

products

We offer top-quality products that enrich people's lives. When it comes to safety, environmental sustainability and ethical practices, we have extremely high expectations and standards.

Whether prescription medicines or over-the-counter products, the work of our Healthcare business sector makes a difference to millions of lives around the world. Through our Life Science products, we are dedicated to making research and biotech production simpler, faster and more successful. We continuously work to improve the sustainability footprint of our products. In our Performance Materials business sector, we develop specialty chemicals for particularly demanding applications, such as liquid crystals for energy-efficient displays.

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innovation and digitalization

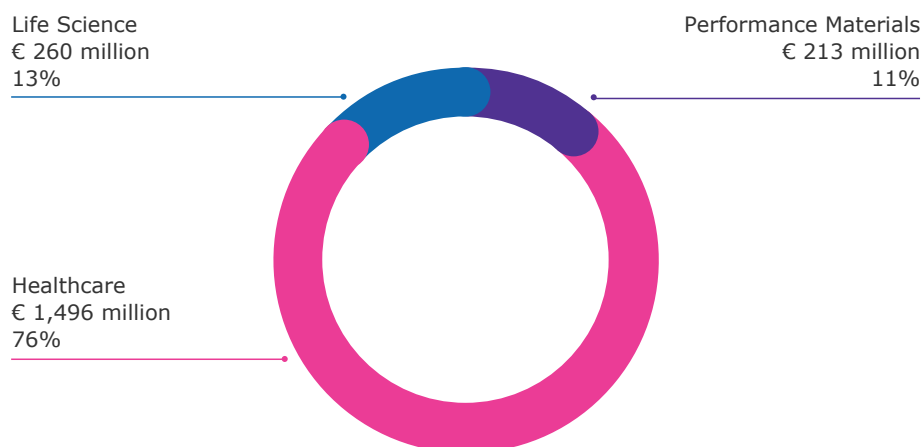
Research and innovation are the basis of our success. In 2016, we spent around € 2.0 billion on research and development (R&D). We develop technologies that enrich people's lives and are constantly on the lookout for groundbreaking developments and trends that can be translated into new products and pioneering business models. In particular, new technologies and the advance of digitalization are enabling us to create innovative products, services and business models that can positively impact lives. We intend to maximize this opportunity.

Our principles

Innovation strategy and organization

Our Group function Strategy & Transformation is in the process of developing a Group-wide innovation strategy. We are analyzing current megatrends, determining the influence they have on our business models, and defining the areas in which we see potential for new business ideas. In doing so, we are thinking far beyond our core business. To find novel approaches, we enter into strategic alliances with organizations that embody different perspectives. Many such potential partners are based in Silicon Valley, CA (USA), one of the key regions in the global high-tech industry. Here, we too are expanding our presence as a science and technology company.

Research and development costs by business sector – 2016



We are investing in forward-looking ideas. Our Corporate Ventures Fund provides up to € 300 million for investments in start-ups that will advance or complement our business models.

To maximally leverage the opportunities of digitalization, we form strategic partnerships with companies such as the California-based Palantir Technologies, with whom we joined

forces in January 2017. We hope to bolster patient outcomes by using their sophisticated data analysis capabilities to improve and accelerate the development, commercialization and distribution of drugs.

You can find more information on our strategic approach under Research and Development in our Annual Report for 2016.

Innovation Center – Making room for ideas

At our Innovation Center in Darmstadt, we offer our employees and external partners space and support to cultivate their ideas. We teach them innovative methods and provide the necessary infrastructure to advance pioneering projects.

Our work focuses on four strategic projects:

- **Accelerator:** Numerous start-ups around the world are working on innovative business models for our business fields. Our global Accelerator program supports such start-ups in the early stages of their development. In return, we gain insight into the highly innovative start-up community and can identify market trends early on.
- **Internal innovation projects:** We want to better harness the great innovation power within our company. We therefore offer our employees from all over the world the opportunity to work at our Innovation Center on select projects for up to a year. As well as receiving financial support for their projects, employees have access to select experts who provide input across all stages, from the seed of the idea to product development.
- **Innovation Think Tank:** In our Innovation Think Tank, we work with internal and external experts, research institutes and other companies to analyze current trends and technologies.
- **Innovator Academy:** The Merck KGaA, Darmstadt, Germany Innovator Academy aims to bolster our company's capacity for innovation by organizing needs-based training courses and workshops with internal project teams, think tank participants and start-ups.

Innospire – Mobilizing employees

The goal of our innovation initiative Innospire (a combination of innovation and inspiration) is to mobilize the innovative potential of our people. Every two years, we call upon them to submit ideas for new products and develop business plans during a multi-stage process. You can find more information under Employees (p. 72).

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 together with the Technical University (TU) of Darmstadt. Furthermore, in supporting TU Darmstadt's HIGHEST 1877 start-up program, we are promoting the innovative ideas of local start-ups.

We also collaborate with various schools in the vicinity of our global headquarters in Darmstadt. For example, we provide STEM subject teachers with educational materials and organize annual events devoted to STEM teachers such as Merck KGaA, Darmstadt, Germany Science Days, where they learn how to incorporate new technologies into their science classes. We regularly invite groups of students to Merck KGaA, Darmstadt, Germany to explore our research activities, or to our Children's University in an attempt to stimulate their thirst for knowledge. Moreover, for over 30 years we have been hosting the "Jugend forscht" student competition.

You can find more information on our educational initiatives under Community (p. 95) and in our "Fostering talent (p. 181)" story.

Digitalization as a driver of innovation

Digitalization is revolutionizing markets and business models. This technological change is also an important driver of innovation and is changing the pace at which new ideas are entering the market. We are constantly exploring new ways to leverage this potential and currently expect advances in the following areas:

- **Research and development:** Digital technologies enable us to access large quantities of data and quickly analyze it. We can use this information to accelerate our research and development activities. Particularly in our Healthcare business sector, we hope to accelerate the development of new drugs so as to provide patients with faster access to medicine with increased efficacy.
- **Supply chain management:** Digital technologies help us enhance our supply chain management process. By collecting all data pertaining to our supply chain centrally, we have access to crucial real-time information. This allows us to predict and respond quickly to issues such as supply bottlenecks worldwide, ensuring a more reliable supply of medicines.
- **Customer interaction:** Thanks to modern data collection and analysis techniques, we can make more efficient use of customer-relevant data to more fully understand our customers. Furthermore, digital platforms offer us new ways to interact with our clientele. By better understanding their needs, we can adapt our products and services accordingly.
- **Digital product innovations:** Digitalization is enabling us to expand our existing products and develop new products, services and business models. For instance, we are enhancing existing products with new digital services such as Baby Wish (p. 28). This platform educates couples on fertility issues and provides healthcare professionals with scientific information. Moreover, we are working to raise health awareness and improve patient treatment through e-health programs such as the Diabetes Online Risk Assessment (DORA).

Vocational training and continuing education

Innovation culture and digitalization are new topics at our Merck KGaA, Darmstadt, Germany University for managers. In early 2017, we entered into a partnership with the Stanford Graduate School of Business, which will be teaching classes on these topics for us. Furthermore, under the banner of "Work 4.0", we are integrating new digital technologies into our vocational training programs and offering our employees a modern, innovative working environment. You can find more information under Employees (p. 64).

Data protection

Data protection is essential to implementing digitalization in a responsible manner, which is why we strictly adhere to all data protection guidelines, monitor the various regulatory frameworks, and respond immediately to changes. You can find more information on data protection under Strategy & management (p. 11).

Progress

Intelligent packaging processes and drug information in real time

Our Smart Packaging project allows us to make our drug packaging processes more efficient and flexible. By connecting our packaging machines via an Internet of Things, we can improve their accuracy and reliability 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 will be able to decrease packaging waste and lead times when changes have to be made to the product information. This also means that, when new information about a product is discovered, we can inform our customers more quickly. We are also exploring options for active packaging that will allow patients to look up the latest information in real time on their smartphones.

In good hands: the Baby Wish digital platform

Through our fertility medicines, technologies and services, we are providing the support clinics need to help couples conceive. We also offer more direct aid to impacted individuals. Launched in April 2017, our Baby Wish digital platform

features information on infertility and treatment options. In July 2016, we launched a different platform that provides healthcare professionals with access to the latest digital scientific information on infertility. Through this medium, we are helping providers offer the best care for couples seeking advice.

First Merck KGaA, Darmstadt, Germany hackathon in Africa

As part of our Accelerator program, we support and organize hackathons in which young entrepreneurs from various sectors collaborate to quickly develop solutions to specific issues. In 2016, we hosted a hackathon in Accra, Ghana that was attended by approximately 150 social entrepreneurs from western Africa. At this gathering, dubbed Health Hack Accra, 29 teams of biomedical engineers, scientists, programmers, and university students had 48 hours to create solutions and business models to tackle Africa's toughest health challenges. With a focus on reproductive and maternal health, access to health, non-communicable diseases, and infectious diseases, this hackathon led to the development of 28 innovative solutions. Our Innovation Center is supporting the top three solutions in partnership with the Impact Hub in Accra:

- CrowdAfrica: A crowdfunding platform for healthcare.
- Peach Technologies: An electronic patient file.
- dynaMix: An awareness platform for reproductive health that also aims to increase the availability of contraceptives in rural regions.

Online campaign for diabetes

In Africa, approximately 62% of diabetes cases go undiagnosed. To improve early diagnosis and promote awareness for diabetes, we joined forces with various partners in March 2015 to launch a digital initiative known as DORA (Diabetes Online Risk Assessment). 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 whether they are at risk of developing diabetes. Since its launch, the DORA website has received more than 401,500 hits, with 74,294 coming from people who took the assessment.

sustainable product design

Respect for the environment and natural resources is at the heart of sustainable conduct. We too see this as our duty. Our Performance Materials business sector produces materials that our customers can use to develop more sustainable products. Take for example liquid crystals that increase display efficiency, or materials that continuously improve solar cells and organic photovoltaics.

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 at the very start of product development.

Our principles

Performance Materials

Our Performance Materials business sector manufactures numerous products that help our customers develop sustainable and environmentally compatible products. Our requirements are set out in the following guidelines:

- Our Product Safety Chemicals Policy: This specifies our Group-wide product safety requirements.
- Our 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 industry and customer-specific requirements. Furthermore, this policy forbids the use of acutely toxic, mutagenic or otherwise hazardous substances that remain in the end product.
- For Display Materials products as well as Pigments & Functional Materials products, we adhere to our customers' Halogen-free Policy.

Across all our manufacturing facilities, our raw materials for the cosmetics industry fulfill the high standards of the Cosmetics Directive, for example Good Manufacturing Practices (EFfCI GMP).

Best practice examples to improve sustainability

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

Energy-efficient displays

Liquid crystals (LCs) ensure high picture quality in computer monitors and televisions, reducing their energy requirements. This is because our PS-VA technology (polymer-stabilized vertical alignment) arranges the liquid crystals so as to better utilize the backlighting, which is a display's

largest power consumer. Thanks to PS-VA technology, devices consume significantly less energy than precursors.

Self-aligned vertical alignment (SA-VA) is the next-generation liquid crystal technology in development, with the first SA-VA products expected on the market in 2017. SA-VA helps conserve resources and is environmentally sustainable because less energy and solvent are required to manufacture the displays. Moreover, it is more efficient as fewer process steps are necessary. Since SA-VA technology can be used at lower temperatures, it is also suitable for sensitive materials such as those in premium products or pioneering applications such as flexible displays.

Mobile device displays have increasingly high resolutions but are still expected to be as energy-efficient as possible. This is exactly 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 so that it can also be used in applications such as LCD televisions.

Switchable windows

Windows that darken in a matter of seconds are now a reality thanks to our liquid crystal window (LCW) technology. Because they also reduce heat input from sunlight, initial estimates show that these windows can lower the energy consumed by building climate control systems by up to 40%. Commercialized under our Icrivision™ brand, this technology thus renders conventional sun shading redundant. We are currently investing € 15 million in the construction of a production facility for liquid crystal window modules in the Netherlands. The manufacture of these switchable glass modules is scheduled to begin there at the end of 2017. More information can be found in our story "Exploring the future (p. 177)".

OLEDs

Organic light-emitting diodes (OLEDs) likewise increase the energy efficiency of displays. They furthermore provide brilliant colors and razor-sharp images. Over the past several years, we've been researching innovative printing processes to efficiently produce large-screen OLED displays. To this end, we've been partnering closely with printer manufacturers. 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 have made at the Darmstadt site in recent years.

