

# What are pharmaceutical companies doing to tackle AMR?

Key findings and recommendations from 2018  
Antimicrobial Resistance Benchmark

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# The Access to Medicine Foundation

access to  
medicine  
FOUNDATION

- 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



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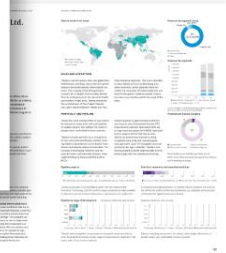
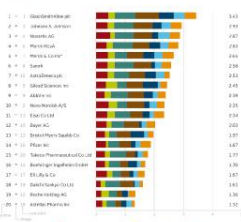
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# What we do

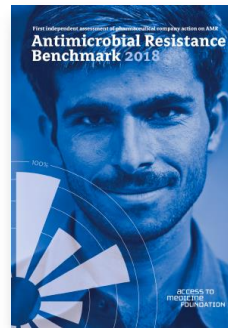
access to  
medicine  
FOUNDATION

## ACCESS TO MEDICINE INDEX

### 2016 ACCESS TO MEDICINE INDEX - OVERALL RANKING



## AMR BENCHMARK



### A RESEARCH & DEVELOPMENT

#### WHAT THIS AREA COVERS

The Benchmark will capture companies' R&D activities targeting infectious diseases. It will map R&D and reward efforts to target pathogens whose distribution and drug resistance makes them a priority target for R&D. It will also recognise companies that plan for the stewardship and accessibility of new products that target priority pathogens, following market entry.

### B MANUFACTURING & PRODUCTION

#### WHAT THIS AREA COVERS

The Benchmark will compare company strategies for limiting the impact of antibiotic manufacturing on resistance. It will assess how companies take antibiotic discharge into account in their manufacturing and environmental risk-management strategies. It will also ask how companies maintain the quality of their antibiotics.

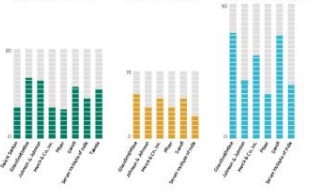
### C APPROPRIATE ACCESS & STEWARDSHIP

#### WHAT THIS AREA COVERS

The Benchmark will assess companies' access strategies for antimicrobial medicines in low- and middle-income countries, alongside their global stewardship strategies for antibiotics. The aim is to understand how companies approach these two challenges, including whether and how each company integrates these approaches.

## ACCESS TO VACCINES INDEX

### RESEARCH & DEVELOPMENT PRICING & REGISTRATION MANUFACTURING & SUPPLY

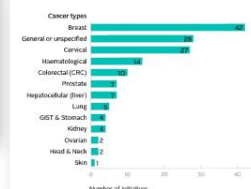


## THEMATIC STUDIES

### Improving access to cancer care

10 May 2017

A first analysis of pharmaceutical company actions in low and middle income countries

