



Annual Responsibility Review 2016



2016 was a transformative year for Shire. We are bigger and more impactful now, but our focus is the same: to meet the needs of people around the world with rare diseases. As we evolve and strengthen our leadership position, our approach to Responsibility will be fundamental to our success and our ability to help people with life-altering conditions to live better lives.

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Jonus – Living with Hemophilia

Jonus is now in elementary school. His mom, Athena, and the rest of his family are doing everything they can to make sure Jonus gets to enjoy his childhood. Whether that's riding his bike, listening to music or playing computer games.

This is Shire

Shire is the leading global biotechnology company focused on rare diseases. We research, develop, and market innovative medicines that have the potential to transform the lives of people with rare – and often unmet – medical needs.

Our focus on rare diseases

Rare diseases are often misunderstood, under-diagnosed, and are potentially life threatening. With a sharp focus in this area, we strive to address significant unmet needs in order to transform patients' lives and place underserved patient communities at the center of all we do.

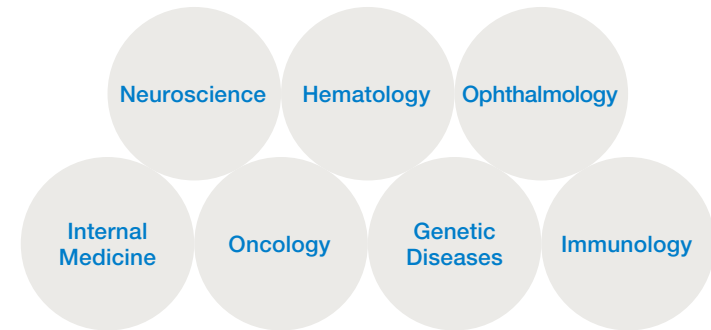
Rising to the challenges associated with our core purpose requires unique capabilities. This is why we aim to attract and nurture outstanding talent, and encourage all of our employees to contribute at their full potential. We have approximately 24,000 employees who come to work every day with a common goal: to develop and deliver breakthrough therapies that enable people with life-altering conditions to live their lives to the fullest.

Our strategy

At Shire, we are dedicated to building and sustaining leadership across our seven therapeutic areas. Through our extensive product portfolio, innovative development pipeline, and collaboration with partners across the healthcare ecosystem, we strive to earn the trust of our patients, their families and physicians, and all others who support and advance their care. Working together, the possibilities for our patients, healthcare partners, employees, and shareholders are remarkable.

More details are available in our Annual Report at shire.com

Our therapeutic areas



Global reach



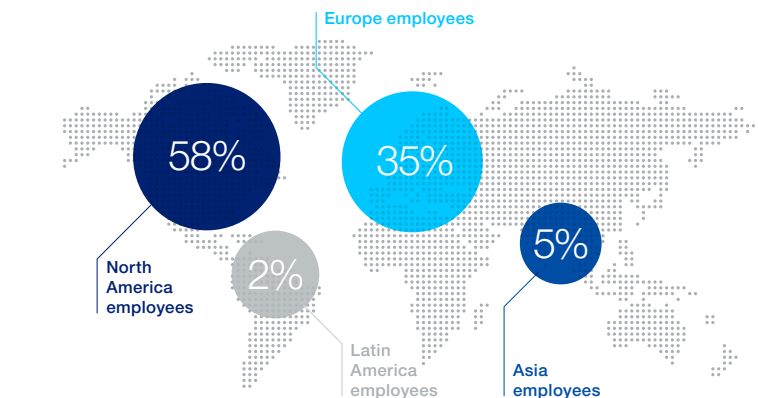
100+

Our products are available in more than 100 countries.



68

We have offices in 68 countries.



24,000 employees

We now sell our products in over 100 countries and have roughly 40 programs in clinical development, of which about 20 are in the later stages of development. We employ approximately 24,000 talented people and have commercial operations in 68 countries. We are committed to developing a diverse organization that values all genders, cultures, ages, and experiences.

Chief Executive Officer's letter



2016 was a transformative year for Shire, in which we became the leading global biotechnology company in rare diseases.

Along with our employees around the world who bring their incredible talent and passion to work every day, I'm proud of the milestones we've achieved in service to patients and all those who support them on their journey. I also know that we have only scratched the surface and that, as a global leader, many great responsibilities lie ahead.

Responsibility and responsible leadership permeate everything we do. At Shire, we address significant unmet medical needs and work tirelessly to improve people's lives with breakthrough medicines. Meeting the fundamental objective of responsible leadership is by no means a simple proposition. It is a challenging endeavor that depends on the efforts of our entire organization and the partnerships and trust we develop with our patients and stakeholders.



Together we have a unique opportunity to place underserved patient communities at the center of all we do and have a positive impact on society.



Flemming Ornskov, MD, MPH
Chief Executive Officer

Throughout 2016, we embarked on a number of key activities to improve our approach to Responsibility. First among these was reaffirming our steadfast commitment to Responsibility within our newly combined Company, following our acquisition with Baxalta. During the year we laid solid foundations, including an examination of our most material Responsibility issues and merging many of our related policies, systems, and processes as a newly combined Company.

I am eager to build on the work that we've done and extend our role as a champion for patients and a role model for responsible leadership. We will achieve this by attracting, retaining, and developing our talent, and managing our operations in an ethical and sustainable way. In 2017, we will bring all these areas together to define a long-term strategy for Responsibility.

Our approach to Responsibility thus far has continued to gain recognition. We are a constituent in the FTSE4Good Index Series and ranked first in Newsweek's 2016 Green Ranking. We were also named Pharma Company of the Year by Scrip Intelligence, a significant recognition awarded annually by industry peers, for our enduring commitment to serving patients and families affected by rare diseases.

I am honored to work alongside my colleagues at Shire. Together we have a unique opportunity to place underserved patient communities at the center of all we do and have a positive impact on society. I invite you to explore our Responsibility highlights and progress in this 2016 Annual Responsibility Review.

As always, I thank you for your continued support and partnership.

Sincerely,

Flemming Ornskov, MD, MPH
Chief Executive Officer

Gaining recognition

FTSE4Good

In 2016, we remained a constituent of the FTSE4Good Index Series, a leading responsibility investment index.

Newsweek's Green Ranking

We were ranked as the 'greenest' company in the world from Newsweek, improving on our position of second last year.

Pharma Company of the year

We were named Pharma Company of the year by Scrip Intelligence, a recognition awarded by industry peers for our commitment to serving patients with rare diseases.

Highlights from 2016

We are proud of our accomplishments in 2016 and we will continue to work towards achieving our Responsibility ambitions.



\$1.3bn

invested in targeted R&D during 2016.



60,000

patients supported by our U.S. patient assistance programs.



\$11m

provided in educational grants.



37

clinical programs in our development pipeline.



\$254m

spent on small businesses in the U.S. as part of our Supplier Diversity Program.



Shire's Global Day of Service

In October, we hosted our second annual Global Day of Service. More than one-third of our workforce participated in over 150 volunteer projects worldwide. A total of 25,000 hours were given to community organizations that, in many cases, help children overcome odds.

