

products

Within this chapter:

48	Innovation and digitalization
52	Sustainable products
52	Sustainable product design
55	Packaging and recycling
57	Health for all
57	Global strategy
60	Focus programs
63	Open innovation sharing
65	Pharmaceutical supply chain
67	Prices of medicines
69	Health awareness
72	Product safety and quality
72	Chemical product safety
75	Patient safety
78	Product-related crime
81	Transport and warehouse safety

Innovation and digitalization

Part of the non-financial report

We develop products and technologies that enrich people's lives and are constantly on the lookout for ground-breaking developments and trends. Research and development (R&D) and innovation are the cornerstones of our success. In 2018, we spent around € 2.2 billion on R&D, corresponding to 15% of our net sales. New technology and the advance of digitalization in particular enable us to create innovative technologies, products, services and pioneering business models. At the same time, digitalization is decreasing the time-to-market for new ideas, which creates opportunities we intend to leverage.

Research and development costs by business sector¹ – 2018



¹ Not presented: Research and development costs of € 47 million allocated to Corporate and Other.

Our approach to innovation and digitalization

Our three business sectors Healthcare, Life Science and Performance Materials, have established strategies to drive new product developments for the benefit of patients and our customers. The diversity of these business sectors provides us with a breadth of technologies and depth of market know-how, giving us a competitive advantage in developing new products.

When deciding where to invest, we analyze current megatrends to determine the innovation fields in which we see potential for new business. We endeavor to identify innovation projects that transcend our current portfolio and develop them from the initial idea all the way to a functioning business model. This can only succeed if our business sectors work closely together and if we are open to external momentum. Our **end-to-end innovation process** seeks to achieve exactly that.

Our Group function Strategy and Transformation facilitates innovation between the individual business sectors and beyond our current business scope. It oversees an end-to-end process that ranges from **setting the innovation direction**, through ideation, incubation and growth of projects to establishing long-term business models.

We push the progress of promising projects as quickly as possible from the brainstorming and idea generation stage to an incubation and growth phase, where we provide project teams with a suitable environment to develop their business models and scale-up. Projects are monitored in a lean, gate-based process, with strict criteria applied at each gate to evaluate progress. All activities are **supported by experts** in business model design, business development, market research and agile methodologies. The objective is that, after market launch, the new products or services will make a measurable contribution to our business success.

Driving digital innovations

A major focus of our innovation efforts is digitalization, and we want to leverage related opportunities to boost our business performance. We therefore increasingly form new strategic partnerships with organizations that offer different perspectives. The following areas are those in which we expect to see progress:

- **Research and development:** Digital technologies enable us to access and quickly analyze large volumes of data, thereby accelerating our research and development activities. This is especially the case in our Health-care business sector, where we are working to advance the development of new drugs to provide patients with faster access to effective medicines.
- **Supply chain management:** Digital technologies help us to better manage our supply chain. Collating all data centrally gives us access to crucial real-time data. This enables us to predict supply bottlenecks around the world and respond promptly to make sure medicines reach their destination when needed.
- **Production:** We set up the infrastructure to capture data throughout all stages of our production processes and apply advanced data science methods to optimize our manufacturing methodologies.
- **Digital product innovations:** Digitalization enables us to broaden our existing product portfolio to include, for instance, new digital services. We also promote health awareness and improve disease awareness and patient treatment through innovative e-health offerings such as our Diabetes Online Risk Assessment ([DORA](#)).
- **Interactions with customers:** Thanks to modern data collection and analysis methods, we can make more efficient use of customer-relevant data. This information allows us to adapt our products and services where necessary.

You can find more information on research and development in our [Annual Report 2018](#).

How we drive innovation

The organizational set-up of our research and development activities reflects the overall structure of our company. All three of our business sectors operate their own independent Research and Development (R&D) units, which are aligned with their individual innovation strategies. In 2018, our Group function Strategy and Transformation **developed a new end-to-end process** that covers innovation both between and beyond current business sectors and is responsible for implementation. This function reports directly to the CEO and Chairman of the Executive Board.

Our Innovation Committee (IC) oversees the implementation of innovation projects both between and beyond our business sectors. It is tasked with ensuring that the decision-making process for selecting innovation projects is both transparent and consistent and reviews the progress of ongoing efforts. The committee consists of senior executives from our Group functions and our three business sectors. For projects requiring larger-scale investments, the IC consults our Executive Board.

INFO

OUR THREE INNOVATION FIELDS IN THE INNOVATION CENTER

Bio-Sensing and Interfaces

This innovation field focuses on the interface between the biological and digital world. The goal is to utilize data analytical tools to enable faster and more accurate (remote) monitoring and treatment of health in numerous areas.

Clean Meat

This field concentrates on the biotechnology required to produce meat in laboratories so that it is healthier, more efficiently produced, ethical, and environmentally sustainable.

Liquid Biopsy technologies

This area focuses on non-invasive alternatives to traditional tissue-based diagnostics like liquid biopsy, thereby reshaping methods of detecting and managing various diseases.

Whilst we are open to innovation around the world, many potential partners for these projects are based in Silicon Valley (California, USA), which is one of the key sites in the global high-tech industry. We are therefore currently building an innovation hub in Silicon Valley to be closer to innovation partners there, be it companies or institutions. The Silicon Valley Innovation Hub aims to scout new technological opportunities and establish partnerships and projects within our three innovation fields.

Discovering new technologies through collaboration

In 2018, our Silicon Valley Innovation Hub signed a partnership agreement with, among others, the Bao Group at Stanford University. Using our liquid crystals as the enabling technology, Bao is working on Liquid Crystal Elastomers, often referred to as **artificial muscle**, making it the most promising candidate for developing wearable haptic sensor-actuator systems.

Our China Strategy and Transformation Group is responsible for driving our strategy in this fast-evolving market. The China Innovation Hub was set up in 2018, with the mission to **boost innovation through collaboration** between current businesses, and cooperate with Chinese start-ups, academic institutions, business partners and local governments to explore new innovation fields. In spring 2019, the first batch of start-ups will be hosted by the China Innovation Hub.

M Ventures is our strategic, corporate venture capital arm. It invests in innovative technologies and products with the potential to significantly impact our core business areas. M Ventures has a significant focus on **early stage**

investing and company creation, including the creation of spin-offs to leverage our science and technology base, and takes an active role in its portfolio companies. The fund has a total volume of € 300 million and has the mandate to invest in the areas of Healthcare, Life Sciences, Performance Materials and New Businesses.

Our commitment: Protecting innovative ideas

We are committed to ensuring the confidentiality of sensitive information, especially of intellectual property in digitalization projects, and to protecting our innovative ideas. Our Policy for Data Protection and Personal Data Privacy defines the standards that govern how we process, save, use, and transfer data. You can find more information on data protection under [Compliance](#).

Spotlight on the Innovation Center

We completed the construction of our new Innovation Center in Darmstadt (Germany) and moved into the premises in early 2018. It was officially inaugurated during our 350th anniversary celebrations on May 3, 2018 which were attended by German Chancellor Angela Merkel.

The Innovation Center offers our people and external partners an optimal environment in which to cultivate their ideas and scale them up to viable new business. We provide the infrastructure needed to advance **cutting-edge projects**, along with state-of-the-art methods and tools. It currently hosts 22 innovation projects. In September 2018, the Innovation Center was nominated for the National German Sustainability Award.

Our bi-monthly Innovators' Club brings together a diverse range of external and internal experts to share insight and debate about a range of topics, from curiosity research and new work order to novel innovation methodologies. These events are open to anyone with an interest in innovation, from start-ups to company experts and other interested employees, and even other organizations.

Synergizing external ideas: Start-ups and cross-industry collaboration

Numerous start-ups around the world are working on new technologies and innovative business models. The "Merck Accelerator" supports selected enterprises in their development, with a focus on initiatives that align with our business sectors and other current trends. In return, we gain insights into the innovative start-up scene and are able to identify **emerging market trends** early on. Our primary goal is to link these start-up companies with our innovation projects or our business sectors for future collaboration. In 2018, we accepted ten start-ups into the Accelerator at our Darmstadt headquarters. Following the end of this three-month program, we are already working on an innovation project with one of the start-ups and are in talks with eight others regarding future collaboration.

In 2018, we started our Africa Satellites program in Nairobi (Kenya), Lagos (Nigeria) and Cape Town (South Africa). These satellite engagements will enable us to foster our network in the African founders' scene and to scout cutting-edge start-ups for our Accelerator program. As part of the program we organized a hackathon in Cape Town

(South Africa). Also in 2018, we started to accept applications to our China accelerator program, which will be run by the China Innovation Hub from 2019 onwards.

Our Accelerator is complemented by hackathons, two of which were carried out at the Innovation Center in 2018. One of them was a so-called Makerthon in collaboration with Deutsche Telekom. Over three weeks in late 2018, almost 80 young students and professionals provided hardware solutions to different challenges where **healthcare and technology intersect**. At a final pitch event at our Innovation Center, the teams were offered the opportunity to present their solutions to the two host companies.

We support the start-up program HIGHEST 1877, which is run by the Technical University (TU) of Darmstadt (Germany). We were Silver Sponsors of the Startup and Innovation Day held in October 2018 and also participated as jury members.

In 2018, we continued our two-year partnership with the European Space Agency (ESA) through which we hope to leverage synergies in areas such as innovation, digitalization and materials research. We hosted astronaut Thomas Reiter, who gave a speech to our R&D employees about research options in space, and we took part in the panel discussion "Space Meets Non-Space" at the ILA Berlin, a leading aviation industry exhibition. We were also a partner of the "Space Exploration Masters", initiated by the European Space Agency (ESA), which annually awards the best business ideas that bring the benefits of space exploration closer to society by way of products and services.

Channeling internal ideas to generate innovation projects

We want to maximize the innovative power within our company, which is why we give our employees around the world the opportunity to present their ideas to us via various channels. Our objective is to identify ideas between our business sectors and beyond our current scope that have the potential to become viable new businesses. Our **Innospire** (innovation and inspiration) initiative encourages employees to submit ideas for new products, services and business models. The best suggestions are then developed into business plans in a multi-stage process. More information on this topic can be found under [Employee engagement](#).

The most promising ideas that are sourced through channels such as Innospire become innovation projects, and we offer employees the chance to focus on their innovation project by hosting them in the Innovation Center. In addition to financial backing we provide a protected ecosystem and dedicated support, as well as clear governance and decision-making to efficiently grow and scale innovation projects into sustainable future businesses.

Our **Innovator Academy** strives to unleash the innovation potential of idea-givers, internal project teams, members of Think Tanks and start-ups. It offers a wide range of development programs, methodologies and online and offline trainings. Besides an online training platform, webinars are offered introducing employees to the topics and contents of the Innovation Center through practical examples.

Third Displaying Futures Award

The aim of our annual Displaying Futures Award, run by our Performance Materials business sector, is to support teams from academic and institutional backgrounds. In 2018, the target topic area was **"smart medical devices"**. Submitted by creative minds and start-ups from 19 countries, the number of ideas we received rose from 69 in 2017, to 97 in 2018. A panel of judges selected the three winning teams by considering important criteria such as innovativeness, business potential and social impact. The winners enter into a year-long partnership with our company, which will culminate in a final event in summer 2019 where they will be able to pitch their ideas to investors.

Maximizing the opportunities of digitalization

Through our strategic partnership with Palantir Technologies, a company based in California (United States), we are able to use their data analysis capabilities to improve and accelerate the development, commercialization and delivery of new medicines. The access to Palantir technology has enabled us to create tools that help to improve patient retention, increase sales rep efficiency and aid in strategic targeting to deliver effectively on our product launches. We can also now integrate and analyze large amounts of data to improve our operational excellence.

Syntropy

Syntropy is a joint venture being formed by Merck and the California software company Palantir Technologies. The partnership aims to give scientists and research centers access to a technology platform that integrates different types of datasets across an organization into a singular point of access. In this way, experts can collaborate more effectively on research on cancer and many other diseases.

Advances in medical research over decades have created a wealth of knowledge about diseases and how to treat them. This includes biomedical data. Massive amounts of this data are trapped within silos and between institutions and are inaccessible to the scientists and clinicians who need it to advance their research. Syntropy will **create a network** that drives discovery and improve human lives.

Improving customer experience through artificial intelligence

We are currently developing **chatbots**, which are text-based dialogue systems that enable people to ask computer systems questions in natural language – exactly as they would write messages to another person. This means we are available to answer questions from our customers 24 hours a day. In the future, for example, patients with multiple sclerosis will be able to order refills for their RebiSmart® injection device via chatbot. Future chatbots may even be capable of reminding patients to order a refill. Chatbots are more cost-effective for us than traditional customer services.

Development of a Global Data Science Team

In 2018, we built up a global data science team of around 30 data scientists to leverage the huge potential in advanced

analytics and machine learning. The team works with eCommerce data to provide insights to our customers and business teams in Life Science, using **image recognition techniques** to support the work of clinicians and researchers in our Healthcare sector, and assisting in the research and innovation process in Performance Materials. In addition, we have established a global data science community, bringing together over 250 analytics professionals from around our company. One milestone of this development was when around 120 employees participated in our first internal Data Science conference in June 2018.

Promoting visionary research

During our 350th anniversary year we were the main sponsor of the Curious2018 - Future Insight Conference. The conference, which took place in July in Darmstadt (Germany), brought together top scientists from around the world to discuss the future of science and technology. More than 60 renowned speakers, including **six Nobel laureates**, presented their work to around 1,300 invited guests. We intend to establish Curious Future Insight as a flagship conference, a forum at which the brightest minds in science and entrepreneurship can share their work and develop visionary solutions to tackle global challenges. The conference will take place again in July 2020.

During the conference we also launched the **Future Insight Prize** to stimulate innovative solutions enabled by ground-breaking science. We want to help drive the development of what we call dream products. These are products that don't yet exist but that might solve some of the existential challenges to mankind. We plan to grant up to € 1 million every year for the next 35 years to researchers who contribute to making these dream products a reality. The first Future Insight Prize will be awarded in 2019, for achievements in the field of pandemic preparedness.

In 2018, we also held the **Innovation Cup Anniversary Edition**, which brought together some of the brightest students from all over the world with experienced professionals to develop new ideas into convincing business plans. A jury made up of top scientists and entrepreneurs selected the best business plan and awarded € 20,000 to the winning team. In addition, in 2018, we started a series of science competitions and rolled out the **350th anniversary research grants**.

Rewarding inclusive innovation

In September 2018, we hosted the European final of the "Inclusive Innovation Challenge" in Darmstadt (Germany) as the exclusive European partner. The competition was initiated by the Massachusetts Institute of Technology (MIT) Initiative on the Digital Economy and aims to **accelerate technology-driven solutions** enabling greater economic opportunity for employees around the world. The challenge awards over US\$ 1 million in prize money. Organizations and companies from around the world can take part with technological solutions to shape the future of work.

sustainable products

sustainable product design

Respect for the environment is at the heart of sustainable conduct. We see it as our duty to not only conserve resources when developing our own products, but to also help our customers increase the sustainability of theirs. Our Life Science business sector develops solutions to make research and biotech production simpler, faster and more efficient, while our Performance Materials business sector focuses on solutions for the electronics market, for example semiconductor or display materials.

