Overall Performance

2020 2021

49% 46%▼

Merck & Co, Inc (MSD)

Large R&D-based pharmaceutical company

Stock exchange: NYSE • Ticker: MRK • HQ: Kenilworth, NJ, US • Employees: 74,000

PERFORMANCE

MSD performs below average overall in its evaluated Research Areas compared to the other large research-based pharmaceutical companies in scope.

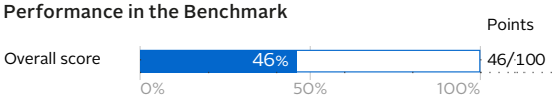
R&D: MSD is a middle-performing company in the R&D Research Area. Its 13-project pipeline has three vaccines. Three projects target critical and/or urgent pathogens. MSD has made a general commitment to expanding access to its products.

Responsible Manufacturing: Performs well. Reports environmental risk-management strategy for own sites and suppliers; quantifies discharge levels at own sites.

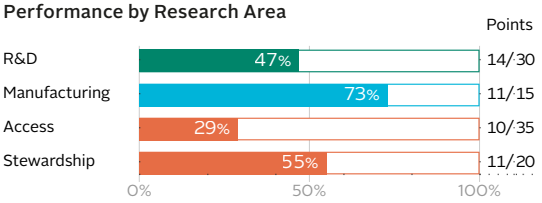
Appropriate Access: Performs less well. Discloses limited information on registration filings for its on- and off-patent products. Discloses some strategies to expand access and ensure continuous supply of its relevant product.

Stewardship: Middle-performing. It fully decouples incentives for sales agents from antibacterial sales volumes in the UK. It publicly shares aggregated results of its surveillance programmes. It reports broad conflict of interest mitigation for its educational programmes. It does not adapt brochures of packaging for patients.

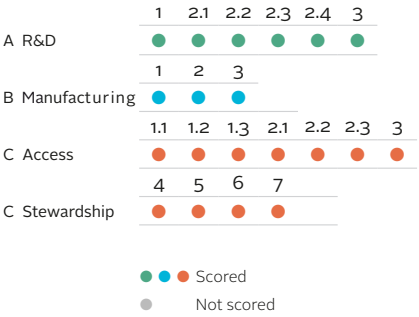
Performance in the Benchmark



Performance by Research Area



How Merck & Co was evaluated



OPPORTUNITIES FOR MSD

Develop and disclose project-specific plans to improve access and stewardship for R&D projects in late-stage development. MSD reports a commitment to expand access through broad registration, including in LMICs, and supports appropriate and responsible use of their antibacterial medicines. MSD can develop project-specific access and stewardship plans for all its late-stage R&D projects. For example, for its *S. pneumoniae* vaccine V116 it can commit to fast registration in countries with the highest burden of disease, and develop a pricing strategy that considers the ability to pay of target populations in those countries.

Expand its environmental risk-management strategy to suppliers and ensure compliance at all sites with antibacterial discharge limits by tracking and publicly disclosing progress and results. MSD reports to set limits and to quantify the discharge levels at its own sites. It can extend this practice to suppliers' sites and track compliance of both own and suppliers' sites with discharge limits and publicly disclose the results. To provide clear evidence of its progress, it can publicly report compliance at all sites. Disclosure of information, including the results of audits and antibacterial discharge levels of its own sites and suppliers' sites, is important. It can also publicly disclose the names and locations of its suppliers and waste-treatment plants for increased transparency.

Expand registration of medicines and vaccines to more access countries. MSD reports that ceftolozane/tazobactam (Zerbaxa®) was filed for registration in 25 access countries. It can file its antibacterial and antifungal medicines and vaccines (e.g. Zinplava™, Recarbio™ and Pneumovax 23®) in more countries, including low-income countries, with a high burden of disease. It can improve disclosure on where its medicines are registered and made available.

