Patient health and safety

“Companies need to incorporate patient evidence at all stages of the medicine R&D cycle as well as decisions on access and availability – with the meaningful involvement of patients and their patient organizations. Only a collaborative and holistic approach can bring about sustainable solutions.”

Nicola Bedlington, secretary general, European Patient Forum

2017 highlights

- Introduced a companywide patient engagement strategy to systematically embed patient engagement in the way we work
- Created a new organization to oversee global suppliers in clinical development
- Began providing easy-to-understand summaries for patients in Phase IIb and III studies
- More than 99% of regulatory inspections had no major findings
- Reached out to more than 1300 patient organizations to ensure we understand patient perspectives
- The Novartis Foundation and partners launched Healthy Schools for Healthy Communities in South Africa
- Healthy Family celebrated 10 years in India and is planned to expand over the coming years
- Nine illegal pharmaceutical manufacturing facilities and assembly lines were dismantled, and more than 7 300 illegal online pharmacies were shut down as a result of our actions to combat counterfeit medicines

Key challenges

- Developing effective strategies to interrupt the transmission of leprosy and ultimately eliminate the disease
- Our Healthy Family program in Indonesia discontinued due to challenges in successfully adapting the program to local realities
- Developing novel distribution channels to improve access to our high-quality antimalarial for people relying on the private sector
Why it is important

The safety of patients is one of the foundations of healthcare delivery, yet a number of adverse events occur each year. According to the World Health Organization, in a study across low- and middle-income countries, the rate of adverse events was around 8%, of which 83% could have been prevented and 30% led to death. Moreover, approximately two-thirds of all adverse events in healthcare happen in low- and middle-income countries.1

Counterfeit and falsified medical products also pose a global public health risk. They often cause treatment failure, disability or even death, and can lead to the emergence of resistant forms of infectious agents. Due to high demand and low production cost, falsifying medical products is a highly profitable business. In the US, the Center for Medicine in the Public Interest puts the worldwide sales of counterfeit medicines at around USD 75 billion. This number is expected to rise by 90% in the next five years.

At the same time, educating patients to become more knowledgeable is one way to help ensure that health treatments have the desired effects. This can only be done if people are given the background and understanding needed to make the right decisions – something that is especially necessary in lower-income environments, where awareness about many diseases (especially chronic diseases such as hypertension, diabetes and cancer) is low.

How we approach it

The health and safety of patients is at the very core of our mission. We cannot hope to find new ways to improve and extend people’s lives if we cannot assure the people who use these medicines that they are both effective and safe.

Throughout the lifecycle of our medicines, we work to ensure the best balance of benefit and risk by having a variety of systems and processes in place for a continuous and systematic review of the data collected for all products in our portfolio, including those on the market and those that are still in development. These processes are designed to help us maximize the safety and therapeutic benefits for patients.

We focus our patient health and safety activities in three key areas: pharmacovigilance, safety profile and quality of drugs; health education and prevention; and combatting counterfeit medicines.

We also work with patients to ensure they have a voice in how our products are developed. Patients are often well positioned to understand the challenges of their disease. By proactively interacting and engaging with patients and the patient and caregiver community, we seek out and use their insights to inform decision-making throughout the development and commercialization process for our medicines. In 2017, we began building a companywide patient engagement strategy that is intended to systematically and consistently embed patient engagement in the way we work. As a first step, in early 2018, we will publish an updated Commitment to Patients and Caregivers, which outlines how we plan to help patients and caregivers better understand what they can expect from Novartis.

Novartis continues to maintain close interactions with national health authorities in a number of countries such as China to improve pharmacovigilance processes, with the ultimate goal of providing patients with a better risk-benefit assessment.

Pharmacovigilance, safety profile and quality of drugs

Our safety efforts begin at the earliest stages of research, right at the conception of a potential drug target through the proof of concept and eventually into clinical trials. Clinical studies are an essential part of the development and registration of new innovative medicines, biosimilars and generics. These studies are possible only because subjects consent to participate and test new medicines. The ethical principles that protect the safety and well-being of the clinical study subjects are outlined in the Declaration of Helsinki.