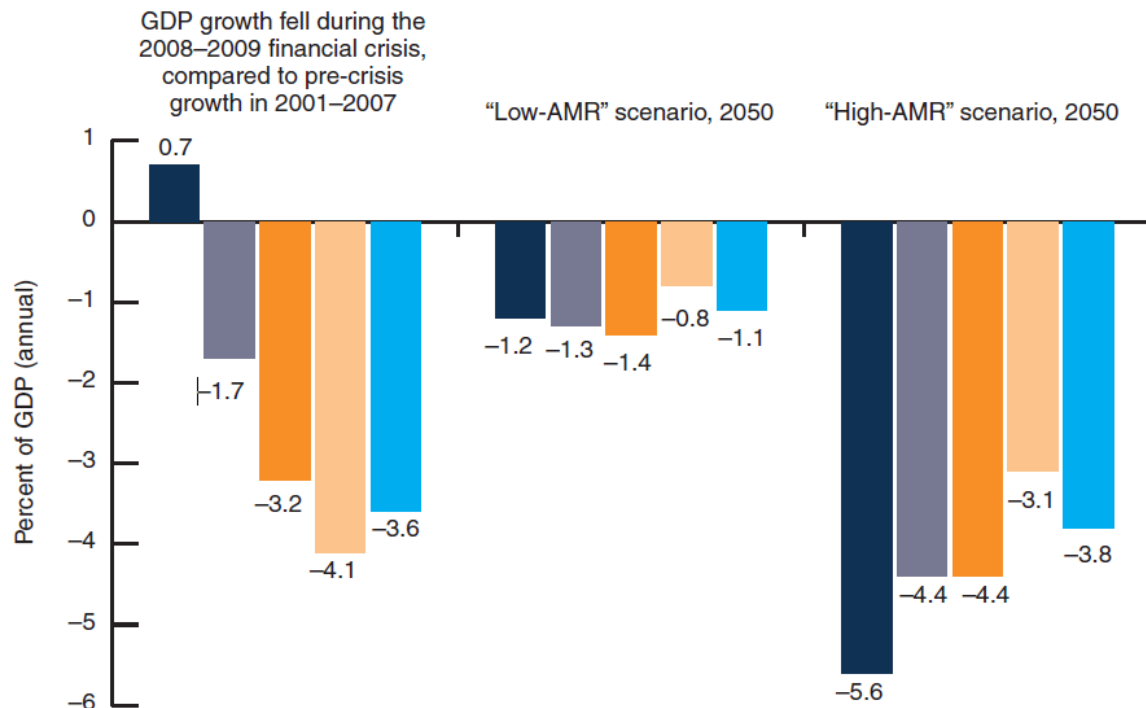


## ADVANCING THE DEBATE



# 2018 Antimicrobial Resistance Benchmark

# AMR affects LMICs the most



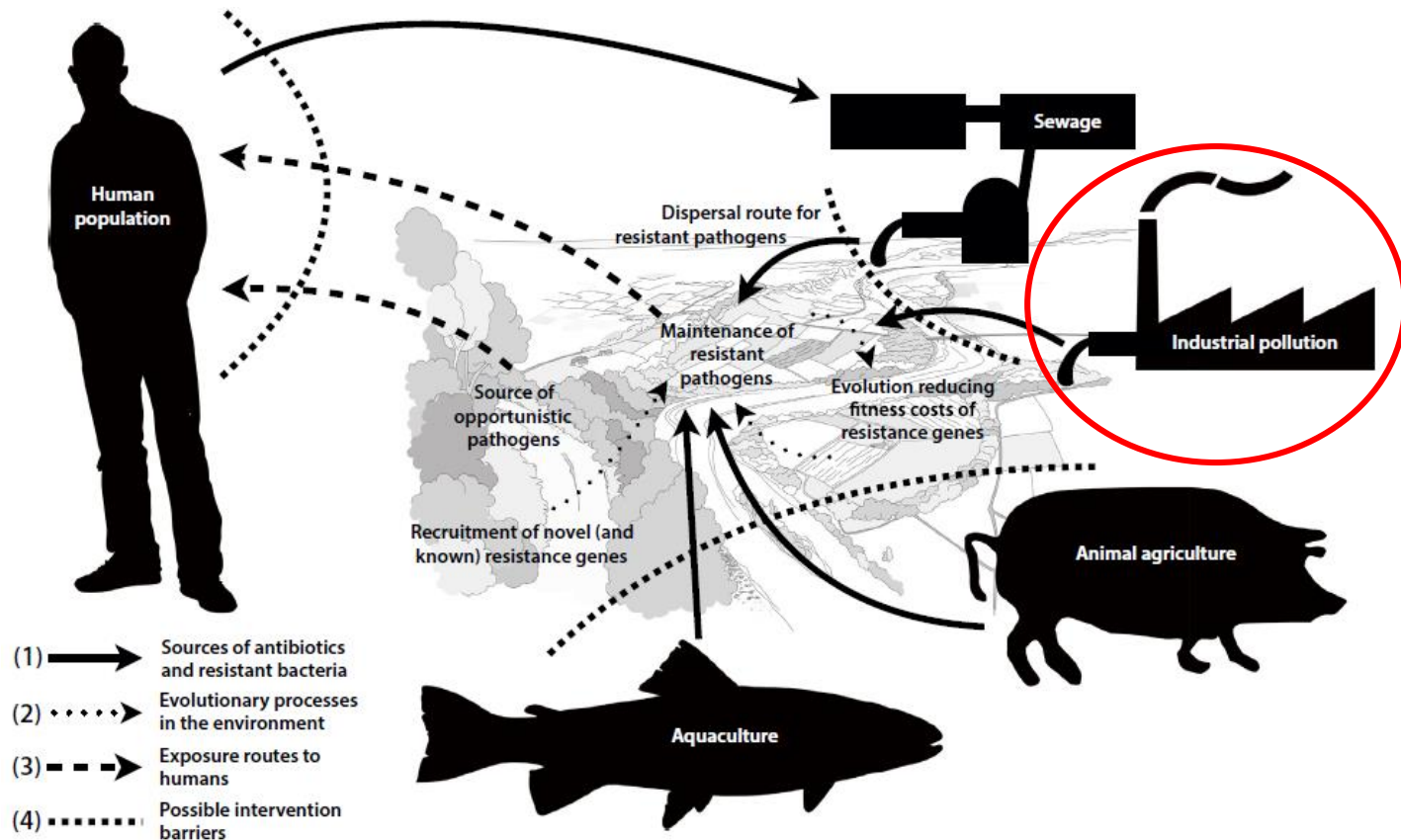
Country group: ■ Low-income ■ Lower middle-income ■ Upper middle-income ■ High-income ■ World