Fully decouple incentives for sales agents from sales volumes. MSD runs a pilot in the UK, in which it fully decouples incentives for sales agents from sales volumes of antibacterial medicines sold in UK hospitals. It can expand this practice to all countries it operates in and to all antibacterial and antifungal medicines.

Publicly share raw data from surveillance programmes. MSD runs multiple AMR surveillance programmes. It can publicly share raw data from these surveillance programmes: SMART, PACTS and STAR - anonymised and in a freely accessible format. Additionally, either MSD or the managing partners can publicly share raw data from the CANWARD and BSAC surveillance programmes.

CHANGES SINCE 2020

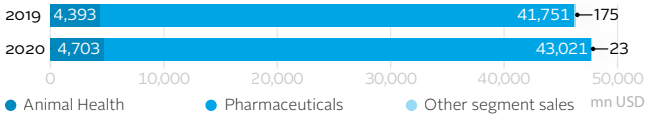
- In May 2020, MSD's technology and services provider ILUM Health Solutions combined with UPMC Infectious Disease Connect Inc. to share expertise and resources to enhance patient care, optimise antimicrobial therapy and reduce potential for drug resistance.
- In 2020, MSD expanded the functionality of the global SMART surveillance website, and it will put a mechanism in place for researchers to request access to anonymised raw data.

* All companies were assessed based on data submitted to the Benchmark in the current and previous periods of analysis, as well as information the companies have made publicly available, or that are accessible through other sources. For the 2021 Benchmark, MSD declined to submit data to the Antimicrobial Resistance Benchmark.

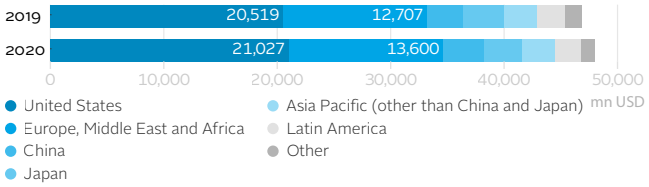
SALES AND OPERATIONS

Therapeutic areas: Cardiovascular, Diabetes, Hospital acute care, Immunology, Neuroscience, Oncology, Vaccines, Virology.
Business segments: Animal health, Pharmaceuticals
Product categories: Animal health, Innovative medicines, Vaccines
M&A since 2020: None in the antibacterial and/or antifungal sectors

Net sales by business segment



Net sales by region



PIPELINE *for pathogens in scope*

Pipeline size: 13 projects targeting pathogens in scope** (10 antibacterial medicines; 3 antibacterial vaccines).
Development stages: 2 clinical projects, including V116, a Phase II pneumococcal vaccine; and 7 discovery/preclinical projects.
Novelty: 0 novel clinical-stage medicine projects.
'Critical' and/or 'urgent' pathogens: 3 projects, relebactam/imipenem/cilastatin (Recarbrio™) targets carbapenem-resistant *Enterobacteriaceae*. It is active against *Klebsiella pneumoniae* carbapenemase (KPC), but not metallo-beta-lactamase (MBL)- producing *Enterobacteriaceae*. Fidaxomicin (Dificid®) targets *C. difficile*.
Regulatory approvals: 4 approvals. In July 2019, Relebactam/imipenem/cilastatin (Recarbrio™) was approved by the FDA for the treatment of complicated urinary tract infections (cUTI), including pyelonephritis, and complicated intra-abdominal infections (cIAI). In June 2020, Recarbrio™ received supplemental approval by the FDA for the treatment of hospital-acquired and ventilator-associated bacterial pneumonia (HABP/VABP) in adults. In January 2020, Fidaxomicin (Dificid®) paediatric adaptation was approved by the FDA. In July 2021, Vaxneuvance™, pneumococcal conjugate vaccine (15-valent) was approved by the FDA.

