

products

29 Innovation and digitalization
32 Sustainable products
38 Access to health
46 Prices of medicines
47 Health awareness
50 Chemical product safety
53 Patient safety

55 Counterfeit products
57 Transport and warehouse safety
59 Responsible marketing
61 Bioethics
63 Clinical studies
67 Animal welfare
70 Interactions with health systems

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 groundbreaking developments and trends. Research and development (R&D) as well as innovation are the cornerstones of our success. In 2017, we spent around € 2.1 billion on R&D. In particular new technologies and the advance of digitalization are

enabling us to create innovative products, services and pioneering business models. At the same time, digitalization is decreasing the time-to-market for new ideas, creating opportunities we intend to leverage.

Research and development costs by business sector – 2017



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 our business sectors provides us with a breadth of technologies and depth of market know-how, giving us a competitive advantage in developing new products. In 2017, we established an organization to seize this opportunity by facilitating innovation between the individual business sectors and beyond our current strategy. Our **new Group function Strategy and Transformation** 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 are investing in forward-looking ideas. In 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 impetus. Our **end-to-end innovation process** seeks to achieve exactly that.

Based on this approach, we source and advance ideas and projects from the brainstorming stage onwards. Following the ideation phase, promising projects progress to an incubation and growth phase, where we provide project teams with a suitable environment in which to develop their business models. Project progress is monitored in a lean, gate-based process – applying strong criteria to evaluate the advance of the projects at each gate. All activities are **supported by experts** in business model design, business development and market research, as well as 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. We want to leverage the opportunities this provides to boost our business performance and are therefore increasingly forming

new strategic partnerships with organizations that offer different perspectives. We expect to see progress in the following particularly promising areas:

- **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 Healthcare 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. By collating all data centrally, we have access to crucial real-time data. This enables us to predict supply bottlenecks around the world and respond promptly, making sure medicines reach their destination.
- **Interactions with customers:** Thanks to modern data collection and analysis methods, we can make more efficient use of customer-relevant data. This information helps us to understand our customers more fully and facilitates our dialogue with them, allowing us to adapt our products and services where necessary.
- **Digital product innovations:** Digitalization enables us to broaden our existing product portfolio, for instance to include new digital services. Moreover, we intend to promote health awareness and improve patient treatment through innovative e-health offerings such as DORA (Diabetes Online Risk Assessment).

You can find more information on research and development in our Annual Report 2017.

How we're driving innovations

The organizational set-up of our research and development activities reflects the structure of our company. In line with their individual innovation strategies, all three of our business sectors operate their own independent Research and Development (R&D) units. On top of that, our Group function Strategy and Transformation has developed a new end-to-end process for innovation both within and beyond its current innovation strategy and is responsible for its implementation. This function reports directly to Stefan Oschmann, 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 furthermore reviews the progress of ongoing efforts. The committee consists of senior executives from our Group functions and our three business sectors. If we participate in projects requiring larger-scale investments, the IC consults our Executive Board.

Even though we are **open to innovation** around the world, many potential partners for innovation projects are based in Silicon Valley, California (USA) – one of the key sites in the global high-tech industry. We are therefore currently building an innovation hub in Silicon Valley to be in closer proximity to the innovation partners there, be it companies or institutions. The head of our future hub is moreover building up a team of technology scouts to tap into the Silicon Valley innovation ecosystem. Also in 2017, we established the China Strategy and Transformation Group, which is responsible for driving our strategy, innovations and digitalization efforts between and beyond our business sectors in this fast-evolving market.

Our strategic Ventures Fund provides up to € 300 million for investments in start-ups. The fund is structured to enable us to invest in **external independent start-up companies** aligned with the strategies of Healthcare, Life Science and Performance Materials, as well as to invest in brand new businesses.

Our commitment: Protecting innovative ideas

To ensure the fully confidential handling of sensitive information, especially intellectual property in digitalization projects, and to protect our innovative ideas, we adhere strictly to all data protection regulations. 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 (p. 11).

Spotlight on the Innovation Center

Having started operations in the modular Innovation Center in May 2015, we completed the construction of our **new Innovation Center in Darmstadt** and moved into the new premises in early 2018. It will be officially inaugurated during our 350th anniversary celebrations in May. The Innovation Center offers our people and external partners an optimal environment in which to cultivate their ideas. We provide the infrastructure needed to advance cutting-edge projects, along with state-of-the-art methods and tools. Our work focuses on the following initiatives.

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

Numerous start-ups are working on new technologies and innovative business models. Our global **Accelerator** program supports these enterprises in the early stages of their development, with a focus on projects in the fields of 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. Moreover, we aim to link these start-up companies with our innovation projects or our business sectors for future collaboration.

Our Accelerator is complemented by **hackathons** that we supported in 2017 in countries such as Israel, the United States, Germany, and Italy, as well as a **Virtual Challenge** in Africa. A hackathon is an event at which students and young professionals from various disciplines collaborate to quickly develop solutions to specific issues. We ran Africa's first-ever hackathon in 2016, which led us to invite the start-up Peach Technologies to join our 2017 Accelerator in Nairobi, Kenya. At this event, they developed an electronic patient file and prevailed against 200 competitors.

The 198 participants of our Virtual Challenge, an online competition, tackled real-life problems in Africa in an effort to devise solutions. Examples included improving healthcare delivery and outcomes, safe food production and water sanitation. We provide six months of funding and support for the best idea to come out of the Virtual Challenge. In 2017, we selected Zelij Invent, a project that put forward a solution for producing flooring products made out of plastic waste. Its application will be fast tracked to the shortlist for the Accelerator.

We also supported the start-up program Highest 1877 run by the Technical University (TU) of Darmstadt. In March 2017, we teamed up with TU Darmstadt to organize a roundtable for entrepreneurs at our Innovation Center, which was attended by around 50 start-up founders and other key actors in the field of innovation and entrepreneurship.

At the end of 2016, we entered into a **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. Within this framework, in 2017 we joined forces with Airbus to sponsor the Sustainable Exploration Challenge within the ESA Space Exploration Master's program. The competition is specifically aimed at start-ups and endeavors to find solutions capable of supporting human life in space – for instance by making use of special chemical and biological processes. Furthermore, we hosted the Space2Health hackathon at our Innovation Center in October 2017, where participants developed solutions for specific challenges using data from the health and aerospace industries.

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 businesses. Within our **Innospire** (innovation and inspiration) initiative, we encourage our 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. You can find more information on this topic under Employee engagement (p. 82).

Since 2015, our **Innovation Think Tank** has been analyzing current trends and technologies to generate new ideas for innovation projects. Here, we work closely with internal and external experts, research institutes and companies. Through **open campaigns**, we support idea-givers right from the initial idea through to the development of a business plan. Our employees can submit their ideas online and develop them to maturity with our support through resources such as online courses.

The most promising ideas sourced through these ideation channels become innovation projects. We offer employees the chance to focus on their innovation project by hosting them in the Innovation Center. In addition to financial support 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.

Innovator Academy: Supporting innovation programs

Within our Innovator Academy, we run needs-based training sessions and workshops for idea-givers, internal project teams, members of think tanks, and start-ups. In May 2017, we launched "traintoinnovate.com", an online platform that provides the participants in our Innovation Center access to programs with additional information and methods for innovation. Employees can also use this platform for independent study and to share their ideas with others.

Second Displaying Futures Award

The aim of our Displaying Futures Award, run by our Performance Materials business sector, is to support **teams from academic and institutional backgrounds**. In 2017, the target topic area was "flexible applications in the field of hybrid electronics". Submitted by creative minds from 22 countries, the number of ideas received rose from 31 in 2016 to 69 in 2017. The three winning teams focused on future-oriented technologies such as portable biomonitoring devices, soft robotics, electronic sensors, and packaging; they were evaluated on innovative value, business potential, and impacts on society and the environment. The Displaying Futures Award is worth a total of US\$ 150,000.

Fostering young talent: An investment in the future

Well-trained talent is the best foundation for future innovations, which is why we endeavor to spark **young people's interest in science**. Students who are curious about chemistry and biology can use our Junior Lab and livfe BioLab to conduct their own research and experiments. We run both laboratories in partnership with the Technical University (TU) of Darmstadt.

Beyond youth labs, we also partner with various schools in the vicinity of our global headquarters in Darmstadt. For

example, we provide STEM teachers with educational materials and organize annual teacher events such as Science Days, where they learn how to incorporate new technologies into their science classes. Moreover, we regularly invite groups of students to our company to explore our research activities and have been hosting the "Jugend forscht" student competition for over 30 years. You can find more information on our educational initiatives under Community (p. 114).

Maximizing the opportunities of digitalization

In early 2017, we launched a strategic partnership with Palantir Technologies, a California-based company. We intend to use Palantir's **data analysis capabilities** to improve and accelerate the development, commercialization and delivery of new medicines.

To harness these capabilities, we have established three joint initiatives. Medical Research & Drug Development aims to accelerate the drug manufacturing process; Global Patient Intimacy intends to enhance patients' experience with our products, and Global Supply Chain focuses on improving demand-forecast accuracy in our supply chains. As well as these initiatives, we have built capacities for data analysis within our own company. In the future we hope to make use of Palantir technology in all three of our business sectors.

Smart packaging processes and drug information in real time

Our Smart Packaging project allows us to make our drug packaging processes more efficient and flexible. We have connected our packaging machines via the Internet of Things and are currently assessing the potential of this technology to improve the accuracy and reliability of our machines while also increasing their output. Additionally, our new predictive maintenance capabilities will reduce machine breakdowns. By connecting systems across the entire organization and

using advanced analytics, we can decrease packaging waste and lead times when changes need to be made to product information. This means that we can pass newly discovered information on to our customers more quickly. We are also exploring options for active packaging that will allow patients to look up the latest information on their smartphones.

Improving customer experience through artificial intelligence

We are currently developing **chatbots**, text-based dialogue systems that enable people to ask computer systems questions in natural human language – exactly as they would write messages to another person. This means we are available to answer our customers' questions 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 extra supplies as soon as they run the risk of no longer observing the recommended dosage. Moreover, chatbots are more cost-effective for us than traditional customer services.

Online diabetes campaign

In Africa, approximately 62% of diabetes cases go undiagnosed. 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). Thanks to this initiative, people in South Africa, Namibia, Kenya, Ethiopia, Ghana, Nigeria, Mozambique, and Mauritius can use their smartphones or computers to take an **online test**. In just a few clicks, they can ascertain how high their risk is of developing diabetes. Since its launch, the DORA website has received more than **740,000 hits**, with more than 100,000 coming from people who have taken the test.

sustainable product design

Respect for the environment and natural resources is at the heart of sustainable conduct. As a major actor in numerous sectors, we see it as our duty to not only conserve resources in developing our own products, but also to help our customers increase the sustainability of theirs. For instance, our Performance Materials business sector manufactures liquid crystals that make displays more energy efficient, while our Life Science business sector develops technologies and solutions to make research and biotech production simpler, faster and more successful. Here too, we take sustainability into account right from the earliest stages of product development.

Our approach to sustainable product design

Due to the different contributions of our individual business sectors to sustainability, sustainable product design is approached differently by each respective sector.

Performance Materials 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.

In our Life Science business sector, we particularly endeavor to reduce the impacts of our products on health and the environment. This applies to their **entire lifecycle**, 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.

How we include sustainability in product design

In Performance Materials, we have established the Performance Materials CR Committee with representatives from all four business units and other relevant internal stakeholders. The committee functions as a platform to discuss corporate responsibility issues and meets three to four times per year.

The CR group 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, and DOZN™, a web-based tool for the quantitative assessment of greener alternatives.

The responsibilities described here likewise apply to packaging (p. 36) as well as reuse and recycling (p. 37).

Our commitment: Chemicals and product policies

To meet the **product safety regulations** relevant to our company, our Regulatory Affairs Group Policy (p. 50) details our Group-wide processes for managing and implementing product safety, including the necessary management structures.

In addition, the following guidelines set out several requirements for sustainable product design within our Performance Materials business sector:

- Green Product Policy: This 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 (EFCI GMP).

Our processes for sustainable product design

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

- Through our Design for Sustainability program (DfS), we have developed a comprehensive approach to increasing the sustainability of life science products through the analysis of different sustainability criteria.
- Green chemistry assessment tool: In addition to our DfS program, our Life Science researchers are developing innovative solutions in line with the 12 Principles of Green Chemistry developed by chemists Paul T. Anastas and John C. Warner.
- Through our self-developed web-based tool DOZN™, we can assess the green alternatives of various chemicals, thereby creating transparency for our customers.

Current product examples from Performance Materials

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

Energy-efficient displays

Liquid crystals ensure high picture quality in computer monitors and televisions, while also making them more power efficient. This is because our PS-VA technology (polymer-stabilized vertical alignment) arranges the liquid crystals so as to make better use of the backlighting, the display component that consumes the most power. PS-VA equipped devices require significantly less energy than their predecessors.

Self-aligned vertical alignment (SA-VA) is the next-generation liquid crystal technology now in the pipeline, with the first SA-VA products expected on the market in 2018. **SA-VA helps conserve resources** and is even more environmentally sustainable because less energy and solvent are required to manufacture the displays. Moreover, its manufacture is more efficient as it requires fewer process steps. Since SA-VA technology can be applied 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.

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 furthermore enhances picture resolution. We are currently working to advance this technology for non-mobile applications such as high-resolution flat-screen LCD televisions, where UB-FFS can help boost energy efficiency.

Optimizing liquid crystal production

By enhancing the standard C-C coupling reaction – where two hydrocarbon fragments are coupled via a new carbon-carbon bond – during the manufacture of liquid crystals,

we have considerably reduced production waste while also saving € 12 million in production costs. Moreover, this change means we used fewer **carcinogenic, mutagenic, and/or reprotoxic (CMR)** substances.

Switchable windows

Windows that can be darkened in a matter of seconds are now a reality thanks to **our liquid crystal window (LCW) technology**. The darkened windows also regulate the heat generated by direct sunlight while creating a certain sense of privacy. Commercialized under our **licrivision™** brand, 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. In 2017, we received the Frost & Sullivan Technology Innovation Award in the Smart Glass Industry category in recognition of our smart windows. We have invested € 15 million in the construction of a facility in the Netherlands to manufacture these switchable glass modules, which will start deliveries in 2018.

OLEDs

Organic light-emitting diodes (OLEDs) likewise increase the energy efficiency of displays while also providing brilliant colors and razor-sharp images. Over the past several years, we've been collaborating closely with printer manufacturers to research **innovative printing processes** for the efficient production of large-area OLED displays. In September 2016, we opened a new production plant for OLED materials at our site in Darmstadt. Costing around € 30 million, this plant represents one of the largest single investments we've made at the Darmstadt site in recent years.

Innovations in photovoltaics

We supply the photovoltaics industry with materials for the production of solar cells. These materials enable the realization of innovative applications for photovoltaics, such as flexible, semi-transparent and lightweight solar cells that can be used in buildings, on curved or straight surfaces, and even in clothing. Take for instance the solar trees that we've installed next to our Innovation Center in Darmstadt. The **organic photovoltaic modules** used in the trees were manufactured with our printable formulations of modern high-performance polymers. The energy generated is stored during the day and used to illuminate the trees at night.

More natural-based cosmetics

In 2017, we teamed up with French company Agrimer to co-develop RonaCare®RenouMer, a skin care product that is extracted from a natural sea algae. Responding to the ever-growing popularity of natural cosmetics, we are working closely with our customers in the cosmetics industry to manufacture products such as RenouMer. We develop cosmetic formulations that comply with strict criteria. By the end of 2017, approximately one-third of our cosmetic raw materials met the criteria of Ecocert's Cosmos standard for organic and natural cosmetics.

Alternative to plastic microbeads

We manufacture mineral-based pigments and functional fillers used by the cosmetics industry in formulations for various purposes. Our RonaFlair® functional fillers series provides an alternative to plastic microbeads contained in skin care products. Through this range, 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.