Source: The World Bank 2016



Source: REACT 2014

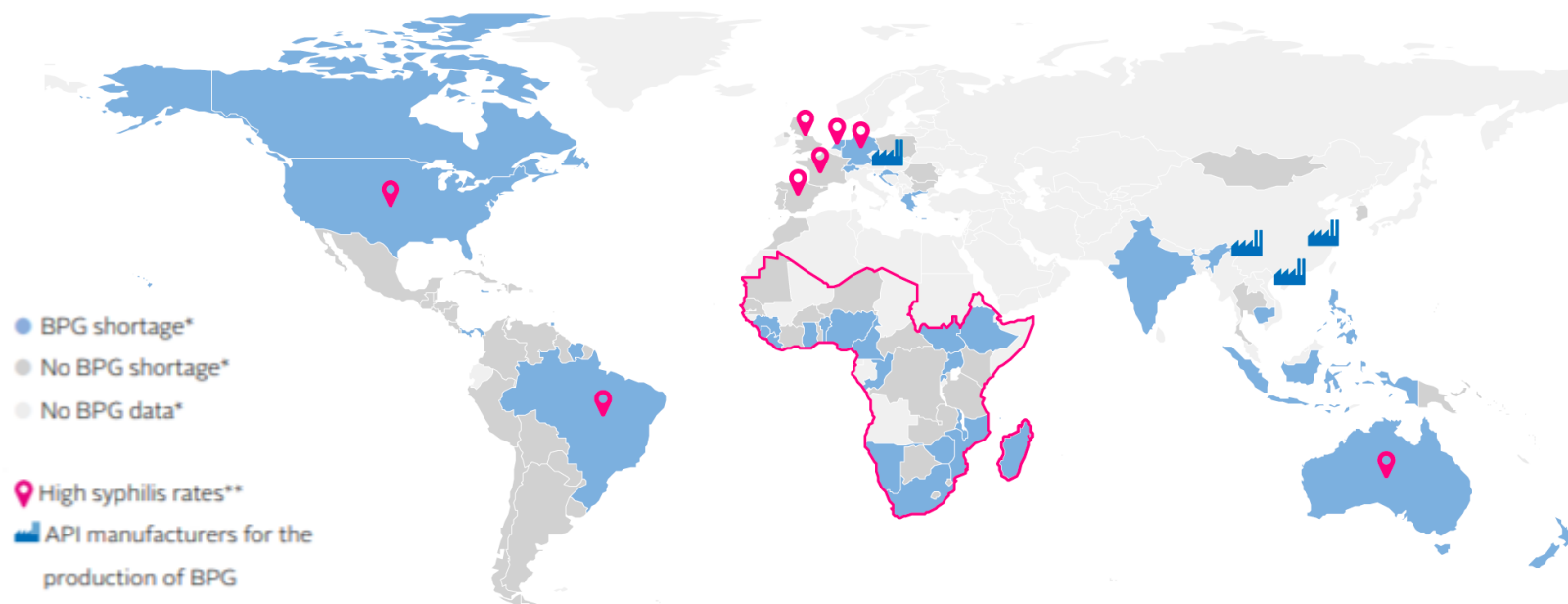
# Impact of environment on antibiotic resistance development



