Merck & Co, Inc

Large R&D-based pharmaceutical company
Stock exchange: NYSE • Ticker: MRK • HQ: New Jersey, USA • Employees: 69,000

**PERFORMANCE**

Merck & Co, Inc is middle-performing in its evaluated Research Areas when compared to other large R&D-based pharmaceutical companies in scope.

**R&D:** Middle-performing. Pipeline consists of 12 projects for medicines and vaccines for priority pathogens. It has commitments to expanding access and affordability and is active in intellectual capital sharing.

**Responsible Manufacturing:** Performs well. It has a comprehensive environmental risk-management strategy for own sites and suppliers, however reports less information than the leaders on the progress in the implementation of discharge limits.

**Appropriate Access:** Performs less well. Discloses limited information on where it registers its relevant products. It partners with organisations including Association Africaine des Centrales d’Achats de Médicaments Essentiels (ACAME) and Developing Countries Vaccine Manufacturers Network (DCVMN) to ensure continuous supply.

**Stewardship:** Middle-performing. It has educational programmes with broad conflict of interest (COI) mitigation. It is involved in multiple surveillance programmes and publicly shares results. It does not report adapting its brochures and/or packaging to facilitate appropriate use.

**SALES AND OPERATIONS**

**Therapeutic areas:** Cardiovascular diseases; Diabetes; Infectious disease; Oncology; Women’s health

**Business segments:** Animal Health; Pharmaceuticals

**Product categories:** Animal health; Innovative medicines; Vaccines

**Manufacturing & supply:** No information available

**M&A since 2018:** None in the antibacterial and/or antifungal sectors

**PIPELINE** for diseases in scope

**Pipeline size:** 12 projects for priority pathogens* (9 antibacterial medicines; 2 antibacterial vaccines; 1 antibacterial and antifungal medicine combination)

**Development stages:** 5 clinical projects, including V114, a Phase III 15-valent pneumococcal vaccine candidate, which has been reported to be non-inferior to Pfizer’s Prevnar 13® and includes 2 additional pneumococcal serotypes, and 7 discovery/pre-clinical projects

**Novelty:** No novel clinical-stage medicine projects

**Regulatory approvals:** 2, for ceftolozane/tazobactam (Zerbaxa®) for the treatment of cIAI and cUTI in July 2019 and for relebactam/imipenem/cilastatin (Recarbrio®), for the treatment of cIAI and cUTI in July 2019

**Access plans:** Unknown if its 5 late-stage R&D projects have project-specific access plans, but the company has a general commitment to increasing affordable access to antibiotics.

**Stewardship plans:** Unknown if its 4 late-stage R&D medicine projects have project-specific stewardship plans, but the company has a general commitment to increasing access and affordability.

**PORTFOLIO** for diseases in scope

**Mid-sized portfolio:** At least 25 products (20 unique INNs): 15 antibacterial medicines; 5 antibacterial vaccines; 5 antifungal medicines

**Essential medicines:** 32% (8) of products are on the 2019 WHO EML

**AWaRe medicines****: 1 Access group; 2 Watch group

**Anti-TB medicines****: 1 product

**Revenues by product (2018)**

<table>
<thead>
<tr>
<th>Product</th>
<th>Revenues (bn USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccines</td>
<td>4.6</td>
</tr>
<tr>
<td>Pharmaceuticals</td>
<td>6.8</td>
</tr>
<tr>
<td>Other</td>
<td>30.9</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>42.3</strong></td>
</tr>
</tbody>
</table>

**Revenues by region (2018)**

<table>
<thead>
<tr>
<th>Region</th>
<th>Revenues (bn USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe, Middle East &amp; Africa</td>
<td>3.6</td>
</tr>
<tr>
<td>USA</td>
<td>12.2</td>
</tr>
<tr>
<td>Asia Pacific, Japan</td>
<td>42.3</td>
</tr>
<tr>
<td>Rest of World</td>
<td>18.2</td>
</tr>
</tbody>
</table>

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.