Displaying Futures – Annual dialogue

Pioneering advances are only possible through close collaboration with our partners. We seek to engage with trailblazers who look far into the future and conceive **groundbreaking technologies**. To encourage this dialogue, we instituted the annual Displaying Futures symposium, which took place in November 2017 for the eighth time.

Held in Tokyo (Japan), this year's conference was dedicated to the topic of **"Digital Transformations"**. We examined digital transformation from various angles and explored current societal trends, asking ourselves how we as Performance Materials can advance various ideas and also serve as a source of inspiration for research and development efforts.

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 enabling 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 product life cycle stages. 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.

35%

of our product development projects currently meet three or more product sustainability criteria thanks to our DfS process.

We intend to incorporate our suppliers into our DfS program as well. In 2016, we launched a pilot project to define the relevant requirements for our vendors. In particular, our objective is for our suppliers (p. 104) to become engaged in Together for Sustainability (TfS), a chemical industry initiative.

Green chemistry assessment tool

In addition to DfS, our Life Science researchers are developing innovative solutions in line with the 12 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. In total, we offer more than 750 products that align with the Principles of Green Chemistry, making them a greener alternative to conventional products.

Through our self-developed web-based tool DOZN™, we can assess the green alternatives of various chemicals, thereby creating transparency for our customers. Under DOZN™, the **12 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 based on the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) as well as the Material Safety Data Sheet information on each substance. One score is given for each of the 12 principles, enabling an easy comparison of the products. The approach of the evaluation system has been verified by an independent body. To date, we have used this matrix to assess and improve more than 40 products. The DOZN™ processes and methods were validated by an environmental consulting company, and a peer-reviewed paper was published in March 2017.

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

Under our DfS approach, we have significantly reduced the environmental footprint of our EZ-Fit™ Manifold laboratory filter. In comparison with its predecessor the Hydrosol Manifold, the EZ-Fit™ Manifold requires 47% less raw material. Its packaging consists of 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. In 2016, we furthermore expanded our range to include a disposable filtration device used to determine the microbial count in liquid samples. Thanks to DfS, we have in particular improved the packaging of these products.

Greener chemistry

In 2017 we received the European Bio-Based Chemical Innovation of the Year Award for our greener solvent Cyrene™. **Bioderived from waste cellulose**, this solvent is used as an alternative to dimethylformamide (formic acid), which has been the subject of increasing criticism in recent years due to its mutagenic effects. Through Cyrene™ and other greener solvents, we are helping our customers in the pharmaceutical and agrochemical industries make their production processes safer and more environmentally sustainable. We've teamed up with leading institutions and start-ups to co-develop further such green solvents. In contrast to conventional solvents, these are based on **natural resources** such as corn cobs and sugar cane bagasse, making them more eco-friendly, more biodegradable and easier to recycle. In 2017, we published the results of these R&D efforts in leading trade journals.

Eco-friendly lab water use

In mid-2017 we launched Milli-Q® IQ 7000, our new lab water purification and monitoring system. This product uses mercury-free UV oxidation lamps and has a hibernation mode to save energy while still preserving system water quality.

packaging

Packaging protects our products from external influences and ensures that they reach the customer undamaged. It also prevents materials from leaking. Our packaging must therefore remain intact across the entire life cycle of our products – from transport and storage, through usage to disposal. Beyond safety, we also endeavor to design packaging that uses as few resources as possible. We are therefore working to reduce the amount of material required, as well as increasingly utilizing eco-friendly materials where possible. In the process, we ensure that the quality and safety of our packaging are not adversely impacted.

Our new sustainable packaging strategy

We aim to deliver our products in packaging that is safe and easy for our customers to handle, and as sustainable as possible. The more than 300,000 products in our Life Science portfolio – ranging from biochemicals to lab chemicals, from filter materials and systems to instruments – pose a variety of challenges when it comes to packaging. We strive to improve the sustainability of this packaging through measures such as **reusable packaging systems** or by avoiding the use of polystyrene. To achieve this goal, we are in the process of defining our new sustainable packaging strategy for Life Science to formalize our approach and set meaningful targets. This strategy is built on the three pillars of optimizing resources, choosing more sustainable materials, and recapturing post-use value. We are establishing priorities, goals, and specific initiatives to support them in the coming years. In doing so, we are continuing to position ourselves vis-a-vis our customers as an ambitious partner committed to the circular economy.

Making packaging more sustainable

A great deal of our packaging is based on wood fiber. We are constantly working to increase the share of corrugated cardboard boxes certified to the standards governing **sustainable forestry**. These include the Sustainable Forestry Initiative (SFI), the Forest Stewardship Council (FSC) and the Programme for the Endorsement of Forest Certification Schemes (PEFC). In adhering to these standards, we are doing our part to prevent deforestation.

Cellulose and air cushions replace polystyrene and foam

In the past, we secured glass reagent bottles 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. It is also difficult to recycle and takes up a lot of space. By contrast, molded

pulp components can be easily recycled with other paper materials and compacted together for storage and transport. We have therefore initiated a substitution program in which we are developing solutions to replace EPS as far as possible with molded **components made of cellulose and recycled paper pulp**. In doing so, the safety of the packaging is always our top priority.

When shipping items from our major distribution centers in the United States and Germany, a large portion of our reagent bottles are secured using molded pulp components. Since 2017, we've been using molded pulp inserts to pack our 4X4 liter bottles in shipping boxes, thereby replacing around 350,000 EPS parts per year. We are currently conducting safety tests on new pulp designs for shipping other bottles of various sizes. As of 2018, our 6x0.5 liter and 1x4 liter reagent bottles are also to be secured using molded pulp. Overall, we use a total of 324 metric tons of molded pulp packaging material each year. In addition to these measures, in 2017 we replaced foam packaging with biodegradable air cushions at our distribution center in Allentown, Pennsylvania (USA).

As well as finding eco-friendlier alternatives to ship our products safely, we are working with Biogen, a specialist biotech company, to develop a more sustainable bulk-packaging design to transport our Millistak+® Pod Disposable Depth Filter. We are currently conducting a Life Cycle Assessment, with promising initial results. We expect a 21% reduction in used corrugated cardboard, which translates to a **19% decrease in greenhouse gas emissions** from the production of packaging materials. In addition to these savings, the large packages will cut down our delivery trips by 12%, thus further reducing emissions and energy use. Moreover, 70% less time is required in the processing of products and their packaging.

More cardboard instead of plastic

The analytical technique of titration is utilized in laboratories to assure the quality of various products by verifying the purity of the raw materials. Although the necessary solvents are conventionally packed in plastic bottles, we use Titripac® because it offers an eco-friendlier alternative for supplying solvents to our Life Science customers. Using a cardboard carton and plastic liner with an integrated withdrawal tap, we 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. In 2016, Titripac® was recognized with the Green Good Design Award **for sustainable product design**.

Reusing 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 U.S. customers the option of sending us back these boxes. If they are still fully functional we reuse them – and with more than 20,000 boxes used per year, this significantly reduces waste.

Integrating stainless steel canisters in production

In Korea and Taiwan, our Performance Materials liquid crystal mixtures are delivered to display manufacturers in stainless steel canisters, an approach we extended to China in 2017. Our customers utilize these Standard Canisters from our company directly on their production lines without decanting. The empty canisters are then sent back to us and cleaned. In 2017, 1,512 standardized canisters were in circulation within this closed system, allowing them to be **reused over multiple years**.

Steel instead of glass

Thanks to our bulk product delivery system, our solvents are delivered to our U.S.-based Life Science customers in special

reusable steel containers such as the EMD ReCycler®. We started the program with containers of 18 and 50 liters in 2010. Since then we have filled more than 12,000 reusable containers annually. Over the years we have partly shifted to containers of 1,250 liters, which now make up roughly 10% of all containers filled.

Our customers can return the empty containers to us for refilling, enabling us to significantly reduce the consumption of primary packaging materials. Since the stainless steel containers are shipped without additional packaging, we also save a lot of the packaging material normally needed to ship glass bottles, which must be packed in boxes and cushioned by molded components.

In Europe, we also deliver solvents required in bulk for preparative chromatography in **reusable stainless steel containers**. Our customers send the empty containers back to us, where they are properly cleaned and then reused. Approximately 70,000 of our stainless steel containers are currently in circulation across Europe. The rate of return is at around 90%.

Reuse and recycling

Many of the products we supply to our Life Science customers are used only once and then discarded. This is necessary in certain cases to minimize the risk of contamination and is thus common practice within the industry. Moreover, this approach helps reduce costs as our customers don't have to clean disposable products, thereby saving time and resources such as energy and water. However, these products do consume a great deal of material, so we've put recycling programs in place to help our customers properly dispose of and recycle our products and packaging.

Our Design for Sustainability program

Our Design for Sustainability (DfS) program encourages our Life Science business sector to design 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.

Recycling program updated

In cooperation with Triumvirate Environmental, a waste-management company based in Massachusetts (USA), we

launched a comprehensive recycling program at the beginning of 2015 to serve our Life Science customers in the United States. Under this initiative, 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 and Recycling Programs.

We are continuing to expand this program throughout the United States and are exploring options for extension to other regions such as Europe and Asia. Since the program is dependent on the technology provided by Triumvirate, we would require new processing plants, as well as licenses, transportation and trained personnel in the respective regions.

Triumvirate's innovative process enables the recycling of biohazardous waste that contains multiple types of plastic and other materials. Our partner has developed a sterilization and shredding component that is combined with an extrusion process to make multiple plastic lumber products. Since launching the program, we have recycled 1,347 metric tons of waste generated from the use of our products, with 901 metric tons in 2017 alone. The program now serves 11 customers, almost twice as many as in 2016.

Access to health strategy

Across the globe, two billion people do not have access to medicines. The World Health Organization (WHO) and the World Bank have estimated that 400 million people lack access to effective and affordable health services, especially in low- to middle-income countries. However, according to WHO, these regions also bear approximately 90% of the world's disease burden. In cooperation with strong partners, we're working to tackle this complex challenge by researching innovative solutions, developing new approaches and improving existing programs to help people at the point of care. Moreover, we're striving to make health solutions affordable, raise awareness of diseases and teach people how to manage them.

Our approach to help improve healthcare

We seek to improve **access to high-quality health solutions** for underserved populations and communities in low- and middle-income countries, a goal that underlies our Access to Health (A2H) approach.

To achieve this aim, we're leveraging our expertise from all our business sectors. However, we're aware that individual companies and organizations can only do so much to improve access to health, which is why we **collaborate closely with a wide range of partners**. To bolster the impact of our A2H efforts, we participate in industry-wide initiatives and work with other businesses to develop new approaches.

Our A2H strategy focuses on the following four areas:

- **Availability:** We research, develop and refine health solutions that address unmet needs, tailoring them to local environments.
- **Affordability:** We seek to provide assistance to those who are unable to pay for the health solutions they require, including addressing challenges surrounding pricing and intellectual property. Further information can be found under Prices of medicines (p. 46) and Community (p. 110).
- **Awareness:** We help raise awareness for diseases and therapies (p. 47) by empowering medical professionals, communities and patients to make informed decisions.
- **Accessibility:** We promote initiatives that strengthen supply chains (p. 44) and develop localized health solutions. Medicines should reach the people who need them quickly and safely.

How we're improving access to health

Our Access to Health unit investigates the factors that make it more difficult for underserved populations to receive healthcare, working with various partners to develop **ways to reduce these barriers**. Our A2H team is backed by a steering committee comprising representatives from our Healthcare and Life Science business sectors, along with representatives from our subsidiaries. The committee ensures that the programs developed support our business strategy and can be implemented locally in order to have the desired effect.

To support this objective, in 2015 we established the Open Innovation Committee, a body dedicated to overcoming access barriers in regions with major unmet needs. The committee helps to promote **intellectual property as an enabler of innovation**, allowing access to our knowledge and compound library to accelerate early discovery with leading partners in areas of high unmet need. For now, our efforts are focused on areas where we have no portfolio or competencies. The Open Innovation Committee is co-chaired by our the heads of our Access to Health and International Patents units.

Our commitment: Our Access to Health Charter

Our Access to Health Charter sets out guidelines on the following:

- Our approach
- Pharmaceutical product donations
- Fake medicines
- R&D for neglected tropical diseases and priority communicable diseases
- Pharmaceutical product pricing
- Intellectual property rights

Sharing and protecting intellectual property

When it comes to access to health, pharmaceutical manufacturers' approach to their intellectual property plays an important role. In most developing countries, we often do not file or enforce patents. In markets where we do register product patents, we are committed to **sharing data with researchers** and to improving public access to clinical study data. We report on the patent status of our products via publicly accessible databases. 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 and prevent anticompetitive effects as well as geographic limitations. We consider joining patent pools when they are relevant to our portfolio and meet all our efficacy, quality, and safety requirements.

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**. For example, approximately 95% of the 2013 WHO Essential List of Medicines are off-patent. Through our initiatives and partnerships, we provide access to patent information and in some cases also access to parts of our compound libraries for efforts such as open innovation research projects.

Agreements and guidelines on intellectual property

A great deal of time and money is required to develop new drugs – without any guarantee of success. It can take ten to 15 years for an effective health solution to be market-ready. Pharmaceutical companies therefore need a **solid, transparent and reliable legal framework** to protect their intellectual property rights and enforce their patents, which provide a sufficient period of time and degree of protection to compensate for R&D costs.

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 2001 Doha Declaration (Special Declaration on the TRIPS Agreement and Public Health). The Doha Declaration extends the deadline for least-developed countries to apply TRIPS provisions to pharmaceutical patents until 2033.

45

medicines provided by us are listed on the WHO Essential Medicines List and/or are classified as first-line treatments, such as bisoprolol/amlodipine, metformin (Glucophage®) and praziquantel.

New initiative improves access to patent information

We are a founding member of the Patent Information Initiative for Medicines (Pat-INFORMED), which was established in 2017 by 20 leading research-based biopharmaceutical

companies. Pat-INFORMED will act as a global gateway to medicine patent information, offering new tools and resources to determine the existence of patents relevant to products sought by national and international drug procurement agencies. The transparency to be provided by Pat-INFORMED seeks to make it easier for drug procurement agencies to **access a basic body of patent information** necessary to implement disease management strategies, or other work addressing public health needs. The initiative is backed by the World Intellectual Property Organization (WIPO) and the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA).

Open innovation collaboration: WIPO Re:Search

We are one of more than 100 members of the WIPO Re:Search platform, whose goal is accelerating early discovery for infectious diseases as well as sharing members' knowledge and intellectual property. This platform is sponsored by the World Intellectual Property Foundation (WIPO). We initiated our first WIPO Re:Search partnership in 2015, joining forces with the University of Buea in Cameroon in a bid to use compounds from our library to develop a treatment for onchocerciasis (river blindness). In 2017, we reached the final phase of the initial screening of a variety of compounds. Also in 2017, we entered into a partnership with the University of California, San Diego (USA) to **share compounds from our compound library** under the WIPO Re:Search open innovation umbrella. This is part of our joint effort to identify potential cures for leishmaniasis, Chagas disease (American trypanosomiasis) and human African trypanosomiasis (HAT - sleeping sickness).

Open innovation collaboration: Drugs for Neglected Diseases Initiative

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

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 A2H efforts. In 2017, we collaborated within the BSR Healthcare Working Group to draft a new working paper on innovative financing models (p. 44). Moreover, we drove the development of the BSR working paper entitled "Advancing Access to Healthcare Metrics".

New initiatives for non-communicable diseases

At the World Economic Forum held in Davos, Switzerland in January 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.

Best practices recognized by the Access to Medicine Foundation

In 2017, a report published by the Access to Medicine Foundation provided the first comprehensive landscape of company activities illustrating how 16 pharmaceutical companies are improving **access to cancer care** in low- and middle-income countries. We were included in the study, which mentioned our access initiatives in this area, including our intellectual property approach and patient access programs (p. 46) for improving access to cancer medicines.