# Global penicillin shortage due to fragile antibiotic supply chain

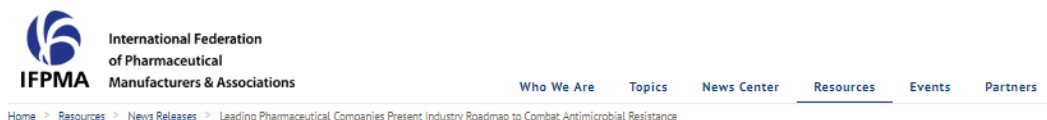
## Penicillin is now in scarce supply, because:

- Global need is high but mainly driven by resource-limited countries
- Penicillin G (BPG) offers little profit
- Supply chain is reliant on only four API manufacturers
- Production levels kept low



# Industry commits to tackle AMR

- Davos Declaration – January 2016
- Industry Roadmap for Progress on Combating Antimicrobial Resistance – September 2016



## Leading Pharmaceutical Companies Present Industry Roadmap to Combat Antimicrobial Resistance

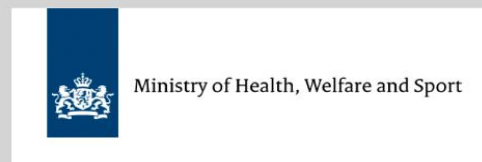
1. **Reduce the environmental impact from the production of antibiotics**, including a review of the companies' manufacturing and supply chains, and work with stakeholders to establish a common framework for assessing and managing antibiotic discharge;
2. **Help ensure antibiotics are used only by patients who need them**, recognizing this requires concerted efforts from many stakeholders, through continued provider and patient education, an examination of the companies' promotional activities, sharing of surveillance data with public health bodies and healthcare professionals, and collaboration with stakeholders to reduce uncontrolled antibiotic purchase;
3. **Improve access to current and future antibiotics, vaccines, and diagnostics**, including working with stakeholders to strengthen global health systems and address access bottlenecks; establishing new business models that balance access needs, appropriate antibiotic use, expanded vaccine coverage and adequate return to companies; and working to reduce the prevalence of substandard/counterfeit antibiotics in high-risk markets; and
4. **Explore new opportunities for open collaborations between industry and the public sector** to address challenges in the research and development of new antibiotics, vaccines, and diagnostics, recognizing the value these bring to society.