Innovations in photovoltaics

We supply the photovoltaics industry with materials for the production of highly efficient 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 or even in clothing.

Phasing out plastic microbeads

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

Through their use in cosmetics and other products, plastic microbeads end up in marine and terrestrial ecosystems, and are facing public criticism because they are not biodegradable. Through our alternative mineral products, we are supporting, for example, the declaration of Cosmetics Europe, which advocates a phase-out of microplastics in rinse-off products by 2020.

Increase in natural cosmetics

An ever-growing number of consumers place importance on natural cosmetics. Together with our customers in the cosmetics industry, we are responding to this rising demand by developing cosmetic formulations that meet strict criteria. The majority of our cosmetic raw materials meet the criteria of Ecocert's Cosmos standard for organic and natural cosmetics.

Life Science

We endeavor to reduce the environmental and health impacts of our Life Science products. This applies to their entire life cycle, from manufacture and use to end of life. At the same time, we want to make our products more efficient and user-friendly. That is why, right at the beginning of the product development phase, we ask ourselves how to best reconcile these requirements.

With our Design for Sustainability (DfS) program, we have developed a comprehensive approach. 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 score card. When developing a new product, our aim is to improve on as many of these criteria as possible. To understand the potential impacts on the environment within different product life cycle stages, we conduct product life cycle analyses. The results 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.

Through our DfS process, we have improved the product properties across 32% of our BioMonitoring product developments and product updates in at least three of our self-defined sustainability criteria. We will be incorporating our suppliers into our Design for Sustainability program as well. In 2016, we launched a pilot project to define the relevant requirements for our suppliers.

In addition to following this design process, our Life Science research teams are developing innovative solutions in line with the 12 Principles of Green Chemistry formulated 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. Under the green chemistry approach, researchers look for alternative, ecologically sustainable reaction media with higher reaction rates and lower reaction temperatures to make production more energy efficient. In total, we offer more than 700 products that align with the Principles of Green Chemistry, making them a "greener" alternative to conventional products.

A 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.

More environmentally compatible laboratory filters

Using 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, we require 47% less raw material for the EZ-Fit™ Manifold. 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 clean 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, which is used to determine the microbial count in liquid samples. Thanks to our DfS approach, we have particularly improved the packaging of this product.

Greener chemistry

In comparison with conventional alternatives, our greener solvents are based on natural resources such as corn cobs and sugar cane bagasse. They are more ecologically sustainable, easier to recycle and more biodegradable. Take for example the solvent Cyrene™, which we launched onto the market in 2016. It is bioderived from waste cellulose and 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. With Cyrene™, we are helping our customers in the pharmaceutical and agrochemical industries make their production processes safer and more environmentally sustainable.

Instruments for biofuels

Our Guava® HT series of flow cytometers is helping to drive biofuel research and development. For example, our customers are using the Guava instruments to find an algae species that is suitable for diesel production. Our flow cytometers are also being used to produce ethanol from sugar; they test which bacteria digest sugars and thus produce gases that can be refined into ethanol.

Energy-efficient sterility tests

Using the DfS approach, we have reduced the energy consumption of our Steritest™ Symbio pumps for sterility tests by 15% to 30% compared with its predecessor.

Tool to assess the sustainability performance of chemicals

In 2016, we introduced a tool called Dozn™ to assess the green alternatives of various chemicals, thereby creating transparency for our customers. Based on the 12 Principles of Green Chemistry, we evaluate how our products score in three main categories, namely improved resource allocation, efficient energy use, and minimized risk to humans and the environment. One point is given for each of the 12 principles, allowing an easy comparison of the products. The results of the evaluation are verified by an independent body. To date, we have used the matrix to assess and improve more than 40 products.

Progress

Displaying Futures: Annual conference on the future of display technology

Pioneering advances such as our efficient UB-FFS display technology are only possible through close collaboration with our partners. We seek to engage trailblazers who look to the future and conceive groundbreaking technologies. This is

why we instituted the annual Displaying Futures Symposium, which was held in 2016 for the seventh time.

In September 2016, the symposium centered on the theme "Driving Forces – Inspired by Performance Materials". At our Group headquarters in Darmstadt, experts from various fields discussed the future of mobility, from cars that communicate with one another to self-driving vehicles.

In 2015, we hosted two events with differing focuses. In October, we met with architects and designers in Chicago, IL (USA) to discuss materials that would transform architecture. We also took the opportunity to introduce our liquid crystal window technology to a large audience. In November, international experts from fields such as displays and electronics gathered together in San Francisco, CA (USA) under the banner "The Future is HOW? Inspired by Performance Materials". Attendees discussed how materials and high-tech chemicals could be used in future applications.

Award-winning programs

In 2015, we were granted the German Innovation Award in recognition of our UB-FFS technology (p. 29), which lowers the power consumed by mobile device displays.

Three of our Life Science products, Titripac®, EZFit™ Manifold and SNAP i.d.® 2.0, were honored in 2016 with the Green Good Design Award for sustainable product design. This award was also given in honor of our Design for Sustainability program, which enabled us to improve these products.

In recognition of close collaboration across company boundaries, we received the Enterprise Innovation Award from the Technical University of Darmstadt in June 2016. In a joint project with Siemens, we developed high-performance materials for energy-efficient generators. These innovative materials not only make the generators more efficient and more powerful, but also allow the construction of buildings that help conserve resources.

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 product's entire life cycle – from transport to storage, and from usage to end of life.

Beyond safety, we also strive to design packaging that uses as few natural resources as possible. We are therefore working to reduce the amount of material required and are increasingly utilizing environmentally sustainable materials where possible. In the process, we ensure that the quality and safety of the packaging is not adversely affected.

Our principles

Sustainable packaging strategy

We aim to deliver our products in packaging that is safe and easy for our customers to handle, as well as sustainable.

The more than 300,000 products of our Life Science business sector – ranging from biochemicals to lab chemicals, from filter materials and systems to instruments – pose a wide range of challenges when it comes to packaging. We strive to improve the sustainability of their packaging through measures such as reusable packaging systems, or by avoiding the use of polystyrene. Our sustainable packaging strategy for our Life Science business sector stipulates the framework for this approach. A variety of guidelines help our experts to consider sustainable packaging alternatives and implement them during the product development stage.

We also work to enhance the sustainability of our packaging design for our Performance Materials products such as liquid crystals and pigments (p. 32).

Certified cardboard boxes

The majority of the corrugated cardboard boxes we use worldwide are 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).

A variety of solutions for an extensive product portfolio

Our initiatives for sustainable packaging systems are as varied as our product portfolio. Here are several examples:

Cellulose instead of polystyrene

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 storage room. By contrast, molded pulp components can be easily recycled with other paper materials and compacted together for storage and transport. We have a substitution program in place that is working on solutions to replace EPS with molded components made of cellulose and recycled paper pulp.

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. In 2015 and 2016, we conducted numerous safety tests on various molded pulp part designs to pad 4X4 liter bottles in shipping boxes. In 2017, we plan to start using pulp components for this package size, which will replace approximately 350,000 molded EPS parts per year. We are currently conducting safety tests on various pulp designs for shipping individual bottles of various sizes.

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 packaged in plastic bottles, we use Titripac® because it offers a more environmentally compatible alternative for supplying solvents to our Life Science customers. By employing a cardboard carton and plastic liner with an integrated withdrawal tap, we made the packaging more recyclable while also cutting down the weight by more than half. As a result, the greenhouse gas emissions arising across the entire life cycle of the product 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 must be kept cool during shipping and are therefore packed in special Styrofoam® boxes. To mitigate waste, we offer our U.S. customers the option of sending us back these boxes. If they are fully functional, we reuse them, which, at more than 20,000 boxes per year, reduces waste. We are in the process of expanding this program to serve customers outside of the United States as well.

Reusing liquid crystal canisters

In Korea and Taiwan, our Performance Materials liquid crystal mixtures are delivered to display manufacturers in stainless steel canisters. Our customers utilize these standardized

canisters directly on their production lines without decanting. The empty containers are then sent back to us and cleaned. Within this closed system, these canisters can be reused over several years.

Steel instead of glass

Thanks to our EMD ReCycler® bulk product delivery system, our solvents are delivered to our U.S.-based Life Science customers in special reusable steel containers. They can return the empty containers to us for refilling. Through this program, we are significantly reducing the consumption of primary packaging materials. Because the stainless steel

containers are shipped without additional packaging, we are also saving 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 quantities for preparative chromatography in reusable stainless steel barrels and drums. Our customers send the empty containers back to us, where they are properly cleaned and then reused. Approximately 20,000 of our stainless steel barrels and 20,000 stainless steel drums are currently in circulation across Europe. The rate of return is 90% for the barrels and around 50% for the drums.

Reuse and recycling

Through our recycling programs, we help our customers dispose of our products and packaging.

Our principles

Design for Sustainability

Our Design for Sustainability (DFS) program encourages our Life Science research & development teams 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.

Progress

Recycling program updated

Many of the products we supply to our Life Science customers are used once and then discarded. This is necessary to minimize the risk of contamination and is common practice within the industry. Moreover, this approach helps reduce costs because our customers don't have to clean disposable products, thereby saving time and natural resources such as energy and water. Recycling the plastic in these products is not easy, primarily due to inadequate recycling options, challenging material properties, and stringent regulatory requirements.

In cooperation with Triumvirate Environmental, a waste management company based in Massachusetts (USA), we launched a 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 and recycled in its entirety. This program has thus replaced our previous individual initiatives, which included our Biopharma Product Recycling Program as well as our Ech2o™ Collection and Recycling Program for water filter cartridges. These processes were not efficient because the various materials had to be separated before recycling.

Our partner company Triumvirate Environmental has developed an innovative process for recycling challenging waste streams. This method recycles 100% of the product without needing to first decontaminate or separate the materials. Triumvirate Environmental then takes the recycled mass and manufactures plastic materials that are used in the construction industry for items such as speed bumps. Since launching the program, we've recycled approximately 450 metric tons of waste generated from the use of our products. Six of our customers are already participating in the program.

We are currently investigating how we can expand this initiative beyond the United States to markets in Europe and Asia.

Access to Health

Across the globe, approximately 400 million people lack access to effective and affordable healthcare, especially in low- to middle-income countries. However, according to the World Health Organization (WHO), these regions 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. To achieve this, health solutions must be affordable and accessible (p. 40). Beyond these efforts, we're also raising awareness (p. 41) for diseases and teaching people how to manage them. The Access to Medicine Index has recognized the progress we've made on improving access to health (A2H). In 2016, we were ranked fourth, moving us two places higher than 2014.

Our principles

Our strategic approach

We endeavor to improve access to high-quality health solutions for underserved populations and communities in low- to middle-income countries. This goal forms the heart of our A2H approach. Indeed, Stefan Oschmann, Executive Board Chairman and CEO, focused on accelerating access to health in such regions during his presidency of the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) from 2014 to the end of 2016.

At the World Economic Forum held in Davos, Switzerland in January 2017, we joined forces with 21 other leading

pharmaceutical companies to announce Access Accelerated, a global initiative that seeks to improve both treatment and prevention of non-communicable diseases in low- and middle-income countries.

To improve access to health solutions, we're leveraging the expertise from all our businesses. We're aware that individual companies and organizations can only do so much to improve access to health, which is why we closely collaborate with a wide range of partners.

Our A2H strategy focuses on the 4 As:

- **Availability:** We research, develop and refine health solutions that address unmet needs and are tailored to local environments.
- **Accessibility:** We promote initiatives that strengthen supply chains (p. 39) and develop localized health solutions in order to deliver and reach out efficiently at the point of care.
- **Affordability:** We seek to provide assistance to those who are unable to pay for the health solutions they need. Further information can be found under Prices of medicines (p. 40) and Community (p. 96).
- **Awareness:** We contribute to raising awareness (p. 41) by empowering health workers, communities and patients so that they can make informed decisions.

The 4 As



Our A2H Charter defines our guidelines for the following topics:

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

In the 2015-2016 period, we aligned our A2H strategy and goals (p. 133) with the Sustainable Development Goals (p. 147) of the United Nations. These efforts were recognized in the 2016 Access to Medicine Index (p. 36).

Effectively managing our A2H programs

Our Access to Health (A2H) unit investigates the factors that make it more difficult for underserved populations to receive healthcare, working with various partners to develop ways to lower these barriers. Our A2H team is backed by a steering committee featuring representatives from our Healthcare and Life Science business sectors as well as representatives from our subsidiaries. In this way, we ensure that our programs support our business strategy, can be implemented locally and have the desired effect.