** Listed on the 2019 WHO EML (Section 6).**

All companies were assessed based on data available in the public domain, including information the companies have made publicly available. This was supplemented by data submitted directly to the Benchmark by the companies. Merck & Co, Inc declined to submit data to the 2020 AMR Benchmark.
OPPORTUNITIES FOR MERCK & CO, INC

Remain engaged in R&D for antibacterial medicines and vaccines. Merck & Co, Inc is one of the few large research-based pharmaceutical companies still active in R&D for antibacterial medicines and vaccines. It is critical for the development and commercialisation of new products that large research-based pharmaceutical companies remain engaged in this space, either through acquisitions and in-licensing or through discovery.

Follow up to public commitments and increase public disclosure on environmental risk management. Following up on its commitments as a signatory to the Industry Roadmap for Progress on Combating AMR, Merck & Co, Inc can work with stakeholders to develop a practical mechanism to publicly disclose (1) a list of its suppliers and waste-treatment plants and (2) the results of environmental audits and the levels of antibacterial discharge from its own sites and the sites of its suppliers.

Expand registration and ensure adequate supply of antibacterial medicines in more access countries. Merck & Co, Inc can disclose more information regarding the access countries in which it has filed its antibacterial medicines for registration and to which it ensures a continuous supply.

Scale up UK pilot and fully decouple sales incentives from sales volumes. In order to mitigate the risk of inappropriate use of its antibacterial and/or antifungal medicines, Merck & Co, Inc can build on its current pilot in the UK and fully decouple sales incentives for sales volumes.

Publicly share raw data from its surveillance programme SMART. Merck & Co, Inc can share publicly (e.g., with the AMR Register) the raw data collected for its long-term, multinational surveillance programme SMART.

CHANGES SINCE 2018

- Received FDA approval in July 2019 for relebactam/imipenem/cilastatin (Recarbrio®) for the treatment of adults with complicated urinary tract and complicated intra-abdominal bacterial infections.
- Received FDA approval in June 2019 for cetolozane/tazobactam (Zerbaxa®) for the treatment of hospital-acquired and ventilator-associated bacterial pneumonias.
- Started a pilot in January 2019 where it would not reward its sales agents based on antibacterial sales volumes in UK hospitals to help prevent the inappropriate use of its antibacterial medicines.
- Reflects emerging resistance trends and guidelines for healthcare professionals (HCPs) in its marketing materials from 2018 onwards to address appropriate use.

PERFORMANCE BY RESEARCH AREA

A RESEARCH & DEVELOPMENT

A.1 No information on relevant R&D investments

Merck & Co, Inc does not report publicly, or to the Benchmark, how much it invested in R&D for antibacterial medicines, antifungal medicines and/or vaccines in 2017 and 2018.

A.2.1 One of the largest pipelines evaluated

Compared to the large research-based pharmaceutical companies evaluated, this pipeline is among the largest. The company reports 12 projects targeting priority pathogens in its pipeline, 11 of which target bacterial pathogens, including two vaccine and nine medicine projects. The other project, in discovery stage, targets both bacterial and fungal pathogens. Of the 12 projects, three are in discovery stage, four are in pre-clinical development and five are in clinical development. Two of its clinical candidates, cetolozane/tazobactam (Zerbaxa®) and imipenem/cilastatin/relebactam (Recarbrio®), were approved by the FDA in June and July 2019, respectively. Merck & Co, Inc disclose that they run an active in-house antibacterial discovery programme, demonstrating its ongoing commitment to early-stage discovery work. It also states that it generally does not publicly disclose candidates in Phase I or earlier.