PORTFOLIO *for pathogens in scope*

Comparatively small portfolio: At least 19 products: 12 antibacterial medicines; 4 antibacterial vaccines; 3 antifungal medicines
On-patent medicines: 6 (bezlotoxumab, ceftolozane/tazobactam, fidaxomicin, imipenem/cilastatin/relebactam, posaconazole, tedizolid)
On-patent vaccines: 3 (Liquid PedvaxHIB®, Pneumovax® 23, Vaxelis®)
Off-patent/generic medicines: 7 of 10 were selected for analysis** (benzathine benzylpenicillin [A], caspofungin [F], clotrimazole/betamethasone [F], daptomycin [R], ertapenem [W], gentamicin [A], moxifloxacin [W])
AWaRe medicines*:** 2 Access group; 4 Watch group; 2 Reserve group

Pipeline for priority pathogens

Products on the market

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT Evaluated: medicine & vaccine pipelines for priority** bacteria & fungi

Pipeline targeting priority pathogens: 13 *As at 24 September 2021*

Discovery	Pre-clinical	Phase I	Phase II	Phase III	Approval
Protein synthesis inhibitor [*M. tuberculosis*]	♦ *Shigella spp.* vaccine		♦ *S. pneumoniae* vaccine adult (V116)	Sivextro® - additional population: paediatric [Gram positive bacteria]	♦ *S. pneumoniae* vaccine (Vaxneuvance™) [FDA/Jul-21]†
Partnership with Orchid Pharma, India - Bacteria & fungi	Compound screening ALIS (MOA) [*M. tuberculosis*]				Fidaxomicin (Dificid®) [*C. difficile*] [FDA: Jan-20]: additional population: paediatric
	ATP synthase inhibitor 1 mo GLP safety studies [*M. tuberculosis*]				Relebactam/imipenem/cilastatin (Recarbrio™) [*Enterobacteriaceae*] [FDA/Jul-19] cUTI, including pyelonephritis and cIAI
	In vivo preclinical PK/PD dose ranging project [*M. tuberculosis*]				[FDA/Jun-20] HABP/VABP
	Diarylquinoline (TBAJ-587) [*M. tuberculosis*]				

♦ = Vaccine
GLP = Good Laboratory practice
PK/PD = Pharmacokinetic/pharmacodynamic
cUTI = Complicated urinary tract infection
cIAI = Complicated intra-abdominal infection
HABP = Hospital-acquired bacterial pneumonia
VABP = Ventilator-associated bacterial pneumonia
† Approved after the end of the period of analysis.

** See Appendix V for information about eligibility for R&D projects and Appendix VII for eligibility criteria of products.
*** Listed on the 2019 WHO EML.

A.1 Investments in R&D

MSD does not disclose publicly, or to the Benchmark, its R&D investments during 2019 and 2020 in antibacterial and antifungal medicines and/or vaccines for pathogens in scope. MSD has pledged USD 100 mn to the AMR Action Fund over the next ten years.

A.2.1 Medium-sized pipeline

The company has 13 projects targeting pathogens in scope: 10 medicines and three vaccines, all targeting bacterial pathogens. Out of the 13 projects, two are in discovery stage, five are in preclinical development, two are in clinical development and four received marketing approval.

A.2.2 MSD extending indications for their antibacterials

MSD's clinical-stage medicine pipeline consists of both innovative and adaptive R&D projects. Relebactam/imipenem/cilastatin (Recarbrio™) received first marketing approval in July 2019 from the FDA for the treatment of complicated urinary tract (cUTI) and intra-abdominal infections (IAI). Recarbrio™ does not meet any of WHO's innovativeness criteria. MSD has three adaptive projects aiming, respectively, to extend the indications of fidaxomicin (Dificid®), relebactam/imipenem/cilastatin (Recarbrio™) and tedizolid (Sivextro®).

A.2.3 Three vaccine candidates

MSD reports three vaccine projects in its pipeline. It includes one innovative candidate in preclinical development targeting *Shigella spp.* and two adaptive vaccine candidates targeting *S. pneumoniae:* V114 and V116.