25,000
volunteering hours

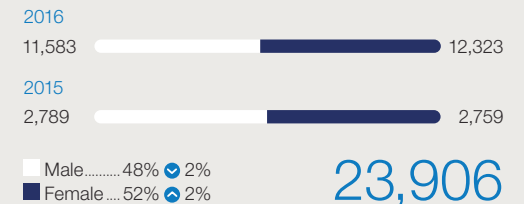
Employee statistics

Employment by region as at Dec 31, 2016

North America.....	58%
Europe.....	35%
Latin America.....	2%
Asia.....	5%



Shire global employees gender split as at Dec 31, 2016



[READ MORE ON PAGE 34 →](#)

Highlights from 2016 continued

CEO Awards

Our CEO Awards are given to colleagues who have demonstrated outstanding performance, making a significant difference to our stakeholders and colleagues, and, most importantly, in the lives of our patients. In 2016, 164 employees from nine countries received an individual or team CEO Award.



Over
\$100,000
saved

Our facility in Vienna, Austria, implemented multiple energy conservation projects, such as converting to LED lighting and optimizing cooling and ventilation. These efforts made annualized savings of over \$100,000 and reduced energy consumption by 1.6 million kWh.

ShireLearns Hub

This year, we launched the ShireLearns Hub, a new online platform that provides employees with access to training, webinars, reading material, and links to partner sites. Since launch, 4,500+ employees have used the resource.



\$3m

committed over three years to the SeriousFun Children's network.

SeriousFun Children's Network

In February of 2016, we committed \$3 million over three years to SeriousFun Children's Network, a global non-profit organization comprised of 30 camps and programs serving children with serious illnesses and their families, always free of charge. SeriousFun Children's Network aims to foster independence, resilience and personal growth, and help children to see beyond the limits of their medical conditions.

Our support will enable nearly 1,000 children, many with rare diseases, to attend SeriousFun's transformative camps and Family Weekend programs. In the summer of 2016, 15 Shire employees from around the world had the unique chance to volunteer as counselors at SeriousFun camps, volunteering over 1,500 hours with campers. In total, our employees donated approximately 5,000 hours of volunteering with SeriousFun through on- and off-site programming throughout the year.

Global EHS policy

One of our most important tasks in 2016 was to develop Shire's new global Environment, Health, and Safety (EHS) policy for our newly combined Company. This policy outlines our commitments, within our operations and across the entire value chain.



66%
of total waste diverted from landfill.

21st Century Cures Act

We played a fundamental role in shaping U.S. healthcare legislation through the 21st Century Cures Act. The Act was passed in December 2016, paving the way for improved services and training for Medicare patients with Hemophilia.

Our approach to Responsibility

Responsibility is central to our overall success

Responsibility is deeply embedded within our organization. Our approximately 24,000 employees lead the way in ensuring we have a positive impact on society. In addition to their day-to-day focus on underserved patient communities and a commitment to doing the right thing at work, they are also involved in our communities.

Meeting ever-changing stakeholder expectations and anticipating emerging risks, issues, and opportunities continue to be integral to how we run our business, ensuring we stay accountable for our social, economic, and environmental impacts.

Our approach to Responsibility is divided into four broad areas as described in this report.

1

Supporting our patients

Every day, we strive to make a meaningful difference in the lives of the patients who count on us. This is our primary Responsibility. It starts with understanding and responding to the unmet needs of patients, families, and caregivers affected by rare diseases. Part of this involves raising awareness of the conditions we treat and providing evidence-based information to help patients receive accurate and timely diagnosis and treatment. We also strive to break down barriers limiting availability, access, and affordability of treatments once patients have been diagnosed. We believe that the best way to deliver on these responsibilities is through collaboration with patients, industry leaders, and advocacy organizations in our key therapeutic areas.

[READ MORE ON PAGE 11 →](#)

2

People and culture

Our approximately 24,000 employees come to work every day with a common purpose: to develop and deliver breakthrough therapies that enable people with life-altering conditions to live their lives to the fullest. But we can only be truly successful if we attract, develop, and retain world-class employees, provide them with a safe work environment, and promote healthy lifestyles and behaviors. By investing in training and development, we aim to create a high-performing, healthy, and inclusive workplace where everyone is encouraged to excel.

[READ MORE ON PAGE 26 →](#)

3

Sustainable operations

Managing the environmental and social impacts of our operations, products, manufacturing, and sourcing is an important part of our commitment. We work with business partners, contractors, and suppliers to ensure the products we deliver are safe, effective, and of the highest quality. Operating responsibly and using resources efficiently involves setting and living up to exacting standards, and supporting our partners and suppliers in doing the same.

[READ MORE ON PAGE 35 →](#)

4

Ethics and transparency

Upholding high standards of ethics and transparency is fundamental to everything we do. We hold ourselves accountable for operating ethically and responsibly and ensure we are transparent with our stakeholders. This includes implementing the right policies and procedures so that we meet the highest standards of integrity across all parts of our business and in all our business relationships.

[READ MORE ON PAGE 44 →](#)

Our approach to Responsibility continued

Responsibility within our newly combined Company

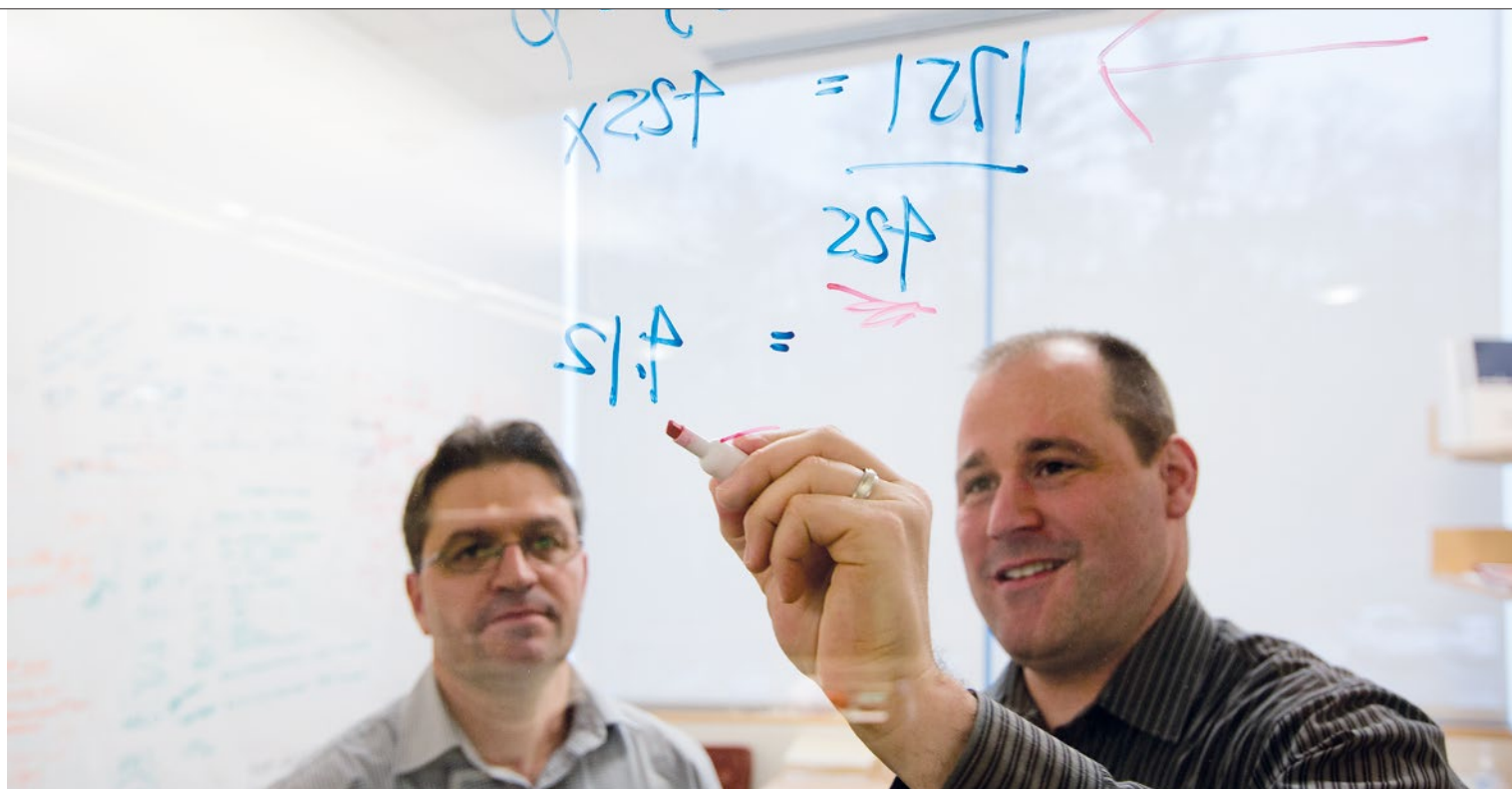
A key component of our approach to Responsibility is looking to the future to identify opportunities where we can use our skills and resources for the greatest impact. With our significant growth and changes in 2016, we commissioned external Corporate Responsibility consultants to conduct an extensive materiality assessment to identify and help prioritize our Responsibility issues.