A.2.2 No clinical-stage novel projects

Merck & Co, Inc’s clinical-stage medicine pipeline for priority pathogens consists of both new and adapted R&D projects. It does not currently include candidates that are considered novel. However, during the period of analysis, Merck & Co, Inc received a market approval for a new, non-novel candidate, cilastatin/imipenem/relebactam (Recarbrio®), for the treatment of complicated urinary tract and intra-abdominal infections.

Pipeline targeting priority pathogens: 12 As at 16 October 2019

<table>
<thead>
<tr>
<th>Discovery</th>
<th>Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compound screening</td>
<td>ATP synthase inhibitor 1 mo GLP safety studies - M. tuberculosis</td>
<td>Diarylquinoline - M. tuberculosis</td>
<td>In vivo pre-clinical pharmacokinetic/pharmacodynamic dose ranging project - M. tuberculosis</td>
<td>Fidaxomicin (Dificid®) - C. difficile - (Adaptation - paediatric) - C. difficile-associated diarrhoea</td>
<td>Relebactam/imipenem/cilastatin (Recarbrio®)** - GNB (including CRE) - cIAI and cUTI (Approved July 2019, FDA)</td>
</tr>
<tr>
<td>ALS (MOA) - M. tuberculosis</td>
<td></td>
<td></td>
<td></td>
<td>Cefotolozane/tazobactam (Zerbaxa®) - GPB - Adaptation (additional indications) - HABP and VABP</td>
<td>Cefotolozane/tazobactam (Zerbaxa®) - GNB - Adaptation (additional indications) - HABP and VABP (Approved June 2019, FDA)</td>
</tr>
<tr>
<td>Partnership with Orchid Pharma, India - Bacteria &amp; fungi</td>
<td>Protein synthesis inhibitor - M. tuberculosis</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

* Bacteria and fungi that have been identified as priority R&D targets for limiting AMR, by either the WHO and/or the Centers for Disease Control and Prevention (CDC). See Appendix V.
infections.

A.2.3 Two vaccines in the pipeline
Merck & Co, Inc reports two vaccine projects in its pipeline. These include one new project (to prevent *Shigella* spp. infections) and one adapted project (against *S. pneumoniae*).

Its *Shigella* vaccine is being developed through Hilleman Laboratories, a joint-venture partnership between Merck & Co, Inc and Wellcome Trust.

A.2.4 Three candidates targeting critical and/or urgent priorities
Merck & Co, Inc has three candidates targeting critical and/or urgent priority pathogens that qualify for analysis. All candidates are for antibacterial medicines in clinical development: fidaxomicin (*Dificid®*), in Phase III and which targets *C. difficile*; ceftolozane/tazobactam (*Zerbaxa®*), recently approved for HABP and VABP and which targets CRPA; and imipenem/cilastatin/relebactam (*Recarbrio®*), which was recently approved for cIAI and cUTI and targets CRE. These pathogens are among those that have been identified as critical and/or urgent R&D priorities for limiting AMR by WHO and/or the US Centers for Disease Control and Prevention (CDC).

A.3 Three intellectual capital sharing initiatives
Its three relevant initiatives include being part of Hilleman Laboratories, a joint-venture partnership between Merck & Co, Inc and Wellcome Trust. The joint venture is responsible for the development of a *Shigella* vaccine, among others. In addition, Merck & Co, Inc reports a similar research centre based in Spain, collaborating with the University of Granada and receiving funding from the regional government of Andalusia. Further, the company is part of the TB Drug Accelerator Programme, a consortium of research institutions and pharmaceutical companies that is developing new treatments for tuberculosis (TB).

A.4 Commits to expanding access and affordability practices
Merck & Co, Inc does not publicly report any specific access or stewardship plans for its five late-stage medicine and vaccine projects targeting priority pathogens. The company has made a general commitment to expanding access to its products through broad registration and to improving affordability and it supports the appropriate and responsible use of them.