In 2016, we were ranked fourth in the Access to Medicine Index, which assesses the degree to which companies have improved **access to medicines in developing nations**. The foundation highlighted several of our initiatives as being best practices, including our endeavors to combat infectious diseases (p. 41) and counterfeit pharmaceuticals (p. 55), strengthen transparency in the drug supply chain (p. 44), and boost health awareness (p. 47). They also recognized our efforts to align our access targets (p. 148) to the UN Sustainable Development Goals (p. 161).

Engaging stakeholders

Partnerships and dialogue are key instruments for improving access to health. Our partners include multilateral organizations, government agencies and NGOs, as well as academic institutions, health industry associations, companies, and experts from the private sector.

Our Access Dialogue Series

In 2017, our Access Dialogue event series put the spotlight on open innovation and intellectual property, as well as supply chain and delivery challenges in developing countries. We engaged our public and private stakeholders to discuss ways of eliminating access barriers to health. We initiated this event series in 2013 to provide a platform for public- and private-sector stakeholders to exchange information and share best practices on broadening access to health.

Discussions at a global level

In 2017, we participated in many other events, a selection of which are presented below:

- Two workshops hosted in Amsterdam in June and September 2017 by the Access to Medicine Foundation.
- "The Global Debate on Intellectual Property, Trade and Development: Past, Present and Future - A Conference in Honour of Pedro Roffe", held in Geneva in June 2017.
- "CAMP-N" (a coalition for access to medicines and products for non-communicable diseases) held on the eve of the UN General Assembly in New York in September 2017.
- Panel session at the World Health Summit to discuss supply chains and improving access to health, held in Berlin in October 2017, co-hosted with Roche and Novartis.
- Panel session on "Accelerating Innovation & Access to Vaccines" at the WIPO Global Challenges Seminar on Vaccines in Geneva in November 2017, including the launch of the new Global Challenges Report and the Access to Vaccines Index published by the Access to Medicine Foundation.
- Belén Garijo, CEO Healthcare, represented our company at the fifth anniversary of the London Declaration to Combat Neglected Tropical Diseases. You can find more information on the London Declaration under Infectious diseases (p. 41).
- Fourth Global Forum on Human Resources for Health under the banner of "Building the health workforce of the future": Attended by over 1,000 delegates from around the world, it was the largest open conference on human resources for health-related issues.
- You can find details on the Accessibility Platform dialogue series on local supply chain challenges under Supply chain (p. 44).

Activities at the local level

In 2017 we also actively engaged stakeholders on a local level, examples of which include:

- We continued our Unmasking Your Thyroid awareness and education campaign in the Philippines. You can find more information under Health awareness (p. 47).
- As part of our Prediabetes and Thyroid Care initiative, we partnered with the Mexican Society of Nutrition and Endocrinology to train 500 health workers in Mexico.

Employee events raise awareness

We seek to motivate and inspire our employees to actively engage in our access to health efforts. In this vein, in April 2017 the Access to Health team organized an event at which various internal and external experts presented our range of initiatives and efforts. Speakers included Peter Hotez from the National School of Tropical Medicine in Houston, Texas (USA), who discussed the topic of science and humanity, emphasizing how important it is to redouble efforts in neglected tropical disease drug discovery.

infectious diseases

Many infectious diseases endemic to developing countries are barely known in industrialized nations. Referred to as neglected tropical diseases, these infections consequently attract little public attention and research funding. One poignant example is schistosomiasis, an insidious parasitic disease that still lacks a treatment suitable for children under six. Malaria, too, continues to pose a threat to public health. According to estimates by WHO, nearly half of the world's population is at risk of malaria. Although a large range of approved products and investigational compounds are available to treat malaria, the number of resistant pathogens is on the rise. New treatments and health solutions are therefore urgently needed. Bacterial infections and antimicrobial resistance also pose global challenges that are becoming increasingly acute. Urgent action is needed to prevent and control these issues.

Our approach to preventing and treating infectious diseases

We seek to improve healthcare in developing countries by creating novel and integrated health solutions for infectious diseases and ensuring the sustainable implementation of these innovations. Our Group-wide initiatives and programs particularly address the **key unmet medical needs** of women and children, with a focus on schistosomiasis, malaria, bacterial infections, and antimicrobial resistance. Here, our integrated strategy is centered not only on developing and providing medicines, but also on improving diagnosis, countering disease transmission, and disease control, as well as strengthening local health systems.

Our comprehensive global health portfolio includes programs for the following:

1. Development of a pediatric formulation to treat schistosomiasis
2. Development of a new active ingredient to treat and prevent malaria in children
3. Screening of our compound library in search of potential new active ingredients to treat schistosomiasis and malaria
4. Development of diagnostic kits for schistosomiasis and malaria
5. Development of products and technologies to enhance prevention

Our efforts to address bacterial infections and antimicrobial resistance concentrate on

- developing assets for antibiotic quality and laboratory capacity to detect antimicrobial resistance,
- improving the use of antibiotics by healthcare providers and patients,
- helping define industry-wide guidelines for the control of antibiotics.

Beyond these efforts, we also sponsor capacity building educational programs and initiatives to enhance research capability and infrastructure in African countries.

How we structure our activities to fight infectious diseases

Our Global Health Institute is responsible for our Group-wide initiatives, programs and sponsorships pertaining to infectious diseases. Our experts there collaborate closely with our Healthcare, Life Science and Performance Materials business sectors to synergize their strengths and competencies. For instance, the internal collaboration with Performance Materials aims at introducing the malaria claim for our insect repellent IR3535®.

We also **cultivate partnerships with leading global health institutions and organizations** in both developed and developing countries. Take for instance the Pediatric Praziquantel Consortium, a public-private partnership that is working to develop pediatric formulations to treat schistosomiasis in children under six.

Our commitment: Guidelines and voluntary commitments

Our programs and initiatives to fight infectious diseases are part of our efforts to improve access to health (p. 38). Our Infectious Diseases Research and Development guideline is particularly relevant here.

Our Global Health Institute acts in alignment with the United Nations Sustainable Development Goals (SDGs (p. 161)). In particular, the Institute's initiatives and programs aim to address SDGs 3, 4, 6, 9, and 17.

We were among the first organizations to endorse the **London Declaration** when it was launched in 2012 to fight neglected tropical diseases. Participating companies, governments and private organizations promise to help control or even eliminate the top ten most prevalent of these infections. We are particularly engaged in the fight against schistosomiasis.

Battling schistosomiasis

In 2017 we continued our schistosomiasis research to combat this disease.

Around 10% of the approximately 220 million patients worldwide with schistosomiasis are younger than six years old. These children cannot be treated with praziquantel, the standard therapy for this parasitic disease. While clinical data is lacking, there is also no formulation of this drug suitable for **children under six**. This is a situation we intend to change. Since July 2012, we have been working within a consortium of partners from industry and science, as well as with funding organizations, to develop a pediatric formulation of praziquantel. In 2016, we initiated a Phase II study in Côte d'Ivoire that aims to assess the efficacy and safety of two different formulations for orodispersible tablets in schistosomiasis-infected children under the age of six. We expect to have the initial results by mid-2018. In 2017 the Japanese Global Health Innovation Technology Fund awarded the consortium an additional research grant in recognition of its efforts, the third time it has received this honor.

Partnering to find new solutions

Since 2017, we've been collaborating with the Australian Institute of Tropical Health and Medicine at James Cook University in Townsville, Queensland, and Baylor College of Medicine in Houston, Texas (USA) to research new biomarkers in order to develop **diagnostic tools for schistosomiasis**. Also in 2017, we established a drug discovery platform to search for new, long-lasting compounds to treat juvenile forms of schistosomiasis, improve efficacy and prevent reinfections. In addition, through academic collaborations, we aim to research a new genome editing method for vector control to combat schistosomiasis.

Fight against malaria

Malaria control also requires an integrated approach. As a science and technology company, we are well-positioned to help improve the treatment of malaria, as well as to develop and enhance diagnostics and prevention. In our efforts we closely collaborate with a wide range of partners.

Accurately diagnosing malaria

Sometimes malaria is hard to distinguish from other febrile infections. We are developing reliable diagnostics so that antimalarials are only administered to patients who are actually suffering from the disease.

Our Global Health Institute is currently developing a **novel malaria detection and typing assay** 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. In 2017 the project made progress in the preclinical phase, yielding promising results. We expect to register this new malaria diagnostic kit in 2020.

Enabling the treatment of children

In September 2017 we initiated the Phase I study of our anti-malarial drug program. 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. Performed in Australia, the Phase I study in healthy volunteers will allow us to assess the safety of the compound. A malaria human-blood challenge model will allow us to obtain an early read-out of the compound's anti-malarial activity to confirm the potential for a single-dose cure. Phase I and challenge model results are expected in the second quarter of 2018. These activities are being supported by the Wellcome Trust, a biomedical research charity based in London.

Developing new lead programs

Initiated in 2015, our strategic collaboration with the University of Cape Town in South Africa has led to the development of a **new research and development platform**. It leverages our proprietary compound library to identify new lead programs for the treatment of malaria, targeting liver-stage forms and long-lasting compounds to improve post treatment prophylaxis. In a separate collaboration, we are in the process of developing a new cell model of liver-stage malaria infection.

Preventing and controlling transmission

To help prevent malaria from spreading, 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 in a bid to foster the malaria claim for this insect repellent. IR3535[®] is already being utilized to help prevent the spread of the Zika virus and Dengue fever, and is particularly suitable for children and pregnant women.

Dialogue and best practice sharing on infectious diseases

In 2017 the experts of our Global Health Institute continued to engage major stakeholders in a dialogue on infectious diseases, attending and holding meetings at around 30 international conferences and events, including:

- The Keystone Symposia conference on Malaria, held in Kampala, Uganda in February 2017
- The International Society for Neglected Tropical Diseases (ISNTD) Festival, held in London, United Kingdom in February 2017, where we received the ISNTD Award for Scientific Engagement
- The Towards Elimination of Schistosomiasis (TES) Conference, held in Yaoundé, Cameroon in March 2017

- The NTD Summit 2017, held in Geneva, Switzerland in April 2017. In the context of this event, Belén Garijo, Executive Board member and CEO Healthcare, represented our company at the fifth anniversary of the London Declaration. We also announced the Global Health Institute at this event.
- The Sixth International Conference on Vivax Research (ICPVR) in Manaus, Brazil in June 2017
- The World Health Summit in Berlin, Germany in October 2017
- The European and American Congresses on Tropical Medicine and International Health (ECTMIH & ASTMH), held in Antwerp, Belgium in October 2017 and in Baltimore, Maryland (USA) in November 2017

In 2017, our Global Health Institute furthermore joined advocacy initiatives such as the Worldwide Malaria Campaign and became a member of key stakeholder groups including the Swiss NTD Alliance and the Swiss Malaria Group.

Building capacities in the health industry

Under our integrated approach to fighting infectious diseases, we have continued to enhance health capacities in and for the developing world.

We sponsor three PhD fellowships as part of a partnership

launched in 2015 with the University of Namibia. In support of governmental malaria control programs, these scientists are studying the extensive spread of malaria pathogens in Namibia, Botswana and Zambia, and are also working to characterize parasite subtypes that occur in the populations in these African countries.

In addition to doctoral fellowships, we also co-sponsor several international fellowship programs for postdoctoral researchers from developing and emerging countries via our collaboration with the European and Developing Countries Clinical Trials Partnership (EDCTP). As well as receiving training on clinical aspects such as clinical trial practices and clinical management, these research fellows are also given the opportunity to work for a period of up to 24 months at leading pharmaceutical enterprises, including our company. On returning to their home countries and academic institutions, they then have the **key resources** needed implement their research in line with international regulatory requirements and standards.

In 2017 our Global Health Institute provided the support needed to expand research infrastructure in several countries. For instance, we have been sponsoring a newly established gynecology ward in the District Hospital of Akonolinga, Cameroon, along with a clinical center in Côte d'Ivoire, where we're also conducting the Pediatric Praziquantel Program's Phase II study on the treatment of schistosomiasis in very young children.

pharmaceutical supply chain

In many parts of the world, medicines are not always available where they are urgently needed. We want patients in low- and middle-income countries to have fast, safe and affordable access to medicines. We believe that efficient supply chain management is key to accomplishing this, as is support for local manufacturing in line with our high standards.

Our approach to efficient supply chain management

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.

Hand in hand with our partners we endeavor to improve supply chains, even in developing countries, and to guarantee **the targeted supply of medicines**. To this end, we partner with pharmaceutical companies and other supply chain stakeholders. We manufacture some of our products directly in the regions where they are needed, thereby shortening the distance to the consumer. Furthermore, thanks to local manufacturing we can offer medicines in these countries at considerably lower prices than in Europe.

How we organize our supply chains efficiently

Global Planning is the unit responsible for our efficient medicine supply chains and is part of the Biopharma Supply Network Operations unit within our Healthcare business sector. Global Planning collaborates with our Access to Health unit (p. 38) 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. We thus fully comply with the internationally harmonized guidelines set out in Good Manufacturing Practice (GMP) and Good Distribution Practice (GDP). This also applies to contract manufacturers.

Our **uniform quality assurance system** ensures that our quality standard is adhered to everywhere. 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 one another's improvements.

Through our Virtual Plant Teams, we provide our contract manufacturers with the support they need to comply with our quality standards. In Africa, Asia and Latin America, our external partners are each assigned a production expert from our company to act as a virtual site leader and provide guidance. Our Virtual Plant Teams were recognized as a best practice in the 2016 Access to Medicine Index.

Leveraging organizational and technological possibilities

Accurate business forecasts are the foundation of **efficient supply chain management**. In 2017, we harmonized our Biopharmaceutical business planning processes across the Group and joined them together. We furthermore rolled out a special platform enabling us to plan specific demand for medicines centrally. This data is used to manufacture and deliver medicines according to demand, which allows us to prevent local inventories from running out or expiring. Our activities start with demand forecasts compiled at the local level, which are rolled out to the regional level and finally aggregated at the global level. All units involved coordinate with one another at least once a month.

In 2015, we rolled out a software-based solution for our customers in northwestern Africa. They can visit our e-shop at any time to quickly and easily order medicines that have been approved by the respective regulatory authorities. The system makes demand more transparent while also reducing lead times and miscommunications.

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

In 2016, we launched NTDeliver, a digital information tool supporting **transparent supply chains for medicine donations**. This tool was developed under the auspices of the Neglected Tropical Diseases Supply Chain Forum, a public-private partnership. Forum members include the World Health Organization (WHO), the Bill & Melinda Gates Foundation, the logistics firm DHL, and six pharmaceutical companies that run donation programs: Merck KGaA, Darmstadt, Germany, MSD Sharp & Dohme, GlaxoSmithKline, Pfizer, Johnson & Johnson, and Eisai. NTDeliver transparently displays the deliveries from the donating companies – from purchase orders made by WHO through to delivery to the first warehouse in the destination country. Moreover, in 2017 we ran a pilot that also tracked the deliveries all the way

to the treatment point in the destination country, providing end-to-end visibility of our shipments. This improves coordination of our efforts on the last mile as well as providing us, the local experts and WHO with a more transparent overview of in-country inventory.

Further partnerships

In addition to these initiatives, we are also a founding member of the Accessibility Platform, which convened in 2017 to discuss local supply chains during our Access Dialogues (p. 40). This is an informal effort spearheaded by the private sector that aims to raise awareness of supply chain issues as part of the access to health challenge. It also 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**.

Promoting local production

At the end of 2017 we inaugurated a new production facility in Nantong (China) that will soon supply China directly with our pharmaceutical products. In India and Indonesia, too, we manufacture drugs for diabetes, cardiovascular conditions, and diseases of the lower respiratory tract. This allows us to supply medicines faster and more affordably to local markets, as well as to neighboring countries such as Sri Lanka and Myanmar.