Our materiality process

To conduct our Responsibility materiality assessment, we consulted a comprehensive set of information sources, beginning with more than 40 internal and publicly available documents to develop Shire's material issue list. From this initial review we identified nearly 300 topics across our value chain. These topics were then amalgamated into Shire's top 20 Responsibility issues.

To prioritize the issues, we engaged more than 30 functional leaders across the Company, gathering input on how the issues could impact Shire's business today and in the future. To assess their input, we considered the following criteria:

- The degree of impact the issue may have on [Shire's four strategic drivers](#) of growth, innovation, efficiency, and people.
- The degree to which the issue is significant to Shire's patients, operations, and manufacturing and sourcing footprint.
- The extent of Shire's ability to directly influence the issue.



We also engaged more than 20 external stakeholders – including patient organizations, supply chain experts, investors, policy and media specialists, and industry and non-profit leaders – to gain their views on the issues most relevant to Shire. We conducted additional assessments with supply chain experts and investors to deepen our understanding of these stakeholder groups' expectations of our newly combined organization.

To capture the viewpoints of our employees, we also ran a Responsibility materiality survey for all employees and received over 5,500 responses.

We completed our research with a workshop for members of Shire's Responsibility Sponsor Network — a group of senior leaders dedicated to implementing Responsibility strategies across the organization — to discuss and validate the materiality results.



5,500

We ran a Responsibility materiality survey for all employees and received over 5,500 responses.

Moving forward

Over the coming months, we will work to understand our key challenges and opportunities and refine our efforts to meet the evolving needs and expectations of all our stakeholders. Our aim is to define a long-term, sustainable Responsibility strategy with clear metrics and goals. We will also continue to monitor other issues that may rise in significance and become increasingly important to our business, our patients, and key stakeholders.

Our approach to Responsibility continued

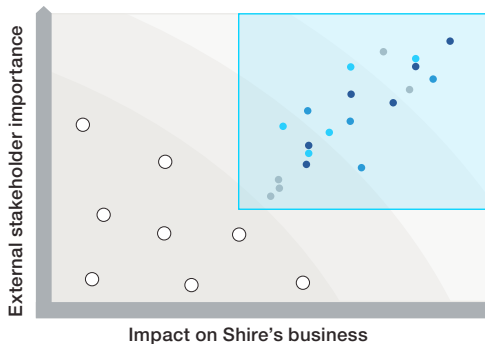
Shire's Responsibility materiality matrix

The Responsibility materiality assessment has reaffirmed the ongoing priority of several top issues, including improving access to medicine and ensuring product quality, safety, and efficacy. It also highlighted the importance of attracting and developing Shire's talent, and ethics and transparency.

Given the increased size and scope of our newly combined Company and our greater focus on operational sustainability and third party manufacturing and sourcing, the assessment highlighted several growing areas of importance, including responsible manufacturing and sourcing, and addressing key environmental impacts across the value chain.

The materiality matrix to the right shows our prioritized Responsibility material issues. The issues in the upper-right region represent some of the greatest opportunities for us to make a positive impact on business and society, due to their high importance to stakeholders and to our business. Issues in the lower-left region are of fundamental or emerging importance to Shire and our industry, requiring continued diligent management. All issues on this matrix are important to Shire and our stakeholders.

Complete universe of material issues



Top 20 Responsibility Material Issues



* Matrix is not drawn to scale

Our approach to Responsibility continued

Governing Responsibility

From our Executive Sponsor for Responsibility, who is a member of Shire's Executive Committee, to our core Responsibility team and champions across the Company, we have voices promoting Responsibility throughout our organization.

Our overall approach to Responsibility is championed by our CEO, supported by the Executive, In-line, Pipeline, and Corporate Committees, and endorsed by Shire's Board of Directors.

Our Responsibility Sponsor Network is critical to shaping our Responsibility efforts. Alongside our Executive Sponsor, the Network comprises nearly 20 senior leaders and advisors who provide strategic advice and help execute Responsibility initiatives within their functions.

The Network also includes leads for specific issue areas, many of which have been highlighted through our Responsibility materiality assessment. These Network leads are responsible for developing strategies and goals for their respective focus areas and monitoring progress.

Our core Responsibility team supports the Responsibility Sponsor Network and manages other Responsibility working groups. It also oversees internal and external Responsibility communications and works with sponsors and stakeholders to identify risks and opportunities.

This year we joined the Pharmaceutical Supply Chain Initiative, (PSCI), to access useful resources that will help us develop and maintain a responsible supply chain.

PSCI

PHARMACEUTICAL SUPPLY CHAIN INITIATIVE

Stakeholder engagement

Engaging thoughtfully with our key stakeholders plays a central role in defining our approach to Responsibility. Our key stakeholders include patients, physicians, advocacy organizations, industry associations, policymakers, business councils, supplier groups, investors, and, of course, our own employees.