Information on clinical studies and their results serves patients and their healthcare providers directly, as well as the public at large. Such information can help interested individuals make informed decisions about their potential participation in a clinical study. For clinical study registration and results reporting, there are a number of national requirements that vary between countries and are continuously evolving. In May 2005, Novartis became one of the first pharmaceutical companies to publish clinical trial results for innovative medicines, regardless of outcome, on a publicly accessible website: www.novartisc clinicaltrials.com. This site includes the results from all phases of interventional trials for innovative products within one year after each trial is completed.

While disclosing trial results is vital, the summaries can be too technical or scientific for the general public and patient populations to make use of. In 2016, we therefore began providing non-technical summaries to patients participating in Phase I/IIa interventional general medicine clinical trials. In 2017, we began providing non-technical summaries to trial investigators to share with their patients for Phase IIb and III studies for our interventional innovative medicine trials initiated within the year. These will be published on www.novartisc clinicaltrials.com alongside the technical summaries.

Together with preclinical safety data, the adverse events collected in clinical trials and spontaneously reported for marketed products provide critical information for characterizing the safety profile of a drug. This safety data is closely scrutinized by regulators when assessing whether the benefits of a drug are expected to outweigh the potential risks, which is a prerequisite for gaining marketing approval and keeping the medicine on.

the market. Post-marketing pharmacovigilance activities play an important role in our ability to gain a deeper understanding of the safety profile of a specific product once it is approved for marketing and becomes available to a wider number of patients in normal clinical practice.

For example, each year the Novartis Chief Medical Office and Patient Safety Organization (CMO & PS) must oversee the submission of more than a million individual case safety reports (ICSRs) to health authorities worldwide – reaching more than 1,500,000 in 2017. Compliance in reporting ICSR to health authorities remained at a very high level across divisions and even increased marginally in the Innovative Medicines and Alcon Divisions in 2017. These ICSR record any adverse events experienced by patients using our medications and are an important source of pharmacovigilance data. Taken together, they form the basis for periodic safety update reports (PSURs), which provide an update on the global safety profile of a medicine and conclude with a risk-benefit balance. PSURs are also submitted to health authorities, who confirm the positive risk-benefit balance of our medicinal products and verify that they remain safe to be on the market. The CMO & PS has excelled in this area, with consistent rates of above 99% in 2017 for on-time regulatory submissions.

The Novartis safety risk management process begins early in the development of new products. Safety management teams (SMTs) develop safety monitoring and risk management plans for each product when it enters development. These plans are regularly updated as new safety information for a product becomes available.

Significant safety- and product-related risks are escalated to the Portfolio Stewardship Board (PSB). The PSB is a standing, cross-functional senior executive board that is chaired by the Head of CMO & PS and that reports to senior management in Global Drug Development. Its decisions and recommendations are made independently of project teams and business franchises, with the intent to put patient safety first.

Many of our clinical trials employ third-party/external service providers (ESPs) that deliver various support services. We recognize the need to ensure all ESPs meet the standards to which we hold ourselves accountable. In 2017, we therefore created a new organization within Global Drug Development called the External Development Organization, which functions as a central hub for global supplier oversight.

Our reputation as a healthcare provider is founded on the quality of our products. It is our obligation and commitment to deliver reliable and safe medicines on time, every time – and our Quality organization safeguards our ability to do this. The team’s scope is broad: It must ensure the quality of our products over their entire lifecycle, from the early stages of product inception, through clinical development, manufacturing and supply, all the way to market exit or withdrawal. The team also helps support and control activities for the design, conduct, safety management, monitoring, reporting and documentation of clinical trials.

We can measure the success of our Group quality activities through a number of indicators. Health authority inspections of our manufacturing facilities are one way to determine if we are on track. Regulatory inspections with no major findings remained high at 99.1% in 2017, and all were deemed good or acceptable, except for a Russian Ministry of Industry and Trade inspection at Alcon’s plant in Puurs, Belgium, which requires further action before being closed out.

**Health education and prevention**

Patient education and awareness is an important step in improving health and well-being, and in increasing disease prevention and health-seeking behavior. We consistently engage in education and awareness activities in disease areas across our portfolio. Partnerships (Sustainable Development Goal 17) across the public and private sectors are key to the way we work.

The Novartis Foundation has an array of projects focused on interrupting the transmission of leprosy, with the ultimate goal of eliminating the disease. These include efforts to improve early detection by developing a molecular diagnostic test and a remote diagnostic tool, strengthening screening programs, and implementing education campaigns to increase awareness about the disease.