Supporting regional vaccine manufacturers

In partnership with the Developing Countries Vaccine Manufacturers Network (DCVMN), we sponsor **educational programs for vaccine manufacturers** in developing and emerging markets and pass on our knowledge to ensure the safe, high-quality production of vaccines. Since 2014, we have conducted more than 12 training sessions as well as various technical workshops in the Asia-Pacific region and Latin America. In 2017, three seminars were held in Vietnam, India and China.

prices of Medicines



Part of the non-financial report

The growing need to provide healthcare in aging societies poses major challenges to health systems. While reforms often focus solely on the price of medicines, it is important to consider the costs of medicines within the context of overall health systems. Medicine expenditures make up an important but still small portion of total spending. According to the OECD, spending on prescription medicines generally accounts for around 10%-16% of total healthcare spending in many OECD countries. Furthermore, science and innovative medicines are currently transforming care and allowing the treatment of many chronic diseases – the biggest cost-drivers – more effectively, thus achieving overall cost savings in health systems. At the same time, our commitment to creating a healthy society means that we must take a responsible approach to pricing our medicines.

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're working to prevent cost from becoming a barrier to treatment. We therefore adapt our prices based on local market access and regulatory considerations such as health system capacity and financial standing, infrastructure, legal requirements, and unmet medical and treatment needs. Partnering with governments and other key stakeholders, we adjust our prices in different geographical or socio-economic environments to take account of **patients' ability to pay**. In addition, we continuously monitor the dynamic healthcare environments, pricing and reimbursement systems, and legal and regulatory guidelines, adjusting our prices as necessary.

Patients are at the very heart of our health solutions. We support patient access programs, flexible pricing, differential pricing, and risk sharing agreements. Moreover, we seek to improve data efficiency in health systems in order to achieve an optimal distribution of funds and resources. By following this approach, we balance our commitment to improving access to our products with our dedication to maintaining a sustainable medical innovation environment for future generations of patients.

How we set medicine prices

Our Global Pricing and Market Access unit reports to the Chief Marketing and Strategy Officer of our Healthcare business sector. This team sets our initial prices in coordination with the respective businesses. Our 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. As a key component of our overarching efforts to improve access to health (p. 38), medicine pricing adheres to the stipulations of our A2H Charter. Our approach is also informed by our Pricing of Medicines guideline. Furthermore, our Patient Access Programs Policy defines standards that enable us to offer medicines at reduced prices through our patient access programs.

Implementing our pricing

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. Based on the results, we define guidelines and, if necessary, adjust our prices to keep them affordable for patients. Our investment in enabling technology and our dedication to patient access allow us to make timely **strategic pricing and reimbursement strategy** decisions. We also make our products affordable to different patient segments within individual countries by participating in **government tenders**, establishing **second "lower-price" brands** or operating **patient access programs**.

Innovative contracting models

We are committed to advancing value-based healthcare through innovative pricing and contracting mechanisms in full compliance with applicable 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 **prompt access to our innovations**. Examples of such models include a shared-risk agreement recently established in the UK that will provide immediate access to Mavenclad® for MS patients, while the health service only has to pay for medicines for those patients that respond to the drug.

Government tenders to serve low-income patients

We work in partnership with governments and stakeholders on innovative, **differential pricing schemes**. 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. For instance, we supply reduced-price products to governments in Africa, Asia, Latin America, and the Middle East.

Second “lower-price” brands

We have established second “lower-price” brands of some of our existing brands. In South Africa, for instance, a second brand of our antihypertensive agent Concor® (named Ziak®) is available at discounted prices.

Patient access programs

Worldwide, we operate patient access programs that allow us to make our products **more affordable** to different patient segments within individual countries. These include programs in China to expand access to our oncology drug Erbitux®, which is used to treat conditions such as colorectal cancer. One example is our Erbitux® China Patient Assistance Program (ECPAP). Launched in 2012 in collaboration

with a local charity, ECPAP is geared primarily toward low-income patients, providing them with the drug free of charge. Since 2015 we have also been partnering with the China Charity Federation (CCF) and helping cover the costs of treating middle-income patients. In some cases, we split these costs with patients and a local insurance fund. To date, around 10,000 patients in China have benefited from our ECPAP donations.

We run similar assistance programs in other countries such as India, where we also offer Erbitux® at discounted prices. In South Africa, we support the Savanti Patient Access Program, which enables patients to be treated with Erbitux® at a lower co-payment rate.

Health awareness

Many people are ill without realizing it. The result? Although effective medicines and therapies are available, these individuals do not receive treatment, or don't receive it in time. To prevent such an outcome, 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 possess the appropriate knowledge and information.

Our approach to raising health awareness

Awareness plays a key role in our strategy to improve access to health (p. 38). 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**.

In our educational campaigns for prevention, early diagnosis and awareness, we often join forces with strong partners. We also seek to build the capacities of medical professionals working in the fields of research, technology and healthcare.

How we're building awareness

Our efforts and the strategic direction of our awareness activities are aligned with our respective businesses. Thus, our various business units plan and implement our diverse awareness projects either on a global level, or through their national and local offices, organizing local projects according to the specific needs of the area in which they operate. In our global campaigns they are additionally responsible for local mobilization.

In 2017 we launched a foundation, a philanthropic limited liability company (gGmbH) that consolidates key initiatives as part of **our efforts to support the community by building health awareness**. A Board of Trustees consisting of members of the Board of Partners and the Executive Board of Merck KGaA, Darmstadt, Germany monitors the foundation's activities and acts in an advisory capacity.

Our commitment: Access to health through awareness

Awareness forms part of our A2H strategy, which is laid out in our Access to Health Charter. Our awareness campaigns are also subject to the responsible marketing (p. 59) principles set out in guidelines such as our “Pharma Code for Conducting Pharmaceutical Business and Pharmaceutical Operations”. They are also governed by our 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 to raise awareness of various diseases across the globe. Our efforts concentrate 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 cancer), thyroid disorders, diabetes, and multiple sclerosis (MS). In our awareness-raising activities we frequently collaborate with patient advocacy groups. In the 2017 period, we conducted or participated in multiple campaigns, enabling us to reach millions of people.

Awareness and knowledge transfer for thyroid disorders

Throughout 2017, we worked to raise awareness of thyroid disorders. On the global level, we updated our Thyroid Aware website and joined campaigns in support of International Women's Day (IWD) and International Thyroid Awareness Week (ITAW). Within the ITAW we connected with more than 5,000 healthcare professionals (HCPs) and reached more than 2,500 people through our own events, of which more than half were directed at HCPs. Furthermore, over 158,000 people followed our own social media activities in 16 countries during the week.

~13

million: During ITAW, we reached 13 million people through news coverage, social media and events. This was the ninth time we have participated in ITAW.

On the regional level, our National Endocrinology Congress in South Africa reached more than 2,000 people, including 300 HCPs. Other regional activities during ITAW 2017 included a public seminar held by our subsidiary in Indonesia in collaboration with the Ministry of Health, bringing together 100 HCPs and 250 members of local communities and non-governmental organizations. Our subsidiary in Jordan sent a bus around the country to carry out testing and raise awareness of thyroid disorders in women (p. 50). It was approached by an estimated 1,100 women. In Saudi Arabia, we partnered with the Ministry of Health in a long-term awareness program named "Fly like a butterfly" and signed a memorandum of understanding to raise awareness of thyroid disorders. In Russia, our employees and endocrinologists shared their expertise on thyroid disorders and treatment options.

In the Philippines, we held our Unmasking Your Thyroid campaign for the third time in collaboration with the Philippine Thyroid Association (PTA) and the Philippine Ministry of Health. In its efforts to educate people on thyroid disease, this initiative utilizes a wide variety of media. It also offers training to health workers located in village communities, with approximately 250 people participating in 2017. Another integral feature of the campaign are **workshops for general practitioners**, which have provided 380 physicians with advanced training on the diagnosis and treatment of thyroid disorders since 2016. Furthermore, together with the PTA and healthcare provider Healthway, we've been offering training on accurately diagnosing thyroid disease since March 2017.

Awareness campaigns for cancer

In September 2017, we supported the fifth annual **Head and Neck Cancer Awareness Week**, an initiative of the Make Sense campaign. Under the banner of "Supporting Survivorship", teams from our Group came together in a global effort spanning nearly 30 countries to post more than 670 messages and pictures of themselves holding messages of support for head and neck cancer survivors. All images and videos were shared on our #SpeakUp wall microsite and our social media channels. Overall, our efforts generated more than 31,000 hits on social media.

On February 4, 2017, we joined **World Cancer Day** (WCD), an initiative driven by the Union for International Cancer Control (UICC) that aims to **bring the cancer community closer together**. We evolved the UICC's three-year campaign "We can. I can." and the 2017 motto "Support Through Sport" into our own call to action: "We can. I can. Jump in!" Participants were asked to submit images of themselves jumping in order to show their support in the fight against cancer. Our people worldwide provided over 500 photos from across 37 countries. The campaign was also opened to external audiences and received over 3,000 likes on social media.

In March, we recognized the colorectal cancer (CRC) **Awareness Month** 2017, an annual initiative to raise awareness of **CRC**, its symptoms and the importance of early diagnosis. As part of this initiative, we developed a multi-faceted campaign platform, as well as a website with an interactive pledge map, CRC quiz and factsheet. In total, we received pledges from six continents and over 60 countries.

World Multiple Sclerosis Day Activities

In May 2017, we supported World Multiple Sclerosis (MS) Day, an annual MS International Federation (MSIF) initiative. Under the banner of "Life with MS", the campaign reflected the need for better understanding and a clearer focus on the needs of care partners living with MS sufferers. Under this umbrella, we launched the global campaign "MS2020".

As part of the MS 2020 campaign, we announced a collaboration with the International Alliance of Carer Organizations (IACO). In partnership with IACO, we undertook a survey to deepen our understanding of the unmet needs of **MS care partners**. A preliminary analysis revealed that 41% of MS care partners suffer from anxiety, 38% from depression and 34% from insomnia. Additional data showed that many care partners suffer from chronic pain and worry about issues such as finances, intimacy, divorce, and parenting.

Also on World MS Day, we held a Tweetathon in which employees across 19 countries took part, sharing details of local awareness-raising activities under the hashtags #MS2020 and #LifeWithMS. Activities ranged from a sponsored run in the Netherlands to an outdoor photo exhi-

bition in Norway. The content was viewed over 70,000 times, and local events run by our teams involved more than 1,500 external participants from the MS community and beyond.

Initiatives and programs from our Foundation

Launched in 2017, the Foundation sponsored by Merck KGaA, Darmstadt, Germany manages key parts of our efforts to support underserved communities by building healthcare capacities and raising awareness. The foundation is also driving many of our existing initiatives and programs.

Instigating cultural change

Through our “More than a Mother” initiative, we aim to empower infertile women through access to information, education and health, as well as by encouraging a change of mindset. Defining interventions to break the stigma surrounding **infertility and infertile women**, the campaign was launched in Kenya in 2015 and is still being conducted in many Asian and African countries today. To further this cause, the Foundation sponsored by Merck KGaA, Darmstadt, Germany is constantly seeking ways to engage government agencies and representatives in dialogue, leading it to take part in the 19th General Assembly of the African Union in 2017. Furthermore, we reached agreements with the several governments, including Uganda and Tanzania, to collaborate more closely on health awareness.

“More than a Mother” features an initiative called “Empowering Berna”, which helps infertile women to start their own business and thus achieve financial independence. The project was rolled out across six African nations in 2016 and expanded to include three additional countries in 2017. To date, more than 1,000 infertile women from Central African Republic, Côte d’Ivoire, Ethiopia, Ghana, Kenya, Liberia, Nigeria, Sierra Leone, and Uganda have been enrolled in the project.

By the end of 2017, 23 embryologists and fertility specialists had taken part in our Merck KGaA, Darmstadt, Germany Embryology Training program, a three-month practical seminar on fertility management also offered within the “More than a Mother” campaign.

Building healthcare capacities

Through our Merck KGaA, Darmstadt, Germany Capacity Advancement Program launched in 2012, we’re collaborating with academic institutions in various countries across Africa, Asia, Latin America, and the Middle East to train **medical professionals**. Through this effort, we are helping to build medical capacity and raise public awareness for diseases such as diabetes, hypertension and cancer, as well as infertility.

By the end of 2017, this program had reached more than 25,000 students from universities in Angola, Ethiopia,

Ghana, India, Indonesia, Kenya, Mozambique, Namibia, Uganda, Tanzania, and the United Arab Emirates, providing them with clinical diabetes and hypertension management training in a bid to equip them with skills to better treat and prevent these diseases. Our goal is to reach more than 30,000 students through this program by the end of 2018.

In 2017, we once again presented our Diabetes and Hypertension Awards to 37 medical students from over 30 universities in Africa and Asia. Through these awards, we have been building a platform of diabetes and hypertension experts across the globe and driving awareness in these fields since 2015.

To promote medical and scientific education, in October 2017 we hosted our fourth Africa Asia Luminary Congress in Cairo, which was attended by more than 450 African physicians, political decision makers and researchers. The event focused on contributions to socio-economic development in developing nations through sessions led by top international experts in diabetes, fertility, oncology, cardiology, family medicine, women’s health, and research.

Raising local awareness

Our Community Awareness Program offers **easy access to information and educational materials** tailored to local needs. We disseminate this information through broad-based social media campaigns and use videos and posters to amplify the initiative’s reach. By partnering with healthcare, policy makers, institutions, governments, ministries of health, and teams of interdisciplinary experts, we have successfully launched a wide range of targeted initiatives.

Bolstering STEM education

Through our STEM Program, we are seeking to encourage more young people, especially women, to pursue an **education in STEM fields**. The third UNESCO Africa Research Summit of Merck KGaA, Darmstadt, Germany (MARS) once more offered a key platform to pave the way for young researchers in Africa. Held in Mauritius in November 2017, the event focused on the role of scientific research in response to the latest developments in cancer management and vaccines. We use this annual conference as an opportunity to present the Best African Woman Researcher Award and the Best Young African Researcher Award. UNESCO-MARS Research Award winners go on to become ambassadors for our STEM Program within their home countries.

Fighting cancer and its effects

Our Cancer Access Program was launched in 2015, with the specific aim of educating people about cancer and cancer treatment. Our “re than a Patient” initiative empowers African female cancer survivors to establish their own small business as a farmer or to open a shop. Thanks to the program’s training and support, they are able to lead an independent and productive

life. To achieve this goal, we partner with cancer patient advocacy groups and cancer institutions across Africa.

Our Africa Oncology Fellowship Program focuses on increasing the number of oncologists in African nations and other developing countries. To this end, we have been offering various **fellowships** in collaboration with universities in Kenya, Egypt and India since 2016. By the end of 2017, 20 fellows had participated in this initiative.

Su-Swastha in India: Providing healthcare to rural regions

In India, around 700 million people reside in rural areas and have no access to effective, affordable healthcare. This is because medical facilities are concentrated in India's megacities, which account for 80% of the country's healthcare professionals and 70% of its hospital beds. Through our Su-Swastha project we are working to improve healthcare in rural India. Our goal is to provide inexpensive medicines while also educating local patients and physicians on everyday health issues and their treatment. Medical professionals hold weekly community meetings on topics such as coughs, childhood ailments and prevention. Moreover, the program also provides patients with **free check-ups** and offers continuing medical education to help doctors advance their medical capacities. In 2017, a total of 482 community meetings were held, reaching 11,250 people directly. Every year around 70 workers from the health industry participate in our continuing education programs, with 346 people having received training since 2012. Due to its business model, the project is currently running self-sustainably. It was recognized as a best practice in the 2016 Access to Medicine Index.

Healthy Women, Healthy Economies initiative

We aim to help women unlock their **economic potential** and in doing so create an impact for global economic growth. Nearly one in four women worldwide are held back from achieving their full economic potential due to preventable causes, such as a wide range of communicable and non-communicable diseases. Healthy Women, Healthy Economies has taken up this challenge. In 2014, under the auspices of the Asia-Pacific Economic Cooperation (APEC), we collaborated with representatives of the United States and other governments to launch this public-private partnership (PPP). Comprising public and private sectors as well as non-governmental organizations, this initiative has developed a policy toolkit with recommendations to improve women's health.