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**B RESPONSIBLE MANUFACTURING**

**B.1 Comprehensive environmental risk-management; less information on discharge limits for own sites and suppliers**

Merck & Co, Inc reports a comprehensive strategy to minimise the environmental impact of wastewaters and solid waste from antibacterial manufacturing at its sites, with an aim to limit AMR. This includes audits generally every 1—2 years, depending on risk. The company reports setting discharge limits for antibacterials manufactured at its sites based on PNECs to limit AMR (or more stringent PNECs).

Merck & Co, Inc expects third-party suppliers of antibacterial APIs and drug products to follow its standards and guidelines, including limits. The company reports being in the process of reviewing suppliers’ operations to assess good practice in controlling releases of antibacterials into the environment and reports having provided them with the limits their discharges should meet. It expects external private waste-treatment plants to comply with its environmental standards and guidelines, but there is limited information on how plants are audited. Merck & Co, Inc reports using no external private wastewater-treatment plants. Wastewater is either treated on-site before being discharged to surface-water bodies or sent to local municipal wastewater-treatment plants.

**B.2 Publicly discloses some information on environmental risk management**

Merck & Co, Inc publishes some components of its environmental risk-management strategy. Further, it is a member of the AMR Industry Alliance, which publishes a list of recommended antibacterial discharge targets. The underlying methodology was summarised in an open-access journal article co-authored by Alliance members including Merck & Co, Inc.

Merck & Co, Inc does not publish: (1) the results of environmental audits, whether conducted at its own sites, the sites of suppliers or external private waste-treatment plants; (2) a list of these suppliers and waste-treatment plants; or (3) the levels of antibacterial discharge from its own sites.

**B.3** Has system to maintain production quality for own and suppliers’ sites; no requests for official corrective action

Merck & Co, Inc reports having a system to maintain high-quality antibacterial production, consistent with international GMP standards. The company reports requiring suppliers to abide by regulatory and company quality standards, regardless of geography, including submitting suppliers to a qualification process prior to establishment of a commercial agreement. Audits are risk-based and the company reports tracking implementation of corrective and preventive actions. The Benchmark found no requests for official corrective action from the FDA or EMA related to non-conformities with cGMP at Merck & Co, Inc’s own sites or any subsidiaries.*

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**C APPROPRIATE ACCESS & STEWARDSHIP – ACCESS**

**C.1 Filed to register relevant on-patent products in 3 access countries on average**

Merck & Co, Inc performs less well than its peers in this area, as it publicly discloses limited information regarding the access countries in which it has filed relevant on-patent products for registration. It does report that one antibacterial, such as imipenem/cilastatin, have been filed for registration in several access countries.

**C.2.1 Basic strategy for ensuring affordability**

For its relevant on-patent products, Merck & Co, Inc considers affordability when setting prices. It works with governments and non-governmental organisations to build effective vaccination delivery programmes. It uses tiered pricing based on factors such as the country’s level of development, actual health spending and the number of people at risk of infection in the population. However, it does not disclose the products or countries to which this pricing strategy applies.

Merck & Co, Inc does not disclose how it plans to increase the affordability of such products over the next five years.

**C.2.2 Pricing strategies for off-patent products**

Companies were not scored for this indicator as the available data was insufficient for a comparative analysis. Merck & Co, Inc does report that it takes socioeconomic factors into account when determining prices for off-patent antibacterial or antifungal medicines or vaccines.
C.3 Some strategies to ensure the continuous supply of relevant products
Merck & Co, Inc performs less well than other large research-based pharmaceutical companies evaluated, as it discloses limited information publicly on the steps it takes to ensure the continuous supply of its relevant products to access countries. It discloses some strategies for achieving this aim. It partners with various organizations including the African Association of Essential Drugs National Purchasing Centres (ACAME) for Sub-Saharan Africa and the Developing Countries Vaccine Manufacturers Network (DCVWN). To mitigate against falsified medicines reaching the supply chain, it has several strategies, including product security features, publication of authorised distributors on its website, awareness-raising initiatives and its Merck Anti-Counterfeiting operations to address large-scale criminal enterprises.

