

6th Indian Pharmaceutical Forum

25/02/2021

Koen Laenen - Medicines For Europe
Senior Quality and Regulatory Affairs Manager

Medicines for Europe - Structure



The European Green Deal

#EUGreenDeal

Pharmaceuticals Regulatory tool

EUROPEAN
COMMISSION

Brussels, 11.3.2019
COM(2019) 128 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN
COUNCIL, THE EUROPEAN PARLIAMENT, THE EUROPEAN ECONOMIC AND SOCIAL



APOTEK



KÄPF



Stockholms läns landsting



Landstinget i



against
Antimicrobial



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Germany's AOK announces discount agreements for 119 drugs

By Tom Brockbank, Senior Consultant, Pricing & Market Access



- 1 15 November 2018
- 2 EMEA/CHMP/SWP/4447/00 Rev. 1
- 3 Committee for Medicinal Products for Human Use (CHMP)

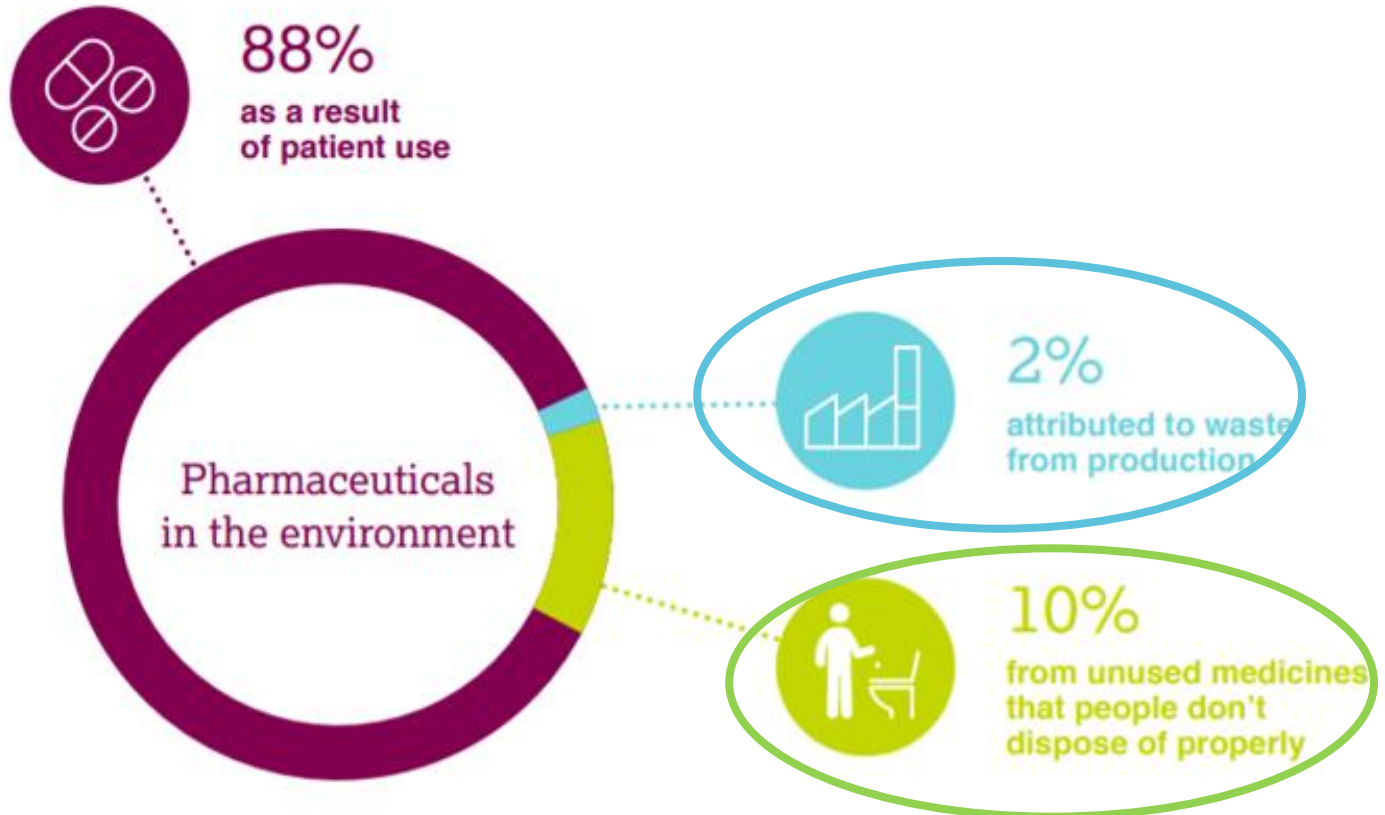
- 4 Guideline on the environmental risk assessment of medicinal products for human use
- 5
- 6 Draft