Under this program, we have 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 2017, we had reached nearly eight million people in the Philippines through our campaign. In Jordan, we collaborated with the NGO Royal Health Awareness Society to likewise train health workers on thyroid disorders in women. Moreover, in 2017 we formed a partnership with the Wilson Center. Hand-in-hand with this U.S.-based research institute we're gathering data and increasing awareness to illustrate how important women's health is to their participation in the economy. Furthermore, we are developing policy recommendations designed to support women in both paid and unpaid work in an effort to achieve greater work-life integration and improve their overall health and well-being. Another collaboration with the University of Miami's Department of Public Health Sciences is currently focused on women's unpaid labor in China, Canada, Chile, Mexico, and Peru.

chemical product safety



Part of the non-financial report

Many of our chemicals are classified as hazardous substances and are therefore subject to an array of national and international regulatory requirements to ensure that they do not pose any risk to people or the environment. Fulfilling these statutes and guidelines is crucial to our business activities. In addition, we strive to meet the expectations stakeholders such as customers and employees have of a comprehensive risk management system.

Our approach to safe chemical products

Product safety is our top priority. Starting in the development stage, we investigate the potential impacts chemical

substances may have. Along the entire value chain of our chemical products – from import or production through commercialization, handling, recycling, and disposal – 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 use them safely.

How we ensure the safety of chemical products

Our Life Science and Performance Materials business sectors each have their own Product Safety units. Working in close collaboration, these units are responsible for all product

safety activities such as registering chemical products, classifying hazardous substances and communicating risks through safety data sheets and labels. In addition to these activities, they also assume similar duties for our Healthcare business sector.

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.

Our Group-wide governance unit Regulatory Affairs (EQ-R) ensures that steps are taken to address gaps in regulatory compliance as soon as these arise. Reporting directly to the head of our Group function Corporate Environment, Health, Safety, Security, Quality, EQ-R is independent of our business sectors and is 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: Observing 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, in 2017 we adopted the 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 German federal law on protection from hazardous substances (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.

REACH registration on schedule

We are working to register all our chemical substances under REACH. We successfully completed registration phase 1 in 2010 and registration phase 2 in 2013. The next step, part of phase 3, is due by June 2018 and requires us to evaluate and register all substances produced or imported in quantities ranging from one to 100 metric tons annually. This process now also includes the substances added to our portfolio through the acquisition of Sigma-Aldrich and is on schedule.

In line with the Strategic Approach to International Chemicals Management (SAICM), a global policy framework overseen by the United Nations, **requirements for registering and licensing chemicals** are being recognized in a growing number of countries. Thanks to our experience in implementing REACH, we are well prepared for such a procedure and have already initiated the registration process for select substances.

Transcending laws

In an effort that transcends 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 we've registered under REACH 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 seek to ensure that our chemical products can be safely used later down the road. All our product innovations undergo a formal **EHS analysis**, which examines aspects such as their impact on human health and the environment. Before launching a new product, we evaluate all relevant hazardous substance data and classify it accordingly. In conducting these safety assessments, Regulatory Affairs provides advice and support to employees in our Life Science and Performance Materials business sectors.

Safe 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 business sectors, we can use nanoscale materials to develop **products with new functions and properties** – meaning, for instance, that resources and energy can be used more efficiently. In our Healthcare business sector, we partner 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 the suitability of nanoparticles as vehicles to deliver active pharmaceutical ingredients to the required site of action.

However, the special structure of nanoparticles can also entail 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 precau-

tionary principle and taking nanomaterial safety issues very seriously. In doing so, we consider Group-wide requirements for safety as well as environmental and health protection, employing our existing processes and systems for product safety. Whether using nanomaterials in pharmaceutical and chemical laboratories, production plants, filling plants, or warehouses, we abide by our Group-wide Policy for Use and Handling of Nanomaterials.

In the manufacture and processing of our products, we adhere strictly to all statutory regulations and other applicable standards, such as the guidelines 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.

Consolidating knowledge of nanotechnology

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 participate in committees and working groups such as the Nano-coordination group of the VCI's Technology and Environment committee, as well as Responsible Production and Use of Nanomaterials, a joint technology working group of DECHEMA (Society for Chemical Engineering and Biotechnology) and the VCI. Under the auspices of the VCI, we furthermore help to review current scientific literature in order to glean new findings on 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 chemical products. These brochures contain instructions for 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 41 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.

~23

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

Since all these documents must be kept up to date and consistent, in 2017 we automated the majority of our Group-wide hazard communication processes. Now the aim is to centralize the creation of safety data sheets in our business sectors. Within Performance Materials, for instance, we began drafting all safety data sheets Group-wide using a single system this year.

Informing customers and increasing awareness

All information on the safe use of our products is also available on our website, where our customers can additionally access the ScIDeX[®] program. This tool allows them to check whether they can use a chemical agent safely in line with the EU chemicals regulation REACH.

We aim to **increase awareness for 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 chemicals in safety cabinets and warehouses.

patient safety



Part of the non-financial report

The safety of patients treated with our medicines is a critical priority. That is why we consistently monitor risks and adverse effects as they arise, and take the necessary action to minimize them. Through rigorous benefit-risk assessments, we ensure that the benefits of our drugs always outweigh the risks for patients.

Our approach to ensuring patient safety

Our pharmaceutical products need to be effective in treating the respective disease while also posing as little risk as possible to patients. To ensure their safety, every new medicine passes a series of precisely defined development stages. Prior to using a drug in humans, we first 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 dose. This also helps us determine the dose that humans can safely tolerate. Only once this is complete do we perform clinical studies (p. 63) 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**. We only submit an application for marketing authorization to the regulatory authorities if the medicine has a positive benefit-risk profile.

Continual monitoring

After a drug is launched, the number of patients being treated with it increases significantly. In certain circumstances, rare adverse effects that go undetected during clinical development may occur, which is why we continually monitor and update the benefit-risk profiles even after market launch. For new products approved in 2017, we introduced educational materials for patients and healthcare providers on potential risks.

Pharmacovigilance is the process of continuously monitoring a drug to detect, assess and understand adverse effects in an effort to take appropriate action to minimize risk.

We always provide physicians and patients with the latest information on the safety of our drugs. This applies to the entire life cycle of a product, ranging from development, market launch and commercialization to expiration of the marketing authorization.

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, and articles published in medical and scientific journals. In 2017 we launched a new methodology and technical system providing effective, state-of-the-art capabilities for signal detection and management using data collected worldwide and big data analytics.

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

To meet the growing demands of our innovative R&D pipeline, Global Patient Safety underwent a strategic reorganization and specialization process in 2017. This resulted in two dedicated units specializing in the co-development and benefit-risk management of our investigational pipeline products, and in the global pharmacovigilance of our broad portfolio of products marketed worldwide. This specialization has already created new capabilities in advanced benefit-risk management, big data analytics, advanced signal detection technology, and pilot processes in patient-centric adverse effects collection.

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. As required, it initiates 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

To evaluate benefits and risks, we have introduced a **Benefit-Risk Guide** to our Global Patient Safety unit. This manual builds on the results of a joint initiative of the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA) in which we are involved. We benefited from the recommendations when compiling the documentation for marketing authorization of the drug cladribine. Subsequently we made use of these learnings for the documentation required for the marketing authorization of avelumab.

In producing pharmaceuticals, **quality assurance** is a key aspect. The Current Good Manufacturing Practice (CGMP) regulations ensure that pharmaceuticals meet the standards set for identity, purity, potency, and safety. Compliance with these regulations is mandatory for pharmaceutical companies and is closely monitored by health authorities. As a pharmaceutical manufacturer, we have appropriately trained employees, as well as suitable facilities, processes and procedures in order to meet all requirements.

We want our pharmaceutical products to be readily available to physicians and patients and always arrive on time. For this to happen, our **distribution processes** must function reliably all over the world. By continually auditing our distribution network, we ensure that both our subsidiaries as well as our partners and contractors adhere to our quality and safety requirements. All distribution activities must comply fully with Good Distribution Practices (GDP).

Meeting statutory requirements

We always adhere to all statutory pharmacovigilance regulations in force in those countries where we market our products and are continuously working to incorporate requirement changes in our Group-wide standards and processes. In 2017, for instance, we upgraded our safety database and the associated reporting processes to meet the new requirements of the European Medicines Agency (EMA).

Collecting information and checking processes

In March 2017 we rolled out agReporter, a mobile app for reporting adverse effects from the use of our products. This tool was initially intended for use by field nurses and our sales representatives. Furthermore, we plan to add a **patient-friendly interface** to the app, thereby putting patients center stage in our efforts to consistently collect adverse effects data.

Supervising drug safety

Regulatory authorities conduct regular inspections to verify that we are complying both with statutory requirements as well

as 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 European Medicines Agency. In 2017 **pharmacovigilance inspections** were conducted in Canada, Colombia, France, Japan, and Switzerland. All inspections have continually confirmed the proper functioning of our Pharmacovigilance system.

Furthermore, we perform our own audits to ensure that all our departments, subsidiaries, vendors, and licensing partners involved in pharmacovigilance consistently meet all requirements across the globe. In 2017, we found no significant deviations from these requirements. Such audits help us hone our pharmacovigilance processes so that they surpass statutory requirements.

Labeling of products

Package inserts inform physicians and patients on how to properly use the respective drug. In accordance with statutory regulations, the insert contains all relevant information such as ingredients and 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.

We review and update all package inserts as necessary, ensuring that they contain the latest information about our medicinal products. These leaflets also reflect changes initiated by our MSEB, such as new warnings. 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 performing regular audits. In addition, all our Biopharma employees receive basic pharmacovigilance training once a year that covers how to report adverse effects from our products.

Through such training, all employees are kept consistently up-to-date. This includes their professional expertise and training on internal standard operating procedures and other relevant requirements. In this way, we ensure adherence to Good Pharmacovigilance Practice (GVP) requirements. We provide our training via a global e-learning platform.

In 2017 we initiated a pharmacovigilance campaign in Mexico to raise awareness for adverse effect reporting. This effort is targeted at both patients and health workers (such as health authorities, physicians and nurses) along with our own Marketing

& Sales people. To ensure the campaign's success, we offered a special training program for our Marketing & Sales staff, who also receive additional informational material every two months. Moreover, we are conducting a poster campaign to make health sector employees more aware of the importance of reporting adverse effects.

Sharing expertise with other countries

We also work to transfer our drug safety expertise to other countries, especially those where health workers still lack the necessary **knowledge regarding pharmacovigilance**. In November 2017 we launched the "Africa kommt!" project in an effort to educate trainees from Africa on the safe use of pharmaceutical products, with the ultimate goal of them subsequently implementing the educational content in their home countries.

counterfeit products



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 too, however, such products are becoming increasingly available on the market through unlicensed internet pharmacies and underground business-to-business (B2B) platforms, ultimately posing a risk to public health. Chemical products can furthermore be used for illegal purposes such as the manufacture of illicit drugs.

Our approach to anti-counterfeiting

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 crime are identified, we also cooperate with customs authorities in the respective countries, along with Interpol, the World Customs Organization, various health authorities, and our peer industry. Our guidelines, standards and processes apply to all our business sectors and markets worldwide, thus protecting our reputation as a supplier of quality products.

What we mean by product crime

1. Counterfeit products: In line with the Trade-Related Aspects of Intellectual Property Rights Agreement (TRIPS) and WHO standards, 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/altered packaging and/or incorrect brand names
- with an authentic active agent, but not one produced under GxP conditions
- that have expired
- that were removed from the legal supply chain (e.g. through theft).

2. Illegal diversion of products: This term refers to the diversion of either chemical or pharmaceutical products from within the legitimate supply chain for illegal export, for use in the production of illegal 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're tackling product crime

Our Group function Corporate Security coordinates all our anti-counterfeiting activities. All such efforts are carried out under the supervision of our 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, violations are first investigated by the unit in charge.

Group-wide anti-counterfeiting network

Our Anti-Counterfeiting Operational Network (MACON) is responsible for globally monitoring and implementing **all anti-counterfeiting measures** for our products. Along with coordinating preventive measures 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, MACON is coordinated by our Corporate Security unit. All MACON activities are now overseen by the new Global Anti Product Crime unit, created in 2016.

To investigate suspected cases, MACON collaborates with the appropriate 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 2017, MACON reviewed and investigated approximately 128 cases, including inquiries from authorities that arose during back-tracking investigations. We furthermore uncovered four underground laboratories that were counterfeiting several of our products.

Our commitment: Group-wide guidelines and standards

Our Crime Relating to Products guideline of Merck KGaA, Darmstadt, Germany describes our goals and strategies for combating counterfeiting. Our Group-wide Product Crime Investigation Standard sets out binding 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 future incidents more effectively. Implemented at the end of 2017, our "Data and Documentation Quality Management" SOP details the associated process.

Tracking system for chemical substances

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

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

We believe that patients should be able to determine the identity and authenticity of a pharmaceutical product themselves. We are therefore rigorous in meeting the requirements of the EU Falsified Medicines Directive, for instance by applying a **unique serial number** to our pharmaceutical packaging. In the United States, this practice has been required by the Food and Drug Administration (FDA) since the start of 2018. We were the first company to have complied with this requirement by the end of 2015. As an EU company, we are likewise legally mandated to label all pharmaceutical packaging with a unique product identifier by February 2019. We are in the process of implementing this provision.

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

- We apply Security M, a security label containing our color travel pigments, to some of our products, taking a risk-based approach to identifying those products that should be labeled in this manner. The Security M enables users to **easily verify the authenticity** of our products and is considerably harder to counterfeit than the holograms commonly used.
- Through our **Track & Trace system**, pharmacists and distributors of our products can trace the supplier of the medicine to verify its authenticity. Having implemented this system for all our pharmaceutical products in the United States and China, in 2017 we expanded it to Colombia as well. We intend to furthermore include Europe, the Middle East, Egypt, and Russia by the end of 2018.
- Our free **Check My Meds app** for smartphones allows patients in the United States and since 2017 also in 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 back 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. With this compact test kit, counterfeit medicines can be detected quickly, easily and inexpensively, a tool that especially benefits developing and emerging countries. You can find more information on this project under Community (p. 111).
- We offer our customers in the pharmaceutical industry **Candurin® pearl effect pigments**, which feature unique color properties that make tablets and capsules more difficult to counterfeit.

Industry-wide exchange

In an effort to fight product 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 Manufacturers e.V. (vfa). We also support industry-wide initiatives. For instance, we work 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. Our Chief Security Officer is the Vice Chair of the PSI Board of Directors. Furthermore, we are a member of Rx-360, a consortium of global pharmaceutical manufacturers and suppliers that aims to prevent counterfeit products through the **introduction of a global quality assurance system**.

Educating our employees and business partners

We endeavor to raise awareness of product crime among our employees and business partners, educating our people worldwide on the subject. In the countries where we don't have our own subsidiaries, we offer training for our business partners.

All staff involved in security, such as Product Crime Officers, participate in **onboarding and training programs** aimed at building their capacities and promoting idea sharing. We are constantly refining these programs and adapting them to new trends. In 2017, for instance, we held incident reporting & intelligence systems training for our Product Crime Officers.

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). In doing so, we also ascertain the extent to which our **security requirements** are being implemented. In general, our contract partners meet these requirements. However, special security audits are conducted if significant deviations are identified. Such audits are also conducted 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. This auditing system is based on the EMA ICH Q10 pharmaceutical quality assurance standard. In 2017, we conducted ten security audits of our partners worldwide, who have since taken the necessary corrective action.

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 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 prevent 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. We ensure safety and compliance with these rules through our standards, regular audits of our sites and employee training.

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 (p. 87)), 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 advise the site director on issues regarding 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 third-party warehouses. Before signing a contract with a warehouse provider, we assess whether they properly adhere to national and international storage and transport regulations and if they are able to implement 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. The Warehouse Safety standard, for instance, defines measures to prevent substances from leaking or igniting. According to this standard, risk evaluations must be conducted on all stored substances, and it also sets out special rules of conduct that apply to all warehouse employees.

To ensure third-party warehouses also adhere to our strict safety requirements, our Group standard Warehouse Requirements for Third-party Warehouses defines specific **structural and organizational requirements** for a facility. Before we sign a contract, warehouse providers must submit a statement detailing how they plan to meet our stringent safety standards.