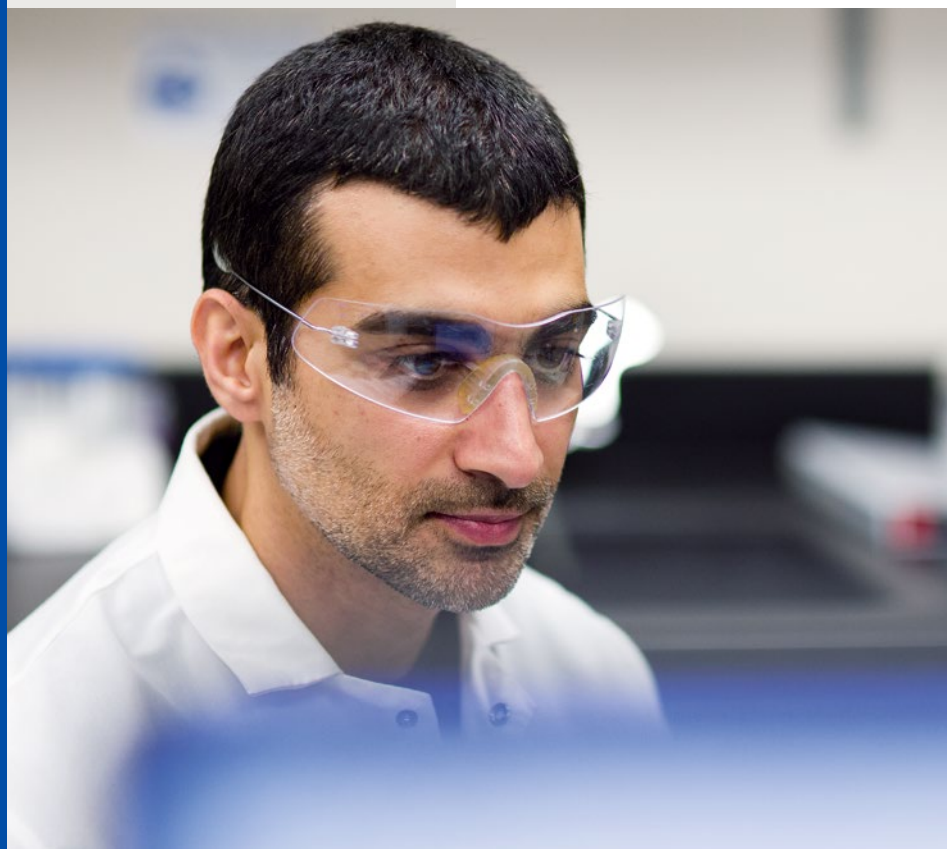
To understand what matters most to them and how we can best address their needs and expectations, we consult with our stakeholders on a range of topics and issues. These include our approach to Responsibility, performance

and reporting, our role in improving access to medicines, and how we help raise awareness of rare diseases. We also communicate our Responsibility priorities and performance through our Annual Responsibility Review and other communications, such as social media, shire.com, and investor presentations.

In 2016, we engaged in a number of industry initiatives focused on Corporate Responsibility. We joined the Pharmaceutical Supply Chain Initiative (PSCI) to access useful resources that will help us develop and maintain a responsible supply chain. We also continued to participate in Business for Social Responsibility's (BSR) Healthcare Working Group, which focuses on the latest issues and trends in the industry, particularly relating to barriers that prevent people accessing healthcare.

Understanding the needs and concerns of our patients is a central priority. In 2016, we continued to partner with patients and patient advocacy organizations to gather vital input and feedback on how our products are helping meet critical health needs. Examples of how we have engaged with these groups can be found in the Supporting our patients section (page 11).

These examples provide a demonstration of our commitment to meaningful stakeholder engagement, where we share our work and how we learn directly from stakeholders. Only by listening to and understanding our stakeholders, especially our patients, and incorporating this learning into our business, can we achieve our goal of making a difference in the lives of our patients and their families.



37

We now have 37 programs in clinical development, including approximately 20 in the later stages; the deepest, and most innovative, pipeline in our 30-year history.

1

Supporting our patients

We strive to make a meaningful difference in the lives of patients with rare diseases. This is our primary Responsibility.

It starts with understanding and responding to the unmet needs of patients and their families and caregivers. We work to break down barriers limiting availability, access, and affordability of treatments. We work in partnership with others to build understanding of the conditions we treat.

- 12 Access to medicines
- 17 Awareness, advocacy, and responsible product use
- 22 Supporting patient and local communities



Access to medicines

Why it matters

There are more than 7,000 known rare diseases affecting 350 million people¹ worldwide. Currently, treatments only exist for 5 percent of these². We are dedicated to improving the lives of rare disease patients by developing innovative treatments and are committed to improving access to essential treatments for those who need them.



5%

Some 7,000 rare diseases have been identified, yet treatment exists for only 5 percent of them.

We are committed to helping people with rare diseases get the correct diagnoses for their conditions as quickly as possible. Receiving the correct diagnosis for a rare disease can be a significant challenge. A typical rare disease patient may see eight doctors — four primary care doctors and four specialists — and receive two to three misdiagnoses before the correct one is given. For those diagnosing, part of the challenge is that rare diseases often hide behind the symptoms of more common illnesses, which makes diagnosis extremely difficult, particularly in children. Beyond the issue of correct diagnosis, living with a rare disease can cause social isolation, economic disadvantage, and emotional strain, which make access to treatment more of a challenge.

Our approach

At Shire, we use our specialist knowledge and expertise to develop innovative treatments and therapies that fulfill unmet patient needs. We help patients access the medical treatment they need by focusing on three areas: **availability, accessibility, and affordability.** Within our newly combined Company, we have been working to expand access programs for our newest therapeutic areas: Hematology, Immunology, and Oncology.

Expanding availability

Improving access to medicines is not only about ensuring that existing treatments are more readily available — it's also about developing innovative, new medicines for rare conditions and disorders. Rare diseases are often the most severe, life-altering and complex conditions, and they disproportionately impact children. Although each disease may only affect a small number of people, we are committed to making scientific breakthroughs in rare diseases where no therapy currently exists. The experience and understanding of rare diseases held by patient associations are invaluable to our research and we work closely with these groups during new treatment development.



I am inspired every day by our brave patients and their families, as well as our team that works to ensure patients have access to their therapies.



Sara Becker
Patient Services Marketing Lead

¹ Global Genes. Global Genes Factsheet on Rare Diseases Available at: <https://globalgenes.org/rare-diseases-facts-statistics/>

² Miyamoto BE, Kakkis ED. The potential investment impact of improved access to accelerated approval on the development of treatments for low prevalence rare diseases. Orphanet J Rare Dis 2011;6:1-13. [page 1]

Access to medicines continued

Improving accessibility

It is important to remove the barriers that prevent patients from accessing the medicines they need. These can include insufficient local healthcare capacity or a lack of suitable transport. With rare diseases, there is also a high chance that healthcare professionals may not have seen a particular condition before. This lack of familiarity and experience can contribute to a long and often frustrating path to diagnosis. Once diagnosed, patients often have to travel long distances to reach specialist centers for the right treatment. The infrastructure for supporting people with rare diseases varies significantly between countries and we work with healthcare providers, patient associations, non-profit organizations, and government bodies around the world to overcome any issues associated with accessibility.