We are currently developing quantitative and qualitative performance indicators to evaluate the efficacy of our programs. Using these indicators, we will assess our strengths and identify areas where we need to improve.

Beyond these efforts, we are also involved in industry-wide initiatives and are working with other companies to develop new approaches to assessing the efficacy of our A2H activities. For instance, in 2016 we endorsed the Business for Social Responsibility's (BSR) Guiding Principles on Access to Healthcare. As a member of the BSR Healthcare Working Group, we contributed to and led the development of the working paper entitled Advancing Access to Healthcare Metrics, which aims to help pharmaceutical and medical device companies improve their performance measurement and reporting on access to healthcare.

Sharing and protecting intellectual property

A great deal of time and money is required to develop new drugs, without a guarantee of success. It can take 10 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 to compensate for R&D costs.

Responsible treatment of intellectual property does not pose a barrier to health. It guarantees safety and high quality for patients worldwide. Most medicines that address the highest burden of disease in developing countries are not protected by patents. For example, 95% of the 2013 WHO Essential List of Medicines are off-patent.

FAST FACT

ESSENTIAL MEDICINES

We provide 45 medicines that are listed on the WHO Essential Medicines List and/or classified as first-line treatments, such as bisoprolol/amlodipine, metformin (Glucophage®), and praziquantel.

Our approach to intellectual property is set out in our Charter on Access to Health in Developing Countries – Rights to Intellectual Property.

In most developing countries, Merck KGaA, Darmstadt, Germany neither files nor enforces 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 provide transparent information on our patents and patent applications via publicly accessible databases. We furthermore approve voluntary licensing agreements of all kinds, including non-exclusive voluntary licenses and legally binding non-assertion covenants or clauses that aim to improve access to health. We also support TRIPS, an international agreement administered by the World Trade Organization (WTO) that addresses trade-related aspects of intellectual property rights, as well 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 on pharmaceutical patents until at least 2033 as per a decision taken by the WTO's council on November 6, 2015. We were in favor of extending this deadline until 2033 and therefore supported this move. Moreover, we support the concept of patent pools. However, we believe that these should be structured to improve access to medicines and should therefore prevent anticompetitive effects as well as geographic limitations. We consider joining patent pools when they are relevant to our portfolio and meet our efficacy, quality and safety requirements.

We share our knowledge and intellectual property and accelerate early discovery for infectious diseases. We are one of over 100 members of the WIPO Re:Search open innovation platform, which is sponsored by the World Intellectual Property Foundation (WIPO). In 2015, we initiated our first partnership as part of this platform, collaborating with the University of Buea in Cameroon. Our common goal is to

repurpose compounds from our library to develop a treatment for onchocerciasis, a disease also known as river blindness. In early 2016, the collaboration received the Pathfinder Award, a grant from the UK-based Wellcome Trust to fund research on this condition.

Our transparent approach to intellectual property was also recognized in the 2016 Access to Medicine Index (p. 36).

Engaging stakeholders

Partnerships and dialogue are key instruments to 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.

Through our Access Dialogues, we have created a platform that allows public- and private-sector stakeholders to exchange information and share best practices. This platform provides a way for participants to collaborate on improving access to health. These dialogues are part of our A2H efforts and commitments around awareness and aim to help stakeholders make well-informed health decisions.

In this vein, we hosted the Innovative Intellectual Property and Access Dialogue in 2015. At this event, we joined forces with leading experts on intellectual property and global health to discuss challenges and potential developments for our intellectual property strategy.

In addition to this gathering, dialogues on challenges in the local supply chain were held in 2015 and 2016 in conjunction with the Accessibility Platform, a multi-stakeholder initiative seeking to ensure that medicines are delivered safely, quickly and efficiently. Further information on the Accessibility Platform can be found under Supply chain (p. 39).

Progress

High ranking in the Access to Medicine Index

Every two years, the Dutch Access to Medicine Foundation assesses the performance and achievements of pharmaceutical companies in terms of their efforts to improve access to medicine in developing countries. The foundation then ranks these companies in their Access to Medicine Index. In 2016, we came in fourth place. The foundation recognized us in particular for aligning our strategy and objectives more closely with the UN Sustainable Development Goals. The following initiatives were singled out as best practices:

- Our transparent approach to intellectual property (p. 35) and sharing of intellectual property through research partnerships.
- Our leading role in raising health awareness, such as our thyroid disorder campaigns (p. 173) in Indonesia and the Philippines.

- The many years we've devoted to detecting counterfeit medicines using the GPHF Minilab® (p. 99).
- The expansion of our Su-Swastha program (p. 42) in rural India, aimed at supplying high-quality health products at affordable prices and establishing the required infrastructure.
- Our support for the network of vaccine manufacturers in developing countries (p. 39).
- Our Virtual Plant Team platform (p. 39), which we're using to ensure globally harmonized quality standards in local production facilities.
- Our continuous and holistic efforts in the fight against schistosomiasis, including our Praziquantel Donation Program (p. 97) in partnership with WHO.

Discourse to improve healthcare

Our Chairman of the Executive Board and CEO, Stefan Oschmann, took part in various events in the 2015-2016 period. For instance, at an event hosted in September 2015 to mark the 70th General Assembly of the United Nations, he gave a speech on the role of private industry in global healthcare. Oschmann also spoke on this topic in May 2015 at an event held on the occasion of the 68th World Health Assembly (WHA) of WHO. Moreover, in March 2015 he attended the Independent Expert Group (IEG) on Emergency Preparedness as an industry representative. This gathering was convened by Bill Gates at the request of Angela Merkel, Chancellor of Germany and G7 President.

Discussions at a global level

In the 2015-2016 period, we also participated numerous other events, including the following:

- Building the Path to Universal Health Coverage: Innovative Financing in Access to Medicines, a round table hosted in September 2015 by UNITAID, Norwegian Church Aid and the Medicines Patent Pool (MPP) in Oslo, Norway.
- Munich Security Conference on global security and foreign policy, held in February 2016: forum on current crises and future challenges to international health security.
- Geneva Health Forum (GHF) in April 2016: Event sponsor and organizer of the round table on "Empowerment: Providing tools to make informed health decisions for chronic diseases aligned with the WHO 2030 Health Workforce Strategy".
- Supply Chain Conference hosted by the German Association for Supply Chain Management, Procurement and Logistics (BME) in February 2016; the topic was: "Accessibility Platform: Uniting Stakeholders for Optimal Global Health Impact".
- Event on the occasion of the 69th WHO World Health Assembly in May 2016; the topic was "Strengthening local supply chains through multi-stakeholder initiatives to eliminate barriers to access".

Activities at the local level

In 2015 and 2016, we also engaged stakeholders at a local level. Below are several examples:

- Continuation of our three-year Indonesia Free Anemia campaign: Raising awareness for the causes and treatment of anemia through social media.

- Together against malnutrition: We are supporting the Beyond Zero initiative of the Kenyan government. Our aim is to improve healthcare for mothers and their children.
- Various activities in China: Raising awareness for thyroid disorders through education programs, continuing education for physicians, and research projects. Collaboration with the National Health & Family Planning Commission as well as medical institutions such as the Chinese Medical Association.

Infectious diseases

Many infectious diseases that are 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 also 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. In 2015, roughly 212 million malaria cases worldwide and an estimated 429,000 malaria deaths were recorded. Approximately 92% of these deaths occur in Africa, with 70% in children under five years of age. 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 are therefore urgently needed together with solutions to effectively control malaria.

Our principles

Global Health innovation platform

The experts of our Global Health innovation platform are working on novel health solutions for vulnerable populations in developing countries, especially children and mothers. They promote and implement Group-wide initiatives and programs to address key unmet medical needs related to infectious diseases, with a focus on schistosomiasis and malaria (including co-infections). The team is applying an integrated strategy by concentrating not only on treatment (drugs) but also on detection, transmission and control.

We are focusing our work on three flagship programs:

1. Development of a pediatric formulation to treat schistosomiasis (p. 37)
2. Development of a diagnostic kit for malaria (p. 38)
3. Development of a new active ingredient for the treatment and prevention of malaria in children under six (p. 38)

In implementing our programs, we synergize competencies from our business sectors while also partnering with leading global health institutions and organizations in both developed and developing countries. Consider, for instance, the Pediatric Praziquantel Consortium, a public-private partnership (PPP) that is developing a pediatric formulation to treat schistosomiasis.

Under the Global Health platform, we are also sponsoring education programs and initiatives targeted to health workers in African countries.

Progress

Treating schistosomiasis in children under six

Around 10% of the approximately 220 million people worldwide with schistosomiasis are younger than six years old. These children cannot be treated with praziquantel, the standard therapy for the parasitic disease. This is something we intend to change. Since July 2012, we have been working with partners from industry and research institutes on the development of a pediatric formulation of praziquantel. As part of these efforts, in 2015 we successfully completed two Phase I bioavailability studies in healthy subjects in South Africa, as well as a taste study in children in Tanzania.

In 2016, the Pediatric Praziquantel Consortium initiated a Phase II study in Ivory Coast; the trial aims to assess the efficacy and safety of two different formulations for orodispersible tablets in schistosomiasis-infected children under the age of six. At the same time, we are preparing the Phase III study.

In recognition of all these efforts, the consortium was awarded a prestigious research grant from the Japanese Global Health Innovation Technology Fund in both 2015 and 2016, which followed the one awarded in 2014.

Accurately diagnosing malaria

In many African countries such as Zimbabwe and Uganda, the rate of co-infection with HIV and malaria is very high. In HIV-infected patients who develop a fever, it is therefore very important to establish whether they also have malaria. Current systems, however, are not accurate enough, which often leads to other febrile illnesses being wrongly diagnosed as malaria.

In 2015, we started expanding our Muse® Auto CD4/CD4% diagnostic kit, which until then had been used for monitoring the treatment of HIV patients in Sub-Saharan Africa and other developing regions. With this system, medical professionals can obtain information on the course of an HIV infection. The advantage is that blood samples no longer need be sent to clinics in the cities. The new Muse® malaria diagnostic kit can measure the presence and type of malaria parasite as well as a co-infection with HIV. The system is expected to be launched in 2019.

Promising antimalarial compound

In developing antimalarial compounds, we are collaborating with Medicines for Malaria Ventures (MMV). Since current treatments are increasingly succumbing to drug resistance, MMV is focusing on the development of new compounds.

In March 2015, we obtained the rights to an investigational antimalarial compound from MMV. The compound potentially represents a novel mechanism of action and is intended to be developed for both the treatment and prevention of malaria in young children. This R&D project completed its preclinical phase in 2016 and is preparing for Phase I to start in 2017.

Building capacities in health systems

In addition to financing fellowships in Zimbabwe and Kenya, in 2016 we launched a partnership with the University of Namibia that is sponsoring two PhD fellows in their research. In support of Governmental Malaria Control Programs, these scientists are studying the spread of an extremely widespread malaria pathogen found in Namibia, Botswana and Zambia and are also working to characterize parasite subtypes in the populations in these African countries.

Moreover, we also co-sponsor several international fellowship programs for postdoctoral researchers from developing and emerging countries. In addition to receiving training on

clinical aspects including clinical trial practices and clinical management, these research fellows are given the opportunity to work for a period of up to 24 months in leading pharmaceutical companies (including our company). On returning to their home countries and academic institutions, they then have the key resources needed to lead and implement their research in line with international regulatory requirements and standards.

Deepening the dialogue on malaria and schistosomiasis

In 2015 and 2016, we stepped up the dialogue on infectious diseases with important stakeholders and experts. Among other achievements, we gained a new partner for the Pediatric Praziquantel Consortium, namely the Schistosomiasis Control Initiative (SCI), which is part of Imperial College London in the United Kingdom. SCI works closely with health ministries in African countries and supports the consortium in efforts such as developing the access and delivery plan for our new pediatric drug for children under six.

Furthermore, in November 2015, we joined forces with the University of Cape Town (South Africa) to co-develop R&D platforms for identifying new lead programs for the treatment of malaria, with the potential for expansion to other tropical diseases. As part of the collaboration, research has been conducted using Merck KGaA, Darmstadt, Germany's compound library.