Our approach to sustainable product design

Our individual business sectors take different approaches to sustainable product design. In our Life Science business sector, we aim to reduce the impact of our products on health and the environment. This applies to the **entire life-cycle**, from manufacture and use to disposal. At the same time, we seek to make our products more efficient and user-friendly, asking ourselves right at the start of product development how to best reconcile these requirements.

Our Performance Materials business sector develops and produces numerous products that in turn help our customers manufacture sustainable and environmentally compatible goods. Our aim is to develop smart products that allow people to save energy in everyday life. The avoidance of hazardous materials is a principle that is embedded in the product development process.

How we include sustainability in product design

The Corporate Responsibility (CR) unit within our Life Science business sector is responsible for coordinating and driving product-related sustainability. This includes our Design for Sustainability (DfS) program for **eco-friendlier life science products** as well as **DOZN™**, a web-based tool for assessing greener alternatives.

Our Performance Materials business sector has its own CR Committee comprising representatives from all Performance Materials business units and other relevant internal units. The committee functions as a platform to discuss CR issues and meets three to four times per year.

The responsibilities described here also apply to product **packaging and recycling**.

Our commitment: Chemicals and product policies

To meet the product safety regulations relevant to our company, our **Regulatory Affairs Group Policy** details Group-wide processes for managing and implementing product safety, including the necessary management structures.

Our processes for sustainable product design

Within our Life Science business sector, a variety of approaches help our experts to drive sustainability improvement during the development of products and packaging:

- With our Design for Sustainability (DfS) program, we have developed a comprehensive approach to increasing the sustainability of Life Science products through the analysis of different sustainability criteria.
- Our Life Science researchers are using a green chemistry assessment tool to develop innovative solutions in line with the 12 Principles of Green Chemistry developed by chemists Paul T. Anastas and John C. Warner.
- Our in-house-developed **web-based tool DOZN™** enables us to assess the green alternatives of various chemicals, thereby creating transparency for our customers.

The following guidelines also set out **requirements** for sustainable product design within our Performance Materials business sector:

- The Green Product Policy ensures that we adhere to all national and international laws and statutes (e.g. **REACH** and the European Union **RoHS Directive**), as well as to industry and customer-specific requirements.
- Our raw materials for the cosmetics industry fulfill the high standards of the Cosmetics Directive and are produced in line with Good Manufacturing Practices for Cosmetic Ingredients (**EFfCI GMP**). As part of a regular process we reviewed the EFfCI GMP in 2018 and communicated the results to the plant managers operating in the field of Surface Solutions. A new manual for cosmetic suppliers was also made available in 2018.

Sustainable product design in the Life Science business sector

Through our Design for Sustainability (DfS) program, we have developed a comprehensive approach to increasing the sustainability of Life Science products. The DfS program provides our product developers with a range of tools that enable them to analyze the impact of the product on the following areas: materials, energy and emissions, waste, water, packaging, usability and innovation. For each of these areas we have developed several sustainability criteria that are noted on a **scorecard**. When developing a new product, our aim is to improve on as many of these criteria scores as possible. We conduct product life cycle analyses to understand the potential environmental impacts within different stages of the product life cycle. The findings of these analyses show us how we can improve our products

and are incorporated into subsequent development stages. During this process, experts from R&D, Product Management, Quality, Procurement and other departments are in constant contact with one another. By the end of 2018, 27% of these product development projects met three or more product sustainability criteria.

We are currently working on enhancing our DfS program, with the aim of helping our development teams better account for environmental impacts during the product development process and improving communication of sustainability attributes to our customers. In 2019, we intend to integrate the changes to the program into our product development process. The improvements will especially **involve our suppliers**, with specific criteria aiming at encouraging the majority of them to participate in the [Together for Sustainability](#) industry initiative. In 2018, we ran a first product development pilot project for which we engaged 10 suppliers of consumable parts who represent more than 85% of the manufacturing cost of the product.

Green chemistry assessment tool

In addition to DfS, our Life Science researchers are developing innovative solutions in line with the twelve Principles of Green Chemistry developed by chemists Paul T. Anastas and John C. Warner. These aim to make research **as environmentally compatible as possible** and to minimize negative impacts on human health. More than 750 greener alternatives to conventional products have been made available so far.

Our in-house-developed [web-based tool DOZN™](#) enables us to assess the green alternatives of various chemicals, thereby creating transparency for our customers. Under DOZN™, the twelve Principles of Green Chemistry provide a framework for rating our products **in three major stewardship categories**, namely "Improved resource use," "Increased energy efficiency" and "Reduced human and environmental hazards." The system calculates scores on each substance based on a range of data that includes the Globally Harmonized System of Classification and Labelling of Chemicals ([GHS](#)) as well as the Material Safety Data Sheet information. To date, we have used this matrix to assess and improve more than 40 products. It is our goal to make the tool available to our customers in 2019, so that they can evaluate the environmental footprint of their activities.

Wide range of solutions

Our Life Science portfolio comprises a broad array of products, each with different properties that are taken into consideration when applying our DfS approach and the Principles of Green Chemistry. The following examples illustrate the results.

Greener laboratory filters

We have significantly reduced the environmental footprint of our [EZ-Fit™ Manifold](#) laboratory filter, and it now requires 47% less raw material than its predecessor, the Hydrosol Manifold. The packaging is 100% recyclable cardboard and, overall, 99% of its parts are recyclable. Because the heads can be easily removed for cleaning, it is no longer necessary

to autoclave the whole device, which saves energy and results in a 91% reduction in the carbon dioxide emissions produced during cleaning.

Greener chemistry

Our greener, **bio-based solvent** Cyrene™ is derived from waste cellulose. This solvent is used as a more sustainable alternative to substances such as dimethylformamide (formic acid), which is classified as teratogenic. Through Cyrene™ and other [greener solvents](#), we are helping our customers make their production processes safer and more environmentally sustainable. Cyrene™ was shortlisted for the "innovation of the year" at the Ethical Corporation's 9th Annual Responsible Business Awards in 2018. We've teamed up with leading institutions and start-ups to co-develop other green solvents. In contrast to conventional solvents, these are based on natural resources such as corn cobs and sugar cane bagasse, making them eco-friendlier, more biodegradable and easier to recycle.

Eco-friendly lab water use

In mid-2017, we launched Milli-Q® IQ 7000, a new lab water purification and monitoring system. It uses mercury-free UV oxidation lamps and has a hibernation mode to save energy while still preserving system water quality. We were able to reduce the system footprint by 25%, and the cartridges by 33%, all of which **cut down on the amount of plastic used**, packaging and transportation, as well as waste levels.

Current product examples from Performance Materials

Our Performance Materials products help boost sustainability in a variety of ways:

Energy-efficient displays

Our [liquid crystals](#) provide high picture quality in LCD TVs, computer monitors and many more electronic devices, while also making them more power efficient. Self-aligned vertical alignment (SA-VA) is the next-generation liquid crystal (LC) technology and was launched in 2018. SA-VA helps conserve resources and is **even more environmentally sustainable** because less energy and solvent for the orientation layer are required to manufacture the displays. Moreover, its manufacture is more efficient as it requires fewer process steps. Furthermore, since SA-VA technology can be processed at lower temperatures, it is also suitable for sensitive materials such as those used in premium products, or for forward-looking applications such as flexible displays. Our [reactive mesogen](#) materials can also be used for ultra-thin optical films to improve the visual performance of LC and OLED displays, making them suitable for potential new flexible-type displays.

Mobile-device displays have increasingly high resolutions yet are still expected to be as energy-efficient as possible. This is where our liquid crystals for touchscreen applications come in. Based on ultra-brightness FFS technology ([UB-FFS](#)), these liquid crystals provide displays with 15% more light transmission. This can reduce the energy consumption of smartphones and tablets by around 30%,

thereby **prolonging battery life**. UB-FFS also enhances picture resolution. Devices with the innovative UB-Plus liquid crystal technology and with a significant reduction in energy consumption are expected to enter the market in 2019.

Switchable windows

Windows that can be darkened in a matter of seconds are now a reality thanks to our **liquid crystal window** (LCW) technology. These darkened windows regulate the heat generated by direct sunlight. The LC material was commercialized under our **licrivision®** brand, and in October 2018 a new brand for the product was launched under the name **eyrise™**. Initial estimates show that this technology can lower the energy consumed by building climate control systems by up to 40%, thus replacing conventional sun shading. We have invested € 15 million in the construction of a facility in the Netherlands to manufacture these switchable glass modules, which began deliveries in 2018. In response to market demand, we prioritized solar control during 2018, and we have three sophisticated architectural projects in the pipeline to be fitted with solar control LCWs.

We were able to realize the first commercial project in October 2018: large solar control windows for the company Orkla in Oslo (Norway). Furthermore, we presented a selection of these innovative architectural solutions at the trade fair "BAU 2019", where we focused on our **eyrise™** technology. Among other things, we showed an iconic building design by renowned Brazilian architect Oscar Niemeyer. The building is currently being constructed for the company Kirow Ardelt in Leipzig (Germany). We also help partner companies build their own window production using our liquid crystal materials.

OLEDs – organic light emitting diodes

Organic light-emitting diodes (OLEDs) increase the energy efficiency of displays while also providing brilliant colors and razor-sharp images. To further enable unique display applications and efficient production of large-area OLED displays, we are developing high performance OLED materials for vacuum evaporation methods and printing processes.

Our OLED production is designed with cost and resource efficiency in mind. Here, we also work together with our customers: When OLED materials are installed, some production material always remains in the used containers and machinery. Our customers can collect this residual

production material and send it back to us. We then prepare it so that it reaches its original quality again and can be reused. This approach saves **valuable resources** and benefits the environment.

Life cycle approach to benefit our customers

At the plants where our effect pigments are produced, we focus on saving energy and reducing CO₂-output. In 2018, this led to an 18% overall CO₂-reduction for plants, which operate for our Surface Solutions portfolio. This is especially relevant for those customers who want to reduce their upstream **CO₂ footprint**. We also conducted a gap analysis on the origin transparency of raw materials, the sustainability in product development and product sustainability. In the Surface Solutions area of our Performance Materials business sector, we use around 600 metric tons of renewable materials for the production of commercial products. This is mainly by extracting the natural compound glycerol from a variety of plant-derived oils.

More natural-based cosmetics

Responding to the ever-growing popularity of natural cosmetics, we are working closely with our customers in the cosmetics industry. Our cosmetic formulations comply with strict criteria and by the end of 2018, 68 of our cosmetic pigments and actives were certified according to Ecocert's COSMOS standard for organic and natural cosmetics. We also obtained **halal certificates** for our **Eusolex T** and UV-Titan product ranges. Our aim is to develop more natural-based raw materials for use in cosmetics in the future.

Alternative to plastic microbeads

We manufacture mineral-based pigments and functional fillers that are used by the cosmetics industry. Our **RonaFlair® functional fillers** series provides an alternative to plastic microbeads that are used in skin care products. Through this range of 27 innovative products, we are supporting initiatives such as the declaration of Cosmetics Europe, which advocates a phase-out of microplastics in rinse-off products by 2020. Microbeads are tiny, non-biodegradable polymer particles that cannot be filtered out by wastewater treatment plants. They end up in marine and terrestrial ecosystems, where they can harm the organisms living there. We are continuing to develop other functional fillers that don't make use of microbeads.

packaging and recycling

Packaging protects our products from external influences and ensures that they reach the customer undamaged. Packaging must therefore remain intact across the entire product life cycle to guarantee safety. We are working to reduce the amount of material we use, as well as increasingly utilizing eco-friendly materials where possible. We have also put recycling programs in place to help our customers properly dispose of and recycle our products and packaging.

Our sustainable packaging strategy

We aim to deliver our products in packaging that is safe and easy for customers to handle, and as sustainable as possible. With more than 300,000 products in our Life Science portfolio – ranging from biochemicals to lab chemicals, from filter materials and systems to instruments – we face a variety of challenges when it comes to packaging. We strive to improve the sustainability of this packaging to help both us and our customers reduce the environmental impact. To achieve this, we have developed a sustainable packaging strategy for Life Science that is built on the three pillars of optimizing resources, using more sustainable materials and designing for **circular economy**. In 2018, goals and targets were defined in collaboration with internal stakeholders from Sourcing, Distribution and the Global Packaging Material group. In December 2018, we started implementing and internally communicating our sustainable packaging plan.

We have set four goals that build on these three pillars:

- Reduce amount of packaging
- Achieve zero deforestation
- Improve plastic sustainability
- Maximize recycling

Internal targets relating to these goals have been defined up to the year 2022 and we have identified initiatives that will be implemented in order to achieve them.

Design for Sustainability program

Our Design for Sustainability (DfS) program supports our Life Science business sector in creating products with reduced life cycle impacts. This process focuses on utilizing recyclable or reusable materials that can be easily recovered or separated. Through DfS, we are continuously working to reduce the **ecological footprint** of our products and make disposal as easy as possible for our customers.

Making packaging more sustainable

A great deal of our packaging is fiber derived from wood. We are constantly working to increase the proportion of corrugated cardboard boxes certified to the standards governing **sustainable forestry**, including the Sustainable Forestry Initiative (SFI), the Forest Stewardship Council (FSC) and the Programme for the Endorsement of Forest Certification Schemes (PEFC). As part of reaching our “zero deforestation” goal by ensuring that none of our fiber-based packaging materials contribute to deforestation, we are currently defining new procedures on how to track the percentage of wood- and fiber-based packaging materials that are certified

by at least one of these standards, so that we can report this figure in the future.

Cellulose and air cushions replace polystyrene and foam

In the past, glass reagent bottles were secured using expanded polystyrene (EPS) molded foam to prevent them from breaking during transport. While EPS, also known as Styrofoam®, is an excellent cushioning material, it is manufactured from non-renewable petrochemicals and difficult to recycle. By contrast, molded pulp components can be easily recycled with other paper materials and compacted together for storage and transport. We employ a substitution program in which we replace EPS as far as possible with molded components made of cellulose and recycled paper pulp.

We are already using molded pulp inserts to pack some of our 4x4 liter, 4x2.5 liter and 6x1 liter bottles in shipping boxes, thereby replacing around two million EPS parts per year. We are currently conducting safety tests on new pulp designs for shipping other bottles of various sizes. Overall, we used approximately 669 metric tons of molded pulp packaging material in 2018.

We seek **eco-friendly alternatives** to ship our products safely, which is why we are also working with a specialist biotech company to develop a more sustainable bulk-packaging design to transport our Millistak+® Pod Disposable Depth Filter. A life cycle assessment showed that we achieved a 24% reduction in used corrugated cardboard, which translates to a 17% decrease in greenhouse gas (GHG) emissions from the life cycle of the packaging materials. Moreover, 70% less time is required at our customers in the processing of products and their packaging.