Increasing affordability

We believe that the cost of medical treatments should not be a barrier to patient access. In the U.S., we provide patient assistance programs to help those struggling to afford their treatment. Outside of the U.S., we currently have 10 patient assistance programs in five countries (Argentina, Canada, Chile, China, and Uruguay) in the areas of Hematology, Immunology, Genetic Diseases and Internal Medicine. More broadly, we work to develop a global environment in which treatments can better reach those who need them, through compassionate or early access programs. We aim to partner with rare disease communities to support and inform the stakeholders involved in making decisions about the regulation, funding, and policy for rare diseases.

Read more online

Our position on [Access to Innovative Treatments](#)

Our position on [Offering Compassionate Use to Investigational Medicines](#)



\$1.3bn

We invested \$1.3bn in targeted R&D during 2016, representing 11 percent of Shire's revenue.



60,000

Our U.S. patient assistance programs reached approximately 60,000 patients.



37

We have 37 programs in clinical development, the most robust pipeline in Shire's history.



85,356

We performed 85,356 free diagnostic tests for Fabry, Gaucher, and Hunter diseases, a 139 percent increase from 2015.

What we did in 2016

Improving diagnostic pathways for rare disease patients

It can take longer to diagnose rare diseases than many common diseases. On average, rare disease diagnosis takes 7.6 years in the U.S. and 5.6 years in the UK¹. Rare diseases such as the primary immunodeficiency (PI) disorders Gaucher disease, Fabry disease, and Hunter syndrome can be devastating, as they are difficult to detect and equally difficult to treat.

In 2016, we expanded our free diagnostic testing in more than 50 countries to identify Fabry, Gaucher, and Hunter patients. The service provides physicians with a free diagnostic kit, comprised of a Dried Blood Spot (DBS) card, return envelope, and optional patient consent form. This year, 85,356 tests were performed, 139 percent more than in 2015, and the testing identified 1,164 new patients, an increase of 63 percent from 2015.

We also partnered with the U.S.-based Jeffrey Modell Foundation (JMF) in 2016 to develop software to flag patients at high risk of PI disorders in the U.S. This program has increased the average annual number of patients diagnosed by 79 percent. We also worked with JMF, the International Patient Organization for Primary Immunodeficiencies, and other organizations to support newborn screening in a number of countries for SCID (Severe Combined ImmunoDeficiency), one of the most severe forms of PI.

¹ Shire. Rare disease impact report: Insights from patients and the medical community, April 2013



Access to medicines continued

Dry Eye Disease

In 2016, the U.S. Food and Drug Administration (FDA) approved XIIDRA®, the first commercial drug approved to treat the signs and symptoms of Dry Eye Disease. We also launched the eyelove™ educational awareness campaign, to raise awareness and understanding of chronic dry eye symptoms, and encourage people to make eye health a priority.

Expanding access to Hemophilia treatment

This year, we improved access to Hemophilia care in Poland, ensuring all Hemophilia patients now have access to preventative treatment. In the U.S., we worked with the National Hemophilia Foundation to ensure that care standards for hundreds of Hemophilia patients would not be affected by a step therapy or 'fail first' program proposed by insurers. This means that patients will be able to access the most appropriate and most effective treatment, rather than waiting for other treatments to fail first.

Improving health insurance literacy

If patients struggle to understand how their health insurance works, they may be at risk of missing out on vital treatment. Increasing health insurance literacy, particularly among vulnerable groups, helps rare disease patients build a strong case for optimal care.

MylgSource is one of our programs, which supports patients with PI. This program helps patients understand their insurance and financial support options, puts them in contact with nurse advocates who answer questions about Shire's Immunoglobulin (Ig) treatments, and provides educational resources and tools to manage PI.



250,000

In 2016, 250,000 calls were made or received by OnePath on behalf of patients.

Increasing affordability through dedicated patient assistance programs

We are committed to providing help and support to patients to make sure they get the Shire medicines they may be prescribed. In 2016, our U.S. patient assistance programs reached approximately 60,000 patients.

Shire Cares™ is a U.S. initiative that helps patients with limited financial resources and no prescription insurance. In 2016, Shire Cares helped over 42,000 patients to access medication and treatments for conditions such as ulcerative colitis, Attention Deficit/Hyperactivity Disorder (ADHD), Adult Binge Eating Disorder (BED), Dry Eye Disease, Epilepsy, and end-stage Renal Disease.

OnePath® is another of our U.S. programs supporting access to treatment for patients living with Type 1 Gaucher Disease, Hereditary Angioedema (HAE) and Hunter Syndrome (MPSII), and other conditions such as Short Bowel Syndrome (SBS) and Hypoparathyroidism. Since its inception, OnePath has helped more than 9,000 patients. To help navigate the path to treatment, Patient Support Managers provide streamlined product support, answer insurance and coverage issues, and work with specialty pharmacies to facilitate access to treatment. In 2016, over 250,000 calls were made or received by OnePath on behalf of patients.

Access to medicines continued

Charitable access program

Our charitable access program improves access to treatment and care for patients with Lysosomal Storage Disorders (LSDs) and Hemophilia in 15 countries in Africa, Latin America, and the Middle East. LSDs and Hemophilia affect people all around the world — not just in countries where treatments are available.

This program brings together the collective expertise and resources of Shire, non-governmental organizations (NGOs), medical experts, and patient advocacy organizations to improve infrastructure and build capability in specific countries. This includes raising disease awareness, providing diagnosis education, and developing treatment expertise. We also launched a LSD training program in partnership with FYMCA Medical. This program aims to build knowledge and capability for physicians and increase disease awareness in developing countries.



20

About 20 of our clinical development programs are late-stage programs, and most are expected to launch by the end of 2020, subject to regulatory approval.

Advancing R&D through collaboration

In 2016, we continued to develop our pipeline of new treatments. We focus our research and development (R&D) efforts in our therapeutic areas and we currently have 37 programs in clinical development. About 20 are late-stage programs in Phase 3 of clinical development or later, and most are expected to launch by the end of 2020, subject to regulatory approval. Our commitment to innovation is reflected in our \$1.3 billion investment in R&D, representing 11 percent of our 2016 revenue.

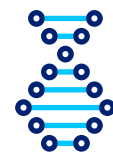
Boston Children's Hospital

Shire and Boston Children's Hospital have an ongoing partnership to develop treatments for children with rare congenital conditions. Using the skills of both partners, the collaboration offers a blueprint for shortening the bridge from the lab to the clinic and is demonstrated by two ongoing projects to develop therapies for children.

Cincinnati Children's Hospital Medical Center

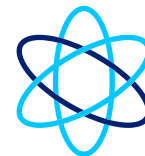
In 2016, we continued our collaboration with Cincinnati Children's Hospital Medical Center to discover and develop novel rare disease therapies. The combination of Cincinnati Children's research capabilities and Shire's research, development, and commercial expertise makes for a powerful partnership. The partnership focuses on programs with the potential to explore developmental therapies within an accelerated three-year timeframe.