Moreover, we took part in the following international conferences and events:

- Workshop entitled "Schistosomiasis in women and its impact on HIV" in Magaliesburg, South Africa in January 2015
- The International Schistosomiasis Conference on schistosomiasis elimination strategies in San Salvador, Brazil in August 2015
- The 9th European Congress on Tropical Medicine and International Health held in Basel, Switzerland in September 2015
- The American Society of Tropical Medicine and Hygiene (ASTMH) conferences in 2015 and 2016 in the United States
- The Better Medicines for Children Conference hosted by the European Medicines Agency (EMA) in London (UK) in October 2016
- The African Society for Laboratory Medicines (ASLM) conference held in Cape Town, South Africa in December 2016

supply chain

We want patients in low- and middle-income countries to have fast, safe and affordable access to medicines. Efficient supply chain management is key to accomplishing this, as is support for local manufacturing in line with our high standards.

Our principles

Efficient supply chain management

Efficient supply chains ensure that patients can be treated quickly and safely. Moreover, they incur lower costs. Our policies and procedures help to ensure that appropriate quantities of our products are delivered in the right condition, at the right place, and on time.

Together with our partners, we endeavor to improve supply chains in developing countries:

- We are a member of the Neglected Tropical Diseases Supply Chain Forum. This public-private partnership works to ensure a good end-to-end supply chain, which in turn will guarantee that the medicines reach the people who need them. Forum members include the World Health Organization (WHO), the Bill & Melinda Gates Foundation, the logistics firm DHL, and six leading pharmaceutical companies which run donation programs: Merck KGaA, Darmstadt, Germany, MSD, GlaxoSmithKline, Pfizer, Johnson & Johnson, and Eisai.
- In the Rx-360 consortium, we are pursuing similar goals: to share best practices with other companies and partners on efficient, end-to-end secure supply chains.
- We are a founding member of the Accessibility Platform. This is an informal effort spearheaded by the private sector which 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 identify opportunities for collective action.

Supporting local manufacturing

In our manufacturing plants in India and Indonesia, we produce various medicines for patients with diabetes, heart conditions and diseases of the lower respiratory tract. This allows us to supply medicines to local markets faster, as well as to neighboring countries such as Sri Lanka and Myanmar. Moreover, we can offer these drugs at considerably lower prices than in Europe.

Our pharmaceutical production plants operate to the same high standard of quality worldwide. We 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 tailored to each site, quality control monitoring, and technology transfer. Our Global Response Team publishes the results of all audits conducted by health authorities across the Group, 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 Merck KGaA, Darmstadt, Germany production expert 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 (p. 36).

Progress

Developing a cross-company database for medicinal products

To make medicines for neglected diseases reliably available in developing and emerging countries, we are working to improve supply chain management. In 2015 and 2016, we therefore collaborated with our partners in the Neglected Tropical Diseases Supply Chain Forum to develop a database to help achieve this goal. All forum members contribute information, which is used to assess the potential need for medicines in the relevant countries. We discuss, for example, which medicines have been ordered by WHO and which products have been supplied to which countries. This provides us with a comprehensive overview of the current distribution of medicines, thus allowing them to more quickly reach the areas where they are needed most.

Supporting regional vaccine manufacturers

We support vaccine manufacturers in developing and emerging countries. Together with the Developing Countries Vaccine Manufacturers Network (DCVMN), we sponsor educational programs and pass on our knowledge to ensure the safe and high-quality production of vaccines. Since 2014, we have conducted more than 12 training sessions as well as a number of technical workshops in Asia-Pacific and Latin America, with eight seminars taking place in 2015 and 2016.

For this initiative, we were honored in the 2016 Access to Medicine Index (p. 36).

Testing software for supply chain management

In the 2015-2016 period, we developed a software-based solution for northwestern Africa to ensure the continuous availability of our drugs, which has improved our inventory and order management. At any time, our customers can go

to our e-shop to quickly and easily order medicines that have been approved by the respective regulatory authorities. The system makes demand more transparent while reducing lead time and miscommunication. After successfully testing the e-shop in Sudan and Ethiopia, we launched the platform in all northwestern African countries in 2015.

prices of Medicines

Merck KGaA, Darmstadt, Germany is committed to ensuring that patients have access to the best possible medicines. This requires optimal pricing, reimbursement, and access conditions for all of our in-line and future pipeline products. Across the world, the healthcare industry is undergoing a unique transformation: National and regional institutions and authorities, which decide on price-dependent market access and reimbursement in many markets, hold a growing role as key stakeholders, together with healthcare professionals, politicians, regulators, patients, and distributors. We are fully determined to continue succeeding in this changing environment.

We believe that the prices of our medicines should reflect their overall value, to include benefits to patients, healthcare systems and payers alike. Value reflects both individual clinical outcomes as well as impact on overall treatment, health system delivery and patient adherence.

Our principles

To meet the needs of patients, our health solutions must be affordable and accessible. In terms of organizational setup, our Group Market Access and Pricing unit reports directly to the Chief Marketing and Strategy Officer of our Healthcare business sector and sets initial prices in collaboration with Merck KGaA, Darmstadt, Germany's individual businesses. Our subsidiaries are responsible for adapting and managing prices at the local level.

Innovative pricing models

We recognize the importance of fairly priced medicines and the fact that individual countries have varying abilities to pay for health solutions. Within a country, too, there are often significant regional and/or socioeconomic differences. We therefore partner with governments and other key stakeholders to develop individual pricing and contracting models. In addition, we continuously monitor the dynamic healthcare environments, pricing & reimbursement systems, guidelines, and policies, adjusting our prices as necessary.

We support product donations, flexible pricing, differential pricing, and post-patent competition between reference products and generics. We conduct yearly reviews of our

pricing strategies to identify ways to continually expand access to health by aligning prices with affordability.

We have developed several product- and market-specific alternative reimbursement and contracting models (ACMs) with payers such as health insurance companies to provide the right patients with prompt access to our innovations. Examples of such ACMs include outcome-based and budget capitation agreements for Erbitux® as well as adherence-based payment agreements for Rebif® and Saizen® in its easypod™ injection device.

We also regularly participate in government tenders for products used in public hospitals serving low-income patients. Beyond this, we have established second "lower-price" brands of existing products. In South Africa, for example, second brands of Concor® and Ziak® (antihypertensive agents) are available at discounted prices.

Low- and middle-income countries

We recognize the importance of affordable access to medicines in low- and middle-income countries. As a result, we are committed to pricing our products responsibly and take part in innovative equitable pricing schemes in partnership with governments and other key stakeholders. In developing countries, we also regularly participate in government tenders. In this way, we're already supplying products to governments at reduced prices in Africa, Latin America, the Middle East, and Asia.

Different kinds of patient support enable us to offer products at a more affordable cost. Our Erbitux® China Patients Assistance Program (p. 41) is a prime example of such an initiative. Our Patient Support Program Policy describes our uniform standards for such efforts.

Progress

Operational pricing and strategic price decisions

In 2016 we implemented a new Group-wide price management system. This global platform enables us to drive strategic price and reimbursement decisions and contains all information needed to set, modify and approve country-

specific prices. It also serves as an analysis tool that enables us to make informed strategic pricing decisions.

Improved access to the oncology drug Erbitux®

In China, we are working with the China Charity Federation (CCF) to expand access to our oncology drug Erbitux®, which is used to treat conditions such as colorectal cancer. For patients with a good prognosis, the Erbitux China Patients Assistance Program (ECPAP) will cover the majority of the costs for Erbitux® treatment. In addition to helping with costs, we also offer free services such as providing

information on this disease, or ensuring that the medicine remains properly refrigerated until reaching patients. From the program's launch in 2011 to the end of October 2016, 6,800 patients had already benefited from ECPAP.

We also run similar programs in other countries such as India, where we likewise offer Erbitux® for the treatment of colorectal and head & neck cancer at reduced prices. Since 2014, this initiative has helped 1,725 patients. In South Africa, we support the Savanti Patient Access Program, which enables patients to be treated with Erbitux at a lower co-payment.

Health awareness

Many people are sick without realizing it. The result? Although effective medicines and therapies may be 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. As part of our strategy to increase access to health (p. 34) in developing countries, we help create awareness by empowering healthcare professionals, communities and patients with appropriate tools, knowledge, information, and skills so that they can make high-quality, informed decisions.

Our principles

Global awareness campaigns

We regularly conduct global campaigns to raise awareness for various diseases. Our efforts concentrate on those conditions in which we have in-depth expertise stemming from our core business. These primarily include cancer (specifically colorectal as well as head and neck cancer), thyroid disorders, diabetes, and multiple sclerosis (MS). In our awareness activities, we frequently collaborate with patient advocacy groups. In the 2015-2016 period, we conducted and/or participated in 17 campaigns, enabling us to reach millions of people. Of particular success in 2016 was the thyroid awareness campaign we spearheaded every year during International Thyroid Awareness Week (p. 42), as were the Make Sense campaign held during Head & Neck Cancer Awareness Week and our World MS Day 2016 campaign.

In addition to these global efforts, we also lead special awareness initiatives to address specific local needs, such as anemia in Indonesia and malnutrition in Kenya. For such programs, we generally cooperate closely with national governments as well as other political actors. You can find more information under Access to health (p. 36).

Vocational training and continuing education for health workers

In developing countries, we empower private and public sector health workers to make decisions on the prevention, diagnosis and treatment of diseases based on the latest medical knowledge. One of our key initiatives is our five-year Capacity Advancement Program (CAP (p. 43)). Among other goals, CAP aims to improve medical training for doctors in Africa, Asia, Latin America, and the Middle East. Further activities include continuing education for medical professionals in India through our Su-Swastha program (p. 42) and vocational training for pharmacy technicians in Tanzania (p. 42).

These efforts form part of our commitment to improving access to health (p. 34) worldwide.

Progress

Social media campaign on head and neck cancer

Every year, we support the Make Sense campaign, an initiative of the European Head & Neck Society. Its objective is to raise public awareness of head and neck cancer and its symptoms in an effort to drive earlier presentation, diagnosis and referral, as well as improve outcomes. Moreover, we hope to dispel the misconception that head and neck cancer primarily impacts older smokers and people with alcoholism, as young adults can also develop this disease. In September 2016, as part of our "Letting our tongues do the talking" campaign, we called on our employees to send us pictures of themselves sticking out their tongues. We subsequently received more than 200 pictures from across 22 countries. Through this effort, we reached around 122,000 people worldwide via our social media channels, thereby raising awareness for head and neck cancer.

Twitter marathon for multiple sclerosis

We endeavor to support people with multiple sclerosis (MS) and regularly work to raise public awareness of this disease. For instance, in May 2016 we joined forces with the MS International Federation (MSIF) and local MS patient advocacy groups to participate in World MS Day. The theme for 2016 was "Independence". With help from our worldwide MS patient ambassadors, we produced two movies entitled "MS – a silent disease" and "MS Does Not Stop Me". These films illustrate how people with MS preserve their independence, refusing to let their disease defeat them. The heart of the 2016 campaign was a 24-hour tweetathon held across 24 countries. Using a variety of hashtags such as #strongerthanMS and #msday24, our employees and various stakeholders across the globe tweeted brief messages on multiple sclerosis. Through this campaign, we also highlighted the efforts of our sites worldwide to support MS sufferers, from fund raising to support local patient advocacy groups to rock concerts. The tweetathon generated a total of 2.7 million responses.

Thyroid health: Focusing on mothers

In 2016, we supported the International Thyroid Awareness Week hosted by Thyroid Federation International (TFI), the eighth time we have done so. A survey we commissioned in 2016 revealed that 84% of mothers worldwide could not correctly identify the most common symptoms of thyroid disorders in their children. Our campaign therefore aimed to help parents recognize the signs. To this end, we partnered with TFI to develop a film, a children's book and additional educational material. These tools utilize two butterfly cartoon characters called "Hypo" and "Hyper" to explain the symptoms of hyperthyroidism and hypothyroidism. The campaign reached around 20 million people across 34 countries. More than 14,500 people additionally received a thyroid check-up and, if irregularities were identified, were advised to see a general practitioner for further testing. You can find more details in our story Enriching lives (p. 173).

Promoting women's health worldwide

Women in the workforce can have a profound impact on a country's productivity and prosperity, but only if they are healthy. In many countries, health issues often prevent women from obtaining and keeping a job, or hinder them from progressing in their career. This poses a challenge for both national economies as well as companies. A study has shown that economic success is predicated not only on increasing women's participation in the labor market, but also on creating gender parity. According to the report by management consultant company McKinsey, these changes could add 28 trillion dollars to global annual GDP by 2025.