More cardboard instead of plastic

Whilst solvents are usually packed in plastic bottles, we use Titripac® because it offers a more eco-friendly alternative. The cardboard carton and plastic liner with an integrated withdrawal tap have made the packaging **more recyclable** while also cutting its weight by more than half. As a result, the greenhouse gas emissions arising across the entire product life cycle are 61% lower than for plastic bottles. Because the withdrawal tap protects the product against contamination, the contents can be used to the very last drop, thereby reducing chemical waste.

Reusing expanded polystyrene (EPS) boxes

Many of our Life Science products need to be kept cool during shipping and are therefore packed in special EPS boxes. To mitigate waste, we offer our customers in the

United States the option of returning these boxes to us. If they are still fully functional, we reuse them. In 2018, this amounted to more than 14,000 boxes being reused at least once, making up around 5% of shipments leaving the three distribution centers where this type of packaging is being used.

Integrating stainless steel canisters in production

In China, Korea and Taiwan, our Performance Materials liquid crystal mixtures are delivered to display manufacturers in stainless steel canisters. Our customers utilize these Merck Standard Canisters directly on their production lines without decanting. The empty canisters are then sent back to us and cleaned. In 2018, 1,374 standardized canisters were in circulation within this closed system, which allows them to be reused over multiple years.

Steel instead of glass

Thanks to our bulk product delivery system, our solvents are delivered to Life Science customers based in the United States in special **reusable** steel containers such as the EMD ReCycler[®]. Our customers can return empty stainless-steel containers to us for refilling, enabling us to significantly reduce the consumption of primary packaging materials. In 2018, we filled more than 14,000 reusable containers.

In Europe, we also utilize reusable stainless-steel containers to deliver solvents that are required in bulk for preparative chromatography. Our customers send the empty containers back to us, where they are properly cleaned and then reused. Approximately 32,000 of these serialized stainless-steel containers are currently in circulation. The rate of return is at around 90%.

New sustainable membrane packaging for cut disc filters

With the objective of helping customers meet their own sustainability goals, we have redesigned membrane boxes

for our cut disc filters. The membrane box packaging has been re-engineered for usability and reduced environmental impact. The newly redesigned membrane box packaging is manufactured using 22% less plastic and replaces polystyrene with polypropylene that has a 43% lower global warming potential than polystyrene. Other environmental impact enhancements include elimination of foam inserts and **local sourcing** of materials, resulting in less transportation and fewer emissions. This new design also reduces GHG emissions by 180 metric tons per year across the entire product life cycle. A life cycle assessment conducted on this new packaging design features the following sustainability improvements over the previous design:

- 22% reduction in weight of product packaging
- 33% reduction in GHG emissions
- 27% reduction in non-renewable energy

Recycling program updated

In cooperation with a waste-management company based in Massachusetts (United States), we employ a comprehensive recycling program for our Life Science customers in the United States. Product waste from their research labs and biopharmaceutical manufacturing operations is collected, sanitized and recycled into plastic lumber. This material can be used in many industries, such as construction, landscaping, transportation and marine construction. The program includes our [Biopharma Recycling](#) and Ech2o Collection **Recycling Programs**.

We are continuing to expand this program throughout the United States and are exploring options in other regions such as Europe and Asia. The program now serves twelve customers. Since launching the program, we have recycled 2,738 metric tons of waste generated from the use of our products, including 1,218 metric tons in 2018 alone.

Health for all

Global strategy

Two billion people across the globe do not have adequate access to health. At Merck, we are striving to make health solutions affordable, raise awareness of diseases and teach people how to manage them. We are working with committed partners to tackle this complex challenge by researching innovative solutions, developing new approaches and improving existing programs to help people at the point of care.

Our approach to improving healthcare of underserved populations

Our aim is to create a healthier future for all: for individuals, communities and countries. We want to use innovation in science and technology to improve the health of underserved populations in low- and middle-income countries. To achieve this, we are leveraging our expertise from all business sectors and collaborating closely with a wide range of partners. We also participate in industry-wide initiatives and work with other businesses to develop new approaches.

In 2018, we refined our **Global Health strategy** for addressing the global needs that impact access to health. Our strategy is designed to overcome access barriers for underserved populations and communities in developing countries in a business-integrated and sustainable manner, thereby creating "shared value." For us, creating shared value means developing business models that increase the value and competitiveness of our company and at the same time solve unmet health needs and bring value to underserved populations, thereby creating a win-win-situation for us and society.

In order to address unmet needs whilst strengthening health systems and our position in the market, we follow three core operating principles:

- **Developing innovative solutions:** we take a leading role in the elimination of schistosomiasis, and we create new integrated drug, diagnostic and vector control solutions for infectious diseases.
- **Engaging cross-sector partners:** we participate in multi-stakeholder global health platforms to help achieve the Sustainable Development Goals. We utilize access alliances for our solutions and create locally based opportunities where possible.
- **Creating business opportunities via a shared value approach:** we help sustainably improve the health of underserved populations by drawing our portfolio from across all three of our business sectors.

We have created focus programs to address our priority areas. We want to be instrumental in the elimination of schistosomiasis and fight malaria and other infectious diseases whilst helping to build local capacity across the value chain and positioning our company as a leading and reliable partner.

Activities within our strategy for global access to healthcare are generally related to one of four areas:

- **Availability:** we research, develop and refine health solutions that address unmet needs, tailoring them to local environments. For example, we are committed to the [Drugs for Neglected Diseases initiative](#).
- **Affordability:** we seek to provide assistance to those who are unable to pay for the health solutions they need, for example through our [Patient Access Programs](#). This also includes addressing challenges surrounding pricing and intellectual property.
- **Awareness:** we help raise awareness for diseases and therapies by empowering medical professionals, communities and patients to make informed decisions. One way to do this is through our [global awareness campaigns](#).
- **Accessibility:** we promote initiatives that strengthen supply chains and develop localized health solutions. Medicines should reach the people who need them quickly and safely, as demonstrated in our [NTDeliver project](#).

How we are improving access to healthcare

Our Global Health unit coordinates the implementation of our strategy for global access to healthcare. Several teams work on ways to investigate and reduce the barriers that make it difficult for underserved populations to receive healthcare.

Our Global Health unit is responsible for Group-wide initiatives, programs and sponsorships that relate to global health topics. Our experts collaborate closely with the Healthcare, Life Science and Performance Materials business sectors to effectively leverage their strengths and competencies.

Integrated into our Global Health unit, the [Merck Global Health Institute](#) seeks to provide **research and development capabilities** in order to engage in health system strengthening programs and develop a sustainable portfolio of treatments, diagnostics and preventive measures against infectious diseases. The Institute operates as a social business enterprise, using innovative financial mechanisms to deliver innovations for those who are most vulnerable: women and children in the developing world.

Our Access to Health subunit investigates the factors that make it more difficult for underserved populations to receive healthcare, working with various partners to develop ways to remove these barriers.

The Merck Praziquantel Donation Program, the third subunit, coordinates our efforts to [eliminate schistosomiasis](#) together with our external partners.

Our commitment: Providing a solid basis for access to healthcare

To demonstrate our commitment to access to healthcare, we publish a dedicated [Access to Health Charter](#) on our website. This charter sets out guidelines on the following:

- Our approach
- Pharmaceutical product donations
- Fake medicines
- R&D for infectious diseases
- Pharmaceutical product pricing
- Intellectual property rights

Every two years, the [Access to Medicine Foundation](#) publishes the [Access to Medicine Index](#), in which it benchmarks 20 of the world's largest research-based pharmaceutical companies on activities and initiatives that experts consider most relevant for access to medicine, ranging from donations, and patents to capacity-building. We use the ranking to inform and, in certain cases, guide our access to health strategy and approach.

We endorsed the [London Declaration on Neglected Tropical Diseases](#) when it was launched in 2012. Participating companies, governments and private organizations promise to help control or even eliminate the top ten most prevalent infections. We are particularly engaged in the fight against schistosomiasis.

Access to Medicine Index Ranking 2018

We have maintained our ranking of **4th place** in the 2018 Index, a recognition of our company's integrated strategy on access to medicine, our efforts across the whole value chain to address the needs of unserved and underserved populations, and our commitment to shared value.

The company has been particularly recognized by the Access to Medicine Foundation for leading practices such as:

- Establishing the Merck Global Health Institute to accelerate R&D, incorporate access provisions and build capacity for [projects and initiatives targeting schistosomiasis, malaria and bacterial infections](#)
- Joining the Drugs for Neglected Diseases initiative's NTD Drug Discovery Booster to accelerate the development of early-stage projects for Chagas disease and leishmaniasis as part of Merck's commitment to [Open Innovation](#)
- Improving access to better therapies in diabetes, cancer, hypertension, and fertility in underserved regions through the Merck Capacity Advancement Program.
- Joining "[Access Accelerated](#)", a global initiative with multiple programs including the Merck Capacity Advancement Program, which affirms our commitment to measuring impact and sharing results publicly via the Access Observatory
- Disclosing publicly the patent statuses for small molecules in scope via the [Pat-INFORMED](#) platform with 20 leading research-based pharmaceutical companies and in collab-

oration with the World Intellectual Property Organization (WIPO)

The 2018 Access to Medicine Index ranking and the report card for our company can be accessed here: www.accesstomedicineindex.org

Partnering to develop clinical capacity and skills

In order to advance global access to healthcare, it is necessary to develop trained and **professional clinical personnel**. We are collaborating with the European & Developing Countries Clinical Trials Partnership (EDCTP), which supports international fellowship programs for post-doctoral researchers from developing and emerging countries. In addition to receiving training on clinical aspects such as clinical trial practices and clinical management, research fellows are also given the opportunity to work for a period of up to 24 months at a number of leading pharmaceutical enterprises, including our own company. They are then able to return to their home countries and academic institutions with the knowledge they need to implement their research in line with international regulatory requirements and standards, as well as to train other local students to also help them enhance own their skills.

Engaging Stakeholders

Partnerships and dialogue are important instruments for improving access to healthcare, and we aim for stakeholder dialogues that have a large-scale relevance and impact. Our partners include multinational organizations, government agencies and NGOs, as well as academic institutions, health industry associations, private sector companies and independent experts on global health topics.

Alliances for better access to health

We are a member of the Business for Social Responsibility (BSR) initiative and have also endorsed the [BSR Guiding Principles on Access to Healthcare](#), which provide a framework for us to refine and enhance our Global Health efforts.

In 2017, we joined forces with 21 other leading pharmaceutical companies to launch [Access Accelerated](#), a global initiative that seeks to improve both the treatment and prevention of non-communicable diseases in low- and middle-income countries.

Our Access Dialogue Series

The [Merck Access Dialogue Series](#) was launched in 2013, as a multi-stakeholder platform for sharing information and **exchanging best practices** on broadening access to healthcare. We are always looking for opportunities for collaborative actions. The outcomes of the series inform and drive our access strategy, plan of action and engagements. This process is intended to be an open space for insightful and critical dialogue on how we and our partners can best use our respective capacities, experience, expertise and competencies to sustainably address access barriers. In 2018, we hosted an event on open innovation and intellectual property as well as supply chain and delivery.

Discussions at a global level

We participated in many events in 2018, that had a global reach or relevance. To position ourselves as a key player for global health, we continued to engage major stakeholders in a dialogue on infectious diseases, and to deepen collaborations with the scientific community through publications and primary roles at international scientific conferences and events. We were also part of stakeholder groups including the [Swiss NTD Alliance](#) and the [Swiss Malaria Group](#).

Selection of events and initiatives:

- International Society for Neglected Tropical Diseases ([ISNTD](#)) conferences in London (United Kingdom) in March and June 2018
- World Malaria Day, including a 'Malaria Screening Campaign and a Scientific Forum' attended by the First Lady of Ghana in Accra (Ghana) in April 2018
- Multilateral Initiative on Malaria (MIM) – 7th Pan African Conference on Malaria, in Dakar (Senegal) in April 2018
- World Health Assembly in Geneva (Switzerland) in May 2018
- 15th [International Symposium on Schistosomiasis](#) in Rio de Janeiro (Brazil) in August 2018
- 9th European & Developing Countries Clinical Trials Partnership ([EDCTP](#)) Forum 2018 in Lisbon (Portugal) in September 2018
- World Health Summit in Berlin (Germany) in October 2018, panel on "Access to Essential Medicines"
- 67th American Society of Tropical Medicine and Hygiene ([ASTMH](#)) in New Orleans (United States) in October/November 2018
- Merck Access Dialogue Series: Supply Chain & Delivery in January 2018 and Innovative Intellectual Property and Access in November 2018
- Hosted Fellows from the African Public Health Leaders Fellowship at our Vevey manufacturing site in November 2018

FOCUS programs

So-called neglected tropical diseases are concentrated almost exclusively in impoverished populations in the developing world. Barely known in industrialized nations, they attract little public attention and research funding. One poignant example is schistosomiasis. Our aim is to help in providing urgent action to prevent and control these neglected diseases, as well as more familiar ones such as malaria.

Strategy for preventing and treating infectious diseases

Our strategy is to not only develop and provide medicines, but also to improve diagnosis, counter disease transmission, increase disease control and strengthen local health systems. We seek to improve healthcare in developing countries by creating **novel and integrated health solutions** for infectious diseases and by ensuring the sustainable implementation of these innovations, many of which are led by our Global Health Institute. Our Group-wide initiatives and programs particularly address the medical needs of women and children.

Our comprehensive Global Health portfolio includes the following programs:

- Development of a pediatric formulation for praziquantel to treat schistosomiasis in children under the age of six
- Development of a new active ingredient to treat and prevent malaria
- Screening of our compound library in search of potential new active ingredients to treat schistosomiasis and malaria
- Development of diagnostic kits for schistosomiasis and malaria
- Development of products and technologies to enhance prevention of disease infection and re-infection

In addition, we engage in activities that address bacterial infections and antimicrobial resistance, for example by developing assets for antibiotic quality and laboratory capacity to detect antimicrobial resistance, improving the use of antibiotics by healthcare providers and patients, and helping define industry-wide guidelines for the control of antibiotics.

Our fight against schistosomiasis

Schistosomiasis, also known as bilharzia, is one of the most prevalent parasitic diseases in Africa, placing a great burden on public health and the local economy. The disease affects over **200 million people worldwide**, with more than 90% of cases occurring in Sub-Saharan Africa. Around 10% of those affected are preschool age children. An estimated 200,000 people die every year from the effects of schistosomiasis, such as liver and kidney infections, bladder cancer and blood loss.

In the 1970s, we partnered with Bayer to develop a medicine called praziquantel. Today, praziquantel remains the standard of care for the effective treatment of schistosomiasis around the world.