R&D pipeline programs



Preclinical

35+



Phase 1

6



Phase 2

10



Phase 3

17



Registration

4



Access to medicines continued

Advancing R&D through collaboration continued

BioPhorum — a cross-industry collaboration

BioPhorum is a cross-industry collaboration of more than 35 biopharmaceutical companies, focusing on strategic development issues that would benefit from a common industry-wide approach. This year, Shire hosted the BioPhorum Development Group's first face-to-face meeting, bringing together 14 representatives from 10 companies. The meeting shared insights into formulation development, particulates, and in-use compatibility, and had a goal of delivering at least one medical publication on standard approaches to building drug product robustness.

Developing pathways for Hemophilia treatment

We are committed to developing products that treat Hemophilia, a disorder that affects the ability of blood to clot. Several of our programs aim to improve the understanding of blood clotting and to provide better prediction tools for thrombotic events. This work has been published in the Journal of Thrombosis and Haemostasis, sharing our understanding and findings with the wider medical profession.

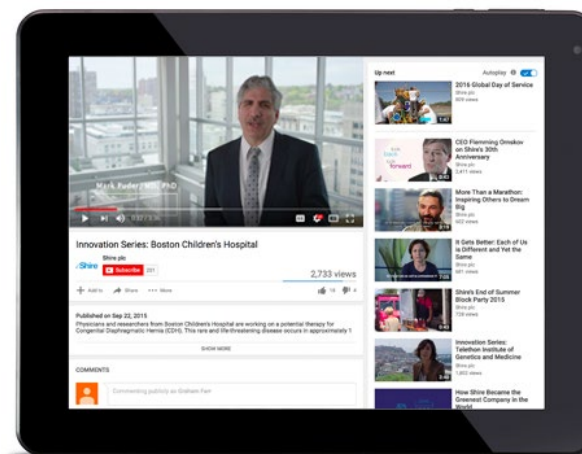
Increasing the understanding of adRP

The Foundation Fighting Blindness is dedicated to funding innovative research for the prevention, treatments and cures for inherited retinal degenerative diseases that lead to blindness. Working in partnership, we launched a new program to further our research on treatments for autosomal Dominant Retinitis Pigmentosa (adRP), a rare genetic disease that leads to the progressive loss of peripheral vision. The disorder varies significantly from patient to patient, making it very difficult to predict the disease's progression. We are conducting a natural history study in an untreated population of 90 patients over a four-year period to gain a better understanding of the natural progression of the disease, with the intention of developing an effective treatment for the disorder.

**FOUNDATION
FIGHTING
BLINDNESS**

Additional research partnerships

Shire's other ongoing rare disease research partnerships include those with the Telethon Institute of Genetics and Medicine (TIGEM), and Armagen. To learn more, watch [Shire's Innovation Series on YouTube](#).



What we will do in 2017

- » Launch an integrated U.S. and international grants and charitable contributions process.
- » Give a greater voice to patients and caregivers by engaging with them through the entire R&D process, from trial design to clinical outcomes.

Awareness, advocacy, and responsible product use

Why it matters

Patients are at the heart of all we do at Shire. Understanding the unmet medical needs of our patients and their families is essential if we want to make a difference in their lives.

Making sure that our products are used responsibly maximizes their benefits and reduces the risk of negative impacts. We know that we cannot address these issues on our own, so we are committed to working with patient associations, industry bodies, non-profits, and others to make a meaningful impact.



Shire's Advocacy team's passion for the communities we serve drives our responsibility to ensure the voice of each patient is heard.



Rodney Dickson
Lead, U.S. Field Advocacy



25+

We took part in more than 25 awareness-raising campaigns throughout the year.

Our approach

One of our most important responsibilities is to increase understanding of rare diseases by sharing our knowledge with patients, families, caregivers, physicians, and policymakers. At the same time, we strive to enhance our own understanding of patients' unique needs. We aim to connect patients with relevant organizations, helping to build networks of individuals in similar circumstances. Our activities are focused on three key areas: **awareness**, **advocacy**, and **responsible product use**.

Raising disease awareness

Many of the conditions we develop treatments for are not widely understood. Low levels of awareness can contribute to misdiagnosis or delayed diagnosis, social stigma, delayed treatments, misuse of treatments, and overall lack of access to treatments — all of which can cause unnecessary stress for patients and their carers. For this reason, we aim to increase understanding and awareness among patients, caregivers, healthcare providers, and the general public.

Fact- and evidence-based information is essential for accurate and timely diagnosis and treatment. We sponsor a variety of research to gather scientific information and build understanding of rare diseases. We then develop balanced, scientifically-rigorous, educational materials and programs in our main areas of expertise — Genetic Diseases, Neuroscience, Hematology, Internal Medicine, Immunology, Oncology, and Ophthalmology.

Awareness, advocacy, and responsible product use continued

Enhancing patient advocacy

We are proud to have a long history of supporting patient advocacy organizations around the world. Collaborating with these groups not only improves our understanding of patient and caregiver experiences, but also helps these important organizations give patients a voice. We adopt an integrated customer journey approach to understand patient experiences better — from pre-diagnosis challenges to managing their condition day-to-day. This helps us identify opportunities to meet patient and customer needs. We strive to understand the frustrations of patients and, in doing so, understand how we can make their lives and experiences better and more fulfilling.

Our Patient Advocacy team works with patient advocacy groups around the world on the shared objective of improving the lives of patients with life-altering conditions. The initiatives and campaigns we run are focused on all aspects of improving the patient experience and include: disease education; raising awareness of clinical trials; decreasing time to diagnosis and treatment; engaging in dialogue with advocates; and championing the patient experience at Shire. The team also recognizes disease awareness days and supports patient advocacy organizations by hosting and participating in internal and external events.

The Patient Advocacy team ensures that the patient perspective is always front of mind within Shire. The more our employees understand the personal burden of disease, the better they will be able to appreciate the emotional, financial and day-to-day challenges that patients, caregivers, and families go through. The team also ensures the patient perspective is represented across Shire engagements. This includes in clinical trial recruitment, internal and external presentations, advisory boards, research projects, educational campaigns, and broad-scale public service announcements.

Our Project Voice initiative aims to connect all Shire employees to the patient experience by identifying patients who are willing to talk about their experiences at internal Shire events. Their stories often focus on the patient journey or give a 'day in the life' perspective, and inform, inspire, and motivate our employees.

Ensuring our products are used responsibly

Shire is committed to making sure that our products are used correctly and responsibly. We oppose the misuse, abuse, and diversion of all prescription medicines approved for treatment of disorders, and in particular Attention Deficit/Hyperactivity Disorder (ADHD).

To combat non-medical use of our products, we work in partnership with a variety of external stakeholders. We have invested in educational tools and support systems for patients, parents, and healthcare professionals on the appropriate diagnosis of ADHD, treatment options, and proper use of our medicines.

Read more online

Our [Patient Advocacy team](#)

Our position on [Public Policy Engagement](#)



\$25.9m

In 2016, Shire made more than \$25.9 million in donations to U.S. healthcare-related charitable organizations.



\$11m

In 2016, Shire provided \$11 million in educational grants, an increase of \$2.4 million from 2015.



180

Our Patient Advocacy team has built relationships with 180 patient advocacy organizations, spanning all of Shire's therapeutic areas.