Healthy Women, Healthy Economies (HWHE) has taken up this challenge. Under the auspices of the Asia-Pacific Economic Cooperation (APEC), we collaborated with representatives of the United States and other countries to initiate

this public-private partnership (PPP) in 2014. Comprising members from the public and private sectors as well as non-governmental organizations, HWHE has developed a policy toolkit with political measures aimed at eliminating labor market barriers that women face due to health issues. In September 2015, the toolkit was rolled out at the APEC Women in Economy Forum.

In a joint effort with the Philippine government, we have launched the first HWHE public-private partnership addressing thyroid health, a problem that disproportionately affects women. In Jordan, we collaborated with the NGO Royal Health Awareness Society to roll out a similar program that likewise aims to bolster awareness for thyroid disorders among women.

Since 2016, we've also been partnering with the American Cancer Society (ACS) to raise awareness of women's cancers. In November 2016, we released a report entitled "The Global Burden of Cancer in Women", which documents the mortality and incidence rate of cancers that affect women and the burden worldwide.

Su-Swastha: Healthcare for rural India

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 urban areas, 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. Healthcare 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 2016, 1,238 community meetings were held, reaching a total of 26,129 people.

For these efforts, we were recognized in the 2016 Access to Medicine Index (p. 36).

Vocational training for pharmacy technicians in Tanzania

The healthcare systems in numerous developing countries are struggling with a shortage of pharmaceutical professionals. For instance, Tanzania has only around 3,000 pharmacists, pharmacy assistants and pharmacy technicians to meet the needs of the country's more than 40 million inhabitants. This imbalance makes it especially hard for people in rural areas to access medicines.

To help relieve this situation, we supported a three-year program to expand vocational training facilities for pharmacy technicians. Under this initiative, which ran from 2014 until

2016, we partnered with the German Society for International Cooperation (GIZ) and the faith-based Kilimanjaro School of Pharmacy, as well as the companies Boehringer Ingelheim and Bayer HealthCare. We worked together to revise existing curricula into a new modular curriculum for a one- to three-year pharmaceutical training program. As a model school, the Kilimanjaro School of Pharmacy furthermore has been furnished with a laboratory and library and is additionally receiving financial support. The Global Pharma Health Fund donated four Minilabs (p. 97) and taught tutors from eight Tanzanian training centers how to use them to properly detect counterfeit medicines.

Expanding our Capacity Advancement Program

Through our Capacity Advancement Program (CAP), launched in 2012, we are collaborating with academic institutions to train medical professionals in the fields of research and development, clinical research, and drug safety to build capacity as well as to raise public awareness of non-communicable diseases (NCD) such as diabetes, hypertension, cancer, and infertility. Across the globe, CAP covers a wide array of initiatives with differing focuses.

By the end of 2016, our Universities Program had reached 17,000 students from universities in Kenya, Uganda, Tanzania, Mozambique, Namibia, Ghana, Ethiopia, Angola, India, and the United Arab Emirates, providing them with European-accredited clinical diabetes and hypertension management training. Our goal is to reach more than 25,000 students through this program by the end of 2018. In 2015 and 2016, we presented the first-ever Merck KGaA, Darmstadt, Germany Diabetes Award and Merck KGaA, Darmstadt, Germany Hypertension Award to 20 promising medical students from universities in Kenya, Uganda, Tanzania, Ghana, Nigeria, the United Arab Emirates, Indonesia, and India, in an effort to drive research and awareness in these fields.

Our Africa Embryology Training Program, which seeks to improve access to fertility care, offers a three-month hands-on course that has already benefited ten African embryologists from Sub-Saharan Africa.

Furthermore, the 2016 Africa Luminary by Merck KGaA, Darmstadt, Germany provided 460 African healthcare providers, policy makers and researchers with development sessions to improve disease management, early detection and prevention of NCDs.

In 2015, we also launched an awareness campaign for diabetes, hypertension, and cancer that has reached over 175,000 people in Kenya. By 2018, we hope to have reached 200,000 people to provide them with services such as diabetes screening.

Through our More than a Patient initiative, we empower women cancer survivors by educating them and helping them start their own small business so as to lead independent lives. Similarly, through More than a Mother, we provide information, education, and healthcare while also working to change the mindset and culture that stigmatizes infertility and infertile women. Through the Empowering Berna Project, we help women in such circumstances to start a business and achieve independence. More than 1,000 infertile women from Ghana, Central African Republic, Ivory Coast, Uganda, Kenya, and Nigeria were enrolled in the project in 2016.

The 2016 Africa Research Summit by the UNESCO and Merck KGaA, Darmstadt, Germany sought to empower women in the fields of healthcare and research, where they are currently underrepresented in Africa. At the summit, we also launched the Best African Woman Research Awards in an effort to promote women's contribution to science, technology, engineering, and mathematics (STEM).

chemical product safety

Many of our chemicals are classified as hazardous substances. However, they must not pose any risk to people or the environment. In developing these substances, product safety is our primary consideration. We fulfill all statutory requirements, often exceeding them, and provide our customers with extensive information so that they understand our products and can use them safely.

Our principles

Statutory regulations and Group-wide guidelines

Numerous national and international regulatory requirements have been put in place to ensure that chemical products do not pose any danger to humans or the environment. We have implemented Group-wide guidelines that guarantee compliance with these regulations at all times when it comes to the import, production, commercialization, handling, recycling, and disposal of our chemical products. We have also signed general voluntary commitments of the chemical industry such as the Responsible Care® Global Charter.

To meet the product safety regulations relevant to our company, our Product Safety Chemicals policy details our Group-wide processes for managing and implementing product safety, including the necessary management structures. These include the Globally Harmonised System of Classification and Labeling of Chemicals (GHS) and its implementation in regional legislation (such as the CLP regulation in the European Union and HazCom 2012 in the United States), the EU chemicals regulation REACH, the U.S. Toxic Substances Control Act (TSCA), and the German federal law on protection from hazardous substances (ChemG). Our Group-wide policy also incorporates legal norms concerning the transport of hazardous chemicals, biocides and cosmetics, as well as the chemicals used in food and animal feed.

Safety analysis during product development

At Merck KGaA, Darmstadt, Germany, 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 impact on human health and the environment. In conducting these safety assessments, Regulatory Affairs provides advice and support to employees in our Life Science and Performance Materials business sectors.

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 for all our chemical products that contains 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 that contain information on the physicochemical, toxicological and ecotoxicological properties of the agent. Our safety data sheets reflect the latest local regulatory requirements and are available in 37 languages as well as 61 language-country combinations. Although not legally required, our non-hazardous substances also come with safety data sheets. In total, we make roughly 22 million safety data sheets available to our customers. Since all these documents must be kept up to date and consistent, in 2015 and 2016, we automated the majority of our Group-wide hazard communication processes and are now harmonizing the systems of our business sectors and sites.

FAST FACT

KEEPING CUSTOMERS INFORMED

All information on the safe use of our products is also available on our website, where 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.

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 Association (ICCA).

Organizational structure for product safety

In response to the acquisition of Sigma-Aldrich, a U.S.-based life science company, we adapted our organizational structures for product safety in the 2015-2016 period. 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 risk assessment, hazard communication in

the form of safety data sheets and safety labels, as well as the registration of chemical products.

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 Corporate Governance unit ensures that critical gaps in regulatory compliance are independently addressed. This unit reports directly to the head of the Group function Corporate Environment, Health, Safety, Security, Quality. Any necessary corrective or preventive action is carried out by the operating units within each business sector.

Take for instance the U.S.-based GHS Compliance Program. Since we had acquired several product portfolios in the United States that lacked safety information, in 2012 we initiated a multinational program to push regulatory coverage and bring the portfolios up to our stringent standards. Our objective was not only to close existing safety gaps, but also to be the front runner in implementing the new GHS requirements under HazCom 2012 in the United States, which took effect in June 2015. We fully achieved this goal while also meeting the deadline.

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 – thus, for instance, helping use resources and energy more efficiently. In our Healthcare business sector, we partner with external companies to explore the use of nanomaterials to improve therapies. Under the auspices of European research partnerships, we are also investigating the suitability of nanoparticles as vehicles for active pharmaceutical ingredients.

However, the special structure of nanoparticles can also entail risks. We assess these risks and furthermore only utilize the new technology with the greatest care. 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. We abide by the precautionary principle and take nanomaterial safety issues very seriously. Our Group-wide Policy for Use and Handling of Nanomaterials governs the handling of nanomaterials, whether used in pharmaceutical and chemical laboratories, production plants, filling plants or warehouses.

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 with information on the proper handling of nanomaterials across their life cycle, including transport, processing, storage, and disposal.

We are continuously engaged in a discourse on the opportunities and risks of nanotechnology. Our internal nano-coordination group consists of analysts, researchers, toxicologists, safety experts, and other professionals from relevant areas of our company. To guide our decisions and actions, we participate in committees and working groups that include other companies, associations and regulatory agencies. Examples of such groups include 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.

Training and awareness

We aim to increase awareness of, as well as provide best practice advice and information on, the safe use of hazardous chemicals. To this end, we regularly conduct seminars worldwide that teach basic lab safety rules such as the handling of flammable solvents and the storage of chemicals in safety cabinets and warehouses.

Progress

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 for us to evaluate and register all substances produced or imported in quantities ranging from one to 100 metric tons annually by June 2018. This process now also includes substances from 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, the Act on the Registration and Evaluation of Chemicals (AREC) took effect in Korea in early 2015. The requirements of AREC are very similar to those of REACH, so much so that AREC is often referred to as "K-REACH". 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.

Drug safety

Our pharmaceutical products must be safe. 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 principles

Benefit versus risk

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. 55) 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 risk-benefit profile. Only if the medicine has a positive risk-benefit profile do we submit an application for marketing authorization to the regulatory authorities.

After market launch, the number of patients being treated with the drug increases significantly. In certain circumstances, rare adverse effects may occur that went undetected during clinical development, which is why we continually monitor and update the risk-benefit profiles even after market launch.

Continual monitoring

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.

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.

Our Global Drug Safety unit is responsible for pharmacovigilance; it continually collects current safety data from a wide variety of sources across the globe, to include clinical studies, spontaneous reports on adverse effects, and articles published in medical and scientific journals. Our experts ensure that all information on the potential risks and adverse effects of our medicines is properly documented, tracked and, if necessary, reported to the respective regulatory

authorities. Global Drug Safety analyzes all data and, as required, uses this to reassess the risk-benefit profile. We then inform the regulatory authorities, physicians and patients about potential risks and changes in the risk-benefit balance.

We always adhere to all statutory pharmacovigilance regulations in force in those countries where we market our products and continuously work to incorporate requirement changes in our Group-wide standards and processes.

Regulatory authorities also conduct regular inspections to verify that we are complying with statutory requirements and our own internal drug safety standards.

Furthermore, we perform our own audits to ensure that all our departments, subsidiaries, vendors, and licensing partners involved in pharmacovigilance are meeting all requirements across the globe at all times.

Medical Safety and Ethics Board

Our Medical Safety and Ethics Board (MSEB) oversees the safety and risk-benefit evaluations of our drugs throughout clinical development and commercialization. As required, it will initiate appropriate measures to minimize risk, such as package insert updates. Our Chief Medical Officer (CMO) is the chairman of the MSEB, which also consists of senior physicians, scientists and experts from our company. Throughout a drug's entire life cycle, the MSEB reviews and assesses all relevant medical, ethical and safety issues. Furthermore, its tasks include the release of new investigational products for first-in-human use after conducting a thorough risk-benefit analysis based on all preclinical examination results.

Product labeling

The package insert informs physicians and patients how to properly use the respective drug. In accordance with the statutory regulations, the insert contains all relevant information such as ingredients and dosage, storage, mode of action, instructions for use, warnings, precautions, and adverse effects. Should the medicine contain ingredients that impact the environment, the package insert may also contain information on the proper disposal of the product.

As necessary, we review and update all package inserts, ensuring that they contain the latest information about our drugs. The leaflets also reflect changes initiated by the MSEB, such as new warnings.

In accordance with statutory requirements, all modifications to the inserts are submitted to the respective regulatory authorities for approval.

Strict quality assurance

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 the 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.

Reliable distribution processes

We want our pharmaceutical products to be readily available to physicians and patients and always arrive on time. Therefore, our distribution process 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).

Employee training

All employees involved in the safety and quality of pharmaceutical products, or in planning, conducting and monitoring clinical studies, are trained according to our global training standards. These standards stipulate how we conduct and document training at all our sites. We verify compliance with these requirements by performing regular audits.

