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Antimicrobial Resistance Benchmark 2018

Guiding pharmaceutical companies to strengthen wastewater management

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HCWH Webinar | Multisectoral approaches to tackle Antimicrobial Resistance | 29 Nov 2018

The Access to Medicine Foundation

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- Research on, and incentives for, pharmaceutical companies and access to medicine
- Independent, non-profit organisation
- Multi-stakeholder approach

Ministry of Foreign Affairs of the Netherlands

UKaid

Bill & Melinda Gates foundation

Supported by Nationale Postcode Loterij
World's third-largest private charity donor

Ministry of Health, Welfare and Sport

What we do

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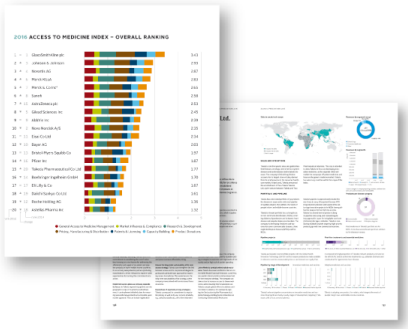
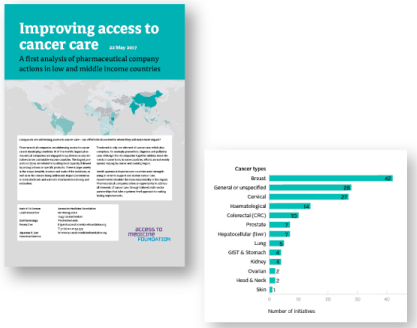
ACCESS TO MEDICINE INDEX



AMR BENCHMARK

ACCESS TO VACCINES INDEX

THEMATIC STUDIES



ADVANCING THE DEBATE

The Antimicrobial Resistance Benchmark

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- A new tool that assesses and compares what pharmaceutical companies are doing to limit AMR
- Fully independent from pharmaceutical companies
- Funded by the UK and Dutch governments

UKaid from the British people

Ministry of Health, Welfare and Sport

Launch of AMR Benchmark at WEF Davos 2018

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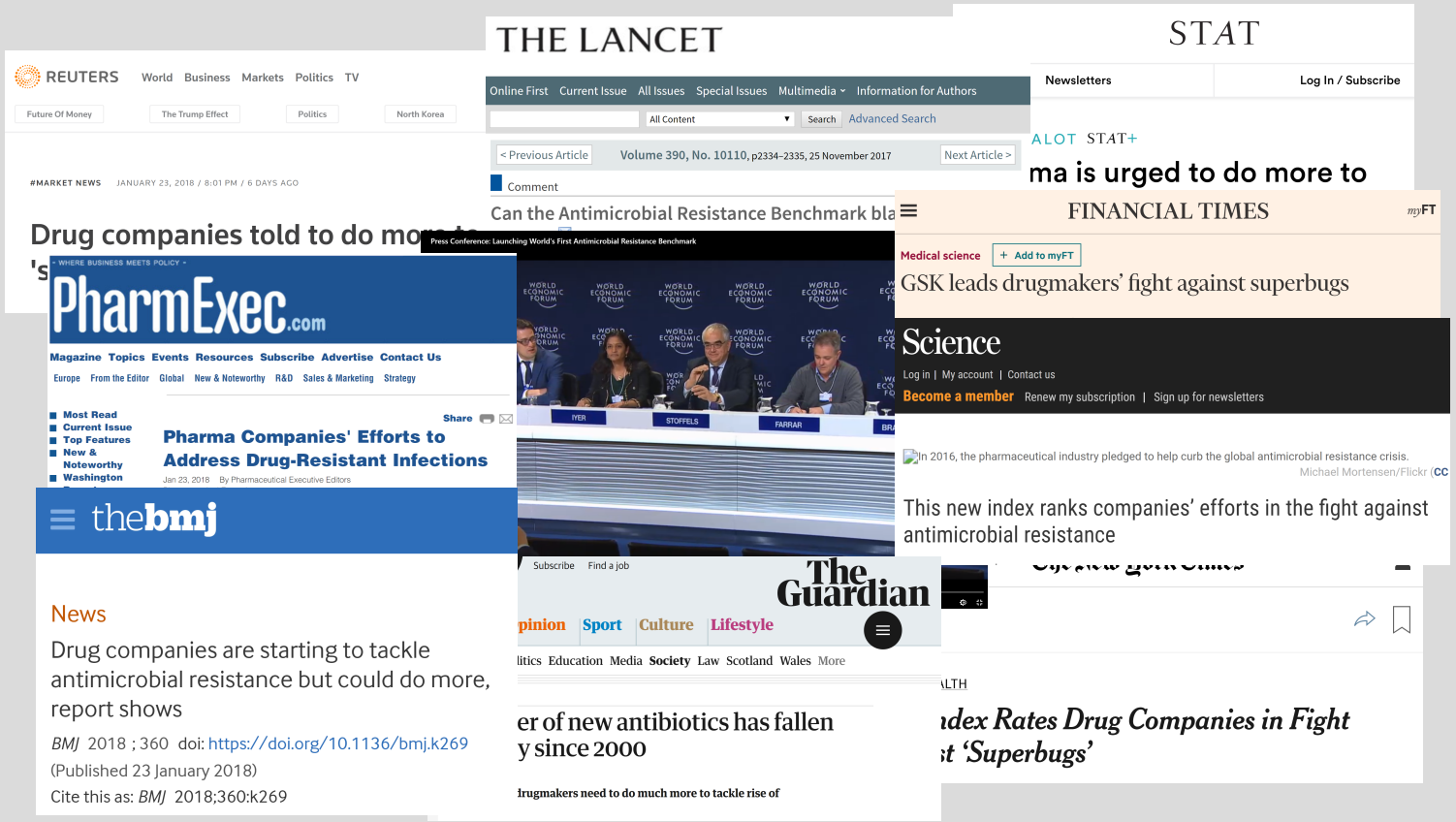