We have been partnering with the World Health Organization (WHO) since 2007, regularly providing them with donations of praziquantel tablets. Over time, we have built up a portfolio of pioneering R&D projects on schistosomiasis. These include:

- a new pediatric formulation of praziquantel to treat children under the age of six
- the screening of our proprietary compound library through a dedicated schistosomiasis drug discovery platform
- the development of innovative and highly sensitive schistosomiasis diagnostic methods
- the setup of approaches for vector control
- health education programs that help prevent transmission

Our fight against malaria

According to estimates by WHO, nearly half of the world's population is at risk of malaria. More than **200 million cases of malaria** and over 400,000 related deaths are recorded every year with 70% in children under five years of age. Around 90 different countries are affected by the disease, with approximately 90% of deaths occurring in Africa.

There is an urgent need for new products to overcome the problem of increasing drug resistance and to achieve the goal of complete eradication. Through our One Merck for Malaria program, we are well positioned to help deliver integrated and sustainable health solutions against malaria (treatments, diagnostics, prevention methods) to endemic countries. In our efforts, we closely collaborate with a wide range of partners in both developed and developing countries.

Schistosomiasis: Over 900 million donated tablets

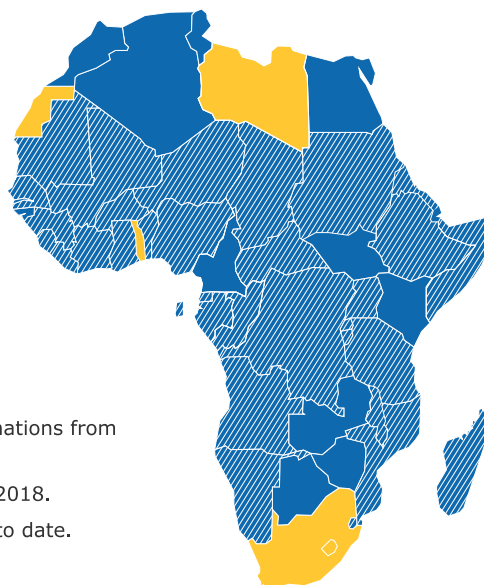
As part of our long partnership with the World Health Organization that dates back to 2007, we agreed to donate praziquantel tablets every year for distribution in African countries. This year, our donation program was expanded to include Burkina Faso, Niger, and Sierra Leone, and now covers a total of 46 countries. In 2018, we donated approximately 200 million tablets for distribution in 34 countries, and we keep our commitment by maintaining production capacities to a level sufficient for manufacturing up to 250 million tablets a year.

Countries that have received donations of praziquantel tablets

Since 2007, we have donated almost **900 million** tablets of praziquantel, which is enough to treat around 360 million school-aged children.

- African countries that started receiving tablet donations from us since 2007*.
- ▨ African countries to which we donated tablets in 2018.
- Countries that have received no donated tablets to date.

* Launch of our Praziquantel Donation Program.



Schistosomiasis Health Education Project

We have been working with the [NALA](#) Foundation since launching the Schistosomiasis Health Education Project in 2017. Through this partnership, we are donating nearly € 300,000 over a period of three years to support the Federal Ministry of Health in Ethiopia in promoting the long-term behavioral change that is needed to help **eliminate schistosomiasis** and other neglected tropical diseases. The project targets a population of 850,000 in Bench Maji, a region in southwestern Ethiopia, with a focus on approximately 260,000 students in 290 schools and includes distribution of customized educational material and improving water sanitation and hygiene facilities through a community-based approach. In 2018, activities were launched in all 74 schools of the Bero and South Bench districts of the Bench Maji region, reaching almost 70,000 students in total. The goal for 2019 is to extend this model to two other districts.

Central platform in the battle against this parasitic disease

Since schistosomiasis is a complex disease, a coordinated, multi-sectoral approach is needed to combat it. We joined forces with international partners from various sectors to address the remaining gaps in the fight against this infection and initiated the Global Schistosomiasis Alliance ([GSA](#)) in 2014, to coordinate and increase the impact of our efforts. The founding members of the GSA include the [Bill & Melinda Gates Foundation](#), the Schistosomiasis Control Initiative ([SCI](#)), the United States Agency for International Development ([USAID](#)) and [World Vision International](#).

In 2018, the GSA acquired additional international stakeholders as new members. As well as organizing several conferences and key meetings, it took part in various projects aimed at driving local efforts to combat schistosomiasis. The GSA is also working to promote and support an **international action plan** to progress schistosomiasis

control and eventually achieve elimination of the disease. The GSA continues with its efforts to raise awareness through campaigns such as [#MakingSchistory](#), which began in 2017.

Partners in schistosomiasis research

The need for a more sensitive diagnostic is crucial in the fight against schistosomiasis. Since 2017, we have been collaborating with the Australian Institute of Tropical Health and Medicine at James Cook University in Townsville (Australia) and with the Baylor College of Medicine in Houston (United States) to research new biomarkers in order to develop diagnostic tools for schistosomiasis. A collaboration with the Bill and Melinda Gates Foundation and the Foundation for Innovative Diagnostics started in 2018, with the objective of developing innovative **rapid diagnostic solutions** for schistosomiasis.

Praziquantel is an effective and well tolerated drug, but it is not active against all development stages of the parasite. Research activities have continued in collaboration with many partners in developing and developed countries. This discovery work searches for new, long-lasting compounds to treat juvenile forms of the parasite, improve efficacy and prevent reinfections. One potential compound has been identified and is currently in the pre-clinical research phase. We also continued supporting academic research into a new genome editing method for **vector control** to combat schistosomiasis.

We have been fostering research and development as well as manufacturing capacities and know-how in endemic countries through collaboration with local academic and public institutions. We have been implementing a series of research programs on schistosomiasis involving African post-doctoral researchers. New initiatives and opportunities were also assessed to tackle female genital schistosomiasis and its impact on HIV/AIDS.

Consortium for the development of Pediatric Praziquantel Formulation

If left untreated at preschool-age, schistosomiasis can have long-term effects such as stunted growth and an impaired learning ability, causing chronic diseases like bladder cancer or genital schistosomiasis. Since July 2012, we have been working within the [Pediatric Praziquantel Consortium](#), with representatives from both the public and private sector including funding organizations, with the goal of developing a pediatric formulation of praziquantel for all children under the age of six.

Following initial Phase I studies and a taste evaluation, we completed a Phase II study in Ivory Coast to assess the efficacy and safety of two different formulations for orodispersible tablets in schistosomiasis-infected children under the age of six. The results indicate that both formulations are well tolerated and confirmed one formulation for further development. The process for the active pharmaceutical ingredient has been developed and is being transferred to a contract manufacturing organization.

In 2018, two new partners joined the Consortium: the Kenya Medical Research Institute (KEMRI) and the Université Félix Houphouët-Boigny in Ivory Coast. Both will play an important role in implementing the **Phase III trial**, which is due to start in the first half of 2019. This trial comprises the confirmatory clinical study in schistosomiasis-infected preschool-age children and is co-funded by the Consortium, the European & Developing Countries Clinical Trials Partnership (EDCTP) and the Global Health Innovative Technology Fund (GHIT Fund). Regulatory submission is planned in 2020, and we expect the product to be available for launch in the first endemic countries in Africa in 2021.

Accurately diagnosing malaria

Malaria is hard to distinguish from other infections that cause a high fever. Reliable diagnostics are needed to correctly identify patients suffering from the disease so that the appropriate treatment can be administered to the right population. We have been working on a kit containing a **novel malaria detection and typing test** adaptable to the MUSE[®] cytometry platform. It aims to accurately diagnose malaria and measure the type of malaria parasite as well as the infection level. This malaria kit was launched for research use in 2018. At the end of 2018, we sold the underlying technology platform developed by our Life Science business sector to the U.S. laboratory supplier Luminex, which is now commercializing the diagnostic kit.

Enabling the treatment of children

We have been developing a new, **innovative drug** for the treatment of malaria since 2015. The new compound is intended to be developed as a single-dose combination treatment to treat and potentially prevent malaria in children. The Phase I study in healthy volunteers in Australia allowed the safety of the compound to be assessed, and a Phase Ib study provided data to support clinical proof of principle. These clinical activities have been supported through a grant by the [Wellcome Trust](#), a biomedical research charity based in London.

The program is progressing towards the next phase, which entails the development of the asset in combination with another anti-malarial compound in acute uncomplicated malaria. The clinical development plan is also being defined with new clinical studies in patients to start in late 2019 or early 2020.

Developing new lead programs

Our strategic collaboration with the University of Cape Town in South Africa has led to the development of a new research and development platform. In 2018, this collaboration, including our collaboration with the Medicines for Malaria Venture, was extended to continue screening activities with the aim of identifying **new therapeutic solutions** for malaria while building research capacity in and for Africa. This program continues to leverage our proprietary chemical library of almost 100,000 compounds to identify new lead programs for the treatment of malaria, targeting liver-stage forms of the parasite and long-lasting compounds to improve post treatment prophylaxis. This program is co-funded by the [German Federal Ministry of Education and Research](#).

A separate collaboration involving two research centers in Portugal, Instituto de Biologia Experimental e Tecnológica (IBET) and Instituto de Medicina Molecular (IMM), saw progression in the development of a new cell model of liver-stage malaria infection. This model could serve as a screening tool for novel anti-malaria drugs.

Preventing and controlling transmission

To help prevent the spread of malaria, we are working to improve access to insect repellent as a vector control method. Through internal and external collaborations, we are working towards demonstrating the **efficacy of IR3535[®]** against malaria in Africa. IR3535[®] is used in insect repellents for complementary prevention from vector borne diseases, such as malaria, dengue fever, Zika, Chikungunya, and Lyme disease. The repellent has the major advantage of being very safe for all age groups including children as well as for pregnant women and lactating mothers.

In 2018, we entered a partnership with the [Infanta Malaria Prevention Foundation](#) and with [ASPIRx](#), a Ghanaian bio-pharmaceutical manufacturer. This supports the National Malaria Control Program of the Ghana Health Service by exploring development of solutions based on IR3535[®] for malaria prevention in vulnerable communities.

Addressing the global health challenge caused by antimicrobial resistance (AMR)

In order to address the growing emergency of increased bacterial resistance, we have been implementing new collaborative programs to assess the degree of resistance of identified bacterial pathogens. We also focus our efforts on the development of new technological platforms to speed up assessment of the type of infections. A Master's program is currently being run at Makerere University (Uganda) where students are researching ways of tackling the three AMR areas of prevention, detection and management.

open innovation sharing

We consider it our duty and responsibility to share core technological advances in the battle for global access to healthcare. This level of transparency, however, requires a solid, transparent and reliable legal framework to protect the intellectual property rights of pharmaceutical companies and enforce patents, in order to provide time and protection to balance the cost of research and development.

Our approach to sharing and protecting intellectual property

The approach that we and other pharmaceutical manufacturers take to our intellectual property impacts access to healthcare. We often refrain from filing or enforcing patents in developing countries. In markets where we do register product patents, we are transparent and committed to sharing data to the greatest possible extent and improving public access to clinical study data. We report on the patent status of our products via a **publicly accessible database**. Furthermore, we support voluntary licensing agreements of all kinds, including non-exclusive voluntary licenses, legally binding non-assertion covenants and clauses that aim to widen access to health. Moreover, we support the concept of patent pools, but believe that these should be structured to improve access to medicines, prevent anti-competition behavior and overcome geographic limitations. We consider joining patent pools when they are relevant to our portfolio and meet all our efficacy, quality and safety requirements. We are currently only active in the [Medicines Patent Pool](#), which recently extended its scope to include HIV, hepatitis C and tuberculosis.

The responsible treatment of intellectual property does not pose a barrier to health, but rather guarantees **safety and high quality** for patients worldwide. Nearly all medicines that address the highest burden of disease in developing countries are not protected by patents. Studies found that between 90% and 95% of the [WHO Model List of Essential Medicines](#) are off-patent. We provide 46 essential medicines and products, of which 27 are on the WHO Essential Medicines List and 29 are considered to be first line treatments.

Through our initiatives and partnerships, we provide access to patent information. In some cases, we even give access to parts of our compound libraries. This is true for open innovation research projects and collaborative research programs for novel R&D platforms in the search of new active substances.

How we organize access and control of our intellectual property

The Merck [Open Innovation](#) initiative is a collaborative and cross-functional effort led by the Access to Health and the Patents teams. It aims to **mitigate affordability issues** by sharing our intellectual property to accelerate early discovery in diseases that have high unmet needs, where

we do not have expertise. We hope to foster the discovery of new generations of health solutions that tackle the needs of the poorest, with a first focus on neglected tropical diseases (NTDs).

In 2015, we established the Open Innovation Committee to provide technical expertise, strategic guidance and decision-making on our open innovation activities, collaborations and strategy. The Open Innovation Committee is co-chaired by the heads of our Access to Health subunit and the globally acting Patents Healthcare unit and is part of the Open Innovation Initiative.

Our commitment: supporting transparent and reliable frameworks

Our approach to intellectual property is based on the principles set out in our [Access to Health charter](#).

We support [TRIPS](#), an international agreement administered by the World Trade Organization (WTO) that addresses trade-related aspects of intellectual property rights, along with TRIPS addenda such as the Special Declaration on the TRIPS Agreement and Public Health, also known as the 2001 DOHA Declaration. This extends the deadline for the least-developed countries to apply TRIPS provisions to pharmaceutical patents until 2033.

Initiative improves access to patent information

We are a founding member of the Patent Information Initiative for Medicines ([Pat-INFORMED](#)), which was established by 20 leading research-based biopharmaceutical companies. Pat-INFORMED acts as a global gateway to medicine patent information, offering new tools and resources to determine the existence of patents that are relevant to products sought by national and international drug procurement agencies. This transparency should make it easier for drug procurement agencies to access a basic body of patent information necessary to implement **disease management strategies** and other activities that address public health needs. Pat-INFORMED features patent information for small molecule drugs within oncology, hepatitis C, cardiovascular, HIV, diabetes and respiratory therapy areas and any products on the WHO Essential Medicines List that are not within these therapy areas. The initiative is backed by the World Intellectual Property Organization (WIPO) and the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

Pat-INFORMED currently houses information on over 14,000 individual patents, for 600 patent families and 169 so-called INNs, unique names that are globally recognized and used to identify pharmaceutical substances or active pharmaceutical ingredients within medicines that cover a wide range of conditions. The initiative will soon extend to other therapeutic areas and explore the inclusion of complex therapeutics such as biologics.

Open innovation collaboration: WIPO Re:Search

Established in 2011, [WIPO Re:Search](#) is a public-private partnership administered by the World Intellectual Property Organization (WIPO) in collaboration with BIO Ventures for Global Health ([BVGH](#)). We are one of more than 100 members of the WIPO Re:Search platform. The mission is to accelerate the discovery and product development of medicines, vaccines and diagnostics to create **new solutions** for people affected by neglected tropical diseases, malaria

and tuberculosis, by making intellectual property and know-how available to the global health research community. Through the WIPO Re:Search platform we are working on the extension of the collaboration with the University of Buea (Cameroon) and University of California, San Diego (United States) to find potential cures for onchocerciasis, leishmaniasis, Chagas disease and African sleeping sickness.