In this way, employees are kept up-to-date at all times. This includes their professional expertise as well as adherence to GCP, GDP, internal standard operating procedures, and other relevant requirements. We provide our training via a global e-learning platform on our intranet.

Progress

Joint recommendations for improved risk-benefit profiles

To optimize the risk-benefit balance of our pharmaceutical products, we work closely with other companies and public-sector organizations such as health authorities and academic institutions. We are involved in PROTECT, a research project run by the Innovative Medicines Initiative (IMI), which is a joint undertaking between the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA). PROTECT aims to further develop tools and methods used in evaluating the risks and benefits of drugs.

IMI project teams, in which we have taken on a leading role, have established a framework to help accomplish the initiative's mission. Building on this, we have introduced a Benefit-Risk Guide to our Drug Safety unit and have been using this guide as a source of improvement since 2015. We last made use of its recommendations when compiling the documentation for marketing authorization for our cladribine tablets.

No critical observations in pharmacovigilance inspections

In Germany, there are two pharmaceutical regulatory agencies: the German Federal Institute for Drugs and Medical Devices (BfArM) and the Paul Ehrlich Institute (the German Federal Institute for Vaccines and Biomedicines). Both agencies conducted pharmacovigilance inspections on our company in February 2015 on behalf of the European Medicines Agency.

Furthermore, pharmacovigilance inspections were conducted by the respective national authorities in Australia, Austria, Colombia, Ghana, Japan, Spain, Croatia, and the United States in 2015 and 2016.

All inspections have continually confirmed the proper functioning of our Pharmacovigilance system.

Sharing expertise with other countries

We also pass on our drug safety expertise to other countries, especially those in which health workers (such as health agencies, physicians and nurses) still lack the necessary knowledge regarding pharmacovigilance. In 2016, for instance, we supported training events and conferences in Peru, China and Ivory Coast.

At our third Africa Luminary conference, held in Ivory Coast in October 2016, government representatives from Liberia, Uganda, the Central African Republic, Nigeria, and Kenya came together with more than 250 medical professionals as well as our own experts. The theme of the conference was "Unlocking the Pharmacovigilance Power in Africa". Here, we provided information (p. 41) on monitoring the safety of drugs for cardiovascular diseases, thyroid disorders, diabetes, and infertility.

In China, too, we shared our knowledge. In partnership with the China Food and Drug Administration (CFDA), we conducted several training seminars for pharmacovigilance experts from the local Chinese pharmaceutical industry. At these seminars, we not only informed participants of the local drug safety requirements, but also about key global regulations and recommendations. Moreover, in Peru we participated in workshops on collaboration between pharmaceutical manufacturers and health authorities.

counterfeit products

According to the World Health Organization (WHO), a considerable proportion of the medicines in developing countries are illegal, counterfeit or substandard. In industrialized nations, however, such products are also becoming increasingly available on the market through unlicensed internet pharmacies and underground business-to-business (B2B) platforms, posing a risk to public health.

Our company develops and manufactures products of the utmost quality. In order to protect customers and patients, we are deeply committed to fighting product-related crime. For instance, we collaborate with law enforcement agencies and take steps to secure our products against counterfeiting. Our guidelines, standards and processes apply to all our business sectors and markets worldwide, thus protecting our reputation as a supplier of quality products.

Our principles

Organization and guidelines

Our Group function Corporate Security coordinates all our anti-counterfeiting activities, basing its actions on our "Crime relating to products" guideline, which describes our goals and strategies for combatting this issue. All such activities are carried out under the supervision of the Chief Security Officer and the Head of Environment, Health, Safety, Security, Quality (EQ).

Furthermore, all our sites have a Product Crime Officer who investigates potential cases of counterfeiting, acting as the interface between local regulatory and law enforcement authorities, national associations, Group functions, and our sites.

Moreover, our Group Product Crime Investigation Standard has been in place since September 2016. It defines binding guidelines, harmonizes knowledge within the company and provides a more solid legal footing when dealing with illegal products.

Fighting product crime

Our Group-wide Anti-Counterfeiting Operational Network (MACON) is responsible for globally monitoring and implementing all anti-counterfeiting measures for our products. As well as coordinating preventive measures and the development of security systems, it is also responsible for investigations. Discourse between the members of the network creates synergies and bolsters our efforts to fight product-related crime. Comprised of experts from various units such as Legal/Trademarks, Product Security, Export Control, Supply Chain, and Quality Assurance, MACON is coordinated by our Corporate Security unit. In 2015, we expanded the network to include representatives from Global Drug Safety as well as various subsidiaries. All MACON activities are now overseen by the new Global Anti Product Crime unit, created in 2016.

In all relevant cases, MACON collaborates with the appropriate law enforcement agencies and regulatory authorities, allowing us to detect more cases of counterfeiting and take decisive action in pursuing existing cases, especially in high-risk countries. The network reviews and handles up to 100 cases of product-related crime per year, including inquiries from authorities that arise during backtracking investigations. In 2015, we uncovered several underground laboratories that were counterfeiting several of our products.

Moreover, in 2016 we launched a new, Group-wide internal reporting system with which all incidents can be better analyzed and documented. This provides us with a more complete picture of the security situation, better equipping us to prevent such incidents in the future.

FAST FACT

DEFINING PRODUCT CRIME

1. Product counterfeiting: In line with the Trade-Related Aspect 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/alterd 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 illegal purposes.

3. Black market crimes: This refers to the sale of counterfeit and/or diverted products via illegal channels (e.g. the Internet), or for illegal purposes.

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

Tracking system for chemical substances

We have established an internal system to monitor and track chemicals that could be misused to produce illegal weapons, explosives or narcotics. Our tracking system flags suspicious orders and/or orders of sensitive products, which are only released once we have confirmed the existence of a (verified) end-user declaration. Moreover, we collaborate closely with regulatory authorities and law enforcement.

In addition to our 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 fulfilling our commitment to the German Chemical Industry Association (VCI) and to the Guideline for Operators published by the European Commission.

Supporting customers and patients

We believe that patients should be able to determine the identity and authenticity of a pharmaceutical product themselves, which is why we implement the requirements of the EU Falsified Medicines Directive, for instance by applying a unique serial number to our pharmaceutical packaging. In the United States, the Food and Drug Administration (FDA) requires all drug packages to be labeled with a unique product identifier by the end of 2017, which we are currently working to implement.

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

- On all our products, we apply Security-M, a security label containing our color travel pigments. This label enables users to easily verify the authenticity of our products and is considerably harder to counterfeit than the holograms that are commonly used.
- With our Track and Trace shipment tracking system, patients can trace the supplier of the medicine to verify its authenticity. We have already implemented this system for all our pharmaceutical products in the United States and China, and are currently considering expansion to other markets.
- Our free Check My Meds app for smartphones allows patients in the United States to scan the serial number of their medicines and quickly verify their authenticity. In 2015, the trade journal PharmaVOICE listed the app among its top innovative health-focused apps and websites.
- In our Mobile Anti-Counterfeiting System (MAS) project in Nigeria, we are working closely with our suppliers on a text message-based identification system. Patients scratch off a barcode that is printed on the product packaging. They then send this code via text message to an assigned number, which immediately sends them 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 85 different active ingredients. With this compact test kit, counterfeit medicines can be detected quickly, easily and inexpensively in developing and emerging countries. Further information on this project can be found under Community (p. 97).
- 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.

Educating our employees and business partners

We endeavor to raise awareness of product-related crime among our employees and business partners, training our employees worldwide on this subject. In the countries where

we don't have our own subsidiaries, we offer training for our business partners.

Conducting security audits

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, conducting corresponding security audits if significant deviations are identified. This auditing system is based on the EMA ICH Q10 pharmaceutical quality assurance standard. In 2015 and 2016, we conducted 37 security audits of our partners worldwide and subsequently provided them with the results of these audits so that the necessary corrective action could be taken.

Industry-wide exchange and collaboration with authorities

We have joined forces with organizations such as EFPIA (European Federation of Pharmaceutical Industries and Associations), IFPMA (International Federation of Pharmaceutical Manufacturers & Associations) and VFA (German Association of Research-based Pharmaceutical Manufacturers e.V.) in an effort to fight product crime. We also support industry-wide initiatives and collaborate closely with regulatory authorities and law enforcement at the regional, national and international level. We work particularly closely with the Pharmaceutical Security Institute (PSI). This non-profit organization is dedicated to protecting public health by sharing information on pharmaceutical counterfeiting and initiating enforcement actions through the appropriate authorities. In May 2015, we hosted a meeting of the PSI for the first time, at which we engaged in discussions on current trends and holistic approaches to fighting product-related crime. In 2016, our Chief Security Officer was appointed Vice Chair of the PSI Board of Directors.

Furthermore, we are also a member of Rx-360, a consortium of global pharmaceutical manufacturers and suppliers that aims to prevent counterfeit products through the introduction of global quality assurance systems and audit programs.

When cases of product crime are identified, we collaborate with the relevant law enforcement agencies and customs authorities in the respective countries. We furthermore work with Interpol, the World Customs Organization, health authorities, and our peer industry.

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. Furthermore, in 2015 and 2016, we scrutinized our existing communication and information management processes to identify potential improvements, and are now making the necessary changes to optimize these processes.

Progress

New training program developed

In the 2015-2016 period, we devised a training program for all our employees in Security roles, such as Product Crime Officers. Via e-learning modules, the program aims to enhance their competencies and promote best practice sharing. In 2015 and 2016, we held ten training courses at various sites. Moreover, participants shared lessons learned during the MACON summit in Darmstadt in June 2016, which was attended by 25 Product Crime Officers from key countries.

Transport and warehouse safety

We transport and store products and materials worldwide such as chemicals, pharmaceuticals, raw materials, intermediates and waste, as well as technical materials and packaging, all of which could pose a hazard if handled incorrectly. In doing so, we adhere to extremely strict safety regulations Group-wide to prevent danger to people and the environment.

Our principles

Organization and standards

Environment, Health Safety, Security, Quality (EQ) (see Environmental stewardship (p. 77)), the Group function in charge of transport and storage safety, sets Group-wide standards and guidelines. In addition, our individual sites are also subject to various national and international regulations governing environmental protection and public safety, which local site directors are responsible for implementing.

Our sites worldwide generally have a dangerous goods manager who advises the site director on issues regarding the safe transport of dangerous goods while also monitoring compliance with regulatory requirements. This position reflects the EU regulations requiring the appointment of a dangerous goods safety advisor.

In 2014, we acquired the company AZ Electronic Materials and in 2015, Sigma-Aldrich, a U.S.-based life science company. We have since aligned their transport and storage systems with our Group-wide standards and updated them where necessary.

Warehouse safety

Our global safety concepts and standards ensure 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. Special rules of conduct apply to all warehouse employees. In 2015 and 2016, we audited more than 20 of our warehouses and, based on the results, identified areas for improvement.

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 contracts, warehouse providers must submit a statement detailing how they plan to meet our stringent safety standards. Our EHS managers regularly visit third-party warehouses. In 2015 and 2016, we audited ten of these warehouses and developed corrective action plans to address the identified shortcomings.

In Germany, the "Technical Rules for Hazardous Substances" (TRGS) stipulate the storage of hazardous substances in non-stationary containers. In 2016, we decided to introduce these rules for storage at all our warehouse and distribution centers worldwide.

We comply with the current requirements of the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) at all our sites with the exception of India, where the GHS system has not yet been fully integrated into national regulations.

Ensuring transport safety worldwide

We seek for all shipments to reach our customers and sites safely, undamaged and with the required safety information. Several substances that we transport are classified as hazardous materials. Hazardous goods transport – whether by road, rail, plane, or ship – is governed across the globe by extensive regulations such as the "European Agreement concerning the International Carriage of Dangerous Goods by Road" (ADR).

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 sites in those countries with no local regulations on the transport of hazardous materials. We update our Group standard to reflect current requirements every two years and support our local site directors in implementing the relevant changes. On January 1, 2017, we introduced the amended IATA regulations on the transport of dangerous goods by air and the RID/ADR regulations on transport by rail and road.

We regularly perform audits to ensure that our own sites as well as our freight forwarders are complying with transport safety regulations. In 2015 and 2016, no incidents that would have had a significant impact on the environment or community were recorded, nor were there any infringements of international regulations.

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 Information 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.