AMR Benchmark publication: 2-year cycle

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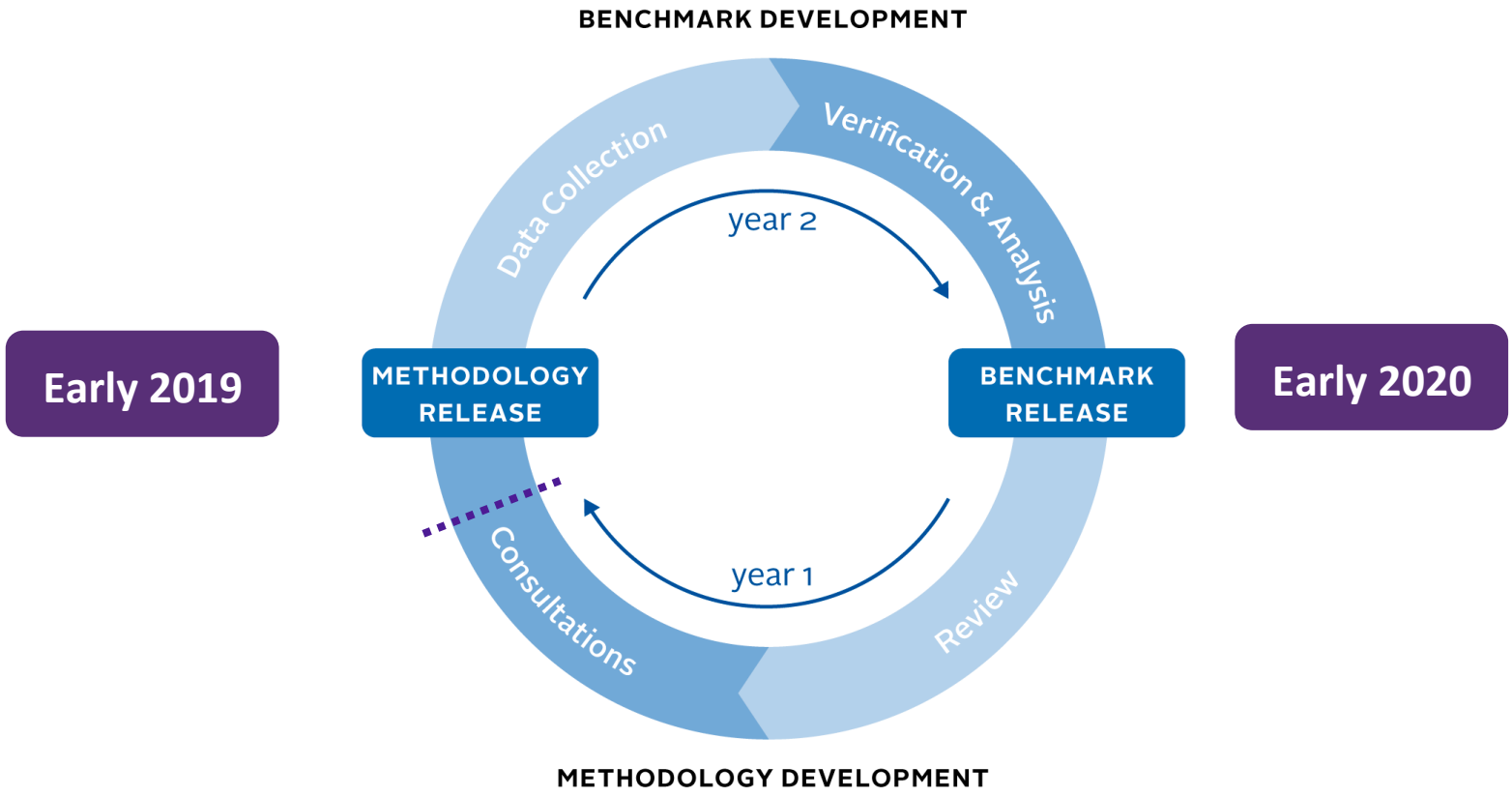