Awareness, advocacy, and responsible product use continued

What we did in 2016

Raising awareness through education

We support patient advocacy organizations in recognizing disease awareness days and months by hosting and participating in internal and external events and awareness campaigns.

Our Fabry Family Tree short film series

Fabry disease is a rare genetic disorder causing a wide range of symptoms, including heart and kidney disease. As part of our work to improve diagnosis of Fabry disease, we worked with Fabry International Network (FIN) to create a compelling story, highlighting Fabry's hereditary impact and how it can be identified in families.

In 2016, we launched a series of short films — Our Fabry Family Tree — that follows a family's journey living with Fabry disease. The trailer for the series launched during Fabry Awareness Month (April) and the three-episode series was subsequently launched on [Shire's YouTube channel](#) and the [fabrydisease.info](#) website.

We support patient advocacy organizations throughout the year by hosting and participating in internal and external events and awareness campaigns.



Spotlight on Gaucher Awareness Campaign

For International Gaucher Day on October 1, 2016, we launched our “Spotlight on Gaucher” initiative on social media. The campaign was endorsed by the European Gaucher Alliance (EGA) and the National Gaucher Foundation (NGF) in the U.S. and reached over 500,000 people. The campaign resulted in a 319 percent increase in traffic to the [Spotlight on Gaucher](#) website, and 333 new members registered for Shire's Rare2Aware community, a gateway to information, news, support and connections for rare disease patients.

More information is available on the [Spotlight on Gaucher YouTube channel](#).



319%

Thanks to the #Together4Gaucher campaign, there was a 319% increase in traffic to the Spotlight on Gaucher website.

Events supported include:

January

- » Thyroid Awareness Month

February

- » MPS Day
- » National Eating Disorder Awareness Week
- » Rare Disease Day

March

- » Bleeding Disorders Awareness Month
- » Hemophilia Awareness Month

April

- » Digestive Disease Awareness Month
- » Fabry Awareness Month
- » IBS Awareness Month
- » World Hemophilia Day

May

- » HAE Awareness Day
- » Mental Illness Awareness Week
- » National Mental Health Month

June

- » Eating Disorders Awareness Day
- » World Hypoparathyroidism Day

July

- » Dry Eye Awareness Month

September

- » Blood Cancer Awareness Month
- » Pediatric Cancer Awareness Month
- » Thyroid Cancer Awareness Month

October

- » ADHD Awareness Month
- » Gaucher Disease Awareness Month
- » International Gaucher Day
- » National Epidermolysis Bullosa Awareness Week

November

- » World Pancreatic Cancer Awareness Month and Day
- » World Prematurity Day

December

- » Crohn's and Colitis Week

Awareness, advocacy, and responsible product use continued

ADHD Awareness Month

Every October, we join with many patient organizations around the world to take part in ADHD Awareness Month. The Month aims to educate and raise awareness of this severely misunderstood disorder, and provides a key opportunity to recognize the true impact of ADHD on the lives of those affected. The theme in 2016 was “knowing is better” and was reflected through a series of activities:

- In My Shoes used virtual reality to allow people to step into the world of a child, adolescent or adult living with ADHD, through multiple real-life 360-degree videos.
- We launched a spoken word video to explain the challenges many adults with ADHD face in seeking accurate diagnosis and appropriate support. The video, entitled “The Truth”, is available to view on [Shire's YouTube channel](#).

Coinciding with ADHD Awareness Month, our annual Excellence in ADHD Patient Group Awards celebrate outstanding projects led by patient advocacy organizations outside the U.S. An international panel of judges awards grants of €10,000, and in 2016 the following groups were recognized for the impact of their innovative work:

- Early Therapy Group, an innovative project for the treatment of pre-school age children with ADHD — Fundación ADANA (Spain).
- ADHD and School — HyperSupers TDAH France (France).
- A foundation for children, teenagers and adults diagnosed with ADHD — TDAH Irapuato (Mexico).



The Coalition to Prevent ADHD Medication Misuse (CPAMM)

In the fall of 2016, continuing our involvement with CPAMM — a coalition working to prevent misuse, abuse, and diversion of ADHD prescription stimulant medication — we helped to launch an educational campaign encouraging parents, caregivers, physicians, college administrators, athletic coaches, and trainers to take action and speak with students about the dangers and consequences of the non-medical use of ADHD medication. To date, this online campaign has received around 15,000 interactions with members of the public. Learn more at cpamm.org



€10,000

Our Excellence in ADHD Patient Group Awards were made to three organizations in Spain, France and Mexico.

Working with patient advocacy organizations

This year, we have engaged with specialist patient advocacy groups in a number of areas to give a greater voice to patients and their families. Some of our activities in this area include:

Hematology: Alongside the European Haemophilia Consortium, we launched the European Inhibitor Network to improve standards of care for patients with Hemophilia inhibitors. Hemophilia inhibitors reduce the efficacy of Hemophilia treatment, making it difficult for these patients to receive appropriate care. In February of 2016, the Network hosted a policy roundtable to raise awareness of the disparities in Hemophilia care across Europe.

Immunology: In October, we hosted events with the Jeffrey Modell Foundation, the Immune Deficiency Foundation, and patients with PI to gather insight into the needs of these patients. The events allowed these groups to share their vision and strategic objectives for 2017 and beyond. Discussions covered issues such as quality control and the process of creating immunoglobulin therapies.

Oncology: In November, we hosted our first-ever Oncology Advocacy Roundtable, bringing together 12 diverse patient advocacy groups. The aim was to listen to these leading non-profits on unmet needs and determine opportunities for collaboration across the entire R&D pathway.

Gastroenterology: During 2016, we held global and local workshops with patient advocacy organizations to better understand the needs of patients with SBS, a rare and potentially fatal gastrointestinal disorder. We also supported the development of a global coalition for SBS, designed to provide support and education to SBS patients across the world.

Awareness, advocacy, and responsible product use continued

Shaping the industry and regulatory landscape for rare diseases

Shire is a member of over 40 pharmaceutical and biotechnology industry groups worldwide including IFPMA, BIO, EFPIA, EuropaBIO, ABPI, Medicines Australia, and Biotec Canada. Through these groups and individually as Shire, we are committed to ensuring that legislation allows patients with rare diseases to receive much needed diagnoses and treatment.

Improving legislation to screen newborns in California

We have been actively involved in helping to pass legislation improving rare disease screening for newborn babies in California. We chaired a working group of patient organizations and industry advocates to support a change in legislation to eliminate delays in newborn screening. The Recommended Uniform Screening Panel (RUSP) is a list of conditions that every baby should be screened for, however, once a condition was added to the RUSP, it could have taken up to eight years for a state to conduct a screening. In September 2016, legislation was passed allowing those in California to screen for diseases as soon as they are added to the list. This bill will help newborns with rare diseases receive much earlier diagnosis and treatment.

In 2016, we played a fundamental role in shaping U.S. healthcare legislation through the 21st Century Cures Act.