Continuously improving safety concepts

Our local EHS and dangerous goods managers regularly review and evaluate our transport and storage activities, informing site directors of shortcomings and opportunities for improvement. Moreover, our sites are audited by EQ every five years.

Based on a strength and weakness analysis of each site, we calculate key performance indicators on transport and storage safety, which help us determine where to institute additional improvements. In 2016, for instance, we developed an e-learning concept for basic management courses on the transport of dangerous goods and launched a subsequent pilot program.

Employee training and internal best practice sharing

We regularly train warehouse workers and all employees involved in the transport of goods on our standards and procedures, as well as on changes to international requirements and incident management.

Furthermore, our EHS managers meet regularly at the EHS conference in Darmstadt, Germany, where they have the opportunity to share experiences and best practices, as well as participate in transport and storage safety training. These

topics are also covered in the three-day orientation seminar that is mandatory for all new EHS managers.

Progress

Award for truck improvements

The safe transport of dangerous goods necessitates safe vehicles, another area we pursue. In 2015, we won the VCI Hesse's Responsible Care competition for our continuous improvements to 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. Over the past several years, our transport employees have worked to continuously hone this system, collaborating with our truck body manufacturers to implement the design changes.

In 2016, we won first prize in the Transport Safety category of the Germany-wide Responsible Care competition in recognition of our "TUIS, Messkonzept Südhessen" project. When a transport or warehouse accident occurs, this system can quickly calculate the rate at which hazardous substances are spilling and spreading.

Responsible Marketing

Pharmaceutical marketing is regulated by legislation worldwide. For instance, manufacturers in Germany 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, side effects, and contraindications of the advertised drug.

Our company commercializes both prescription medicines as well as over-the-counter products. In marketing our products, we voluntarily commit to various standards that exceed statutory regulations. Because patients deserve effective, high-quality treatment, they are always our primary consideration.

Our principles

Guidelines and organization

We adhere strictly to all regulations on pharmaceutical marketing. Our Group-wide Pharma Code for Conducting Pharmaceutical Business and Pharmaceutical Operations defines the relevant standards for ethical marketing practices. This code also governs our interactions with physicians, medical institutions and patient advocacy groups. We furthermore comply with the codes of conduct of national and international industry organizations such as the Code of Practice and Code of Pharmaceutical Marketing Practices published by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA). Our pharmaceutical activities in the United States are governed by a specific US guideline.

All guidelines pertaining to marketing and advertising are part of our Group-wide compliance program, which stipulates that we always conduct business in compliance with the law and according to the highest ethical standards. We regularly review all guidelines, adapting them to new developments.

We have defined processes for all international, national and regional sales and marketing activities, and have appointed individuals responsible at each of these levels. We furthermore conduct regular audits of our sales and marketing activities.

High global standards for advertising materials

Through our Principles of Review and Approval of Promotional Materials and Other External Communications, we ensure that all advertising materials meet our rigorous standards. In 2016, we updated these principles and rolled out a Group-wide review and approval system that meets the latest technical requirements. This system helps us check whether all advertising materials meet our standards. All employees involved in creating advertising materials worldwide have been trained on the updated principles as well as this new system.

Direct marketing only permitted in certain countries

Direct-to-consumer advertising (DTC) for prescription drugs is allowed in some jurisdictions such as the United States and New Zealand. We only pursue DTC campaigns in these countries. 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 treatment.

Compliance violations

The industry associations in which we are members have put in place various reporting channels for people to report any wrongdoing with regard to marketing practices.

Furthermore, we have also established a SpeakUp Line, which 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 corrective and, if need be, punitive action.

Voluntary self-regulation

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 for collaboration between physicians and the industry. When violations of the FSA code are suspected, members and third parties can file complaints directly with an arbitration board. In 2015, we were involved in proceedings that resulted in a fine.

Regular employee training

Individuals responsible for our pharmaceutical advertising, as well as employees working in sales, marketing and regulatory positions, receive regular training on our current guidelines. Furthermore, via our Intranet the responsible

employees also have access to our compliance guidelines on the marketing and promotion of pharmaceuticals.

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 that customer.

Bioethics

Bioethics are foundational to guiding how humans use the rapidly advancing power of life sciences and technology responsibly and ethically to the ultimate benefit of mankind, animals, plants and all living beings. In the course of our Healthcare and Life Science activities, we are faced with various bioethical issues, including stem cell use, animal testing, the use of genetically modified microorganisms, the potential impact of new gene editing techniques such as CRISPR/Cas, and our own clinical research. Beyond compliance with the relevant regulations and laws, we have a strong commitment to conducting research in an ethical manner, which is why we continuously evaluate all manner of positions on controversial topics in order to make informed decisions. In treating patients with our drugs and interacting with participants in our clinical studies, their wellbeing is always of utmost importance.

Our principles

Merck KGaA, Darmstadt, Germany Bioethics Advisory Panel

As a global company, it is important for us to promptly identify and address all international developments concerning bioethical issues. This approach is what enables us to define our own stance, as does the advice of external experts.

To this end, the Merck KGaA, Darmstadt, Germany Bioethics Advisory Panel (MBAP) convenes once a year to advise the company. Consisting of renowned international experts in the fields of bioethics, theology, science, and law, the MBAP is jointly headed by our Chief Medical Officer (CMO) and our

Head of Global Health. 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.

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) guidelines of the International Council for Harmonization (ICH). More details can be found under Clinical studies (p. 55).

Stem cell research

We do not 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 Stem Cells and Human Cloning Principles ensure compliance with our ethical approach. Furthermore, our Stem Cell Research Oversight Committee (SCROC), which was established in 2016, reviews our business strategies as well as all internal human stem cell research proposals to verify compliance with our ethical and legal guidelines. This also includes collaboration with external

partners. The mandate of the SCROC is based on the recommendations of our Bioethics Advisory Panel.

Infertility treatment research

We develop treatments to improve the success rate of in vitro fertilization and are currently revising our Fertility Research Policy based on recommendations from the MBAP. You can find more information under Progress (p. 54).

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 centers for medical biotechnology are in Darmstadt, Boston (MA, USA), Beijing (China), and Tokyo (Japan). Major biotech production sites are located in Aubonne and Corsier-sur-Vevey, Switzerland, the latter of which is one of the largest biopharmaceutical production facilities in Europe.

We manufacture our biotech products according to the highest standards. 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 regulatory changes pertaining to biotech products and adapt our processes accordingly, thus ensuring we adhere to all statutory requirements.

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 new 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.

In 2016, we instituted a new Group-wide policy that sets out our principles for disseminating information regarding off-label use. 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 only provide such information upon direct request to healthcare professionals for medical purposes. 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.

Progress

Merck KGaA, Darmstadt, Germany Bioethics Advisory Panel discussions

In 2015 and 2016, the MBAP discussed the following issues:

1. Selecting partnerships according to ethical standards

We collaborate with numerous partners in research and development, production, and marketing and sales. The MBAP has emphasized that it is crucial to form partnerships with organizations whose values align with ours. Our values are described in guidelines such as our Code of Conduct, our Human Rights Charter and the Merck KGaA, Darmstadt, Germany Responsible Sourcing Principles.

2. Biosampling & biobanking

A biobank is a repository that stores tissue samples and body fluids, as well as coded patient and specimen data. Although these are extremely important to our research, their storage and use for research require adherence to stringent ethical standards, not only in terms of specimen collection, including those for genetic analyses, but also for biobank operation. For this reason, we explain to all study participants the purposes for which we are using their samples. The participants then sign an informed consent form to confirm that they understand and that they authorize the use of their specimens.

Because we might want to use patient samples at a later date in other studies, the MBAP has recommended that we include this possibility in the Informed Consent form for our study participants. Furthermore, in 2017 we will be adopting a policy on patient specimen handling and establishing a committee to advise our researchers on the use of these samples.

3. Fertility and the German Embryo Protection Act

Because we develop therapies to treat infertility, 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? The German Embryo Protection Act provides guidance on such questions. The MBAP has discussed the various issues thoroughly, and, based on these deliberations, we are currently revising our Fertility Research Policy.

4. Use of genome editing systems

We are a leading supplier of gene-editing technologies such as CRISPR/Cas9, which can be used to target and modify specific genes. 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 genetic editing techniques in plant cultivation. Statutes in different countries allow for a

varying degree of latitude in applying this technique, which is why the MBAP has thoroughly discussed the possibilities and ethical boundaries of genome editing systems. The results of this discourse are being incorporated into our new Gene Editing Policy, which is under development. Moreover, in

response to guidance from the MBAP, we are currently working to establish the Genome Editing Consortium, whose tasks shall include determining the responsibility and bioethical role of gene editing tool providers.

clinical trials

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

Our principles

Adhering to the highest standards

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 and 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 scientific questions.

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 include:

- The Good Clinical Practice (GCP) guidelines of the International Council on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use
- The Declaration of Helsinki published by the World Medical Association
- The Belmont Report
- Good Pharmacovigilance/Laboratory/Manufacturing/Distribution Practices (GVP/GLP/GMP/GDP)

- The International Ethical Guidelines for Biomedical Research Involving Human Subjects 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 Japanese Pharmaceutical Manufacturers Association (JPMA), and Pharmaceutical Research and Manufacturers of America (PhRMA)
- The "Principles for Responsible Clinical Trial Data Sharing" published by the EFPIA and PhRMA

Clinical research governance

Our Head of Global Research and Development bears overall responsibility for pharmaceutical development as well as the related governance process. Two committees support this individual in overseeing our clinical studies. The Integrated Clinical Study Committee (ICSC) is responsible for studies in pharmaceuticals 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. Furthermore, in 2015 we also established therapeutic area review boards, which assess proposed study concepts and use their expertise in the various therapeutic areas to advise the ICSC.

Before administering a new drug in human subjects for the first time, we conduct extensive preclinical testing to demonstrate that the medicine has the potential to offer clinical benefits, is sufficiently safe for use in humans, and has a positive risk-benefit profile. Potential risks for subjects are carefully and continuously analyzed before and during the clinical study. Our Medical Safety and Ethics Board (MSEB)

oversees the safety of subjects participating in our clinical studies and, as necessary, also reviews the risk-benefit profiles of the investigational drugs. You can find further information on the MSEB under Drug safety (p. 46) and Bioethics (p. 53).

Our clinical study procedures are regularly audited 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 adapting our processes accordingly.

Conducting clinical studies responsibly

Protecting the safety, wellbeing, dignity, and rights of the volunteers and patients 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, and the confidentiality of all data and information collected is ensured in compliance with statutory regulations.

Prior to enrolling subjects, every clinical trial must 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 informed consent before enrolling in a clinical study. We fully inform subjects 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 posed by potential participants are answered by the clinical investigator or another qualified healthcare professional familiar with the study. As far as possible, non-interventional studies (observational studies) are also assessed by an ethics committee, and subjects are provided with thorough information.

Once started, every study follows precisely defined procedures. This ensures that the study is 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. This approach also ensures that the data are accurately generated, documented and reported in line with all applicable requirements. In the 2015-2016 period, we received no significant complaints regarding this clinical study procedure from 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 pharmaceuticals. Potential adverse effects and risks are taken into consideration in an effort to evaluate the risk-benefit

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 Drug safety (p. 46).

Conducting clinical trials in vulnerable populations

When a drug is intended for use in vulnerable populations, we must sometimes conduct clinical studies in populations such as children or underprivileged individuals. Their wellbeing is one of our top priorities 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 in other, less vulnerable study participants. When performing such studies, especially when informing subjects and obtaining their consent, we comply with all statutory regulations throughout the entire process.

More information can be found under Infectious diseases (p. 37).

Clinical study collaboration

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 – especially contract research organizations (CROs) performing studies on our behalf – to abide by the same set of high standards when conducting clinical studies.

To verify their compliance with Good Clinical Practices (ICH-GCP), our CROs, partners and other vendors are subjected to regular audits as part of our quality assurance efforts. We also arrange for audits of study centers involved in our clinical studies.

In the 2015-2016 period, these audits did not show any indication of studies that were failing to comply with ICH-GCP standards or the Declaration of Helsinki.

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 for clinical studies in 2014. During advisory board meetings, caregivers and representatives from patient advocacy groups are invited to provide feedback on clinical study issues. 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 five-year public-private partnership within the Innovative Medicines

Initiative (IMI) launched in 2012. 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 scientific circles and academic institutes in advancing medical and scientific knowledge. To this end, we provide them with data from our clinical studies to use in their own research. When disclosing data from clinical studies, the privacy of our patients is always safeguarded; national legal systems are always respected, and incentives are always provided for investments in biomedical research.