In Germany, the Technical Rules for Hazardous Substances (TRGS) govern the storage of hazardous substances in non-stationary containers. Across all our warehouse and distribution centers worldwide, we have implemented this regulation's requirements for storing various hazardous materials together and in 2017 we began rolling out **software** that will help us keep track of everything. We also comply with the current requirements of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) at all our sites, with the sole exception of India, where the GHS system has not yet been fully transposed into national regulations.

Our Group Transport Safety standard defines the safety levels for our sites and is based on the United Nations Recommendations on the Transport of Dangerous Goods. This is especially important for facilities in those countries with no local regulations on the transport of hazardous mate-

rials. We update our Group standard to reflect current requirements every two years and support our site directors in implementing the 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 audits every five 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 risk potential to be low.

In 2017, we audited 37 of our warehouses for compliance with our Warehouse Safety and Transport Safety standards. In response to the deficiencies identified by this audit, we are currently optimizing our Group-wide packaging selection process with a focus on our portfolio of acquired Sigma-Aldrich products.

Third-party warehouses and contract transportation companies are also regularly audited by our EHS managers. In 2017, we audited 15 third-party warehouses and external logistics providers, developing corrective action plans where shortcomings were identified. Along with implementing individual corrective measures, we also intend to optimize packaging and disposal processes at our third-party warehouses. In this vein, we are therefore currently compiling **information for off-site warehouses in Asia and Latin America**. Using real-life examples, this brochure will describe and explain our safety concept and guidelines. This is one of the ways we support our providers in meeting our strict requirements.

As a member of the Logistics & Distributors User Group of SQAS, a service provided by the European Chemical Industry Council (Cefic), we receive additional audit reports on our logistics service providers. In 2017 we developed criteria to evaluate these reports, which we subsequently make available to the relevant units in our company.

In 2017, no incidents that could have significantly impacted the environment or community were recorded at our company, our third-party warehouses or logistics providers, **nor were there any infringements** of international regulations.

Continuously improving 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. Based on a **strength and weakness**

analysis of each site, we calculate key performance indicators for transport and storage safety, which help us determine where to institute additional improvements. Rolled out in 2017, our in-house e-learning concept for basic management courses on the transport of dangerous goods is mandatory for all logistics, EHS and dangerous goods managers; additional courses on transport safety and storage are currently under development.

Employee training and best practice sharing

Several 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 changes to international requirements and incident management. All our truck drivers hold a dangerous goods driving license, while in Germany they complete additional training in line with the German Professional Driver Qualification Act (BKrFQG) and on securing cargo. Across the globe, every year we conduct around 1,000 internal and external training seminars on transport and warehouse safety. In some cases, the managers of third-party warehouses also participate in these sessions.

Furthermore, our EHS managers meet regularly at the EHS Conference in Darmstadt (Germany), where they have the opportunity to share lessons learned and best practices, as well as participate in transport and warehouse safety training. These topics are also covered in the mandatory three-day orientation seminar for all new EHS managers.

Such meetings also provide a platform to discuss current issues, for instance transport and warehouse safety during natural disasters such as Hurricane Harvey, which hit the United States at the end of August 2017.

Ensuring correct transport

Our products are primarily delivered to our customers by logistics providers. In Germany, we transport the majority of our hazardous waste ourselves, but do sometimes also enlist the services of other companies 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 expertise 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 transport or warehouse accident occurs, we can use our "TUIS Messkonzept Südhessen" to quickly calculate the rate at which hazardous substances are spilling and spreading.

Making transport vehicles safer

The safe transport of dangerous goods requires safe vehicles, another area we pursue. In the past few years, for instance, we have been constantly improving our **SafeServer truck body technology**. In this design, the aluminum panels integrated into the side walls of the truck render the walls extremely stable, making it largely unnecessary to secure cargo.

Responsible Marketing



Part of the non-financial report

We commercialize both prescription medicines and over-the-counter products. Pharmaceutical marketing is regulated by legislation worldwide. In Germany, for instance, manufacturers are only permitted to advertise prescription drugs to medical professionals such as physicians and pharmacists. In doing so, they must always disclose the active ingredients, adverse effects and contraindications of the advertised drug. In marketing our pharmaceuticals, the wellbeing of patients is always our primary consideration - because they deserve effective, high-quality treatment.

Our approach to responsible marketing

We adhere strictly to all regulations on pharmaceutical marketing. All guidelines pertaining to marketing and advertising are part of our Group-wide compliance program, which requires us to always conduct business in compliance with

the law and **in line with the highest ethical standards**. Our compliance program is complemented by our internal guidelines and various voluntary commitments that, in many cases, exceed the applicable statutory regulations. We regularly review all our internal guidelines, adapting them to new developments.

How we conduct ethical marketing

Our Group Compliance unit is responsible for setting up internal compliance policies and procedures to ensure that our business activities adhere to the statutory regulations applicable to our sales and marketing activities. Our Global Regulatory Affairs unit has also established a dedicated policy and complementary process document on the review and approval of our promotional materials. The necessary training and communication are carried out by each policy owner. On the operational level, the businesses and every

employee involved in our sales and marketing activities must carry out these activities in adherence with our internal policies and procedures. Our Internal Audits unit regularly conducts risk-based reviews of our sales and marketing activities. You can find more details on how we ensure compliance with statutory regulations worldwide under Compliance (p. 11).

Our commitment: Code of Conduct and industry-wide regulations

Our Group-wide "Pharma Code for Conducting Pharmaceutical Business and Pharmaceutical Operations" defines the relevant standards for our ethical marketing practices. It also governs our interactions with physicians, medical institutions and patient advocacy groups. Due to specific regulations in the United States, our pharmaceutical activities there are subject to a specific guideline entitled "Pharmaceutical Operations of Merck KGaA, Darmstadt, Germany and the biopharmaceutical business sector in the United States".

Through our "Principles of Review and Approval of Promotional Materials and Other External Communications", we ensure that **all promotional materials conform to our rigorous standards**. In 2017, we updated these principles along with the associated standard process, focusing particularly on our requirements for scientific communication with health workers. All employees involved in creating promotional materials worldwide have received training on these updates.

Beyond national laws and our own standards, we furthermore comply with the codes of conduct of various industry organizations, such as the Code of Practice and Code of Pharmaceutical Marketing Practices published by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). Moreover, we are a member of the German Association of Voluntary Self-Regulation for the Pharmaceutical Industry (FSA), which has defined its own code of conduct regarding collaboration between physicians and the industry.

Reviewing marketing material Group-wide

Our aim is to review all promotional material end-to-end to ensure that it meets our standards, which is why we apply a **Group-wide review and approval system**. In 2016, we updated this system and harmonized a variety of locally used tools. Since the beginning of 2017, approximately 2,200 Healthcare employees have been using a centralized platform that allows us to streamline the review and approval process more efficiently, while also providing a better overview of global marketing data. This helps us identify opportunities for improvement.

Addressing violations of standards and regulations

A **variety of channels** has been established so that wrongful marketing practices can be reported to the industry associations to which we belong. For instance, when members of the FSA or third parties suspect a violation of the FSA Code, they can file complaints directly with the respective Arbitration Board. In 2017, **no such complaints** were lodged against our company.

In addition to external reporting options, we have also established a SpeakUp Line that allows our employees to anonymously report potential compliance violations. If our marketing or advertising rules of conduct are violated, we have a committee in place to take immediate countermeasures. Appropriate corrective action is taken to deal with violations as required.

We have not identified any significant cases of non-compliance regarding regulations and voluntary codes.

Regular employee training

Employees responsible for our pharmaceutical advertising receive regular training on current guidelines. This particularly applies to individuals working in sales, marketing and drug registration. These seminars are conducted locally in a classroom setting, but are also offered online and as e-learning courses. In 2017 for instance, more than 1,100 employees took part in the training course on the "Review and Approval of Promotional Materials and Other External Communications". Additionally, the **employees in charge** can also access our compliance guidelines on the marketing and promotion of pharmaceuticals via our Intranet.

Direct marketing only in certain countries

Direct-to-consumer (DTC) advertising for prescription drugs is allowed in some countries such as the United States. We only pursue **DTC campaigns** in these jurisdictions. Through direct advertising, we hope to increase people's awareness of certain diseases as well as available therapies, empowering consumers and patients to make informed decisions about their own treatment.

Marketing chemicals

We approach the marketing of our chemical products with the deepest sense of responsibility. For instance, we only supply our chemicals to commercial customers with proven expertise and furthermore provide them with detailed information on the safe handling and use of our products. We have an extensive safety and security network in place to prevent the **misuse of dual-use products**. This network features standardized export control guidelines for these products, which are monitored by our central Export Control & Customs Regulations unit, as well as by trade and export control officers at our local subsidiaries. If we suspect misuse, we terminate our business relationship with the respective customer. In 2017, too, there were attempts to obtain our products for illegal purposes. In questionable cases, we additionally engage the responsible authorities to prevent illegal use.

Bioethics



Part of the non-financial report

Bioethics are foundational in guiding how we use the rapidly advancing power of life sciences and technology responsibly and ethically to the ultimate benefit of society, humans, and other living beings. However, factors such as diverse cultural backgrounds have led to heated debates, with controversy surrounding certain bioethical issues arising from the explosive progress in science and particularly molecular biology. In light of this situation, we believe it necessary to clearly state our position on these issues.

Our approach to ethical business conduct

In the course of our activities, we encounter various bioethical issues, including stem cell use, animal testing, the use of genetically modified microorganisms, the potential impact of new genome editing techniques such as CRISPR/Cas, and our own clinical research. We are strongly committed to conducting research in an ethical manner. In treating patients with our drugs and supplying academic researchers and the biopharma industry with our products, patient benefit and wellbeing are always of utmost importance. When faced with **controversial topics**, we carefully evaluate all relevant positions to ensure we make informed decisions in line with the highest ethical standards.

How we assess bioethical issues

Our Bioethics Advisory Panel (MBAP) of Merck KGaA, Darmstadt, Germany convenes once a year and also provides support when urgent bioethical issues arise. Co-chaired by our Global Chief Medical Officer (CMO) and the head of our Global Health Institute, the MBAP provides clear guidance on bioethical questions, which we take as a basis for our entrepreneurial conduct. For the benefit of our employees, we publish summaries from MBAP meetings on our Intranet.

In 2017, we adapted the organizational structure of the MBAP to reflect the current requirements of bioethical issues so that it now advises on bioethical questions pertaining to all three of our business sectors. Moreover, by appointing external experts from Africa and Asia to the panel, we have also integrated the views of these regions more strongly in bioethical discussions. Our Dedicated Guidance Panels for Genome Editing and Stem Cell topics are also now operating under the overarching MBAP. These panels are responsible in particular for the operational implementation of our positions and are empowered to make decisions regarding specific questions on individual projects. Formed in 2011, the Stem Cell Research Oversight Committee (SCROC) verifies in advance all internal research proposals employing human stem cells, compliance with our ethical guidelines,

and legal requirements pertaining to stem cell research. This also includes collaboration with external partners. The SCROC works under the guidance of the MBAP.

Our commitment: Identifying issues early on

As a global company, it is crucial for us to promptly identify and address new developments concerning bioethical issues in order to define our own stance. Although we align all our business activities with international and national legislation, many bioethical discussions raise questions that far exceed the current purview of legislators, which is why we also seek the advice of external experts.

Bioethics Advisory Panel discussions

In 2017, in addition to organizational changes, the MBAP discussed the establishment of our new Global Health Institute, as well as fertility research (p. 62), stem cell research (p. 62) and genome editing (p. 62). We have submitted the panel's advice and scientific recommendations for publication in a peer-reviewed journal.

Our Global Health Institute aims to improve access to health-care, particularly in developing countries. Its focus areas are addressing the unmet needs of women and children, as well as infectious diseases (p. 41) and antimicrobial resistance. The panel has suggested developing a guideline for the Global Health Institute that would define aspects such as collaboration with partner organizations and research priorities.

Biotechnology and genetic engineering

We utilize genetically modified organisms (GMOs) in our research and development work and have been manufacturing biotech products using GMOs since the 1980s. Without this technology, **the major medical advances** of past years would not have been possible.

Our most important research hubs for medical biotechnology are Darmstadt, Boston (MA, USA), Beijing (China), and Tokyo (Japan). Major biotech production sites are located in Martillac (France), as well as Aubonne and Corsier-sur-Vevey, Switzerland, the latter of which is one of the largest biopharmaceutical production facilities in Europe.

Across our Group, we manufacture our biotech products **according to the highest standards**, and all our biotech activities are subject to strict statutory regulations worldwide. Compliance with these regulations is monitored by our biological safety officers. We continuously track regula-

tory changes pertaining to biotech products and adapt our processes accordingly, thus ensuring we adhere to all statutory requirements.

Using genome-editing applications

We are a leading supplier of technologies such as CRISPR/Cas9, which can be used to target and modify specific genes, a process known as **genome editing**. CRISPR/Cas9 opens up new possibilities in genetic engineering research that could bring about major advances in the treatment of serious diseases or in "green genetic engineering", the use of genome editing techniques in plant cultivation. Statutes in different countries allow for a varying degree of latitude in applying this technique, which is why in 2017 the MBAP once more thoroughly discussed the current possibilities and ethical boundaries of genome editing systems. The results of this discourse have been incorporated into our new Genome Editing Technology Principle, which took effect at the end of October 2017. This principle provides our employees with background information and explains our current stance on such technology. It thus defines a mandatory ethical and operational framework – firstly for us as a supplier of custom targeted nucleases and genetically modified cell lines, and secondly as a user of genome editing technologies for scientific research.

Stem cell research

At present, we neither participate in clinical programs that utilize human embryonic stem cells or cloned **human cells** for the treatment of diseases, nor do we pursue such approaches ourselves. However, we do make use of stem cells in our research. In addition, we offer our customers several select stem cell lines. Our updated Stem Cells Principle, which was discussed by the Stem Cell Research Oversight Committee in 2017 and took effect in October 2017, ensures compliance with our ethical approach. The panel further recommended a new Informed Consent form for the use of induced pluripotent stem cells (iPSCs), which are identical to embryonic cells and can generate every type of cell in the human body.

Fertility research

Because we develop treatments for infertility and seek to improve the success rate of in vitro fertilization, we are frequently confronted with various bioethical issues relating to such treatments. For instance, may embryos resulting from artificial insemination be screened for genetic disorders and then selected on this basis? In such questions, the German Embryo Protection Act is our legislative point of reference. Developed based on guidance from the MBAP, our new Fertility Principle came into force at the end of October 2017. Further discussion topics on the MBAP's 2017 agenda included various issues pertaining to **medical technology and products for fertility research**. We have the support of the panel in establishing a data pool of clinical evidence regarding fertility technologies.

Biosampling and biobanking

Biological samples obtained from patients within clinical studies are indispensable to the development of new precision treatments and advanced diagnostic methods. We handle these samples in a responsible and ethical manner, in compliance with all regulatory requirements, and according to the consent given by patients for the use of their samples.

When conducting clinical studies in which biological samples are collected, we inform study participants upfront about the purposes for which we use their samples. On this basis **participants may consent to the use of their specimens**, thereby enabling us to learn more about the study drug, the disease, or other medical questions. Participants can withdraw their consent at any time.

In addition, study participants are given the opportunity to authorize the use of their biosamples for further medical research beyond the clinical study. This way they help to address future scientific questions and ultimately support medical progress. In 2017 we implemented a policy and a standard operating procedure defining the principles and processes of human biosample management during and after clinical studies.

Biological samples, including tissue samples and body fluids, are permanently stored in biobanks together with the corresponding encrypted patient and specimen data. While these are extremely important to our research, their storage and use for research purposes requires us to adhere to stringent ethical standards. In 2017 we implemented new rules governing biobank operation and the use of stored samples.

