < 50 ppm
• TDS : < 200 ppm
• Antibiotic Contents : < 50 ppb

*Used in-house cooling towers, scrubbers & for Horticulture purpose*

(B) Incinerated Ash
• Calorific Value : < 500 Kcal/Kg
• Antibiotic Contents : < 50 ppb

*Being sent to PPCB approved facility for disposal*

(C) MEE Residue
• Calorific Value : < 1000 kcal/Kg
• Antibiotic Contents : < 50 ppb

*Being sent to PPCB approved facility for disposal*