Drugs for Neglected Diseases initiative

In 2017, we formed a partnership with the Drugs for Neglected Diseases initiative ([DNDi](#)), under which we are involved in the Drug Discovery Booster project for neglected tropical diseases. This project pursues an open innovation approach in which the participating companies simultaneously search for new treatments for leishmaniasis and Chagas disease. We are joined in this project by six other companies (Astellas, AstraZeneca, Celgene, Eisai, Shionogi and Takeda).

pharmaceutical supply chain

In many parts of the world, medicines are not always available where and when they are urgently needed. We want patients in low- and middle-income countries to have fast, safe and affordable access to our products. We believe that this can be accomplished through efficient supply chain management and by utilizing local manufacturing. Our actions in this area reflect our high standards for improving access to healthcare for underserved populations.

Our approach to local supply chain solutions

During product development and manufacturing we favor approaches that enable us to control the cost of goods and allow for local supply chains that strengthen the local economy. This is the model applied in the context of the [Pediatric Praziquantel Consortium](#), for instance, in which the manufacturing and supply are planned to be undertaken locally.

We partner with pharmaceutical companies and other supply chain stakeholders to improve supply chains in developing countries and to guarantee the targeted supply of medicines. We manufacture some of our products directly in the regions where they are needed in order to **build local capacity**, reduce travel time and distance, and achieve cost savings that can be passed on to the consumer.

Our pharmaceutical supply chains are organized efficiently to ensure that our products reach the right place in the right condition and quantity, at an affordable price and on time. **Modern supply chain solutions** allow us to monitor our inventory and current deliveries, as well as to predict expected demand for medicines, partly in real time.

How we organize our supply chains

The Global Planning unit is responsible for our efficient medicine supply chains and is part of Biopharma Supply Network Operations within our Healthcare business sector. Global Planning collaborates with our [Global Health unit](#) and consults experts from other business sectors as needed.

Our commitment: High quality standards for pharmaceutical production

All our pharmaceutical production plants operate to the same high standard of quality worldwide. This ensures full compliance for us and our contract manufacturers with the internationally harmonized guidelines Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP).

In 2018, we refined our "Right First Time" (RFT) concept, which aims to reduce the number of temperature excursions that happen during transportation worldwide. At the same time, we encourage shipping sites and receiving units worldwide to improve their processes together with freight forwarders and carriers.

Our **uniform quality assurance system** ensures that our quality standards are universally adhered to. It comprises training courses, quality control monitoring and technologies that are tailored to each site. The results of all audits conducted by health authorities are published Group-wide, allowing the respective units to share lessons learned and benefit from the improvements of others.

Through our Virtual Plant Teams, we support our contract manufacturers in complying with quality standards. Our external partners in Africa, Asia and Latin America are each assigned a Merck production expert to act as a **virtual site leader** who is able to provide guidance. This approach was again recognized as a best practice in the [2018 Access to Medicine Index](#).

Leveraging technological possibilities for efficient market access

Accurate business forecasts are the foundation of efficient supply chain management. We use harmonized Biopharmaceutical business planning processes across our Group, including a special software platform that enables us to plan centrally for specific demand for medicines. The data generated by the software platform is used to manufacture and deliver medicines according to demand, which allows us to prevent local inventories from running out or expiring.

We employ a software-based solution for our customers in northwestern Africa, which gives them continuous access to our e-shop so that they can quickly and easily order medicines approved by the respective regulatory authorities. The system makes demand more transparent whilst reducing lead times and miscommunications. Combined, both systems enable us to react more quickly to local demands, including in developing markets, than ever before.

Working with partners to achieve more

Our collaborations and partnerships are founded on the Group-wide exchange of centrally stored information, which allows us to organize shared supply chains in a more efficient manner.

Shared data platform for medicine donations

NTDeliver is our digital information tool, which facilitates **transparency in supply chains** for medicine donations that are created through public-private partnerships. Deliveries from companies running donation programs are clearly displayed – from purchase orders made by the World Health Organization (WHO) through to delivery to the first warehouse in the destination country. This improves the coordination of our efforts and provides WHO, the local experts and us with a more transparent overview of the in-country inventory. Following a pilot in 2017, where we tracked deliveries all the way to the treatment point in the destination country, we fully implemented the system in 2018. We started using NTDeliver last mile tracking as a standard reporting tool in the school-based deworming program for schistosomiasis in Kenya. This system is now fully functional

in collecting and consolidating field information and has helped us reach out to more than 12,000 teachers throughout Kenya. In addition to supply chain data, we have started to integrate the first level of impact data requests from the teachers, such as the number of children treated.

Further partnerships

We are a founding member of the Accessibility Platform, which meets to discuss local supply chains during our [Access Dialogues](#). This is an informal effort spearheaded by the private sector to raise awareness of supply chain issues as part of the access to health challenge. It seeks to **increase knowledge-sharing** and information exchange through open, multi-stakeholder dialogue, and to identify opportunities for collective action. We also share best practices with other companies and partners on efficient, end-to-end, secure supply chains. The Accessibility Platform was recognized by the [Access to Medicine Foundation's white paper](#) on "Shortages, stockouts and scarcity: the issues facing the security of antibiotic supply and the role for pharmaceutical companies." In the paper, the Foundation acknowledges that companies have a strong role to play in helping to address supply chain complexities and recognizes the Accessibility Platform as a best practice in information sharing through partnerships.

Promoting local production

Having started to supply pharmaceutical products in 2017, our production facility in Nantong (China) increased its production volume to full capacity in 2018, in order to serve local markets. In addition, we manufacture drugs for diabetes, cardiovascular conditions and diseases of the lower respiratory tract in India and Indonesia. This local capacity building supports local economies and allows us to supply medicines faster and more affordably here and in neighboring countries such as Sri Lanka and Myanmar. In 2018, we further expanded the scope of local production with a contract manufacturing organization (CMO) in Russia.

CURAFA

In 2017, we started the project [CURAFA™](#). The name is derived from the Latin word 'curare', which means care, and the Swahili word 'afya', which means health. CURAFA™ facilities serve as points of care for integrated primary healthcare services and are run by local pharmacists and nurses, who provide **pharmaceutical and clinical services**, medicine, digital health solutions, insurance and financing schemes. The staff is supported by a modern facility with WiFi access and charging stations, tablet PCs and TVs, refrigerators for cold chain medicines, and solar power.

We created the project as part of our vision to achieve primary healthcare for everyone everywhere. Our mission is to address inequalities in primary healthcare access in emerging economies and to enable accessibility, availability and affordability of primary healthcare. We also aim to leverage on-the-ground learning to build a sustainable business model for primary healthcare and provide a space for co-creation with fellow innovators. The project was implemented in collaboration with the non-governmental orga-

nization [Amref Health Africa](#) and benefits patients as well as communities. In 2018, five primary healthcare points were opened in the Kenyan counties Kajiado, Kiambu and Machakos.

Fight against falsified medicines

According to a [WHO report](#) published in 2017, more than 10% of all medicines in developing and emerging countries are counterfeit or substandard, creating a major health risk. The Global Pharma Health Fund (GPHF) is a non-profit initiative funded by our company that is fighting counterfeit medicines with its GPHF Minilab™.

The GPHF Minilab™ is a **portable, compact laboratory** that fits into a tropics-resistant suitcase and can detect fake medicines quickly, easily and cheaply. Around 90 chemical substances can be tested for their authenticity. The GPHF develops these Minilabs, supplies them at cost and provides training on how to use them. The WHO report cites the Minilab as one of the most important tools for detecting poor quality and falsified medicines. As part of a study published in this report, over 20,000 pharmaceutical samples were tested using the Minilab™, with more than 1,000 of them identified as falsified. An [international study](#) conducted by the Difäm-EPN Minilab Survey Group in 2017 also highlighted how the GPHF Minilab™ has helped ensure access to safe medicines in developing countries. The Minilab is currently the only product of its kind.

The majority of Minilabs are deployed in countries in Africa and Asia. These test kits are primarily utilized by national health agencies, often in partnership with the labs of governmental drug inspection centers or within multilateral health interventions led by various UN bodies, aid organizations in the United States and Germany, faith-based networks or the incoming goods inspection unit in the medicines supply chain in all kinds of healthcare facilities, for example medical stores and major hospitals.

Through the [Merck Global Health Institute](#), we are also co-developing a new user-friendly technology that will enable users to detect falsified medicines at the qualitative and quantitative level. Initial models will focus on measuring the presence and quantity of the active pharmaceutical ingredient for malaria and other bacterial infections.

Expanding Minilab use

In 2018, the GPHF developed testing methods for five additional active ingredients, effectively covering a total of 90 active agents from the essential medicines list. Test protocols for ten more active pharmaceutical ingredients were developed and 30 existing protocols reviewed. All test protocols will be put together into a single volume in 2019, and made available in three languages in 2020. By 2020, the Minilab will then cover **100 active ingredients**, ranging from antipyretic, antimalarial and antiviral, to antibacterial and antimycobacterial medicines.

Since 1998, the GPHF has supplied a total of 843 Minilabs to nearly 100 countries, with seven new Minilab shipments made in 2018. The GPHF and its partners held three official seminars for Minilab users in 2018 with 60 participants.

prices of Medicines

Part of the non-financial report

In OECD (Organization for Economic Cooperation and Development) countries, prescription drug costs currently account for between 6% and 29% of total healthcare spending. However, advances in the research and development of innovative medicines are dramatically transforming the healthcare landscape, allowing chronic diseases – the greatest cost drivers – to be treated more effectively and affordably.

Our approach to pricing medicines

We want to ensure that all patients have access to the most effective medicines for their needs, which is why we are working to prevent cost from becoming a barrier to treatment. We are committed to **flexible and fair pricing** – both within and across countries. We therefore adapt our prices based on local market access, also taking into account factors such as health system capacity and financial standing, geographic circumstances and existing infrastructure, statutory requirements, unmet medical needs, and socioeconomic aspects such as the ability of patients to pay. This approach involves working closely with governments and other stakeholders. In addition to these considerations, we continuously monitor dynamic healthcare environments and markets, pricing and reimbursement systems and legal and regulatory guidelines, adjusting our prices as necessary.

We review our prices on an annual basis to ensure they meet patient access needs. To assist this process, we use a consistent, data-driven approach to monitor our local pricing. We also make our products affordable to patients in certain countries by participating in government tenders, establishing second low-price brands or branded generics and operating patient access programs.

Moreover, we support risk-sharing agreements and are working to improve data efficiency in health systems in order to achieve an optimal distribution of funds and resources.

Setting medicine prices

Our Global Pricing and Market Access unit sets initial prices in coordination with the respective businesses. Following a reorganization in 2018, this team now reports to the Chief Operating Officer of our Healthcare business sector. Our individual subsidiaries are responsible for managing prices and continually adapting them to local environments.

Our commitment: Medicine price guidelines and principles

The affordability of our health solutions is part of our broader patient value proposition, which includes increasing [accessibility](#), availability and awareness. Medicine pricing adheres to the stipulations of our overarching [Access to Health Charter](#) and is defined in detail by our [Pricing of Medicines](#) guideline. Our Patient Access Programs Policy furthermore sets out standards that enable us to offer medicines at reduced prices.

Customer-centric contracting models

We are dedicated to advancing value-based healthcare through pricing and contracting mechanisms that comply fully with all local laws. In collaboration with payers such as health insurance companies, we have developed various product- and market-specific reimbursement and contracting models with the aim of providing patients with prompt **access to our innovations**. For instance, we have entered into a risk-sharing agreement in the United Kingdom that provides immediate access to Mavenclad® for patients with multiple sclerosis (MS); under this agreement, the National Health Service only has to pay for medicines for those patients who respond to the drug. Since the start of 2018, under this scheme 488 patients in the United Kingdom have been reimbursed for the cost of the drug.

We have also created contracting models for our oncology drug Erbitux®, our MS drug Rebif® and our growth hormone Saizen® to make it easier for patients to access these medicines. In this vein, we have also capped per patient costs in certain countries and have formed risk-sharing agreements there.

Pricing schemes to serve low-income patients

We work in close partnership with governments and other stakeholders on innovative, differential medicine pricing schemes and furthermore supply products at **reduced prices** to certain countries in Africa, Asia, Latin America and the Middle East. In India, for instance, we are working with public sector representatives such as Bharat Heavy Electricals Limited ([BHEL](#)) and the Oil and Natural Gas Corporation ([ONGC](#)) to develop alternative models for low-income patients and patients who have a limited ability to pay.

Moreover, we regularly participate in government tenders for products that are used in public hospitals serving low-income patients. Many of these tenders take place in developing countries.

Low-price second brands

We have established low-price second brands for some of our existing brands, particularly in countries with a large percentage of **very low-income patients**. In Brazil, for instance, twelve of our products are available as a lower priced version. Other examples of countries where we have established low-price second brands include Mexico, the Philippines, Poland, and South Africa.

Generics

Hand in hand with our partners, we offer branded generics particularly in developing countries to meet the local need for affordable, high-quality medicines that are required to treat the diseases endemic to these nations. In doing so, we ensure better access to reliably high-quality medicines at lower prices. In the Philippines, for instance, four branded generics have been launched to date.

Patient access programs

Worldwide, we operate patient access programs that allow us to offer certain products at **more affordable prices** in several countries. Examples include efforts in China to expand access to our oncology drug Erbitux[®], which is used to treat conditions such as colorectal cancer. Geared

primarily toward low-income patients who receive the drug free of charge, our Erbitux[®] donations have so far benefited around 11,500 patients in China.

We run similar assistance programs in other countries such as India, where we also offer Erbitux[®] at discounted prices. Over 1,700 patients have participated in the initiative. In nations such as China, Peru and the Philippines, we offer free-of-charge biomarker screening that determines whether Erbitux[®] would be a suitable treatment.

In addition to our oncology initiatives, we offer access programs for our drugs Rebif[®], Gonal-F[®] and Saizen[®]. In China, for instance, we operate the Gonal-F-Baby Fund, an access program that provides financial assistance for fertility treatments to low-income couples who have lost their only baby.

Health awareness

Many people are ill but do not realize it. This means that, although effective medicines and therapies are available, these individuals either do not receive treatment or do not receive it in time. To try and prevent this, we conduct global campaigns to raise awareness and improve knowledge of diseases, their symptoms and treatment options. Ultimately, healthcare professionals, communities and patients can only make informed decisions if they have the right knowledge and information.

Our approach to raising health awareness

Awareness plays a key role in our [approach to improving access to healthcare](#). We seek to empower communities, medical professionals and patients with appropriate tools, information and skills so that they can make **high-quality, informed decisions** on prevention, diagnosis, treatment, care, and support.

We often join forces with committed partners to conduct educational campaigns for prevention, early diagnosis and awareness, which also helps to build the capacities of medical professionals working in the fields of research, technology and healthcare.