# The Antimicrobial Resistance Benchmark

- A new tool map how pharmaceutical companies are responding to the rise of antimicrobial resistance
- Fully independent from pharmaceutical companies
- Funded by the UK and Dutch governments
- Full report published in January 2018 at the WEF in Davos



# What the Benchmark does

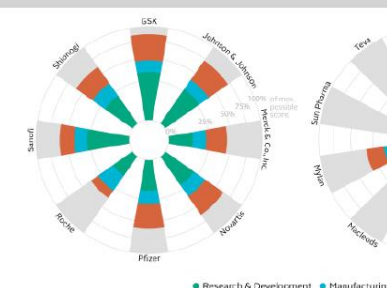
## BUILD CONSENSUS

On the role and responsibilities of pharmaceutical companies, to guide company action on AMR



## TRACK PROGRESS

Covering priority areas in R&D, Manufacturing & Production and Stewardship & Access



## DIFFUSE PRACTICES

Within companies, governments and investors.



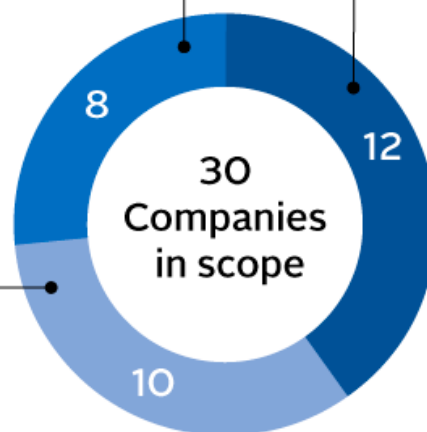
# 2018 Antimicrobial Resistance Benchmark: Company scope

## 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.

# 2018 Antimicrobial Resistance Benchmark: Metrics

## 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

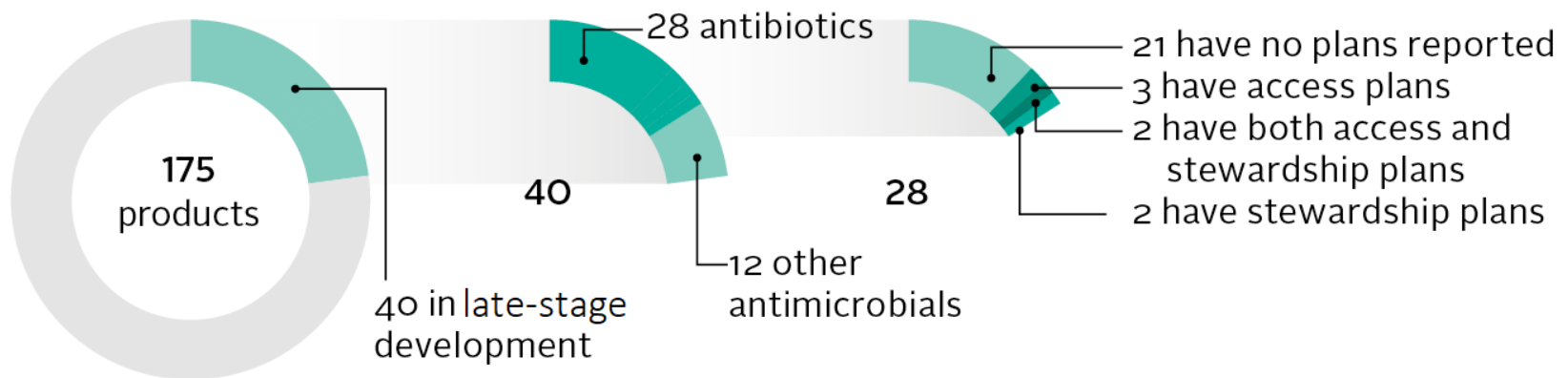
## SCOPES

<b>ANTIMICROBIALS PRODUCTS</b>	On-market medicines; and medicines and vaccines in R&D
<b>30 COMPANIES</b>	Pharmaceutical companies, generic medicine companies, biopharmaceutical companies
<b>INFECTIOUS DISEASES</b>	Bacteria, viruses, fungi, protozoa, helminths
<b>GEOGRAPHIC SCOPE</b>	Global

How is the pharmaceutical industry  
addressing AMR?