C.4 Broad strategy to mitigate COI for all educational programmes
The Benchmark analysed five AMR-related educational programmes for HCPs from Merck & Co, Inc. Merck & Co, Inc reports broad COI mitigation for all five programmes. To mitigate COI for three programmes, it provides financial resources to independent third parties to develop the programmes. Of the two programmes developed by the company, one has all three COI mitigation strategies looked for by the Benchmark: (1) content is developed independently from its marketing department (it is developed by independent third parties); (2) a pledge not to provide financial or material incentives to participants; and (3) it does not use branded materials. However, for the remaining programme, it is unclear whether content is developed independently from its marketing department or whether it uses branded materials.

C.5 Adapts marketing materials to address appropriate use
Merck & Co, Inc engages in practices that aim to address the appropriate use of its antibacterial and/or antifungal medicines via its marketing practices. Under a global policy, all of Merck & Co, Inc’s marketing materials reflect emerging resistance trends and include guidelines for HCPs to raise awareness of AMR and address appropriate use. To this aim, it has developed its Star of Stewardship principles for marketing teams to follow. Under this guidance, all marketing materials must include, e.g., specific indications, treatment duration and dose. After the period of analysis, the company publicly announced that it had started a pilot in January 2019 where it would not reward its sales agents based on antibacterial volumes sold in UK hospitals.

C.6 No information on brochure and/or packaging adaptations to facilitate appropriate use
There is no information regarding Merck & Co, Inc’s adaptations in its brochures and/or packaging to facilitate appropriate use of its antibacterial and/or antifungal medicines by patients beyond regulatory requirements.

C.7 Active in multiple AMR surveillance programmes; openly publishes results
Merck & Co, Inc is active in multiple long-term AMR surveillance programmes. Three programmes are international: the Study for Monitoring Antimicrobial Resistance Trends (SMART); the Program to Assess Ceftolozane/Tazobactam Susceptibility (FACTS); and Surveillance of Tedizolid Activity and Resistance (STAR). These programmes run in 63, 28 and 14 countries respectively. Two programmes are national: CANWARD in Canada; and the BSAC Resistance Surveillance Programme in the UK. All five programmes only share their results in peer-reviewed open-access journal articles. Merck & Co, Inc does not report making antibacterial and/or antifungal consumption data available to national governments or other public health authorities.

DIAGNOSTICS, ANIMAL HEALTH & AGRICULTURE
Activities in this area are not scored by the Benchmark. This information is provided given the importance of diagnostics, animal health and agriculture on the topic of AMR.

Merck & Co, Inc is the only company in scope that is involved in antibacterials for use in animal health and it was an original signatory to the Health for Animals Antibiotic Commitment. Its Position Statement on Animal Health states that it supports the responsible use of antibacterials to treat and improve the health of animals by: (1) conducting research to develop alternatives to antibacterials for animal use; (2) working with regulatory agencies to establish withdrawal periods and submitting data related to resistance development as part of the approval process for antibacterials used in food-producing animals; (3) providing veterinarians, commercial production operations, farmers, ranchers and feed companies with guidelines on resistance management, appropriate dosage, and length of usage to support the appropriate use of antibacterials; and (4) supporting the adherence to guidelines on the prudent use of antibacterials developed by the World Organization for Animal Health (OIE) and adopted jointly by the American Veterinary Medical Association, Federation of Veterinarians of Europe and Canadian Veterinary Medical Association.

Moreover, Merck & Co, Inc is teaming up with the Association of American Veterinary Medical Colleges (AAVMC) through its Animal Health division on an international grant programme designed to help mitigate AMR in animals. The programme is focused on building networks and using communication technology to increase awareness, share ideas and support innovative approaches to improving veterinary medical education at universities around the world.

‡ 102 low- and middle-income countries where better access to medicine is most needed. See Appendix VI.
§ See Appendix VII.