How we build awareness

The strategic direction and the output of all awareness activities are aligned with our respective businesses. This means that the different business units plan and implement our diverse awareness projects either on a global level or through their local offices, with projects organized according to the **specific needs of the local area**. The offices are also responsible for local mobilization during our global campaigns.

Our commitment: Access to health through awareness

Our strategy for addressing access to healthcare incorporates the topic of awareness and is laid out in our [Access to Health Charter](#). Our awareness campaigns are also subject to the respective [marketing principles](#) set out in guidelines such as our "Pharma Code for Conducting Pharmaceutical Business and Pharmaceutical Operations." In addition, they are governed by internal policies and guidance for reviewing our [interactions with health systems](#) and by the review processes for communication materials.

Global awareness campaigns

We regularly conduct campaigns, often in collaboration with patient advocacy groups, to raise awareness of various diseases across the globe. We focus on those diseases that align with **our core competencies**, expertise and experience along the health value chain, in particular cancer (specifically colorectal as well as head and neck), thyroid disorders, diabetes, and multiple sclerosis. During 2018, we conducted or participated in multiple campaigns that enabled us to reach millions of people.

Awareness and knowledge transfer for thyroid disorders

Throughout 2018, we continued our work to raise awareness of thyroid disorders. At the global level, we supported the International Thyroid Awareness Week in May 2018 for the tenth time. This annual awareness campaign, which we run jointly with the Thyroid Federation International (TFI), aims to highlight some of the lesser-known aspects of thyroid disorders.

To mark this year's International Thyroid Awareness Week, we commissioned an international survey, together with the TFI, among hypothyroidism patients in six countries. The results suggest that getting diagnosed can be difficult and distressing for many of those affected by thyroid disorders, with 70% of surveyed patients saying that they found the road to diagnosis stressful.

We hosted a number of our own events during the week, with more than half targeted specifically at healthcare professionals. These events connected us with almost 35,000 people, including around 11,000 healthcare professionals. Furthermore, we reached three million people through our own social media activities in 23 countries and an additional 35 million people were touched by news coverage, social media and events.

At the regional level, we launched an awareness and action campaign with the Vietnam National Hospital of Endocrinology, which highlighted the fact that although many women suffer from thyroid disorders, an estimated 50% go undiagnosed. The campaign offered free screening for thyroid diseases in 15 hospitals nationwide, with around **50,000 screenings** taking place under the supervision and management of the Merck Vietnam representative office.

Awareness campaigns for cancer

Each year in September, we support the Head and Neck Cancer Awareness Week, an initiative by the Make Sense Campaign that is run by the European Head and Neck Society (EHNS). We align with the Make Sense Campaign's three-year theme, "Supporting Survivorship," and demonstrate our commitment to the head and neck cancer community through our own "Stand Up for Survivors" campaign. Our publicity material included a video in which a head and neck cancer survivor discussed the challenges she faced during remission. Partners were encouraged to translate our materials and leverage them locally with stakeholders in their region. We also asked subsidiaries to show their solidarity with survivors by sharing photos on social media that showed them representing the key theme and standing up for survivors.

World Cancer Day

On February 4, 2018, we again recognized World Cancer Day, an annual initiative driven by the Union for International Cancer Control (UICC). This year, we focused on the future possibilities of cancer care with our campaign "We Can. I Can. Help Shape the Future for Patients." **Teams from around the world** got creative, expressing their hopes and aspirations for the future of cancer care through sculptures made from modelling clay. We received almost 330 images of support from 24 countries and our multi-channel social media activity generated over 15,300 views.

Colorectal Cancer Awareness Month

During March 2018, we backed Colorectal Cancer (CRC) Awareness Month, an initiative to raise awareness of CRC, its symptoms and the importance of early diagnosis. Our "gut strength: Targeting CRC Together" campaign encompassed three key themes: together, strength and support. We united on social media to share a message of support through a Thunderclap, which reached over 162,000 people worldwide. Colleagues also showed their commitment to the CRC community by sharing photos of themselves visually representing the key themes and using the campaign hashtag #gutstrength.

World Multiple Sclerosis Day

We participated in the annual World Multiple Sclerosis Day (WMSD) in May 2018. This year's theme was #bringingus-closer to ending multiple sclerosis (MS), which was selected to celebrate advancements in research and care and to look to the future for further developments. A total of **26 Merck organizations** participated in this initiative of the MS International Federation (MSIF) by showcasing their support and activities.

We also announced a new campaign, #MSInsideOut, to support the MS community and deepen understanding of the disease. The initiative involved a collaboration with the social network Shift.ms, which acted as executive producers of a new documentary, "Interpreting MS", which featured unique perspectives from people with MS. The documentary premiered at the 34th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in Berlin (Germany) in October 2018.

To accompany the premiere of the documentary, we published the report "Living with Multiple Sclerosis: The Carer's Perspective", which examines the experiences of those caring for people living with MS. This report was developed in collaboration with the International Alliance of Carer Organizations (IACO) and Eurocarers, the European network that represents informal carers and their organizations. A survey of MS carers across seven countries (Canada, France, Germany, Italy, Spain, the United Kingdom, and the United States) found that almost half of those surveyed became carers when they were 34 years old or younger, and one in three had been caring for somebody for 11 years or more. Furthermore, nearly half reported that their caring responsibilities had negatively impacted their future plans and life goals, while a similar proportion said they suffered from either severe or high stress levels. This emotional toll was compounded by the fact that over half of

the carers surveyed felt that people around them don't truly understand what it means to care for someone with MS. Finally, MS in the 21st Century, an initiative sponsored by our company, launched a [website](#) for discussions between patients and healthcare professionals.

World Malaria Day

Since 2015, Merck has championed World Malaria Day, held annually on April 25, with campaigns that raise awareness for the disease and through engaging in the activities and efforts of the "One Merck for Malaria" program. In 2018, we hosted events in Accra (Ghana), [joining forces](#) with the [Infanta Malaria Prevention Foundation](#) of the First Lady of Ghana and with [ASPIRx](#) to support the Ghanaian National Malaria Control Program. These events, which included a scientific symposium, led to the signing of a Memorandum of Understanding for a consortium to identify and deploy timely and **effective malarial prevention solutions** for vulnerable populations.

World Diabetes Day

We launched a global campaign for World Diabetes Day on November 14, 2018, under the concept: See it. Slow it. Stop it. The aim of the campaign is threefold: helping people spot the risks and symptoms of type 2 diabetes, empowering them take action to slow down progression to type 2 diabetes and ultimately equipping them to help themselves or others prevent type 2 diabetes. We continued our partnership with the International Diabetes Federation (IDF), working on a range of educational activities that aim to raise awareness of prediabetes and diabetes prevention and to globally reduce the rise in type 2 diabetes cases.

Online diabetes campaign

According to the International Diabetes Federation, there were 14 million cases of diabetes in Africa in 2015, a figure expected to more than double by 2040. Moreover, approximately 60% of cases go undiagnosed. Awareness of early symptoms of diabetes is low, even among healthcare professionals. To **improve early diagnosis** and promote awareness of the disease, we joined forces with various partners in March 2015 to launch a digital initiative known as DORA ([Diabetes Online Risk Assessment](#)). DORA aims to expand individuals' knowledge of diabetes by providing free online self-assessment tests to determine their risk of developing the disease. Depending on the outcome of the online test, people have the opportunity to take a free blood test in partnering pharmacies. When this blood test indicates diabetes, they are given a starter pack to help monitor the disease at home. Until recently, DORA had been deployed in Ethiopia, Ghana, Kenya, Mauritius, Mozambique, Namibia, and South Africa. During 2018, the program was extended to Angola, Botswana, Tanzania and Uganda. Since its launch, there have been more than one million visits to the DORA website.

Healthy Women, Healthy Economies initiative

Nearly one in four women worldwide are held back from achieving their full economic potential due to preventable causes, including exposure to a wide range of communicable

and non-communicable diseases. In addition, they spend significant time on unpaid work. This has implications for their own health and well-being. To tackle these challenges, we are committed to [Healthy Women, Healthy Economies](#). Under the auspices of the Asia-Pacific Economic Cooperation (APEC), we collaborated with representatives of several governments to launch this public-private partnership that aims to identify and implement policies that advance women's health and well-being to support their economic participation. The initiative has developed a [policy toolkit](#) with recommendations to improve women's health. We have made Healthy Women, Healthy Economies part of our core commitment by **forming collaborations** to make meaningful change and supporting research to quantify the socio-economic impact of health burdens on women.

Our collaborations

We joined forces with the Philippine government and the Philippine Thyroid Association (PTA) to educate more than 2,000 health industry employees on thyroid disorders, a problem that disproportionately affects women. By the end of 2018, our campaign had reached nearly eight million people in the Philippines.

In Jordan, we collaborated with the Royal Health Awareness Society, an NGO that increases awareness among women about thyroid disease and trains health workers on thyroid disorders in women. We reached over 7,000 patients through the Society's thyroid disease website and an accompanying social media awareness campaign, and engaged and educated over 120 healthcare providers during a scientific event.

We also sponsored and undertook several other projects in Brazil, Spain and the United States.

Quantifying the socio-economic impacts of health burdens on women

In Asia we are working to help our local not-for-profit partners better understand the drivers and impacts of the socio-economic dynamics they will be facing locally. In 2018, we commissioned the Economist Intelligence Unit to study

the demographic trends, childbearing choices and family-related policy decisions in China, Japan and the emerging markets of Southeast Asia.

In the United States, we conduct six studies with the March of Dimes Center for Social Science Research to better understand the relationship between economic and employer policies, women's health and productivity and childbirth. Under a collaboration with the Wilson Center, we supported the development of a policy brief titled "The Juggling Act of Caregiving: Balancing Career, Health, and Gender Roles".

We are also conducting research to understand the full range of impacts that multiple sclerosis has on the lives of women who are affected by the disease in Argentina, Brazil, Chile, Colombia, and Mexico. This research builds on the [European report](#) we launched in October 2017.

Embracing Carers initiative

[Embracing Carers](#) is a global initiative that we lead in collaboration with prominent caregiver organizations around the world. Embracing Carers is designed to increase awareness, action and discussion for the often-overlooked needs of caregivers. We believe that the topic of caregiving is one of the most **under-addressed public health issues** of our time. Caregivers spend so much time looking after someone else that they often do not get the recognition and support they need. We raise awareness of the issues caregivers face, activate stakeholders for deeper engagement, establish global best practices and advocacy resources, and endorse the improved integration of carer support into the entire spectrum of care. In 2018, Embracing Carers supported the self-identification of caregivers, extended the reach of the initiative to Brazil and China, established dedicated disease-specific carer resources, and collaborated with carer communities to develop the first-ever Global State in November 2018, which highlights the needs of unpaid caregivers in Australia, Canada, France, Germany, India, Italy, Spain, the United Kingdom, and the United States.

product safety and quality

chemical product safety



Part of the non-financial report

Since many of our chemicals are classified as hazardous substances and mixtures, we must ensure that they pose no risk to people or the environment. We therefore comply with an array of national and international regulatory requirements, statutes and guidelines, an approach that is crucial to our business activities. In addition, we strive to meet the expectations that stakeholders such as customers and employees have of a comprehensive hazard management system.

Our approach to safe chemical products

Product safety is one of our top priorities. Starting at the development stage, we investigate the potential adverse impacts chemical substances may have. Along the entire value chain of our chemicals – **from cradle to grave** – we fulfill all statutory requirements, often even exceeding them. We furthermore publish extensive information on our website so that both our customers and the general public can learn about our products and how to handle them safely.

How we ensure chemical product safety

Our Healthcare, Life Science and Performance Materials business sectors each have their own organizational structures in place to provide guidance on product safety. These units work in close collaboration with our Group-wide governance function Corporate Regulatory Affairs Chemicals (EQ-R) to ensure our products' safety. Their tasks include registering chemicals, classifying hazardous substances and communicating risks by means of safety data sheets and labels.

Our Group Product Safety Committee (GPSC) monitors regulatory requirements worldwide to check for relevant changes, initiating and reviewing the measures needed to integrate these changes into our processes.

Corporate Regulatory Affairs Chemicals (EQ-R) ensures regulatory compliance Group-wide. Reporting directly to the head of our Group function Corporate Environment, Health, Safety, Security, Quality, EQ-R is independent of our business sectors and not subject to any operational commitments. Any necessary corrective or preventive action is carried out by the operating units within each business sector. EQ-R further supports individual units in implementing and harmonizing efficient processes.

Our commitment: statutory regulations and Group-wide guidelines

We have implemented Group-wide guidelines that guarantee compliance with national and international regulatory

requirements, and have also endorsed general voluntary commitments of the chemical industry such as the [Responsible Care® Global Charter](#).

To meet the product safety regulations relevant to our company, we have enacted our Regulatory Affairs Group Policy, which details our Group-wide processes for managing and **implementing product safety**, including the necessary management structures. The statutory requirements applicable to our operations include the Globally Harmonized System of Classification and Labeling of Chemicals (GHS) and its implementation in regional and national legislation (such as the CLP regulation in the European Union and HazCom 2012 in the United States), the EU chemicals regulation [REACH](#), the amended U.S. Toxic Substances Control Act (TSCA), and the amended German Federal Banned Chemicals Ordinance (ChemVerbotsV). Our Group-wide policy also incorporates legal norms concerning the transport of hazardous chemicals, biocides, cosmetics, and products used in food and animal feed. In 2018, we furthermore implemented our Group Label Standard, which provides a consistent framework for labeling products according to GHS requirements.

In this period, there were no incidents of non-compliance with regulations or voluntary standards involving chemical product labeling.

REACH registration complete

In 2018, we finished registering all substances covered by REACH, doing so within the allotted time. In the third and final REACH registration phase, to be completed by June 2018, we **evaluated and registered all substances** produced or imported in annual quantities greater than one metric ton. This process also incorporated the substances added to our portfolio through the acquisition of Sigma-Aldrich.

In line with the **Strategic Approach** to International Chemicals Management (**SAICM**), a global policy framework, a growing number of countries are recognizing the requirements for registering and licensing chemicals, such as the Toxic Substances Control Act (**TSCA**) in the United States and the Act on the Registration and Evaluation of Chemicals (**AREC**) in Korea. Thanks to our expertise in implementing REACH, we are well prepared for such a procedure and are already registering chemicals as required.

Transcending laws

In an effort that goes beyond statutory requirements, we support the goals of the Global Product Strategy, an international initiative of the chemical industry. In this vein, we publish product safety summaries for all lead substances that we have registered under **REACH**, making them available on the website of the International Council of Chemical Associations (**ICCA**).