# Planning for appropriate access during R&D

- Out of 28 antibiotics in late stages of clinical development, only two have both access and stewardship plans in place.



- Contractual provisions are important to ensure that access and stewardship measures will be applied when a new medicine or vaccine reaches the market.

# Commitment to responsible manufacturing

## Industry Roadmap for Progress on Combating Antimicrobial Resistance – September 2016

The Davos Declaration<sup>1</sup> signed by >100 companies and trade associations in January 2016, called for collective action to create a sustainable and predictable market for antibiotics<sup>2</sup>, vaccines and diagnostics, that enhances conservation for new and existing treatments. It also called for coordinated action to improve prevention of infections, hygiene, stewardship, and conservation measures.

As a group of leading companies supporting the Davos Declaration, we welcome the continued high level political focus on Antimicrobial Resistance (AMR), including discussions at the UN, WHO, G7, G20, the AMR Review team's Final Report as well as regional and national debate. This work has established an ambitious, comprehensive agenda for the world and challenges each key stakeholder group to act and contribute to managing the threat of resistance.

The pharmaceutical industry recognises our responsibility and remains committed to playing a significant part in this long-term effort. Given the unique scientific, economic, public health and environmental challenges presented by AMR, collaboration between stakeholders is essential to maximise progress. We will continue to engage and partner with governments, global institutions, academia, prescribers and patients at global, regional and national levels. Resolving the complex economic challenges for the development, access and appropriate use of new antibiotics, vaccines and diagnostics remains of critical importance for us. It is necessary to attract sustained investment in developing new technologies to combat AMR.

As signatory companies of the Davos Declaration, we are committed to working to reduce the development of antimicrobial resistance, to invest in R&D and to improve access to high quality antibiotics and vaccines. These are ambitious goals, requiring new ways of working and investments of time, money and skilled people. This paper lays out a Roadmap for four key commitments on which the undersigning companies of this document will deliver, as applicable according to their different businesses and capabilities. Although work is underway on most aspects of the Roadmap, the precise end-points are not yet defined in all cases. These commitments therefore reflect our intent to proactively contribute to the fight against AMR, by developing and implementing solutions that will make a difference. We would welcome similar commitments from, and working collaborations with, other companies involved in combating AMR.

- 1) We support measures to reduce environmental impact from production of antibiotics, and will:
  - 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<sup>3</sup>, 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.

“Establish a **common framework for managing antibiotic discharge**, [...] 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** for antibiotics and good practice methods to reduce environmental impact of manufacturing discharges, by 2020.”



# Use of environmental risk-management strategies for responsible manufacturing

- Out of 18 companies assessed in this area, 15 have an **environmental risk-management strategy**. Of these, 12 disclose their strategies publicly.
- 8 companies report that they have **set limits for antibiotic discharge**.
- Yet, **no company discloses publicly its limits** and/or the levels of antibiotic discharge.

		Breadth			Depth					
		Own manufactur- ing sites			Third party man- ufacturing sites of API and Drug Products			External waste treatment plants		
		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	●	●	●	●					



# Improving access to antibiotics in LMICs

## Availability

- Registration
- Exclusive voluntary licensing
- Demand planning
- Local manufacturing

## Accessibility

- Affordability & equitable pricing strategies (e.g., cost margins cap, non-profit model)
- Supply chain strengthening