nability • partnership


Pharmaceuticals in environment

- Complex issue
- Limited information sharing and cooperation throughout the PIE chain => need for discussions and alignment
- New legislation is coming
- Measurement systems for PIE effects are compliant to current legislation, but not future proof => industry's concern on non harmonized approach to address PIE and different expectations might come from different regions in the world, while PIE and AMR are of global concern

Pharmaceuticals in environment



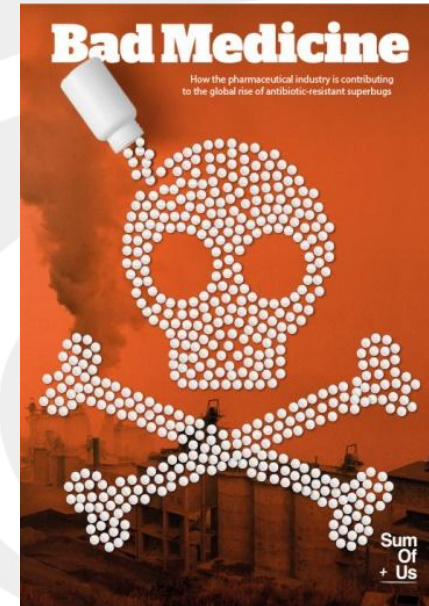
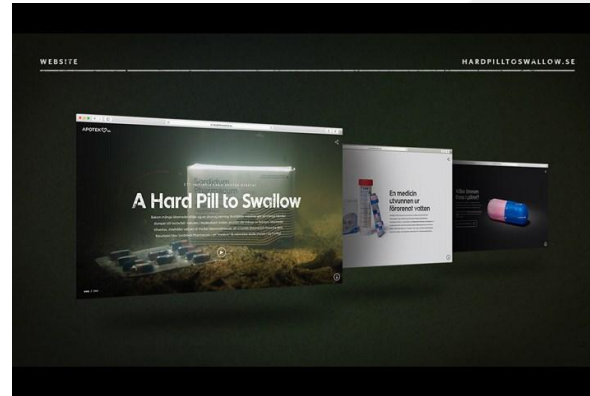
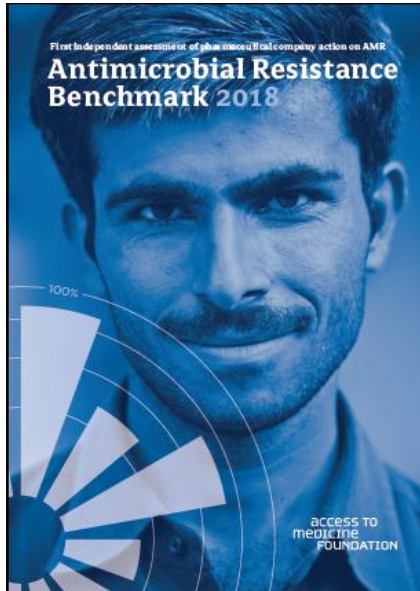
#medsdisposal is a campaign to **raise awareness** on how to dispose of **unused or expired medicines** appropriately in Europe, bringing information on current disposal schemes in European countries to one place.



Pharmaceutical waste (both human and veterinary) should be returned exclusively to community pharmacies. The outer box and paper leaflet should be removed and disposed of according to normal waste management schemes. This applies also to empty glass bottles and blisters. Used needles and sharps should be collected in a syringe container (for sale at community pharmacies) and should be collected in the municipal container park as biohazard waste

[Link : joint initiative on medicines take back in Belgium](#)

Manufacturing effluent management



Many stakeholder reports include manufacturing discharges as a pollution/AMR risk

Manufacturing effluent management

Representatives call for action on antibiotic resistance

Members of Congress are calling on the FDA to do its part in curbing antibiotic resistance by helping hold pharma companies responsible for pollution. It's been reported that drug manufacturers in India will sometimes dump antibiotics into surrounding waters, which can encourage the development and spread of drug-resistant bacteria. Representatives Louise Slaughter (D-NY), Peter DeFazio (D-OR), and Carol Shea-Porter (D-NH) have sent the FDA a letter urging the agency to work with its regulatory counterparts in those countries to make sure they're taking action. "Bacteria have no respect for national borders," they warn. "China and India's [problems] today can easily become our problems tomorrow"