To ensure responsible clinical study data sharing, we also collaborate with the European Federation of Pharmaceutical Industries and Associations (EFPIA) as well as the Pharmaceutical Research and Manufacturers of America (PhRMA). In accordance with their voluntary commitments, we provide qualified researchers from medicine and science with study protocols, anonymized patient data, study data, and clinical study reports.

Publication of clinical studies

We are obliged to disclose information from our clinical studies. We communicate this information publicly in a complete, accurate, balanced, transparent, and timely manner. We publish clinical study designs and results in the international database ClinicalTrials.gov 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. Furthermore, in accordance with EU regulations, we publish results of our clinical studies in the European Union Drug Regulating Authorities Clinical Trials (EudraCT) database, which is run by the European Medicines Agency (EMA).

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.

Clinical studies in developing countries

We conduct all our clinical studies in accordance with local laws and regulations, irrespective of the region or country. In addition, we 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 support the development of their healthcare systems.

In performing clinical studies in developing countries, we apply the same principles that apply when conducting such studies 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; in particular, 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 there is a reasonable expectation that the drug tested will be submitted for marketing authorization and be 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.

Under our Praziquantel Donation Program, we are partnering with the World Health Organization to combat the parasitic disease schistosomiasis in African school children. However, in their currently available form, praziquantel tablets are only suitable for adults and children older than six. For children younger than six, it is currently not possible to properly treat the disease. Within a public-private partnership (PPP), we are researching a new formulation of praziquantel that is also suitable for infants and toddlers. As part of this research, we are currently conducting clinical studies with children in Africa. Further details can be found under Infectious diseases (p. 37).

Progress

Immuno-oncology: Strategic alliance with Pfizer

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 the antibody avelumab as a potential treatment for various tumor types. In 2015, we thus launched JAVELIN, our expansive international clinical study program in which we are investigating the potential therapeutic benefit of avelumab in multiple tumor types. By October 2016, more than 3,000 patients had been evaluated as part of this program, which is investigating avelumab in more than 15 tumor types.

In 2016, we achieved important milestones in the indication of metastatic Merkel cell carcinoma (mMCC), a rare and aggressive form of skin cancer. We submitted the Biological License Application (BLA) for mMCC to the U.S. Food and Drug Administration (FDA) in the third quarter, and the FDA accepted it for Priority Review in November. In October, the European Medicines Agency (EMA) validated for review our Marketing Authorization Application (MAA) for mMCC. To date, there is no approved therapy available for this kind of tumor.

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 the most 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 our patients. We published a position paper on this topic in 2015.

Coming to terms with the past

In the 1950s and 1960s, drugs from various manufacturers were tested on orphans in Germany. The majority of such clinical studies were performed in collaboration with (university) hospitals and general practitioners. By making available files in our historical archives at Group headquarters in Darmstadt, we are now supporting efforts to understand and come to terms with this episode in the history of science. In 2015, we granted a historian access to the files in our corporate archives so that she could do in-depth research for her dissertation. Her scholarly endeavor will ultimately help us all to navigate 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 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, as well as the efficacy of our pharmaceuticals. We enforce stringent animal welfare standards that exceed applicable laws and expect our suppliers, contract research organizations and other partners to do likewise.

The majority of our animal testing is conducted in our Healthcare business sector as part of the official drug approval process. However, animal welfare has also become a more prominent issue for our Life Science business sector. The acquisition of the U.S.-based life science company Sigma-Aldrich in autumn 2015 has increased the number of products of animal origin in our Life Science portfolio. For instance, certain animals are kept so that their blood can be used to produce antibodies. Before the acquisition, Sigma-Aldrich also conducted animal studies as part of contract research work for third parties, a line of business we are continuing to pursue.

Our principles

The 3Rs of animal welfare

In the housing, care and feeding of our lab animals, we are committed to consistently applying the most stringent ethical standards and are continuously working to improve upon them. When conducting research, we adhere to established

methodology and endeavor to use animal alternatives 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. For instance, under the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ Consortium), 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 toward the 3Rs of animal research to advance ethical science in academia and industry. In 2016, one of the Global 3R Awards went to Madhav Paranjpe, a scientist from our Life Science business sector. He was recognized for publishing a study showing how the number of mice used to evaluate the carcinogenicity of a new drug can be reduced by 25%.

Legal requirements

Animal research is only permitted if there are no recognized alternative methods available. However, in many fields, animal studies are indispensable and legally mandated by the ICH guidelines or REACH. The safety of humans is our number one priority. Laws and regulations govern all aspects of animal research, such as the housing conditions of research animals, the conduct and approval of studies, and the reliability and expertise required of all involved individuals.

Group-wide methodology and guidelines

Through our Group-wide Use, Care and Welfare of Laboratory Animals policy, we make a commitment to global animal welfare principles and the highest possible ethical standards in animal research.

This 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've been offering third parties since acquiring Sigma-Aldrich.

In addition to our policy, our Group-wide Animal Science and Welfare manual describes the requirements for implementing, maintaining and improving animal welfare practices.

Organizational structures

Our Corporate Animal Science and Welfare (EQ-A) unit is headed by the Chief Animal Welfare Officer, who is responsible for creating uniform animal welfare standards. The Chief Animal Welfare Officer also initiates audits, sometimes performing these themselves, and consistently works to drive improvements in our own animal welfare practices as well as those of our partners. Moreover, all our animal science and welfare experts meet on a regular basis through our global laboratory animal science network, which monitors the animal welfare units at our sites and supports all projects and processes related to animal science and welfare.

In 2016, we furthermore established the Group Animal Welfare Council, which convenes several times a year. Comprising representatives from all our business sectors, this council monitors policy developments, updating our Animal Welfare Strategy where necessary.

Our sites are generally 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 when not required by law.

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. In 2015, for instance, he chaired the IQ Consortium and currently represents EFPIA on the AAALAC International Board of Trustees, where he ensures adherence to European standards. Moreover, at the end of 2016 he was appointed to the Executive Committee of AAALAC International for a term of three years.

Collaborating with partners and suppliers

We perform the majority of animal studies ourselves and for the most part procure our lab animals from specialized animal breeders. 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 review compliance with this policy by performing regular audits.

The suppliers gained from the Sigma-Aldrich acquisition are also subject to our strict animal welfare requirements. Since 2016, we have been working on harmonizing our standards and developing a suitable audit concept.

Employee training

We regularly provide training to all employees working 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 they are in 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).

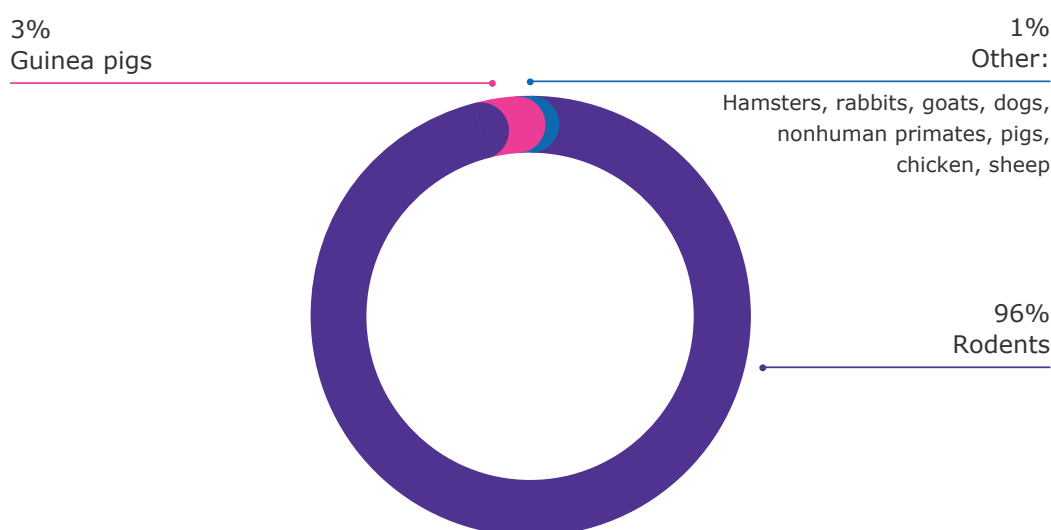
Progress

The majority of laboratory animals are rodents

Roughly 96% 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 side effects with the necessary accuracy and include them in the risk assessment of a substance. In performing tests on non-rodents, researchers must meet additional requirements pertaining to animal care and study design.

Animal types



Auditing our animal research facilities

We perform regular audits on our animal research facilities to ensure adherence to our animal welfare standards. In 2016, for instance, our Corporate Animal Science and Welfare unit conducted three internal audits at our sites in the United States, the United Kingdom and Israel. These audits identified the need for better environmental enrichment to promote species-typical behavior. They also suggested improvements relating to occupational safety, veterinary care and organizational issues. Corrective actions have since been taken.

It goes without saying that we adhere to the highest international animal welfare standards at all times. Since early 2016, 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). One facility in our Life Science business sector is also AAALAC-accredited.

Conducting audits of 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 we feel to harbor potential risks. In the 2015-2016 period, a total of three audits were conducted in European countries excluding Germany. The audit results are shared among Interpharma member companies and treated confidentially.

Developing alternative testing methods

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 acceptance, both animal studies and alternative testing would 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.

Awards for developing alternative testing methods

- 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

We want all patients to receive the best possible medical treatment. To achieve this, it is essential that research institutes, physicians, patient organizations, and other key actors in health systems have access to detailed and current information on diseases and treatments. We help facilitate this access by sponsoring independent initiatives and medical capacity advancement programs, and by donating money and supplies. In addition, we promote outstanding research projects. Since transparency is always our number one priority, we provide detailed reports on donations and activity sponsorship. Furthermore, we are committed to various voluntary requirements within our industry.

Our principles

Statutory and voluntary requirements

We explicitly endeavor to exert no influence over financial or non-financial contributions, nor over the information communicated to key actors in healthcare systems. Consequently, we have committed ourselves to providing transparency. 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". We also adhere to statutory transparency requirements worldwide, such as the stipulations of the Sunshine Laws in the United States, or the Loi Bertrand in France.

Transparently promoting research and education

To support health systems, we make monetary contributions and donate supplies to institutions such as professional medical associations, hospitals and university clinics. These contributions are expressly not intended to influence decisions regarding treatment, prescriptions or purchasing. On our website, we publish all relevant payments to partners in the health industry as well as our R&D spending in the relevant countries. This practice aligns with the code of conduct of the German Association for the Voluntary Self-Regulation of the Pharmaceutical Industry (FSA), as well as the codes of conduct of the pharmaceutical associations in the member states of the EFPIA. We update the disclosed information on an annual basis.

Furthermore, 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, 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 for scientists, physicians, nurses, pharmacists, and other healthcare professionals. We conduct these efforts in a transparent fashion. All direct and indirect financial aid aligns with the principles of the EFPIA.

Partnering with patient advocacy groups

Patient advocacy groups support patients, family members and care givers, providing them with information on disease management. Just like these organizations, we have set ourselves the goal of improving patient quality of life, which is why we endeavor to support their crucial work. We explicitly strive to exert no influence or control over the information that the organizations communicate to their members. We provide the highest level of transparency on our donations by publishing the details of contributions to European patient organizations on our website. This information is updated annually, which enables us to fulfill the commitment we made through our membership in the European Federation of Pharmaceutical Industries and Associations (EFPIA). In 2016, we published a new Group-wide guideline entitled "Good Practice and Process Guidance: Engagement with Patients, Patient Opinion Leaders and Patient Organizations". This document governs our interactions with patients and patient advocacy groups worldwide except in the United States, where a separate regulation applies. It furthermore ensures that patient wellbeing is considered.

Progress

First report in line with transparency initiative requirements

Since 2016, companies in the EU have been required to publish all financial and non-financial contributions to medical professionals and organizations in the healthcare industry not related to research activities. As set out in the transparency initiative of the EFPIA, the information provided must include the name and address of the individual recipient as well as the purpose and amount of the transfer. In 2015, our work focused on informing our partners in the health industry just how important the transparency initiative is to us. We also took steps to ensure data quality and data privacy in all affected countries. At the end of 2016, we reported for the first time in line with the new requirements. Currently, we are involved in new legislative initiatives launched in several European countries as part of the transparency initiative, which will impact our reporting process as of 2017. We will ensure that we fulfill all requirements.