## Acceptability

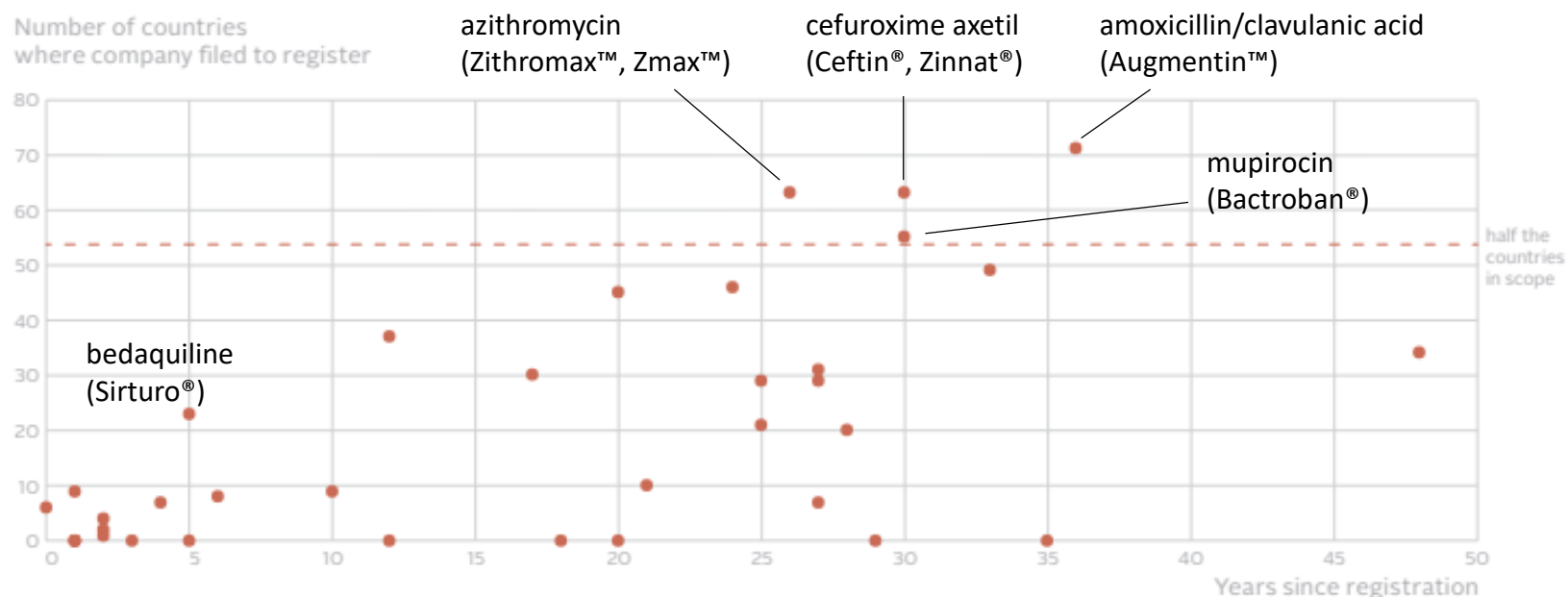
- Labelling adaptations respecting e.g. local languages
- (Taste-masked) paediatric formulations

## Quality

- WHO Prequalification
- Global Fund pre-qualification
- Prevention of substandard and falsified medicines

# Limited registration of new antibiotics

Four antibiotics have been filed for registration in more than half of the LMICs in scope



\* Introduction refers to the year of approval by the US FDA, EMA or Japan's PMDA or the year a product was introduced as reported by the company. Products were included in this analysis only where the year of their first global regulatory approval was reported.

# Enhancing conservation of antibiotics

- Educational stewardship activities
  - Through external organisations to mitigate conflict of interest
- Ethical promotional activities
  - Decoupling sales volumes from sales agents' bonuses
- Brochure & Packaging
  - Stimulating appropriate use of antibiotics
- AMR Surveillance
  - Tracking resistance trends

# Decoupling bonuses from sales volumes for antibiotics

## GSK

- Full decoupling
- All bonuses decoupled from sales volume
- Applies to all sales staff globally
- Changes made in 2013

## Shionogi

- Full decoupling
- Bonuses decoupled from antibiotic sales volume for all sales staff