A.2.4 Two candidates targeting critical and/or urgent priorities

MSD has two medicines in its R&D pipeline targeting pathogens defined as 'critical' by WHO's list of priority pathogens and/or characterised as 'urgent' threats by the US Centers for Disease Control and Prevention (CDC). Relebactam/imipenem/cilastatin (Recarbrio™) targets carbapenem-resistant *Enterobacteriaceae*, and fidaxomicin (Dificid®) targets C. *difficile*.

A.3 General commitments towards expanding access and affordability practices

MSD does not report any specific access or stewardship plans for any of its six late-stage medicine and vaccine projects targeting pathogens in scope. Four out of six projects have ongoing clinical trials in access countries.‡ The company has made a general commitment about registering its products in LMICs, expanding access through broad registration and improving affordability. MSD supports the appropriate and responsible use of its antibacterial and antifungal medicines by supporting hospitals globally to strengthen their AMS programmes.

B RESPONSIBLE MANUFACTURING Evaluated: antibacterials manufacturing (APIs and drug products)

B.1 Environmental risk-management for own sites and suppliers; sets limits at own sites and suppliers

MSD reports a strategy to minimise the environmental impact of wastewaters and solid waste from antibacterial manufacturing at its sites, including audits at least every 1-2 years. It reports setting discharge limits in the receiving environment for all antibacterials manufactured at its sites, based on PNECs to limit AMR, as recommended the AMR Industry Alliance. It also reports quantifying discharge levels but there is no information on the methods used and compliance with set limits.

MSD requires third-party suppliers of antibacterials to follow similar standards, including on-site audits and limits based on PNECs. There is limited information whether it requests and reviews the discharge levels of its suppliers.

MSD expects external private waste-treatment plants to comply with its general environmental standards. It reports auditing external private and public waste-treatment plants but no details on audit parameters are provided. It also does not report whether conservative measures for effluents sent to external public wastewater plants are employed.

B.2 Publicly discloses some information on environmental risk management and commitment to setting limits

MSD publishes some components of its environmental risk-management strategy. It is a member of the AMR Industry Alliance, which publishes a list of recommended antibacterial discharge targets. MSD publishes its commitment to setting these targets. It does not publish: (1) the results of environmental audits, whether conducted at its own sites, the sites of suppliers or external private and public waste-treatment plants; (2) a list of these suppliers and plants; or (3) the levels of antibacterial discharge from its own or suppliers' sites.

B.3 System in place to maintain production quality for own and suppliers' sites; no requests for official corrective action

MSD reports that its own sites and suppliers have a system to maintain high-quality antibacterial production, consistent with international GMP standards. This includes risk-based internal audits and tracking of corrective and preventive actions. It also requires its suppliers to audit their own suppliers. The Benchmark found no requests for official corrective action from the FDA or EMA related to non-conformities with cGMP at MSD's own sites or any subsidiaries that manufacture antibacterials.

C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS

Evaluated: access activities relating to antibacterial & antifungal medicines & vaccines in 102 access countries‡

C.1.1 Limited information on registration filings for on-patent medicines

MSD performs below average as it does not disclose where it has filed five of its six relevant on-patent medicines for registration. However, it publicly reports that its on-patent medicine, ceftolozane/tazobactam (Zerbaxa®), a reserve antibiotic used to treat intra-abdominal infections, acute pyelonephritis, cUTIs and hospital-acquired pneumonia, was filed for registration in 25 LMICs.

C.1.2 Limited information on registration filings for off-patent/generic medicines

MSD's performance is low. It reports no evidence of filing its seven relevant off-patent/generic medicines for registration in access countries.

C.1.3 No information on registration filings for on-patent vaccines

MSD reports no evidence of filing its three relevant on-patent vaccines for registration in access countries.