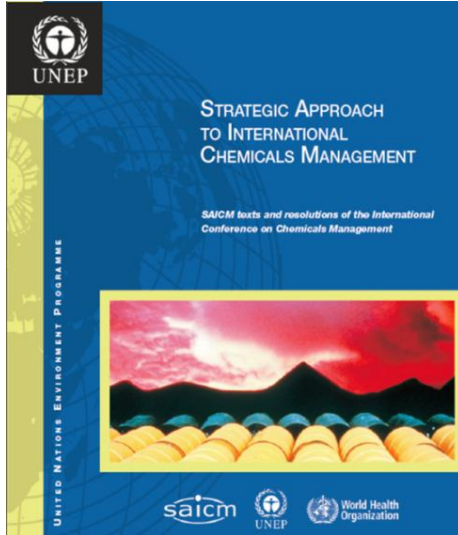
Brussels, 11.3.2019
COM(2019) 128 final

COMMUNICATION FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT, THE COUNCIL AND THE EUROPEAN ECONOMIC AND SOCIAL COMMITTEE

European Union Strategic Approach to Pharmaceuticals in the Environment

परिशिष्ट सं. सी.एल.- 33004/99

REGD. NO. D. L.-33004/99



India may formulate standards for pharma antibiotic residue

Malavika Yyambhara
malavika.yyambhara@indianbusiness.com

NEW DELHI: India could become one of the first countries to set standards for antibiotic residue in the pharmaceutical industry.

Antimicrobial resistance (AMR), refers to the ability of microbes like bacteria, viruses to resist the effect of antibiotics designed to kill them, making diseases caused by them very difficult if not impossible to treat.

The Central Drugs Control Board (CDCB) was tasked with framing the standards that remain to be approved by the environment ministry. "We will be one of the first countries to set such standards," a CDCB official said on the condition of anonymity.

anti-gambling laws on the lines of horse racing. Asked if this was a possibility, he said, "It is not in our purview to discuss such matters."

ations, licensing and brand-sharing agreements," it has said.

allowed for people who can afford it, it said.

Measles virus is a highly contagious virus. In India, as in many other countries, measles is a major cause of death among children. The virus is spread through the air.

India is a major producer of pharmaceuticals. The country's pharmaceutical industry is one of the fastest growing in the world. The industry is also a major source of pollution. The industry discharges large amounts of effluent into the environment. This effluent contains a variety of pharmaceutical residues, including antibiotics. These residues can be harmful to the environment and to human health.

counter availability of these drugs, and indiscriminate use of drugs in the poultry industry to keep the poultry healthy.

However, discharge of effluent from manufacturers of the antibiotics is an important source. Presence of antibiotic residues in high concentrations in the environment can lead to the development of AMR pathogens.

Pharmaceutical industries are considered one of the Grossly Polluting Industries (GPIs) in India. However, standards for antibiotic residues are rarely set, not part of the effluent standards for the industry. WHO has called for better management of pharmaceutical waste but a major challenge is the lack of clear consensus on what constitutes a safe level for antibiotic residues.

...and there are calls for Governments to act

सी.जी.-डी.एल.-अ.-27012020-215690
CG-DI-E-27012020-215690

असाधारण
EXTRAORDINARY
भाग II—खण्ड 3—उप-खण्ड (1)
PART II—Section 3—Sub-section (1)
प्रकाशित
PUBLISHED BY AUTHORITY

सं. 41] नई दिल्ली, बुधवार, जनवरी 23, 2020/भाग 3, 1941
No.41] NEW DELHI, THURSDAY, JANUARY 23, 2020/MAGHA 03, 1941

- ❑ In 2016 several manufactures within the Alliance committed to take key actions to help address risk
- ❑ Initially 13, primarily (not exclusively) large R&D pharma with antibiotic research
- ❑ Expanded to include more large generic pharma companies in 2018...and yet more companies in 2019/2020
- ❑ Medicines for Europe made manufacturing commitments for all the association members, irrespective of being member of the AMR IA.
=> important step as majority of produced and supplied antibiotics are off-patent

Manufacturing effluent management

AMR Industry Alliance publicly committed to:

- develop a Common Antibiotic Manufacturing Framework by 2018
- establish methodology and publish “predicted no effect concentrations” by 2020
- *work with stakeholders to develop a practical mechanism to transparently demonstrate that our supply chains meet the standards in the framework*

Manufacturing effluent management

Making antibiotics responsibly

A common manufacturing framework to tackle antimicrobial resistance



AMR Alliance Science-Based PNEC Targets for Risk Assessments

Active Pharmaceutical Ingredient	PNEC-ENV (µg/L)	PNEC-MIC (µg/L)	Lowest Value (µg/L)
Amikacin	N/A	16.00	16.00
Amoxicillin	0.57	0.25	0.25
Ampicillin	0.60	0.25	0.25
Avilamycin	125.00	8.00	8.00
Azithromycin	0.03	0.25	0.03
Aztreonam	N/A	0.50	0.50
Bacitracin	114.59	8.00	8.00
Bedaquiline	0.08	N/A	0.08
Benzylpenicillin	N/A	0.25	0.25
Capreomycin	N/A	2.00	2.00
Cefaclor	N/A	0.50	0.50
Cefadroxil	0.14	2.00	0.14
Cefalonium	21.10	N/A	21.10

- Review our own manufacturing and supply chains to assess good practice in controlling releases of antibiotics into the environment
- 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
- Work with stakeholders to develop a practical mechanism to transparently demonstrate that our supply chains meet the standards in the framework
- Work with independent technical experts to establish science-driven, risk-based targets for discharge concentrations

Manufacturing effluent management

Reporting Progress - 2nd Progress Report

- Access
- Research & Science
- Appropriate Use
- Responsible Manufacturing

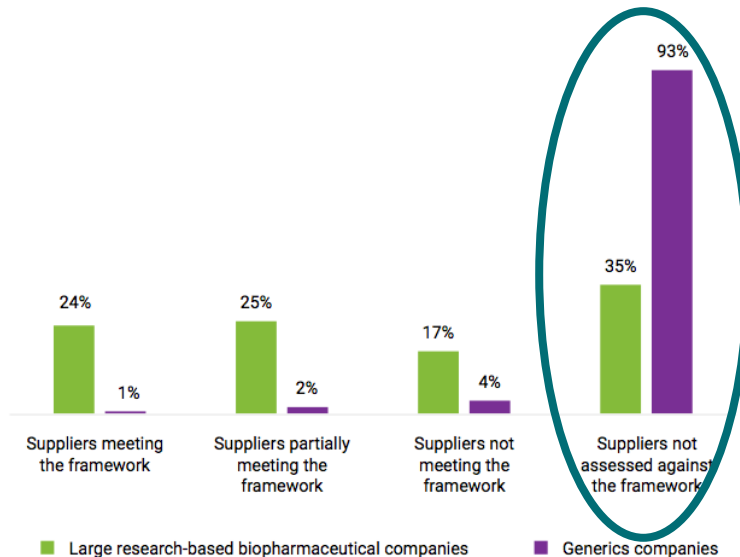


FIGURE 16: SUPPLIER PERFORMANCE AGAINST THE COMMON ANTIBIOTIC MANUFACTURING FRAMEWORK, BY SECTOR (TOTAL: 926 SUPPLIERS).*

Manufacturing effluent management

AMR Industry Alliance publicly committed to:

- develop a Common Antibiotic Manufacturing Framework by 2018
- establish methodology and publish “predicted no effect concentrations” by 2020
- *work with stakeholders to develop a practical mechanism to transparently demonstrate that our supply chains meet the standards in the framework*
- In 2020 the Alliance Manufacturing WG commenced a ~ 24 month project to engage an internationally recognized Standards body - the British Standards Institute - to:
 - 1) develop a Publicly Available Specification (PAS) - a consensus standard (based on the Alliance framework/PNECs) (by 2021)**
 - 2) Subject to agreement, develop a certification scheme (by 2022) - companies may choose to certify products against the standard (from 2023)**

PUBLIC AVAILABLE SPECIFICATION and CERTIFICATION SCHEME

What: Opportunity for greater assurance and transparency to buyers and stakeholders of antibiotics and meeting environmentally responsible manufacturing practices through an independent third party certification.

Why: Greater assurance and transparency for buyers and stakeholders, streamlined risk assessment for suppliers and customers. Bring a uniform and standardized solution irrespective of the location of production.