Safety analysis during product development

We believe that product safety starts during the development stage. By conducting hazard, exposure and risk assessments, we work to ensure our chemicals can be safely used later down the road. All our innovations undergo an **EHS analysis**, which examines factors such as their impact on human health and the environment. Before launching a new product, we evaluate all relevant hazardous substance data and classify the product according to the Globally Harmonised System of Classification and Labelling of Chemicals (**GHS**), along with locally applicable regulations such as **CLP** in Europe. In conducting these safety assessments, our employees in our Life Science and Performance Materials business sectors are advised by their respective Regulatory Affairs unit.

Our approach to nanotechnology

Nanotechnology is a highly innovative field of development that researches and uses structures 50,000 times thinner than a human hair. This technology makes it possible to produce **materials with completely new properties and functions** for a myriad of applications.

Nanotechnology opens up many opportunities for our Group. In our Life Science and Performance Materials busi-

ness sectors, we utilize nanomaterials to develop products with new functions and properties, thereby making resource and energy consumption more efficient. In our Healthcare business sector, we collaborate with research institutes and other European companies to explore the use of nanomaterials to improve therapeutic options. Under the auspices of **European research partnerships**, we are also investigating whether nanoparticles are suitable vehicles to deliver active pharmaceutical ingredients to the required site of action.

Despite their promise, the unique structure of nanoparticles may harbor risks, which we assess in line with statutory requirements such as REACH. Moreover, we only utilize this new technology with the greatest care, abiding by the **precautionary principle** and taking nanomaterial safety very seriously. In doing so, we consider Group-wide requirements for safety, environmental stewardship and health impact mitigation, employing our existing product safety processes and systems. Whether using nanomaterials in pharmaceutical and chemical laboratories, production facilities, filling plants, or warehouses, we follow our Group-wide **Policy for Use and Handling of Nanomaterials**.

In the manufacture and processing of our products, we adhere to all statutory regulations along with standards such as those of the German Federal Institute for Occupational Safety and Health (**BAuA**), as well as the German Chemical Industry Association (**VCI**). We also provide our customers **safety data sheets** containing information on the proper handling of nanomaterials during transport, processing, storage, and disposal.

Sharing nanotech knowledge

Over and above our internal efforts, we continuously engage other companies, associations and regulatory agencies in a dialogue on the **opportunities and risks of nanotechnology**. We also take part in committees and working groups, including the Nano Panel of VCI's Technology and Environment committee, as well as Responsible Production and Use of Nanomaterials, a joint technology working group of the Society for Chemical Engineering and Biotechnology (**DECHEMA**) and the VCI. Under the auspices of the VCI, we furthermore review current scientific literature in order to stay abreast of new advances in nanotechnology.

Standardized product safety information

As part of our efforts to communicate the potential dangers of our products, we provide our customers with in-depth informational material on all our chemicals. These brochures contain instructions on **proper use and handling** to prevent them from posing a danger to people and the environment. Our goal is to give our customers product safety information that has been standardized worldwide.

We issue all chemicals classified as hazardous with **safety data sheets**, which, in accordance with UN regulations, follow a globally harmonized format. These sheets contain information on the physicochemical, toxicological and ecotoxicological properties of the agent, and reflect the relevant regulatory requirements of the countries in which they are published. We therefore produce country-specific safety data sheets in 44 languages for our Performance Materials business sector and in 37 languages for our Life Science business sector. Although not mandated by law, we also provide safety data sheets for the non-hazardous materials and finished medicinal products manufactured by our Healthcare business sector. Since all these documents must be kept up to date and consistent, we have automated the majority of our Group-wide hazard communication processes. Within Performance Materials, we draft all safety data sheets Group-wide using a single system.

In 2018, we also automated most of the safety data sheet creation process for our Life Science business sector and also developed an app that provides our Life Science customers with **access to the latest product safety information**. Covering the whole life cycle of the product along its entire supply chain, the information is available

worldwide in the respective national language and accounts for country-specific regulations. To access it, customers need merely scan the product's barcode or enter it manually.



million safety data sheets in total are made available to our customers.

Informing and educating customers

All information on the safe use of our products is also available on our website, where our customers can additionally access the **SciDeEx[®]** program. This tool allows them to check whether they can use chemicals safely within the boundaries of the REACH exposure scenarios.

Taking a more active approach, we also endeavor to **educate people on the safe handling of hazardous chemicals**, providing users with best practice advice and information. To this end, we regularly conduct seminars and information sessions worldwide that teach basic lab safety rules such as the handling of flammable solvents and the storage of hazardous chemicals in safety cabinets and warehouses.

patient safety

Part of the non-financial report

The safety of patients who are treated with our medicines is our absolute priority. Our pharmaceutical products need to be effective in treating the respective disease while also posing as little risk as possible to patients. That is why we consistently monitor risks and any adverse effects that may arise, and take the necessary actions to minimize them. The benefits of our drugs must always outweigh the risks for patients.

Our approach to ensuring patient safety

Through rigorous benefit-risk management, we ensure that the benefits of our drugs always outweigh the risks for patients. Every new medicine passes a series of precisely defined development stages. Before any drug is given to humans, we conduct extensive preclinical testing both in vitro and in vivo. Through toxicological testing, we determine whether an active pharmaceutical ingredient is toxic to living organisms and, if so, at what dosage. This also helps us determine the dose that humans can safely tolerate. Only when this is complete do we perform [clinical studies](#) to investigate the safety and efficacy of the drug when used in humans. During clinical development, we diligently use all collected data to continuously evaluate the drug's **benefit-risk profile** to be positive, we then submit an application for marketing authorization to the regulatory authorities.

Continual monitoring

After a drug is launched, the number of patients being treated with it increases significantly. In certain circumstances, rare adverse and severe effects that go undetected during clinical development may occur, which is why we continually monitor and manage the positive benefit-risk profiles after market launch. Pharmacovigilance is the process of continuously monitoring a drug to detect and assess signals as part of signal management activities. The aim is to track the adverse effects in an effort to take appropriate action to minimize and communicate the risks in a transparent way. We always provide physicians and patients with the **latest information on the safety** of all our marketed drugs. This applies to the entire life cycle of a product, ranging from development, market launch and commercialization to expiration of the marketing authorization.

For new products, educational materials are developed for patients and healthcare providers to communicate the known and potential risks, and ways to minimize them. We assess the effectiveness of these materials in close collaboration with our Benefit-Risk Action Team. If required, we adjust the content of the materials and their distribution, and describe the results from the effectiveness analysis in our periodic safety reports and risk management plans, which we submit to health authorities for evaluation.

How we monitor patient safety

Our Global Patient Safety unit is responsible for pharmacovigilance. It continually collects current safety data from a wide variety of sources across the globe, including clinical

studies, spontaneous reports on adverse effects, patient support programs, and articles published in medical and scientific journals, and furthermore reassesses the benefit-risk profile on an ongoing basis.

Our experts make sure all information on the risks and adverse effects of our medicines is properly documented, tracked and reported to the respective health authorities in accordance with regulatory requirements. The Global Patient Safety unit analyzes all data and uses this as required to reassess the benefit-risk profile. We then inform regulatory authorities, physicians and patients about new risks, additional risk mitigation measures and potential changes in the benefit-risk balance.

Our **Product Quality unit** (MBQ) processes quality complaints relating to our products. When quality defects may have an impact on patient safety or lead to adverse effects, Global Patient Safety gets involved.

Our Medical Safety and Ethics Board

Our Medical Safety and Ethics Board (MSEB) oversees the safety and benefit-risk evaluations of our drugs throughout clinical development and commercialization. It endorses appropriate **measures to minimize risk**, such as package insert updates. This board is chaired by our Chief Medical Officer (CMO) and consists of experienced physicians, scientists and experts from our company. Throughout a drug's entire life cycle, the MSEB reviews and assesses important medical safety risks and benefit-risk issues, and reviews ethical issues if necessary.

Our commitment: Guidelines and statutory requirements

We follow international guidance and standard procedures such as the International Conference of Harmonization (ICH) guidelines and the Good Pharmacovigilance Practices (GVP) established by the European Medicines Agency (EMA). In addition, we adhere to all statutory pharmacovigilance regulations in those countries where we market our products, and we constantly work to incorporate all required changes in our Group-wide standards and processes. In 2018, for instance, we harmonized the **processing of personal data** worldwide according to [new European legislation on data privacy](#).

In November 2017, the EMA implemented a new process for EudraVigilance to monitor the safety of medicines. This newly established approach provides marketing authorization holders with access to data on suspected adverse effects, requiring them to monitor the EudraVigilance data for safety signals and to report these to health authorities.

In response to these new requirements and to the new data transmission format stipulated by ICH guideline E2B (R3), we upgraded our **Global Safety Database** to ensure the technical capabilities needed to support the coordinated exchange of individual [case safety reports](#).

In 2018, we assessed new country-specific regulatory requirements and implemented necessary changes in order to fulfill them. Examples include the Chinese Food and Drug Administration, the new India Pharmacovigilance Guidance for Marketing Authorization for **post-marketing safety reporting** and the new Canadian requirements for safety signal notification.

In addition to adhering to guidelines and regulations, we have introduced a Benefit-Risk guide to our Global Patient Safety unit, which builds on the results of a joint initiative that we are involved in between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA). These results helped us in compiling the documentation for the marketing authorization of cladribine and avelumab.

Collecting information and checking processes

Our self-developed mobile app, named agReporter, is used to report any adverse effects arising from the use of our products. Although initially intended for use by field nurses and our sales representatives, in 2018 we introduced an interface designed for non-medically trained users, thus making **patient feedback** the core of our efforts to consistently collect adverse effects data. In 2018, the app became available in a total of eight languages, with a Chinese version currently in the works.

In 2018, we introduced a new pharmacovigilance intelligence process to improve internal data analysis and informational output from our various sources. We have developed new capabilities in the following areas:

- advanced benefit-risk management
- big data analytics
- advanced signal detection technology
- pilot processes in patient-centric adverse effects collection

Supervising drug safety

Regulatory authorities conduct periodic inspections to verify that we are complying both with statutory requirements and our own internal standards for drug safety. In Germany, these are handled by the German Federal Institute for Drugs and Medical Devices (BfArM) and the Paul Ehrlich Institute (the German Federal Institute for Vaccines and Biomedicines (PEI) on behalf of the EMA. In 2018, four **pharmacovigilance inspections** were conducted in Japan, Slovakia, Slovenia, and Turkey. Every inspection has confirmed the proper functioning of our pharmacovigilance system.

Furthermore, we perform audits to ensure that all our departments and subsidiaries involved in pharmacovigilance consistently meet all requirements across the globe. In 2018, we conducted a total of 37 audits and found no significant deviations in our pharmacovigilance system from these requirements. We also audit vendors and licensing

partners involved in pharmacovigilance, which help us hone our pharmacovigilance processes so that they surpass statutory requirements.

Innovative signal detection

In 2018, we successfully launched a new methodology and technical system for analyzing and managing large amounts of data from around the world, such as scientific studies and news about side effects. Through this new tool for signal detection, named Empirica, we intend to become more efficient and proactive and improve risk management. It helps us to comply with regulatory timelines for safety signals and other safety-related factors and will ensure that all signal data, documentation and decisions are captured in one place. This allows easy access to and analysis of our data as well as cross-functional collaboration between Global Patient Safety and other internal and external stakeholders. Furthermore, we established a **new signal detection process** that allows us to detect signals directly from the EudraVigilance Data Analysis System (EVDAS) and enables us to comply with any new requirements set by health authorities.

Up-to-date labeling and product information

Our product information explains to physicians and patients how to properly use the respective drug and allows for an informed decision on the treatment. In accordance with statutory regulations, the **package insert** contains all relevant information such as indication and ingredients, as well as dosage, storage, mode of action, instructions for use, warnings, precautions and possible adverse effects. Should the medicine contain ingredients that may impact the environment, the package insert may also contain information on the proper disposal of the product.

As necessary, we review and update all product information documents such as package inserts, ensuring that our medicinal products contain the latest information on safety, efficacy and pharmaceutical formulation. In accordance with statutory requirements, all modifications to the inserts are submitted to the respective regulatory authorities for approval.

Internal and external training

All employees involved in the safety and quality of pharmaceutical products are trained according to our global training standards. We verify compliance with these requirements by producing training compliance reports and performing regular audits.

Our training is delivered via a **global-learning platform**. All of our 20,000-plus Biopharma employees receive basic pharmacovigilance training once a year that covers the procedure for reporting adverse effects from our products. Other training courses keep employees up to date on their professional expertise as well as internal standard operating procedures and other relevant requirements. This ensures adherence to Good Pharmacovigilance Practice (GVP) requirements.

Sharing expertise with other countries

We endeavor to transfer our drug safety expertise around the world, especially in countries where health workers need to build **their pharmacovigilance expertise**. In 2018, we organized a workshop for 96 students from the School of Medicine of the National University in Guatemala, as reporting of adverse drug reactions is often not sufficiently represented in the curricula of medical students. The participants were already examining patients and prescribing drugs on a daily basis, so they considered the workshop to be relevant and applicable in their daily routine.

We also assist Latin American health authorities in implementing electronic reporting processes for adverse effects. Following a pilot project in Ecuador that ended in April 2018, we are supporting the implementation of elec-

tronic reporting in Argentina, El Salvador and Peru. Health authorities in Mexico and Brazil are also moving towards adopting this technology. This program makes us one of the first companies to participate in global electronic reporting.

Our activities in providing **health for all** include involvement in piloting a **social business healthcare platform** in Kenya named **CURAFA**. As part of this project, in 2018 we provided training to two pharmacies on pharmacovigilance awareness and safety reporting procedures, and introduced our agReporter app to the people working there.

Launched in late 2017, we are continuing the "Afrika kommt!" project in an effort to educate trainees from Africa on the safe use of pharmaceutical products. The ultimate goal is for them to eventually take what they have learned and implement it in their home countries.

product-related crime

Part of the non-financial report

According to the World Health Organization (WHO), a considerable proportion of the medicines in developing countries are illegal, counterfeit or substandard. In industrialized nations, however, such products are also becoming increasingly available on the market through unlicensed internet pharmacies and underground platforms, posing a risk to public health. Moreover, chemical products too can be used for illegal purposes such as the manufacture of illicit drugs.

Our approach to product-related crime

Our company develops and manufactures products of the utmost quality. In order to protect both customers and patients, we secure our products against counterfeiting and are deeply committed to fighting product-related crime. For instance, we collaborate with regulatory and law enforcement agencies **at the regional, national and international level**. When cases of product-related crime are identified, we also cooperate with the law enforcement and public health authorities in the respective countries. In taking preventive action, we furthermore partner with representatives from Interpol and the World Customs Organization. Our guidelines, standards and processes apply to all our business sectors and markets worldwide.

What we mean by product-related crime

1. Counterfeit products: In line with the relevant WHO standard, we define a counterfeit product as "a product that is deliberately and fraudulently produced and/or mislabeled with respect to its identity and/or source to make it appear to be a genuine product."

This includes products

- with incorrect active ingredients or concentrations thereof
- without any active ingredients
- with dangerous impurities
- with modified/alterd packaging and/or incorrect brand names
- with an authentic active agent, but not one produced under GxP conditions
- that have expired
- that were diverted from the legal supply chain (for example through theft).