The AMR Benchmark guides and incentivises companies by

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…building consensus and clarifying responsibilities

…triggering positive competition

…enabling private sector accountability

…empowering internal decision-makers

…diffusing good practices

…unleashing pressure from investors

…supporting private sector participation in global health initiatives

The full report

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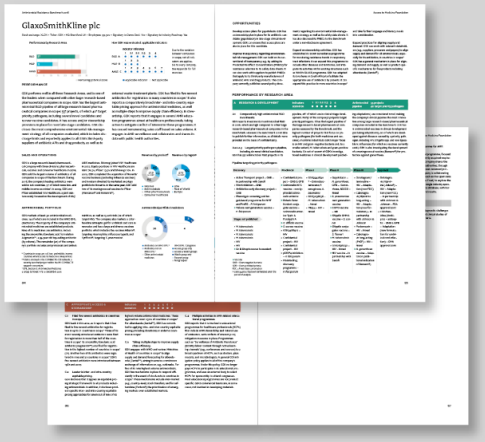

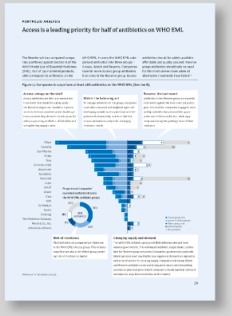

4 KEY FINDINGS

3 CASE STUDIES

1 PORTFOLIO ANALYSIS

1 PIPELINE ANALYSIS

30 COMPANY REPORT CARDS

30 companies across three sub-sectors analysed

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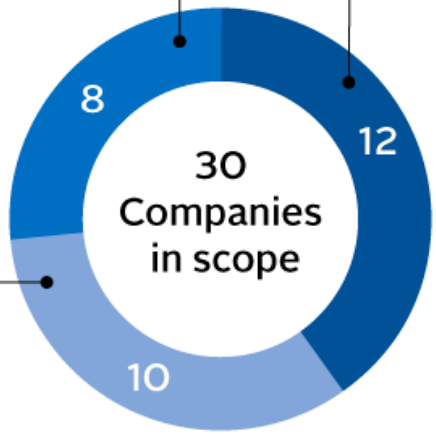
Large research-based pharmaceutical companies

GlaxoSmithKline plc
Johnson & Johnson
Merck & Co., Inc.
Novartis AG
Pfizer Inc.
Roche Holding AG
Sanofi
Shionogi & Co., Ltd.