What: A Publicly Available Specification (PAS) or standard would define methodologies and protocols for auditing antibiotic manufacturing processes within a manufacturing facility, based on AMR IA manufacturing framework and PNECs

How: Use BSI to facilitate, highly respected organization known for their expertise in standards development and 3rd party certification. The focus would be on wastewaters and other waste streams that have the potential to enter the environment and contribute to AMR.

When: Timing could be 24 months to finalize standard and create certification scheme. Individual companies choose to certify: each antibiotic manufacturing process that meet the requirements of the PAS would be so certified.

What about other medicinal products?

Medicines play a **critical role** in ensuring a high level of **public health**, and we believe that political debates on PiE should not overlook the **value** that medicines bring to citizens.

As pharmaceuticals can enter the environment at all stages of the **product's life cycle**, reducing pharmaceuticals in the environment will be the result of **cooperation** between the public and private sector and the consumers they serve.

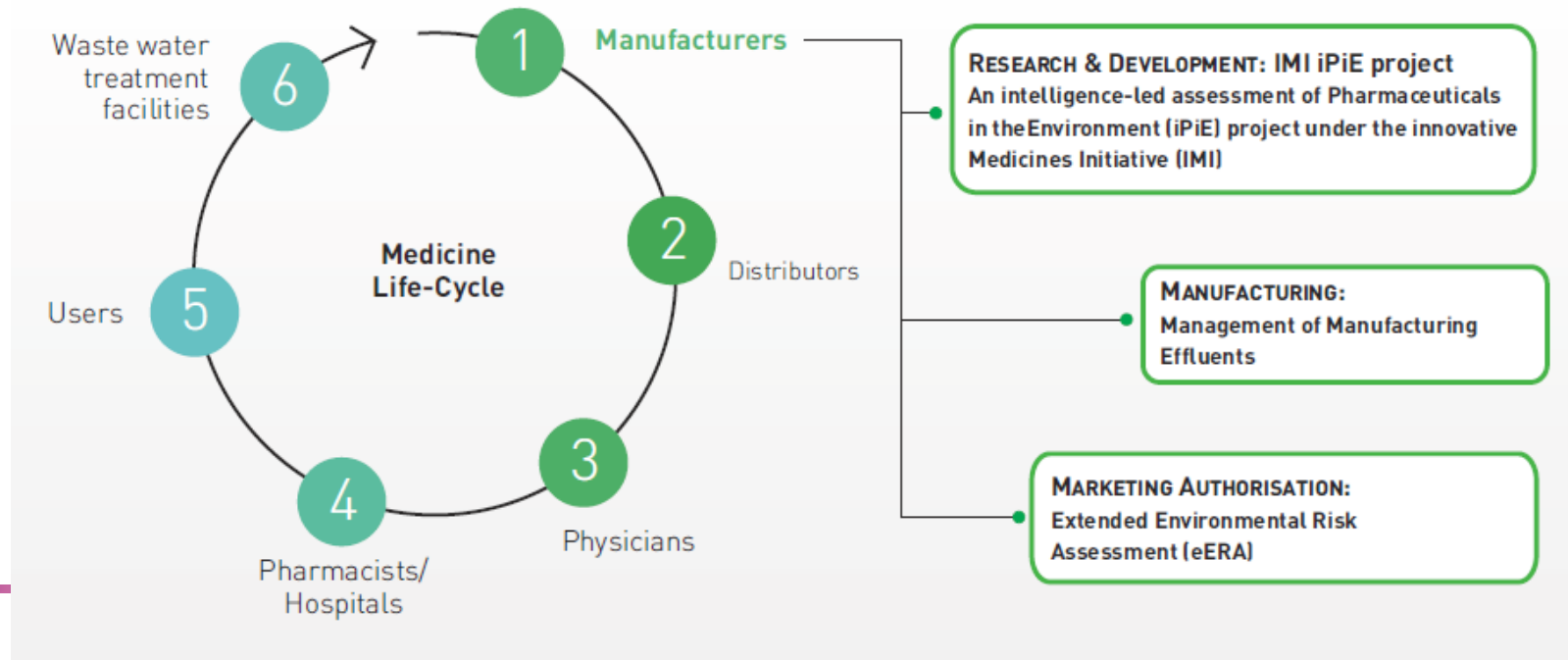
Therefore, all actions should strike the optimal **balance** between **economic costs** and the **benefit of medicines to public health**.