Clinical studies

We discover and develop **innovative medicines** that meet patient needs. In doing so, we adhere to all relevant statutory and regulatory requirements, as well as scientific and ethical standards. For clinical studies, these standards particularly include the Declaration of Helsinki, in which the World Medical Association has formulated ethical principles for medical research involving human subjects, and the Good Clinical Practice (GCP) of the International Council for Harmonisation (ICH). More details can be found under Clinical studies (p. 63).

Off-label use

We endeavor to **drive scientific and medical progress**, often doing so in close collaboration with medical professionals. We regularly receive inquiries about the off-label use of our products, i.e. indications for which the drug was not originally approved. While each medicine is authorized for specific indications, cases do arise in which a physician wishes to prescribe a drug to treat a disease for which it is not approved. Such applications can benefit patients. However, to use a drug in this way, solid evidence must

exist showing that it can be effective in the treatment of the specific disease.

Our principles for disseminating information regarding the off-label use of our products are set out in corresponding globally applicable policies. In particular, we only market our medicines within the scope of the drug's marketing approval. We never share information on off-label use for commercial

ends and provide such information to healthcare professionals only for medical purposes and only upon direct, unsolicited request. The information must be backed by scientific evidence and factually balanced. Our employees are not permitted to make any sort of treatment recommendations for individual patients.

clinical studies



Part of the non-financial report

Our company develops medicines that help people with serious diseases. Before obtaining regulatory approval, we conduct clinical studies with patients and, if necessary, also with healthy subjects to test the safety and efficacy of these products. These trials generally run for multiple years. Prior to doing so, extensive preclinical testing must first be performed to demonstrate that the drug poses no unacceptable risks. This preclinical test phase typically includes procedures such as animal testing. We only test medicines in patients if the compounds show great therapeutic promise and have a positive benefit-risk ratio.

Our contribution to safe and transparent clinical studies

We conduct high-caliber clinical research that always complies with applicable laws and regulations. When performing clinical studies, we adhere to the highest **ethical and scientific standards** worldwide.

We only conduct clinical studies to investigate issues that are relevant to patients, healthcare professionals or society as a whole. In addition to this prerequisite, a sound, established scientific methodology must be available to investigate these scientific or medical questions. We only enroll the number of participants required to answer the respective questions.

Protecting the safety, wellbeing, dignity, and rights of the patients and healthy volunteers participating in our clinical studies is of utmost importance to us. We do not intentionally expose study subjects to undue risk or irreversible harm. Personal data privacy is extremely important to us, and the confidentiality of all data and information collected is ensured in compliance with statutory regulations.

Clinical studies in developing countries

We conduct all our clinical studies in accordance with local laws and regulations. In addition, we also adhere to all relevant international scientific and ethical standards at all times.

We are intentionally expanding our medicinal product development to more diverse markets in order to address the healthcare needs in various regions and countries and to support **the development of their healthcare systems**.

In performing clinical studies in developing countries, where there is usually a lower level of healthcare and less developed healthcare infrastructure, we adhere to the same principles that apply when conducting such trials in industrialized countries. When we perform studies in developing countries, we also:

- only do so in an environment in which the principles of Good Clinical Practice can be upheld; particularly in those places where ethics committees and well-trained Clinical Investigators are present.
- only investigate diseases and innovative medicines that are relevant to the local population.
- only conduct clinical studies in countries where we expect that the drug tested will be submitted for marketing authorization and made available to patients after we have proved its efficacy and safety.
- assure that no subject enrolling in a clinical study is discriminated against on the basis of ethnic origin, gender or socio-economic status.

How we govern clinical studies

Overall responsibility for pharmaceutical development as well as the related governance process is borne by our head of Global Research and Development, who, hand-in-hand with the Chief Marketing & Strategy Officer, co-chairs the Development Operations Committee (DOC). This top-ranking Biopharma committee ensures a cross-functional approach to the governance of drug development.

Under the umbrella of the DOC, two further committees oversee our clinical studies. The Integrated Clinical Study Committee (ICSC) is responsible for studies in pharmaceu-

tics that are under clinical development, while the Global Medical Affairs Decision Board is responsible for studies involving approved medicines. Both bodies consist of medical scientific **experts and executives with long-standing experience** in clinical research. Each committee meets regularly to conduct a comprehensive review of the proposed clinical study concepts to verify that our studies are scientifically sound, have a legitimate scientific purpose, and are performed according to the latest standards and best practices. Our therapeutic area review boards support the ICSC by conducting thorough scientific assessments of new drug/pharmaceutical study concepts.

Before administering a new drug to human subjects, there must be sufficient evidence that it offers a potential therapeutic benefit, is sufficiently safe for use in humans, and has a positive benefit-risk profile. Only after diligently **conducting extensive preclinical testing** do we take the critical step of a first-in-human clinical trial. This important step of exposing humans to an investigational drug is governed by the Human Exposure Group chaired by our Global Chief Medical Officer.

Potential risks for subjects are carefully and continuously analyzed before and during the course of our clinical studies. Our Medical Safety and Ethics Board (MSEB) oversees the safety of subjects participating in our clinical studies and, as necessary, reviews the benefit-risk profiles of investigational drugs. You can find further information on the MSEB under Patient safety (p. 53).

Our commitment: International guidelines and agreements

Our Clinical Research policy provides the framework for conducting clinical studies and ensures that we adhere to all legal, ethical and scientific standards. In addition to the relevant national laws and regulations, these standards also include:

- The Good Clinical Practice (GCP) guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH)
- The Declaration of Helsinki published by the World Medical Association
- The Belmont Report from the Office for Human Research Protections, USA
- Good Pharmacovigilance/Laboratory/Manufacturing/Distribution Practices (GVP/GLP/GMP/GDP)
- The International Ethical Guidelines for Health-related Research Involving Humans published by the Council for International Organizations of Medical Sciences (CIOMS)

- The "Joint Position on the Disclosure of Clinical Trial Information via Clinical Trial Registries and Databases" and the "Joint Position on the Publication of Clinical Trial Results in the Scientific Literature", published by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), the European Federation of Pharmaceutical Industries and Associations (EFPIA), the Japan Pharmaceutical Manufacturers Association (JPMA), and the Pharmaceutical Research and Manufacturers of America (PhRMA)
- The "Principles for Responsible Clinical Trial Data Sharing" published by EFPIA and PhRMA

Regular supervision of clinical studies

Our clinical study procedures are regularly inspected by health authorities to ensure compliance with the applicable laws and guidelines. We also conduct our own internal quality assurance audits. In both cases, we respond immediately to any issues found by defining and implementing corrective and preventive actions to improve our processes accordingly.

Conducting clinical studies responsibly

Prior to enrolling subjects, every clinical trial must first be assessed and approved by a qualified independent **ethics committee**. Furthermore, all regulatory authorizations required in the respective country must be obtained. In accordance with Good Clinical Practice guidelines (ICH-GCP), all subjects must give their explicit informed consent before enrolling in a clinical study. Subjects are fully informed about all aspects of the clinical trial in a language that they understand; this includes the potential risks and benefits from participating in the study. All participants are given ample time and opportunity to inquire about details before deciding whether to participate. All questions are answered by the clinical investigator or another qualified healthcare professional familiar with the study. As far as possible, non-interventional (observational) studies are also assessed by an ethics committee. The subjects are further provided with thorough information.

Every study follows precisely defined procedures to ensure that studies are conducted to the **highest quality standards** in line with good working practices for the development and manufacture of drugs (GxP), the ethical principles of the Declaration of Helsinki, and other international guidelines and regulations. This approach ensures in particular that studies are designed, conducted, recorded, and reported in line with all applicable requirements. In 2017, no significant issues regarding these clinical study procedures were raised by third parties or regulatory agencies.

We continuously collect and communicate safety data for our investigational drugs and promptly provide clinical investigators with important new findings relevant to the safety of subjects. In this way, we ensure the safe use of our phar-

maceuticals. Potential adverse effects and risks are taken into consideration in an effort to evaluate the benefit-risk ratio of our products and manage risk. Product information, including the Investigator's Brochure and Subject Information, is updated accordingly. You can find more information under Patient safety (p. 53).

Conducting clinical trials in vulnerable populations

The implementation of clinical studies in vulnerable populations requires **special attention and care** in order to comply with the highest ethical and scientific standards. When a drug is intended for use in vulnerable populations, such as children or people with mental disabilities, in some cases clinical studies must be conducted in these populations. Their wellbeing is our utmost priority as, in general, these groups are relatively (or absolutely) incapable of protecting their own interests. We therefore only conduct studies with patients from vulnerable populations if there is no other way to achieve conclusive results. When performing such studies, especially when informing study participants and obtaining their consent, we comply strictly with all statutory regulations.

One example of a trial involving vulnerable populations is our praziquantel study in Africa to develop a formulation for children under the age of six. Praziquantel tablets are only suitable for adults and children *older* than six. Due to a lack of clinical data and **no suitable pediatric formulation** of praziquantel, pre-school aged children must currently go untreated. Within a public-private partnership, we are working to develop, register and provide access to a pediatric formulation of praziquantel that is suitable for children under the age of six. To this end, a Phase II study is currently ongoing in Côte d'Ivoire, and Phase I trials have been completed in South Africa and Tanzania. This clinical program was designed in line with U.S. Food and Drug Administration recommendations for pediatric development. It was planned and implemented with the support of regulatory authorities and a panel of international experts, including clinicians from endemic countries. Further details can be found under Infectious diseases (p. 41).

Teaming up to get results

To provide a broad, in-depth basis for the development of new medicines, we frequently conduct clinical studies in collaboration with external partners in academia and industry, as well as with medical scientific advisory boards, service providers and vendors. We expect all our partners to abide by the same set of high standards when conducting clinical research. This applies especially to **contract research organizations** (CROs) performing studies on our behalf.

Our CROs, partners and suppliers are subjected to regular audits within our quality assurance strategy to verify their compliance with Good Working Practices (GxP, for example ICH GCP), other international guidelines and regulations, and

the Declaration of Helsinki. This also applies to study centers (for example hospitals) involved in our clinical studies. In 2017, these audits did not reveal significant non-compliance with the above-mentioned standards.

Close dialogue with patients and advocacy groups

We want to ensure that **patients' voices** and needs are adequately taken into consideration when planning and carrying out clinical studies. To this end, we established Patient Advisory Boards (PABs) in 2014. Our Patient Advisory Boards Charter describes the process on how to involve the Patient Advocacy Groups in our clinical research. During Advisory Board meetings, caregivers and representatives from patient advocacy groups are invited to provide feedback on clinical study matters. This advice and wealth of valuable insight applies to both the design of the clinical trial as well as its operational implementation. Cumulatively, we use this information to render clinical development and clinical studies more patient centric.

Furthermore, we are involved in the European Patients' Academy on Therapeutic Innovation (EUPATI), a public-private partnership within the Innovative Medicines Initiative (IMI) that initially ran from 2012 to 2017. In 2017, we extended our participation in EUPATI for an additional three years. EUPATI is a pan-European project led by the European Patients Forum (EPF); it features partners from patient advocacy groups, universities and not-for-profit organizations, along with a number of pharmaceutical companies. This project focuses on helping patients **better understand pharmaceutical research and development** while also offering them a way to incorporate their needs into the development of clinical studies. EUPATI furthermore aims to improve the availability of objective and reliable information for the public.

Responsible data sharing

We support professional circles in advancing **medical and scientific knowledge**, thereby allowing for informed healthcare decisions for the benefit of patients. To this end, upon request we provide qualified researchers with study protocols, anonymized patient data, study data, and clinical study reports. In doing so, we share data and information in a manner that is consistent with the following joint Principles for Responsible Clinical Trial Data Sharing of the EFPIA and PhRMA:

- Safeguarding the privacy of patients
- Respecting the integrity of national regulatory systems
- Maintaining incentives for investment in biomedical research

Disclosure of clinical studies and publication of results

We are obliged to disclose information from our clinical studies, which we do publicly in a complete, accurate, balanced, transparent, and timely manner, as laid out in our Clinical Trial Disclosure Policy. Our clinical study designs and results are made public in the international ClinicalTrials.gov database run by the U.S. National Institutes of Health (NIH), which can also be accessed via the World Health Organization's International Clinical Trials Registry Platform (ICTRP). Furthermore, in accordance with EU regulations, we publish results from our clinical studies in the European Union Drug Regulating Authorities Clinical Trials (EudraCT) database, which is run by the European Medicines Agency (EMA). If required by local laws and regulations, we publish study results on other publicly accessible platforms. In 2017 we started providing our study participants with Lay Patient Summaries, which explain clinical study results in plain language.

We make sure that results from our clinical studies are published in medical journals in line with applicable laws and industry codes. In doing so, we adhere in particular to the current version of the Good Publication Practice (GPP3) and follow the recommendations of the International Committee of Medical Journal Editors (ICMJE). Our Medical Publications Policy ensures compliance with all relevant standards. Furthermore, we have defined standard procedures for scientific publications on our products.

Immuno-oncology: Major clinical research milestones

Immuno-oncology investigates the extent to which the body's immune system can be activated or strengthened to mount an immune response against cancer. As part of a strategic alliance with the U.S. pharmaceutical company Pfizer, we are studying **avelumab**, an investigational anti-PD-L1 (programmed cell death ligand 1) antibody initially discovered and developed by Merck KGaA, Darmstadt, Germany, as a potential treatment for a broad spectrum of tumor types. Under this collaboration, in 2015 we launched JAVELIN, our comprehensive international clinical study program in which we are investigating the potential therapeutic benefit of avelumab in multiple tumor types. By the end of 2017, more than 7,200 patients had been evaluated within this program.

In 2017, avelumab was granted its first marketing authorization in several countries (including the United States and Japan) and the European Union for treatment in patients with metastatic Merkel cell carcinoma (mMCC), a rare and aggressive form of skin cancer. Subsequently, avelumab was granted regulatory approval by the U.S. Federal Drug Administration for the treatment of patients with locally advanced or metastatic urothelial carcinoma (a malignant tumor of the urothelium that lines the urinary tract) that had progressed following platinum-containing chemotherapy. Meanwhile, avelumab continues to be evaluated in several ongoing registrational Phase III studies across multiple different tumor types, including lung, gastric, ovarian, renal cell, and head and neck cancers.

Enabling early access to new medicines

Not all patients can take part in a clinical study and so must wait for a new pharmaceutical product to be approved. Through our Early Access Program, we are, under specific circumstances, enabling patients to gain early access to new, potentially life-saving medicines. The offer is aimed at people with serious conditions who have already used all available therapies without success. It allows them to obtain medicines that have already been clinically tested but not yet obtained marketing approval. Here too we meet stringent statutory, ethical and scientific standards. By performing a thorough assessment of all available data, we ensure that the potential benefits outweigh the potential risks for patients. We have published a position paper on the Early Access Program on our website.

Coming to terms with the past

In the 1950s and 1960s, drugs from various manufacturers were tested on children living in institutions in Germany. The majority of such clinical studies were performed in collaboration with (university) hospitals and general practitioners. By making files in our historical archives at our global headquarters in Darmstadt available, we are now supporting efforts to understand and come to terms with this episode in the history of science. As part of these efforts, we opened our archives to researchers in 2015. It is important that the findings and completion of their work be awaited before making a final assessment of this complex issue. We guarantee full transparency and will do everything necessary to help the affected institutions come to terms with the past.

Animal welfare

From both an ethical and scientific perspective, animal research is indispensable and is furthermore mandated by law. Through animal studies, we test both the safety of our chemical and medicinal products, and the efficacy of our pharmaceuticals. We enforce stringent animal welfare standards that exceed applicable laws and extend these high expectations to our suppliers, contract research organizations and other partners. We conduct animal testing within our Healthcare business sector as part of the official drug approval process. However, animal welfare is also a prominent issue for our Life Science business sector, which keeps laboratory animals for the production of antibodies, for instance. In addition, our subsidiary Bioreliance conducts animal testing as part of contract research work for third parties.