Generic medicine manufacturers

Aspen Pharmacare Holdings Limited
Aurobindo Pharma Ltd.
Cipla Inc.
Dr. Reddy's Laboratories Ltd.
Fresenius Kabi AG
Lupin Limited
Macleods Pharmaceuticals Ltd.
Mylan NV
Sun Pharmaceutical Industries Ltd.
Teva Pharmaceutical Industries Ltd.



Biopharmaceutical companies with priority R&D projects

Achaogen Inc.
Cempra Inc.
Entasis Therapeutics Inc.
Melinta Therapeutics Inc.
MGB Biopharma
Motif Bio plc
Nabriva Therapeutics plc
Polyphor Ltd.
Summit Therapeutics
Tetraphase Pharmaceuticals Inc.
The Medicines Company
Wockhardt Ltd.

Source: Access to Medicine Foundation

Analytical framework: 3 Research Areas, 17 metrics

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A RESEARCH & DEVELOPMENT

- A.1 R&D Investments
- A.2.1 Pipeline size
- A.2.2 Novelty of pipeline
- A.2.3 Vaccines in pipeline
- A.3 R&D Collaborations
- A.4 Facilitating access and stewardship

B MANUFACTURING & PRODUCTION

- B.1 Environmental risk-management strategy
- B.2 Disclosure on environmental risk management
- B.3 Manufacturing high-quality antibiotics

C ACCESS & STEWARDSHIP

- C.1 Registration of antibiotics
- C.2 Pricing of antimicrobials
- C.3 Ensuring continuous supply
- C.4 Supporting educational stewardship activities
- C.5 Ethical promotional activities
- C.6 Brochure and packaging
- C.7 AMR surveillance
- C.8 Reducing uncontrolled use

Industry commitments: The Davos Declaration, 2016 (+100)

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"Commitments by signatory companies …

Work to reduce the development of antimicrobial resistance …

We support measures to **reduce environmental pollution from antibiotics**, along with a 'one health' approach towards prudent and responsible use, including a global reduction of unnecessary antibiotic use in livestock, and we applaud moves from major food groups to work towards this goal."

Industry commitments: The Industry Roadmap (13)

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i. **Review our own manufacturing and supply chains** to assess good practice in controlling releases of antibiotics into the environment.

ii. **Establish a common framework for managing antibiotic discharge**, building on existing work such as PSCI, and start to apply it across our own manufacturing and supply chain by 2018.

iii. Work with stakeholders to develop a practical mechanism to **transparently demonstrate that our supply chains meet the standards** in the framework.

iv. 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.

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Manufacturing & Production Company performance

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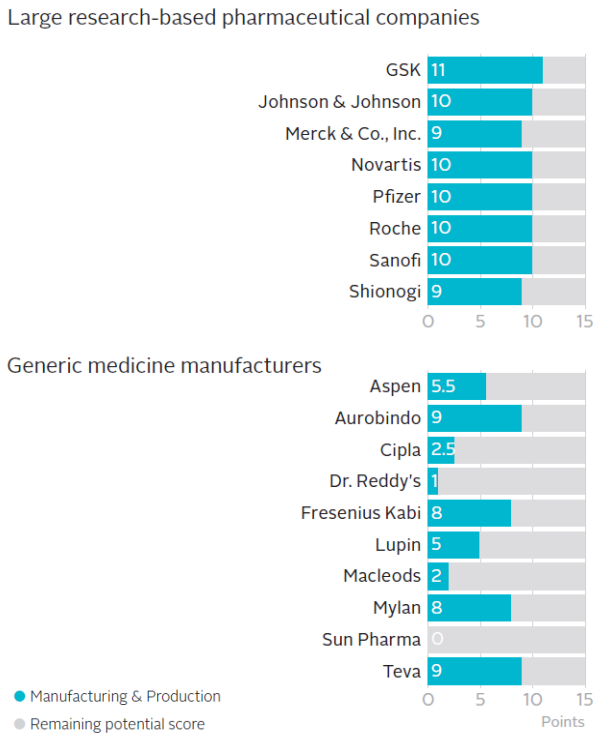
B MANUFACTURING & PRODUCTION