2. Illegal diversion of products: This term refers to the diversion of either chemicals or pharmaceuticals from within the legitimate supply chain for illegal export, for use in the production of illicit drugs, weapons or explosives, or for any other illegitimate purpose.

3. Black market crimes: This refers to the sale of counterfeit and/or diverted products via illegal channels such as the Internet, or for illicit purposes.

4. Misappropriation of products: This refers to theft from production sites and warehouses, or while in transit.

How we are tackling product-related crime

Our Group function Corporate Security coordinates all our anti-counterfeiting activities, all of which are overseen by the Chief Security Officer and the head of Environment, Health, Safety, Security, Quality (EQ). Furthermore, all our sites have a product crime officer who investigates potential cases of counterfeiting, acting as the interface between local regulatory and law enforcement authorities, national associations, our Group functions, and our facilities. Depending on the type, allegations are first investigated by the competent unit. In 2018, conference calls attended by all product crime officers were held every two weeks to discuss strategic matters along with local issues and suspected cases of criminal activity.

Group-wide anti-counterfeiting network

Our Anti-Counterfeiting Operational Network (MACON) is responsible for **globally monitoring and executing all anti-counterfeiting measures** for our products. Along with coordinating prevention and the development of security systems, this organization is also responsible for investigations. Comprised of experts from various units such as Legal/Trademarks, Product Security, Export Control, Supply Chain, Patient Safety, and Quality Assurance, this network is coordinated by our Corporate Security unit.

To investigate suspected cases, MACON collaborates with the competent law enforcement agencies and regulatory authorities. This network has allowed us to identify more **cases of counterfeiting** and take decisive action, especially in high-risk countries. In 2018, MACON investigated and pursued numerous incidents including theft, counterfeiting and illegal diversion in both the legitimate and illegitimate supply chain.

Our commitment: Group-wide guidelines and standards

Our Crime Relating to Products of the Merck Group Guideline describes our goals and strategies for combating product-related crime. Our Group-wide Product Crime Investigation Standard sets out **mandatory requirements** and defines the knowledge sharing process within our company in an effort to provide a solid legal footing for dealing with illicit products.

Enhanced monitoring and reporting systems

We analyze and document all counterfeit product incidents using a Group-wide reporting system. This approach provides us with a **complete picture of the security situation** and enables us to identify possible links between different cases, thus equipping us to combat similar incidents more effectively going forward. Our standard operating procedure "Data and Documentation Quality Management" details the corresponding process and was used in 2018 to standardize and harmonize data quality and reporting across our organization.

Tracking system for chemical substances

We monitor chemicals that could be misused to produce illegal weapons, explosives or narcotics, tracking them through an **internal system** that flags suspicious orders or orders of sensitive products. These are only released once we have confirmed the existence of a (verified) end-user declaration.

In 2018, the integration of Sigma Aldrich into our organization substantially increased the volume of products to be monitored. In an effort to augment process safety and efficiency, we revised our **internal reporting**.

In addition to fulfilling the duties stipulated by **statutory provisions on export control**, we also report suspicious orders, inquiries and requests to the competent authorities. Through these efforts, we are honoring a voluntary commitment of the German Chemical Industry Association (VCI) and meeting the terms of the Guideline for Operators published by the European Commission.

Reviewing our efforts

We evaluate the effectiveness of our measures according to the number of reported, investigated and solved cases, as well as their severity.

Supporting customers and patients

To protect patients, pharmacies must be able to determine the identity and authenticity of pharmaceuticals. We are therefore rigorous in meeting the requirements of the EU Falsified Medicines Directive and, accordingly, have set a goal for February 2019 to apply a **unique serial number** to the packaging of all the prescription medicines we commercialize in the European Union. We have already concluded the preparatory stage of implementation for 73% of our products covered by the directive. In 2018, 32% of these serialized products were in circulation. We are also transposing similar guidelines in many other countries. In the United States, for instance, we were the first company to comply with the 2018 Food and Drug Administration (FDA) product identification requirement.

In parallel to meeting these provisions, we also pursue our own initiatives:

- We apply the Security M label to some of our products, which enables users to **easily verify the authenticity**

of our products and is considerably harder to counterfeit than commonly used holograms. We take a risk-based approach to identifying the products to be labeled in this manner.

- Using our **Track and Trace** system to track the serial numbers of our products, delivery points (such as pharmacies) and distributors can trace the supplier of the medicine to verify its authenticity. So far, this system has been established in the United States, the European Union, China, Egypt, Colombia, Turkey, and parts of the Middle East, with implementation in Russia still underway. Preparations are currently being made to launch Track and Trace in Indonesia and Malaysia.
- Our free **Check My Meds app** for smartphones allows patients in the United States and Colombia to scan the serial number of their medicines and quickly verify their authenticity.
- In our **Mobile Anti-Counterfeiting System (MAS)** project in Nigeria, we are working closely with one of our suppliers on a text message-based identification system. Patients scratch off a barcode that is printed on the product packaging and then send this code via text message to an assigned number. They immediately receive a response telling them whether their code is authentic.
- We sponsor the non-profit Global Pharma Health Fund (GPHF), which supplies **GPHF Minilabs®** to test the quality of 90 different active ingredients. Used primarily in developing and emerging countries, this compact kit can detect counterfeit medicines quickly, easily and inexpensively. You can find more information on this project under [Pharmaceutical supply chain](#).
- We offer our customers in the pharmaceutical industry **Candurin® pearl effect pigments with** unique color properties that make tablets and capsules more difficult to counterfeit.

Industry-wide exchange

In an effort to fight product-related crime, we have joined forces with organizations such as the European Federation of Pharmaceutical Industries and Associations (EFPIA), the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), and the German Association of Research-based Pharmaceutical Companies e. V. (vfa). We also support industry-wide initiatives. For instance, we partner particularly closely with the Pharmaceutical Security Institute (PSI), a non-profit organization dedicated to protecting public health by sharing information on pharmaceutical counterfeiting and initiating enforcement actions through the appropriate authorities. We take an active role in this work through participation in [PSI conferences and network meetings](#). Furthermore, we are a member of Rx-360, a consortium of global pharmaceutical manufacturers and suppliers that aims to prevent counterfeit products through a **worldwide quality control system**.

Raise awareness for product-related crime

We endeavor to raise awareness of product crime among our employees and business partners, educating our people Group-wide on the subject.

All staff involved in security, such as product crime officers, participate in **onboarding and training programs** aimed at building their capacities and promoting best practice sharing. We are continuously evolving these programs and adapting them to new trends. In 2018, for instance, we held 40 onboarding sessions for our product crime officers, covering product-related crime, incident reporting, case management, and cooperation with authorities.

In addition to offering training, we contributed to "Schutz vor Arzneimittelfälschungen: Regelungen zur Arzneimittelsicherheit", a book published in July 2018 by Editio Cantor Verlag that **discusses approaches to combating counterfeit drugs**.

Security audits for contract manufacturers and distributors

We regularly check whether our distributors and contract manufacturers are complying with GMP and GDP (Good Manufacturing Practice/Good Distribution Practice). These audits are based on the [EMA ICH Q10](#) pharmaceutical quality assurance standard. In doing so, we also ascertain the extent to which our **security requirements** are being obeyed by contract manufacturers and distributors, conducting special security audits if a concrete need is identified. Such audits are also conducted standardly when we certify external service providers for our Security M label. This applies to both pharmaceutical contract manufacturers as well as print companies that print packaging. The findings from these audits are a key factor in our decision-making process when considering potential external partners. If any critical defects are found, they must be rectified prior to us signing a deal, or a detailed corrective action plan must be submitted for our approval. In 2018, we conducted four security audits of our partners worldwide, who have since remedied the relevant defects.

Transport and warehouse safety

Part of the non-financial report

We transport and store products and materials worldwide such as chemicals and pharmaceuticals, raw materials, intermediates and waste, as well as technical materials and packaging, all of which could pose a hazard to health and the environment if handled incorrectly.

Our approach to safe transport and storage

We strive for all our shipments to reach our customers and sites safely, undamaged and with the required safety information. Several of the materials we store and transport are classified as hazardous. To minimize danger to people and the environment, we therefore adhere to **extremely strict safety regulations across our Group**. The storage of such hazardous goods and the corresponding transport involved – whether by road, rail, plane, or ship – are governed by regulations applicable worldwide. Our standards cover all stipulated safety guidelines, and we ensure compliance through regular audits of our sites along with training for our employees and the leadership of contract warehouses.

How we achieve transport and warehouse safety

Transport and warehouse safety falls under our Group function Environment, Health, Safety, Security, Quality (EQ) (see [Environmental stewardship](#)), which sets Group-wide standards and guidelines. In addition, our individual sites are subject to various national and international regulations governing environmental stewardship and public safety, which **local site directors are responsible** for implementing.

Each of our sites around the world has an EHS manager and a **dangerous goods manager**, a position that equates to the “dangerous goods safety advisor” required by EU regulations. Both of these people advise the site director on the safe storage and transport of hazardous goods while also monitoring compliance with statutory requirements and our own internal standards.

Our EHS managers are also responsible for **monitoring our contract warehouses**. Before signing a contract with a third-party warehouse operator, we assess whether they properly adhere to national and international storage and transport regulations and if they are able to meet our additional requirements. The findings from this audit are summarized in a statement issued by EHS. If off-site warehouses employ additional subcontractors, these are also included in our audit.

Our commitment: Internal standards and international rules

Our **Group-wide safety concepts and standards** govern the safe storage of hazardous substances. Take our Warehouse Safety standard, for instance, which sets out measures to prevent materials from leaking or igniting and requires us to specify the dangers posed by any stored

substance. Moreover, special rules of conduct apply to all warehouse employees.

Third-party warehouses must also adhere to our strict safety requirements. Before we sign a contract, providers must submit a statement detailing how they plan to meet our stringent safety standards, while audits are performed to ensure compliance from both our own warehouses as well as third-party facilities. To this end, in 2018 we drew up a standardized checklist that helps us assess contract warehouse risks. Furthermore, our Group standard “Warehouse Requirements for Third-party Warehouses” defines specific **structural and organizational requirements**.

In Germany, the Technical Rules for Hazardous Substances ([TRGS 510 Storage of hazardous substances in non-stationary containers](#)) govern the **storage of packaged hazardous materials** and apply across all our warehouse and distribution centers worldwide. We are currently working with the Committee on Hazardous Substances ([AGS](#)) of the German Federal Ministry of Labor and Social Affairs to revise these rules. Beyond complying with these requirements, all our sites fulfill the current requirements of the Globally Harmonized System of Classification and Labelling of Chemicals ([GHS](#)).

Our Group Transport Safety standard defines the **safety levels for our facilities** and is based on the United Nations Recommendations on the Transport of Dangerous Goods. This is especially important for sites in those countries with no local regulations covering the transport of hazardous materials. We update our Group standard to reflect current requirements every two years and support our site directors in implementing relevant changes at the local level.

Enhancing transport and warehouse safety

In addition to the inspections conducted by our EHS and dangerous goods managers, we regularly perform **risk-based** audits across our company to ensure that our sites are complying with warehouse and transport safety regulations. We generally conduct these every four years, performing them more frequently at facilities that pose a potentially higher risk. If major shortcomings are identified, we re-audit the respective site the following year. Conversely, we may decide to extend the period between audits at facilities where, based on the findings from previous audits, we deem the potential risk to be low.

In 2018, we audited ten of our warehouse facilities for compliance with our Warehouse Safety and Transport Safety standards. All audit observations were assessed in terms of the areas where we can improve, with the focal points of the observations being scrutinized and addressed. In response to the deficiencies identified by these audits,

we are currently reviewing and optimizing our processes for **safety-related storage time limits**. For instance, specific transport regulations require time limits, as does the use of stabilizers and desensitizers, while plastic packaging has a limited shelf life due to aging. Moreover, we drafted or revised training documents on load securing, safety data sheets, safety signs, and the safe use of pallet units.

Third-party warehouses and contract logistics companies are also regularly audited by our EHS managers. In 2018, we audited 15 third-party warehouses and external logistics providers, developing corrective action plans where deficiencies were identified. To optimize safety communication, we created **additional informational material and distributed it to all our contract warehouses**.

As a member of the SQAS Logistics & Distributors User Group, a service provided by the European Chemical Industry Council (Cefic), we receive additional audit reports on our logistics service providers and evaluate these against our own set of criteria.

In 2018, no incidents that could have significantly impacted the environment or community were recorded at our company, our third-party warehouses or our logistics providers, nor were there any major infringements of international regulations.

Continuously evolving safety concepts

Our local EHS and dangerous goods managers regularly review and evaluate our transport and warehouse activities, informing site directors of shortcomings and opportunities for improvement. Underpinned by a **strength and weakness analysis of each site**, we calculate key performance indicators for transport and warehouse safety that help us determine where to institute additional improvements.

Employee training and best practice sharing

Multiple times a year, our warehouse workers and all employees involved in the transport of goods undergo training on our standards and procedures, as well as on incident management and changes to international requirements. The e-learning concept we've developed for basic management courses on hazardous material transport is mandatory for logistics, EHS and dangerous goods managers. By the end of 2018, the majority of eligible employees had completed such a course. To bolster this

e-learning concept, we offered further **classes on transport and warehouse safety**. All our truck drivers hold a dangerous goods driver's license, while in Germany they complete additional training on securing cargo, along with training required by the German Professional Driver Qualification Act (BKrFQG). Across the globe, we conduct around 1,000 internal and external seminars on transport and warehouse safety every year. In some cases, the managers of third-party warehouses also participate in these sessions.

To further best practice sharing, our EHS managers meet every three years at our **EHS Conference** in Darmstadt (Germany), where they have the opportunity to share lessons learned and participate in transport and warehouse safety training. These topics are also covered in the mandatory three-day orientation seminar for all new EHS managers. The next EHS conference will be held in 2019.

Ensuring correct transport

Our products are primarily delivered to our customers by means of logistics providers. In Germany, we transport the majority of our hazardous waste ourselves, but do sometimes also enlist the services of contractors if necessary. Furthermore, we participate in the German **Transport Accident Reporting and Emergency Response System** (TUIS) operated by the German Chemical Industry Association (VCI). Within this system, we exchange lessons learned and best practices on chemical transport with experts from other chemical companies and also provide hands-on assistance in the event of a chemical transportation accident. When a transportation or warehouse accident occurs, we can use our "TUIS Southern Hesse Measuring Concept" to quickly calculate the rate at which hazardous substances are spilling and spreading.

Making transport vehicles safer

The safe transportation of dangerous goods requires safe vehicles, another factor we take very seriously. Over the past few years, for instance, we have been constantly evolving our **SafeServer truck body technology**. Under this design, the aluminum panels integrated into the side walls of the truck render the walls extremely stable. In 2018, 14 of our trucks were already running with this technology.