C.2.1 Limited information on strategies to expand access to on-patent medicines

MSD performs below average. It expands access to its on-patent medicines in access countries through differential pricing and public or private partnerships and publicly commits not to enforce patents in low-income countries. MSD does not provide evidence of patient reach and geographic reach in low- and middle-income countries.

C.2.2 Limited information on strategies to expand access to off-patent/generic medicines

MSD's performance is low as it discloses limited information on how it expands access to its seven relevant off-patent/generic medicines. It publicly reports to expand access through differential pricing and public or private partnerships with governments, NGOs and distribution channels. MSD does not provide evidence of patient reach and geographic reach.

‡ 102 low- and middle-income countries where better access to medicine is most needed.

C.2.3 Limited information on strategies to expand access to on-patent vaccines

MSD performs below average as it discloses limited information on how its expands access to its on-patent vaccines in access countries. It publicly discloses having differential pricing and intellectual property policies, and participating in public or private partnerships. To set the price of its vaccines, MSD takes into account the level of economic development, the channel of distribution and the public health needs. It has inter- and intra-country pricing strategies to allow for price flexibility. MSD publicly commits not to enforce patents in low-income countries. MSD does not provide evidence of patient reach and geographic reach for its strategies.

C.3 Limited information on strategies to ensure continuous supply

MSD has an average performance. It publicly reports to ensure accurate demand planning and commits to maintaining a reliable supply of its medicines and vaccines. MSD has supply agreements with local manufacturing partners to allow for local production of its vaccine. To mitigate against substandard and falsified products, MSD uses security features, has a dedicated anti-counterfeiting team in place, and raises public awareness.

C APPROPRIATE ACCESS & STEWARDSHIP – STEWARDSHIP

Evaluated: stewardship activities relating to antibacterial & antifungal medicines globally

C.4 Broad COI mitigation strategies in place for its educational programmes

MSD performs well in the analysis of its top five AMR-related educational programmes for healthcare professionals in conflict of interest (COI) mitigation. To mitigate COI for three programmes, it provides financial resources to independent third parties (CIDEIM, BSAC and the University of Dundee) to develop the programme. One programme (developed by the company) has all three COI mitigation strategies looked for by the Benchmark: (1) content is developed by a third party independent from the company's own marketing department; (2) participants are not provided financial or material incentives (as it is a website); and (3) it does not use branded materials. The remaining programme has one COI mitigation strategy: it is unclear whether content is developed independently from its marketing department or whether it uses branded materials.

C.5 Engages in sales and marketing practices to address appropriate use

MSD performs above average in sales practices. It started a pilot in 2019 where it does not reward its sales agents based on antibacterial volumes sold in UK hospitals. However, outside of this pilot MSD does not report whether it decouples incentives for sales agents from sales volumes to help prevent the inappropriate use of its antibacterial and/or antifungal medicines.

MSD engages in marketing practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines. Its marketing materials reflect emerging resistance trends and/or include treatment guidelines for healthcare professionals: it has developed its Star of Stewardship principles in which all marketing materials must include, e.g. specific indications, treatment duration and dose.

C.6 Does not report adapting brochures and/or packaging to facilitate appropriate use by patients

MSD does not report adapting brochures and/or packaging to facilitate the appropriate use of its antibacterial and/or antifungal medicines by patients.

C.7 Active in multiple AMR surveillance programmes; openly publishes aggregated results

MSD is active in multiple AMR surveillance programmes. It runs the multinational SMART programme, which is focused on respiratory infections and complicated intra-abdominal and urinary tract infections in 63 countries and has been running since 2002. MSD only shares the aggregated results through peer-reviewed open-access journal articles as well as on the online SMART database, a restricted data platform. Additionally, it is planning to make anonymised source data available for researchers upon request through the SMART database. For the remaining programmes, only the aggregated results are shared through peer-reviewed open-access journal articles, as well as on an open-access data platform for the CANWARD programme (a national programme managed by the Canadian Antimicrobial Resistance Alliance).