B.1 Environmental risk-management strategy

B.2 Disclosure on environmental risk management

B.3 Manufacturing high-quality antibiotics

Company performance



Environmental AMR risk-management strategies

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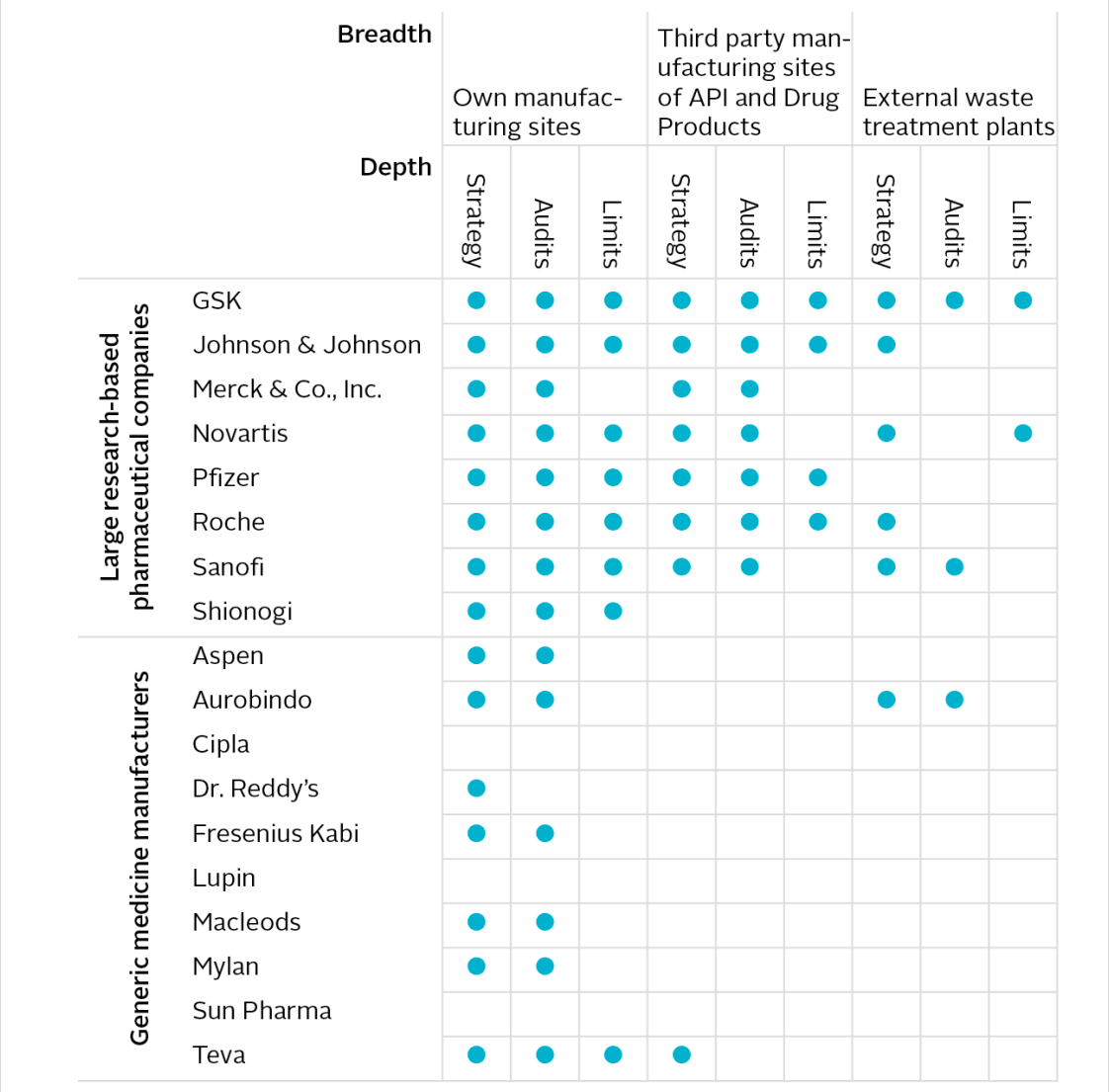