Our approach to animal welfare

Our Group-wide Use, Care and Welfare of Laboratory Animals Policy sets forth our commitment to consistently uphold the highest ethical standards regarding the housing, care and feeding of laboratory animals. When conducting animal research, we pursue tried and tested methods that ensure high-quality results and furthermore strive to replace animal testing with alternative methods wherever possible and permissible by law. We therefore subscribe to the internationally recognized **3Rs for animal-based research**:

- **Reduction** - using the minimum number of required animals
- **Refinement** - minimizing distress or discomfort before, during and after testing
- **Replacement** - replacing animal studies with non-animal systems

We promote the 3Rs outside our company as well. Under the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ Consortium), for instance, we have joined forces with other companies to support the Global 3Rs Awards Program. In partnership with the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International), this initiative recognizes innovative contributions to the 3Rs of animal research to advance ethical science in academia and industry.

How we ensure animal welfare

As head of Corporate Animal Science and Welfare (EQ-A), our Chief Animal Welfare Officer is responsible for creating uniform animal welfare standards. This individual also initiates EQ-A audits, sometimes performing these himself within

our company or on our partners. Moreover, all our animal science and welfare experts regularly interact through our **global laboratory animal science network**. A platform for sharing best practices and lessons learned, this network supports the animal welfare units at our sites along with all projects and processes related to animal science and welfare.

Our Group Animal Welfare Council convenes twice a year. Comprising representatives from all our business sectors, this council discusses relevant developments and makes decisions regarding our Animal Welfare Strategy. In 2017, our efforts focused on creating various guidelines and certifying contract research organizations, other partners and suppliers. To accomplish this, the council is developing a risk-based approach that will also apply to the procurement of products of animal origin.

In most cases, our sites are subject to additional national regulations. In order to assess the quality of animal husbandry practices and ensure compliance with our standards as well as all statutory requirements, we appoint **animal welfare officers** and establish **animal welfare councils** across our Group, even where not required by law. In 2017, for instance, we appointed an animal welfare officer for our Life Science business, who is greatly involved in conducting audits and identifying potential animal welfare risks in our supply chain.

Work with committees and associations

As part of our efforts to improve animal welfare, we are involved in several organizations such as the European Federation of Pharmaceutical Industries and Associations (EFPIA), the German Association of Research-based Pharmaceutical Companies (vfa), and Interpharma, a federation of research-based pharmaceutical companies in Switzerland. Our Chief Animal Welfare Officer has an active role in various committees to advocate our position on animal welfare. Moreover, he represents EFPIA on the AAALAC International Board of Trustees, where he ensures adherence to European standards. At the end of 2016, he was appointed to the Executive Committee of AAALAC International for a term of three years. In addition to these positions, he is a member of the German Federal Animal Welfare Commission.

Our commitment: Group-wide methodology and standards

Through our Group-wide Use, Care and Welfare of Laboratory Animals Policy, we have made a commitment to global animal welfare principles and the highest possible ethical standards in animal research. In 2017, we updated this policy to establish a basis for the work of our Group Animal Welfare Council. The policy further sets out principles on the

housing, care and feeding of laboratory animals. We strive to provide our animals with high-quality living conditions and consistently seek ways to make improvements. This ethos applies equally to the contract animal research services we offer third parties. In addition to our policy, our Group-wide Animal Science and Welfare manual describes the requirements for implementing, maintaining and improving animal welfare practices. Moreover, in 2017 we created a new guideline entitled Housing and Husbandry Practices for Common Laboratory Animals, which applies to our external partners as well. We also drafted a Standard on Vendor Qualification, which describes our criteria for evaluating the quality of our suppliers' and partners' animal welfare practices. This standard took effect in March 2018.

Legal requirements

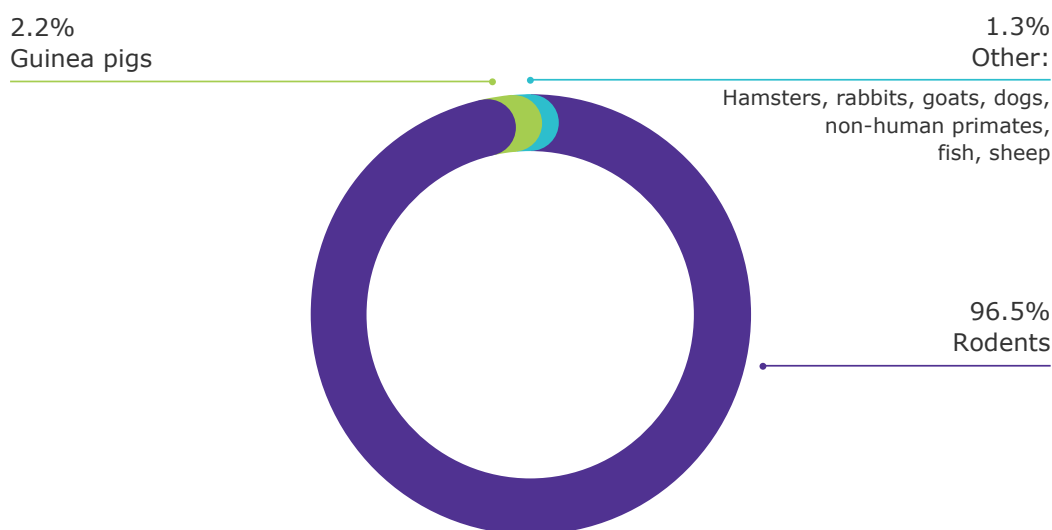
Animal research is only permitted if there are no recognized alternative methods available. In many fields, however, animal studies are indispensable and legally mandated by ICH guidelines or REACH, which place priority on the safety

of humans. Laws and regulations govern all aspects of animal research, such as the housing conditions of laboratory animals, the conduct and approval of studies, and the reliability and expertise of all involved individuals.

The majority of laboratory animals are rodents

Approximately 97% of the laboratory animals we use are rodents (mice and rats). Other animal species are only used if specified by statutory regulations or if deemed necessary for scientific reasons. For example, regulatory agencies sometimes require investigational drugs to also be safety tested on a non-rodent species such as monkeys, dogs or pigs. Guidelines such as REACH also require testing on non-rodents under certain circumstances. This allows researchers to identify potential **adverse effects with the necessary accuracy** and include them in the risk assessment (p. 53) of a substance. In performing tests on non-rodents, we must meet additional requirements pertaining to animal care and study design.

Animal types



Auditing our research facilities

We perform regular audits on our animal research facilities to ensure adherence to our animal welfare standards. In 2017, for instance, our Corporate Animal Science and Welfare unit conducted two internal audits at our Healthcare sites in Billerica, MA (USA) and Ivrea (Italy). We have initiated the relevant corrective measures where necessary. No critical shortcomings were identified during these audits.

It goes without saying that we adhere to the **highest international animal welfare standards** at all times. All our Healthcare laboratory animal facilities have been certified to the standards of the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC International). Furthermore, one of our Life Science laboratory animal facilities has also received AAALAC accreditation.

Collaborating with partners and suppliers

We perform the majority of animal studies ourselves and for the most part procure our animals from specialized breeders or, in very few cases, from our own breeding colony. Sometimes, however, we also hire **contract research organizations** (CROs) to conduct animal research on our behalf. Furthermore, we work with both the private sector and academic institutions. When collaborating with such organizations, we expect them to adhere to the same high standards as we do, as set out in our Use, Care and Welfare of Laboratory Animals Policy. We verify compliance with this policy through a risk-based qualification procedure and, where necessary, also conduct audits, generally every three years. In order to harmonize animal welfare efforts within our company, in 2017 we created a Group-wide standard entitled Housing and Husbandry Practices for Common Laboratory Animals, which also applies to our partners and vendors.

Regularly auditing our partners

We perform regular audits on our animal breeders and contract research organizations to ensure compliance with our animal welfare standards. As part of our work with Interpharma, we have developed a cross-company audit concept that concentrates on those partners that are relevant to the maximum number of companies involved. In 2017, two audits were conducted in Europe. The results are shared among Interpharma member companies and treated confidentially. If critical defects are not corrected, we reserve the right to terminate our collaboration with the respective vendors.

Comprehensive employee training

We regularly train all employees who work with laboratory animals, thereby ensuring that animal studies are conducted according to the latest scientific standards and that animals receive the best care possible. The nature and scope of this training is based on national and international legislation, as well as local requirements. The respective regulatory authorities monitor our activities to ensure compliance. In addition to this training, our employees regularly participate in **external continuing education programs** such as accredited laboratory animal science courses offered by the Federation of European Laboratory Animal Science Associations, the American Association for Laboratory Animal Science, the Society of Laboratory Animal Science, the Laboratory Animal Science Association, and the Interessengemeinschaft Tierpfleger (Community of Animal Caregivers).

How we implement the 3Rs

To minimize the discomfort and distress to animals before, during and after testing (refinement), in 2017 we introduced our own innovative group housing concept for rabbits and rats at one of our sites. By keeping animals together in groups, they are generally healthier and less stressed.

Moreover, we actively support the development of alternative testing methods and their official recognition at an international level. There is a serious need for action here because animal research can only be truly reduced if a new methodology is internationally accepted. Without this **global recognition**, both animal studies and alternative testing have to be conducted in parallel when developing pharmaceuticals intended for worldwide distribution.

To help rectify this situation, we support the European Partnership for Alternative Approaches to Animal Testing (EPAA). This collaboration between the European Commission, European trade associations and companies from various sectors seeks to pool knowledge and resources to accelerate the development of alternative approaches to animal use in regulatory testing. Through our membership in the German Association of Research-based Pharmaceutical Companies (vfa), we also support the set Foundation, which seeks to reduce and replace animal testing. To achieve this objective, the foundation funds projects that conduct research into alternative methods. Our Chief Animal Welfare Officer is currently Vice Chairman of the set Board of Trustees. Our own scientists are also working on developing alternative methods and have received numerous accolades for their efforts:

- 2014: The Hessian Animal Welfare Research Prize for Alternative Methods to Replace or Reduce Animal Testing
- 2010: The IUTox Bo Holmstedt Scientists Award for Alternative Test Strategies according to the 3Rs
- 2009: The Eurotox Gerhard Zbinden Young Scientists Award
- 2008: The Eurotox Bo Holmstedt Young Scientists Award for Alternative Test Strategies according to the 3Rs
- 2007: The Hessian Animal Welfare Research Prize for Alternative Methods to Replace or Reduce Animal Testing
- 2006: The German Animal Welfare Research Prize awarded by the Federal Ministry of Food, Agriculture and Consumer Protection (BMELV) for alternative methods to replace or reduce animal studies
- 2005: The Eurotox Gerhard Zbinden Young Scientists Award

interactions with health systems



Part of the non-financial report

We want all patients to receive the best possible medical treatment. To achieve this, it is essential that research institutes, physicians, patient advocacy groups, and other key actors in health systems have access to detailed and up-to-date information on diseases and treatments. We help facilitate this access by sponsoring independent initiatives and medical capacity advancement programs, as well as by donating money and supplies. In addition, we promote outstanding research projects. In all our endeavors, transparency is our number one priority.

Our approach to interacting with health systems

We support health systems by providing information, making monetary contributions, and donating supplies to professional medical associations, university clinics and other hospitals, as well as to patient advocacy groups. These contributions are expressly not intended to influence decisions regarding treatment, prescriptions or purchasing. Consequently, we have committed ourselves to providing **complete transparency**. We prepare detailed reports on our donations that align with industry-wide codes and with statutory requirements such as those governing data protection. Every year we disclose all transfers of value to healthcare professionals, healthcare organizations and patient organizations. We also report on transfers of value made by our R&D activities in every country where our company operates within the region covered by the European Federation of Pharmaceutical Industries and Association (EFPIA). Furthermore, we fulfill the relevant voluntary commitments of our industry.

How we're ensuring transparency and compliance at an organizational level

In all interactions with health systems, Group Compliance establishes internal policies and related **review processes** to ensure adherence to statutory requirements and transparency obligations. Group Compliance also provides the necessary training and communication to all employees involved. Furthermore, the Global Transparency Operations team of Group Compliance serves as a center of excellence, providing support for transparency reporting and our end-to-end management process for interactions with healthcare professionals, healthcare organizations, patients, and patient advocacy groups.

Our Internal Audits unit monitors the implementation of these initiatives locally. Before entering into a partnership or collaboration with third parties, we also involve our Busi-

ness Partner Risk Management unit in the respective selection process. The Compliance (p. 11) chapter of this report provides more details on how we implement legal requirements across the Group.

Our commitment: Group-wide guidelines and industry standards

Our "Interactions with Patients, Patient Opinion Leaders and Patient Organizations" policy provides a comprehensive framework for our prescription medicines business. For our over-the-counter product business we have a comparable policy that was revised in 2017 and is now in effect throughout the Group. Supplementing this, our guideline "Good Practice and Process Guidance: Engagement with Patients, Patient Opinion Leaders and Patient Organizations" provides additional guidance for our interactions with patients and patient advocacy groups. It furthermore ensures that patient wellbeing is always our top priority. Through this policy, the supplementary guideline and specific local policies, we provide a robust compliance guidance structure to support our employees in conducting **compliant interactions** with patients, patient opinion leaders and patient organizations.

In all transfers of value, we comply with the principles set forth by the European Federation of Pharmaceutical Industries and Associations (EFPIA) in its "Code on disclosure of transfers of value from pharmaceutical companies to healthcare professionals and healthcare organizations". Furthermore, our efforts are aligned with the Code of Conduct of the German Association of Voluntary Self-Regulation for the Pharmaceutical Industry (FSA).

In addition to complying with these codes, we adhere to all statutory transparency requirements worldwide, such as the stipulations of the Sunshine Act in the United States and the Loi Bertrand in France. Specific national laws and requirements are implemented by our local units. In doing so, we consistently adhere to the applicable data privacy legislation and make a best effort to ensure our partners also comply fully.

Through mandatory online training and classroom seminars, the relevant employees are kept up-to-date on our interactions guideline and policy, as well as on important changes to reporting requirements for transfers of value.

Transparent reporting

In 2017, we continued to publish all financial and non-financial contributions made to European medical professionals

and organizations in the health industry. As required by the EFPIA Disclosure Code, this information includes the names of individual recipients and their addresses, as well as the purpose and amount of the transfer. Before publishing, we secured all necessary informed consent forms as required by applicable data privacy regulations. In 2017, as part of the EFPIA transparency initiative, new laws were adopted in several European countries including Greece, Spain, Belgium, and Turkey. These changes have already been incorporated into our 2017 reporting processes. Other than disclosing monetary transfer of value on an individual level, we also published our overall spending on our research & development activities as required by the EFPIA Disclosure Code.

Partnering with patient advocacy groups

Patient advocacy groups support patients, family members and caregivers, providing them with information on disease management. Just like these organizations, our company has also made it our goal to **improve patient quality of life**, which is why we endeavor to support their vitally important work. We provide the highest level of transparency on our donations by publishing the details of contributions to European patient organizations. Updated annually, the 2017 report includes all donation amounts, recipients and the purpose of each donation, thus fulfilling our obligation as a member of EFPIA.

Transparently promoting research and education

We sponsor research and continuing medical education around the world in order to contribute to medical advances that will benefit patients. Through our Grants for Innovation, for example, we support research projects in fertility, multiple sclerosis, oncology, and growth disorders. Through our Global Medical Education unit we also provide grants to continuing medical education providers, enabling them to develop and deliver advanced medical training to scientists, physicians, nurses, pharmacists, and other healthcare professionals. We take an entirely transparent approach to this collaboration as well. All direct and indirect financial aid aligns with the principles of EFPIA. According to our internal "Medical Education Funding Policy", all requests for medical education funding are channeled through an **evaluation process** under the responsibility of our R&D and Compliance functions. This process ensures that all funds for medical education programs are granted according to established internal guidelines and criteria while also complying with all applicable laws and industry codes.

In 2017, we partnered with other experts belonging to a sub-group of the International Pharmaceutical Alliance for Continuing Medical Education (iPACME) to write a joint position paper setting out suggestions for improving and harmonizing **quality standards for continuing medical education (CME)** in Europe. We explicitly invited our stakeholders to take part in this discussion. The position paper was published in July 2017 in the Journal of European CME and is supported by the European CME Forum and the Global Alliance for Medical Education.