The foundation is also looking at ways to interrupt transmission through leprosy post-exposure prophylaxis (LEPP) by providing preventative treatment to close contacts of newly diagnosed patients – such as family members and friends – to decrease the risk of transmission. This program, initially launched in 2014, is now running in Indonesia, India, Nepal, Myanmar, Tanzania, Sri Lanka and Brazil.

Additionally, the Novartis Foundation is working with many partners to address hypertension around the world. In October, the foundation launched Healthy Schools for Healthy Communities together with the University of Basel and other partners. Known locally as KaziBantu, the initiative aims to address poor health in disadvantaged schools in South Africa and is the first

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**Pharmacovigilance, safety profile and quality of drugs performance indicators**

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<th>2017</th>
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<td>Health authority regulatory reporting (ICSRs) per division (%)</td>
<td>Innovative Medicines: 99.2</td>
<td>Sandoz: 98.8</td>
<td>Alcon: 97.4</td>
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<tr>
<td></td>
<td>Sandoz: 96.9</td>
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<td>Alcon: 94.9</td>
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<td></td>
<td>Alcon: 96.5</td>
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<td>Regulatory inspections without major findings (%)</td>
<td>99.1</td>
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1 Compliance by division can only be reported from January to November 2017 due to a change in European regulation as of November 22, 2017, resulting in a change in our reporting configuration.

2 ICSR: individual case safety reports
Novartis Foundation program to involve the education sector. The ultimate goal of Healthy Schools for Healthy Communities is to improve the cardiovascular and overall health of schoolchildren and their teachers.

The Novartis Healthy Family programs are also continuing to evolve. Launched 10 years ago in India under the name Arogya Parivar, Healthy Family is an essential public health tool. Arogya Parivar offers effective, low-cost medications against infectious and chronic diseases that are prevalent in rural India. Healthy Family programs also operate in Kenya (Familia Nawiri) and Vietnam (Cung Song Khoe), and are roughly the same across countries: A social arm conducts health education activities, while a separate commercial arm is responsible for product promotion. Over the years, however, we have learned that we cannot simply replicate a model, given the differences in healthcare infrastructures and systems, stakeholders, regulatory environments and local competition. For example, the program we launched in Indonesia never took off – partly because we only had one product to offer, and also because our operations on the ground were lacking – and it was discontinued in 2017.

Overall, since 2010, more than 40 million people in rural areas have attended health education sessions held by our Healthy Family programs, and more than 3 million patients have received diagnoses and treatments at health camps. Novartis plans to expand Healthy Family to more countries and disease areas in the coming years, while exploring partnerships with other companies and organizations that have complementary expertise and products.

In a partnership with apparel company Levi’s and its supplier Aquarelle, health workers from the Arogya Parivar program in India will train 50 Aquarelle factory workers and supervisors to serve as peer health educators on health topics, including women’s health. These trained workers will then be able to deliver basic health education to their 1000 co-workers in biweekly sessions, supporting the nurse and physician who provide healthcare services at the factory.

In an effort to further strengthen its coffee supply chain in Kenya, Nestlé is partnering with Familia Nawiri to bring health information and care to coffee farmers. A pilot is underway whereby the cooperatives pay in advance the regular USD 2 fee for coffee farmers to attend Familia Nawiri health camps when they are unable to pay out of pocket. This system enables farmers to access healthcare services when they need them, even if they have no cash in hand. Cooperatives usually pay farmers twice a year and deduct this amount when they pay the farmers for their coffee beans.

We are also exploring a collaboration with agribusiness Syngenta; the Kenya Tea Development Agency, one of the largest tea management companies in Kenya; and Living Goods, an NGO that supports health entrepreneurs who teach families how to improve their health and wealth. In particular, we are planning on running health camps in tea-growing areas and other agricultural estates to offer screening, diagnosis and treatments to farmers. We aim to leverage Living Goods’ large network of “Avon-like” health entrepreneurs who go door-to-door to incorporate Familia Nawiri activities in two specific counties.

Photo  Women in the US city of Philadelphia participate in a yoga event run by Living Beyond Breast Cancer, a group that provides information and support for patients and their families.
Counterfeit medicines

We believe counterfeit medicines, including both innovative medicines and generics, pose a significant threat to public health. This is especially true since patients are generally unable to distinguish between authentic, falsified and counterfeit products. Solving the issue requires an ongoing commitment not only from national governments and international health organizations but also from the pharmaceutical industry and other healthcare stakeholders, such as pharmaceutical distributors.