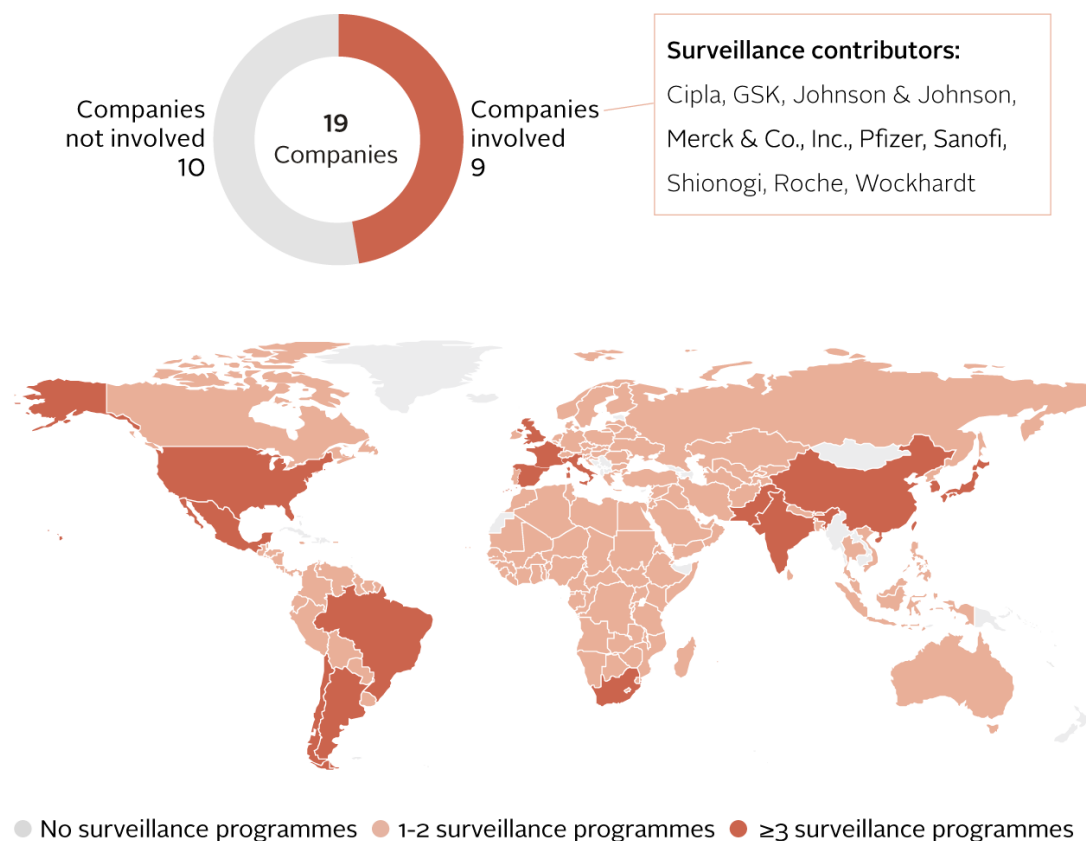
## Pfizer

- Pilot
- All bonuses decoupled from sales volume
- Applies to sales staff in selected geographies
- Starts in 2018

## Novartis

- Adjusting incentives
- Lowering % of bonuses linked to sales volume

# AMR surveillance: need for an harmonised approach



# Driving positive changes in the AMR landscape

## 1. R&D

- Incentives that spur new R&D
- Provisions can help to ensure appropriate availability to these treatments

## 2. Responsible manufacturing

- Define the evidence base necessary for consensus on antibiotic discharge limits
- Focus on environmental surveillance and assessment of the human health impact of antibiotic discharges
- Consider the explicit inclusion of environmental standards in GMP assessments
- Include green criteria into the procurement of antibiotics

## 3. Conservation of antibiotics

- Prevent over-the-counter sales
- Access to diagnostics
- Education and appropriate prescription guidelines
- Collaborate on the harmonisation of surveillance

# Questions?

Access to Medicine Foundation

[www.accesstomedicinefoundation.org](http://www.accesstomedicinefoundation.org)

[www.amrbenchmark.org](http://www.amrbenchmark.org)

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