=> ENVIRONMENTAL CONCERNS SHOULD NOT OVERSHADOW PUBLIC HEALTH BENEFITS

This principle is very much part of the Eco-Pharmaco-Stewardship (EPS).

Eco-Pharmaco-Stewardship (EPS): a life-cycle approach

Objective: Provide knowledge and data to enable science-based assessments of the environmental sustainability of pharmaceuticals



iPIE project: Public-private partnership for improved prediction of the potential environmental risk of pharmaceutical substances (2015–2019)

- ✓ 13 pharma companies, 6 universities, 6 SMEs, 1 regulator
- ✓ Looking to develop tools to:
 - Predict environmental risk earlier in drug developed
 - Screen legacy APIs for environmental risk assessment
 - => 72% of APIs (419/581) screened have a PEC below EMA Phase I PEC Action Trigger of 10 ng/l

Follow-up research programme iPIE PREMIER

- ✓ Review feasibility of greener drug design/ development
- ✓ Develop an EU-wide environmental risk assessment database
- ✓ Implement iPiE tools for prioritisation of legacy APIs
- ✓ Perform intelligent testing and tailored assessment for 20–25 APIs of concern

Industry has been collaborating on pharmaceutical production effluents, their risk assessment and management

- ✓ Collated and compared data from different companies and sites
- ✓ Shared best practice
- ✓ Developed general guidance for effluent assessment and management, with modular maturity ladder concept. Guidance to be incorporated with existing procedures by manufacturers.
- ✓ Collaborating with PSCI and AMR Industry Alliance

Environmental Risk Assessment (ERA) for a new pharmaceutical according to EMA Guideline

- 1-2 years before patent expiration, check
 - ✓ use (sales) amounts in country with highest per capita use,
 - ✓ new in-house environmental or clinical data as well as robust scientific publications on environmental properties
- update existing ERA accordingly

Publish updated ERA prior to loss of exclusivity and give generics companies access to ERA data

- minimise duplication of animal tests,
- prevent multiple generic companies to invest into generation of ERA report
- improve consistency of ERAs,
- updated ERA based on actual use, not on default worst-case assumptions.

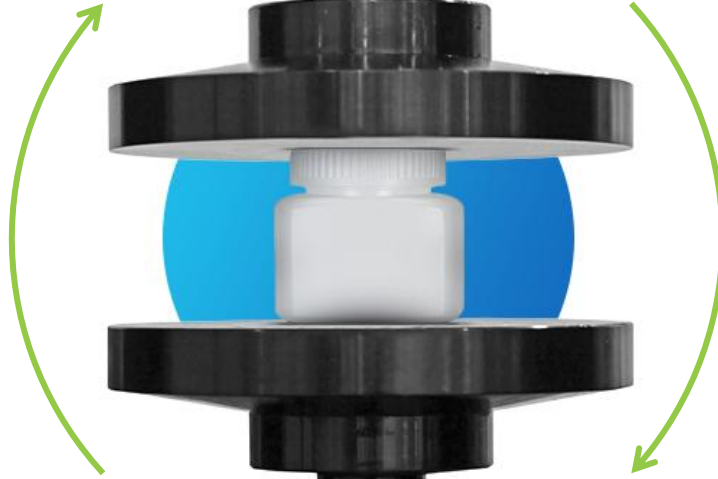
ABILITY TO SUPPLY
IS NEGATIVELY
AFFECTED BY

REGULATORY
COSTS AND
PRICE PRESSURE



REGULATORY
COMPLIANCE COST

- Environmental topics
- GMP / GCP / ...
- Variation Regulation
- PV regulation
- FMD



PRICE

- Pharmaceutical in environment is a complex issue
- PIE and AMR are global concerns and require to be addressed in an holistic approach
- Scientific and risk based approach needed, no blanket approach solutions possible
- AMR a priority topic requiring continued attention from all stakeholders, also pharmaceutical industry => extended engagement from pharmaceutical industry to AMR IA
- Industry as stakeholder very engaged in different aspect of PiE, engagement with policy makers and regulators will be needed to have a universal vision to address issue like manufacturing effluent management and environmental risk assessments.
- Payers need to be aware that price alone cannot be a winning criteria into tenders. Meeting current and future environmental criteria requires investments into manufacturing operations.
- Manufacturing continues to be sustainable, increased regulatory requirements are affecting the price of a product with some products at risk of zero margins

THANK YOU

klaenen@medicinesforeurope.com