With regard to our own portfolio, we take a diverse and multipronged approach. This includes continuously monitoring and improving the security of our distribution chain as well as the security of our product packaging. We investigate and use various technologies to serialize, track and verify products. Serialization is the process of creating a unique number that is applied to each product to provide visibility and full traceability within the supply chain – from the manufacturer to the distributor to the dispensing point (e.g., wholesalers and pharmacists). It is therefore one technology that helps decrease the number of falsified products that enter the legitimate supply chain. We have also implemented a verification features system that enables a fully automated, fast and secure verification of our innovative medicines products, and we monitor our trademarks globally as another mechanism to detect falsified and counterfeit products.

We investigate all reported cases of falsified and counterfeit Novartis products, regardless of where they are made available, including the internet and local markets. All Novartis associates can access a standardized electronic reporting tool for suspected counterfeit and falsified products. We also maintain a global intelligence effort and investigate illegal supply chains to identify the manufacturers, distributors, importers and exporters of falsified and counterfeit medical products, and then report confirmed cases to local law enforcement and health authorities. During 2017, Novartis Global Security, with the support of local law enforcement and health authorities, initiated seizures of counterfeit and falsified products in more than 30 countries globally. As a result, nine illegal pharmaceutical manufacturing facilities and assembly lines were dismantled, dozens of illegal trading and distribution operations were shut down, falsified and counterfeit medical products found on site were seized, and criminals were prosecuted. More than 7,300 illegal online pharmacies, many of which were large clusters operated by criminal organizations, were also shut down. To raise awareness about the dangers of pharmaceutical crime and the necessity of joint collaboration from all stakeholders, Novartis also actively engaged in training of almost 1,000 law enforcement and health authority officials in more than 20 countries.

Our anti-counterfeiting program is governed by a Security Steering Group that comprises three ECN members, including the Group General Counsel; an Anti-Counterfeiting Steering Committee, also sponsored by a member of the ECN; and an Anti-Counterfeiting Working Group composed of representatives from 11 core functions within Novartis. An Anti-Counterfeiting Guideline has been in effect since November 2016, and a position paper on counterfeit and falsified medical products has been publicly available since July 2017.

Counterfeit and falsified products are especially prevalent for malaria medicines in Africa. It is estimated that up to half of malaria patients there buy antimalarial medicines from the private sector, at local market stalls and drug stores. This carries with it the increased risk of purchasing sub-standard or counterfeit medicines because they are cheaper and available. In addition to conducting several market surveys in African countries in 2017, and initiating and supporting subsequent enforcement operations, we are exploring novel distribution channels to improve access to our high-quality antimalarial for people relying on the private sector.

How we perform

Patient health and safety has always been a top priority at Novartis. In 2017, we took further steps to incorporate the patient perspective more deeply into how we run our business. From a safety perspective, our more centralized Group Quality, medical and patient safety organizations help ensure that patients can be confident in the safety, efficacy and quality of our medicines.

While thorough quality and safety systems are necessary to protect the well-being of patients taking our medicines, we must also continuously work with patients and groups representing them to capture their perspectives and ensure that our medicines, clinical trials and other activities are helping patients overcome health challenges.

Our soon-to-be-published Commitment to Patients and Caregivers is planned to be the foundation for all our patient-related activities, and we intend to incorporate patient perspectives into our research, development and commercial activities to an even greater extent. The process to include the patient perspective in clinical trials has been defined, and several projects have been documenting the benefits. For 2018, this means that we will increase our efforts to seek out and use insights from the patient community to inform our decision-making processes, including expanding access to our medicines and improving access to and participation in clinical trials.

At the same time, our anti-counterfeiting efforts continue to make progress, both internally (through our multipronged approach to better monitor our medicines) and externally (through our work to better track down medicines that are fake).

Our health education programs are also growing and, perhaps more importantly, evolving. We are exploring the possibility of expanding our Healthy Family programs into new countries and therapy areas. We are also looking at additional partnerships with other companies and organizations that have complementary expertise and products. The Novartis Foundation takes a strategic approach, working hand-in-hand and on the ground with partners on projects addressing local health needs. The foundation acts as a catalyst, with the ultimate goal of helping evolve every project into scalable and sustainable healthcare solutions and policies that can improve health outcomes long after our involvement ends.