		Breadth	Own manufacturing sites			Third party manufacturing sites of API and Drug Products			External waste treatment plants		
		Depth	Strategy	Audits	Limits	Strategy	Audits	Limits	Strategy	Audits	Limits
Large research-based pharmaceutical companies	GSK		●	●	●	●	●	●	●	●	●
	Johnson & Johnson		●	●	●	●	●	●	●		
	Merck & Co., Inc.		●	●		●	●				
	Novartis		●	●	●	●	●		●		●
	Pfizer		●	●	●	●	●	●			
	Roche		●	●	●	●	●	●	●		
	Sanofi		●	●	●	●	●		●	●	
	Shionogi		●	●	●						
Generic medicine manufacturers	Aspen		●	●							
	Aurobindo		●	●					●	●	
	Cipla										
	Dr. Reddy's		●								
	Fresenius Kabi		●	●							
	Lupin										
	Macleods		●	●							
	Mylan		●	●							
	Sun Pharma										
	Teva		●	●	●	●					

Disclosure on environmental risk-management

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- 15/18 companies assessed have ERMS - 12 disclose strategies publicly
- 8 companies in scope report to have set limits for antibiotic discharge
- 4/8 require upstream suppliers of antibiotic APIs and drug products to adhere to same limits.
- Yet, no company discloses publicly its limits and/or the levels of antibiotic discharge.

Recent developments

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January 2018 | Common Antibiotic Manufacturing Framework

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UNITED AGAINST ANTIMICROBIAL RESISTANCE

COMMON ANTIBIOTIC MANUFACTURING FRAMEWORK

The Antimicrobial Resistance (AMR) Roadmap Companies recognize and understand concerns raised by stakeholders regarding the presence of pharmaceuticals in the environment (PIE). The major source of pharmaceuticals entering into the environment is via patient excretion following use of medicine that is taken to prevent, cure or alleviate a medical condition. A comparatively smaller contribution to PIE stems from emissions from industry during manufacture of the pharmaceuticals.[1]

While the overall contribution of pharmaceutical manufacturing to PIE is relatively low, there is the potential for localized impacts to be created in cases where manufacturing emissions are inadequately managed. Ensuring the use of appropriate environmental risk management measures to adequately control manufacturing effluent emissions remains an important area of focus for the pharmaceutical industry and is an approach already in place in a number of companies.[2] We are aligned in our intent and are ready to build and share common practices.

Reports of active pharmaceutical ingredients (APIs) in water from pharmaceutical manufacturing indicate concentrations have reached potentially harmful levels when wastewater discharges are not sufficiently controlled at some facilities,[3] highlighting the importance of effective control of API emissions from manufacturing, both in

"No untreated discharge of manufacturing waste containing antibiotic."

"Audit reports will remain confidential."

September 2018 | Recommended discharge limits

AMR Alliance Recommended PNECs for Risk Assessments

Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Amikacin	N/A	16	16
Amoxicillin	Testing On-Going	0.25	0.25
Amphotericin B	N/A	0.02	0.02
Ampicillin	0.87	0.25	0.25
Anidulafungin	N/A	0.02	0.02
Avilamycin	N/A	8.0	8.0
Azithromycin	0.02	0.25	0.02
Aztreonam	N/A	0.50	0.50
Bacitracin	100	8.0	8.0
Bedaquiline	0.08	N/A	0.08
Benzylpenicillin	N/A	0.25	0.25
Capreomycin	N/A	2.0	2.0
Cefaclor	N/A	0.50	0.50
Cefadroxil	Testing On-Going	2.0	2.0
Cefalonium	21	N/A	21
Cefaloridine	N/A	4.0	4.0
Cefalothin	N/A	2.0	2.0
Cefazolin	N/A	1.0	1.0
Cefdinir	N/A	0.25	0.25
Cefepime	N/A	0.50	0.50
Cefixime	0.18	0.06	0.06
Cefoperazone	N/A	0.50	0.50
Cefotaxime	0.10	0.13	0.10

(...)

Key takeaways

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Companies should:

- Implement recommended "PNEC-MIC" (or lower) limits for antibiotic discharge across their supply chain
- Move forward with practical ways to disclose more information about suppliers and levels of antibiotic discharge

Governments should:

- Consider explicit inclusion of environmental standards in GMP assessments
- Include "green criteria" into procurement of antibiotics

Academia should:

- Collaborate with governments to further refine evidence base for antibiotic discharge limits
- Collaborate with companies & governments in environmental surveillance and assessment of the human health impact of antibiotic discharges

Thank you

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