Helping to shape the 21st Century Cures Act

During the year, we played a fundamental role in shaping U.S. healthcare legislation through the 21st Century Cures Act, which passed in December 2016. We were involved in two key aspects of the Act:

- **Giving Medicare patients access to self-infusion medication at home**

We joined patient groups and the specialty pharmacy community as the only pharmaceutical company supporting Medicare home infusion legislation. Previously, Medicare — the U.S. federal health insurance program — provided insurance coverage for home infusion of drugs self-administered by a subcutaneous pump, but did not cover associated nursing and training. As a result of the coalition's work, the legislation was passed ensuring that Medicare beneficiaries receive the training, nursing, and support services needed for self-infusion of medication.

- **Extension of the Rare Pediatric Disease Priority Review Voucher**

We led the efforts to reauthorize the Rare Pediatric Disease Priority Review Voucher program. The program provides the sponsor of an approved drug for a rare pediatric disease with a voucher that can be used to prioritize the FDA's review of another drug application. The 21st Century Cures Act extended the Voucher program until September 30, 2020, and expanded the number of eligible rare pediatric diseases covered by the program. The passing of this legislation provides an important incentive for companies to develop drugs to treat more rare pediatric diseases.

Our political engagement work in California will help newborns with rare diseases receive much earlier diagnoses and treatment.

What we will do in 2017

- » Support selected smaller rare disease advocacy groups to grow and expand through mentoring programs.
- » Develop coalitions in cancer care to address areas that have significant unmet needs.
- » Develop and launch a Rare Disease Registry in India.
- » Continue to work with patient groups on legislation to advance the start date of the new Medicare Home Infusion Act and expand it to include intravenous administration.
- » Work to replicate the success of the newborn screening legislation in California in other targeted states.

Supporting patient and local communities

Why it matters

Companies do not operate in isolation and at Shire we are no exception. Our impacts — both positive and negative — extend into the local communities where we live and work. Our responsibilities also extend to the therapeutic communities we serve. This includes patients and their families, and the advocacy and support groups that represent them. We strive to ensure that our impact is a positive one, wherever we operate.



Our approach

Our goal is to help our communities thrive and be healthy in the long term. To ensure the greatest benefit from our activities, we partner with expert organizations and provide support in areas that are closely linked to our business activities and core skills.

We have a particular focus on improving the wellbeing of children and young people that are most in need. We also provide support for communities struck by one-off disasters. To achieve maximum impact, our programs run globally and locally.



Coming to work and knowing that we can positively affect those around us each and every day... now that's inspiration.



Alex Schuman
Responsibility Manager

Supporting patient and local communities continued

What we did in 2016



1,500

Our employees had a unique chance to volunteer as counselors at SeriousFun camps, donating over 1,500 hours.



Working as a counselor at SeriousFun showed how important it is for us to discover and manufacture treatments for rare diseases. It was an exciting experience; I loved meeting new campers and helping them have fun.



Jon Chin
Process Engineer II



Partnership with SeriousFun Children's Network

In February of 2016, we committed \$3 million over three years to SeriousFun Children's Network, a global non-profit organization comprised of 30 camps and programs serving children with serious illnesses and their families, always free of charge. SeriousFun Children's Network aims to foster independence, resilience and personal growth and help children to see beyond the limits of their medical conditions.

Our support will enable nearly 1,000 children, many with rare diseases, to attend SeriousFun's transformative camps and Family Weekend programs. In the summer of 2016, 15 Shire employees from around the world had the unique chance to volunteer as counselors at SeriousFun camps, volunteering over 1,500 hours with campers. In total, our employees donated approximately 5,000 hours of volunteering with SeriousFun through on- and off-site programming throughout the year.

For more information see our video on the first year of our relationship on [Shire's YouTube channel](#).

ACMG Foundation for Genetic and Genomic Medicine

Across the U.S., there is a significant shortage of medical geneticists. With only one geneticist for every 600,000 individuals, the U.S. has less than half of the genetic workforce it needs. As an issue directly related to our business, we announced a \$1.65 million grant to the ACMG Foundation for Genetic and Genomic Medicine. The ACMG Foundation is a non-profit organization that works to attract and fund training for the next generation of medical geneticists and genetic counselors. The Foundation also sponsors important research, and promotes information about medical genetics.

Our partnership aims to advance and improve expertise in medical genetics in the U.S. Over the next three years, the grant will fund 10 one-to-two year fellowship training awards for medical geneticists in three categories: clinical laboratory fellowships, clinical genetics residencies, and medical biochemical genetics subspecialty fellowships. The partnership between Shire and the ACMG Foundation for Genetic and Genomic Medicine will help develop a future generation of geneticists around the world who will be crucial in the diagnosis and care of patients with rare diseases.



\$1.65m

We committed \$1.65m to the ACMG Foundation to fund 10 fellowship training awards for medical geneticists.

Supporting patient and local communities continued

Supporting patient communities through scholarships

As part of our commitment to the rare disease community in the U.S., we offer the Shire ACES (Award for Collegiate Education from Shire) Scholarship. The scholarship provides a \$5,000 educational grant for up to three years to support undergraduate or vocational school costs. The scholarship is open to recent high school graduates and equally qualified students with a rare disease.

In 2016, we increased the number of annual scholarships from one to three. This year's recipients were Britt from South Dakota and Daniel from Arkansas, who have primary sclerosing cholangitis, and Nathaniel from Michigan, who has eosinophilic esophagitis.

We continue to provide annual scholarships to individuals in the U.S. and Canada with ADHD who are pursuing higher education. In the U.S., the 'Michael Yasick ADHD Scholarship by Shire' includes a \$2,000 bursary and a year of ADHD coaching from the Edge Foundation to help recipients overcome the challenges they might face. Since the start of the program in 2011, we have awarded 343 national scholarships and 27 employee scholarships.

In 2016, the Shire ADHD Scholarship Program selected 55 U.S. recipients for a scholarship from more than 2,000 applicants. In Canada, the program awarded bursaries to five recipients from more than 300 applicants. 2016 was the third year that the program supported Canadian adults living with ADHD who are pursuing a post-secondary education. Find out more at shireADHDscholarship.com



2016 Shire ACES Scholarship recipient – Britt, South Dakota.

Since 2010, the Education Advantage scholarship program has awarded over 200 scholarships, totaling more than \$1.3 million, to students with a bleeding disorder. Education Advantage is designed to help recipients pay for school and continue their education. The program is open to anyone with Hemophilia A or B, including those with inhibitors, regardless of which brand of treatment they use. Beginning in 2016, students with von Willebrand Disease were also eligible to apply. In 2016, 16 young people with bleeding disorders were awarded University Scholarships, Community College and Technical Scholarships, or GED Assistance worth up to \$7,000.



200

Since 2010, the Education Advantage scholarship program awarded more than 200 scholarships to students with a bleeding disorder, totaling over \$1.3 million.

Financial support for those in need

We continue to invest in local projects designed to make a difference to disadvantaged young people and their families. Our support ranges from projects providing career inspiration for students with special needs, to helping schools to buy equipment for students with disabilities.

In 2016, we continued our support for Cotting School — a special education school for students aged three to 22 with learning, communication, and physical disabilities, based near our U.S. Operational Headquarters in Lexington, MA. Support in 2016 included:

- A \$25,000 donation to support the school's career program, which places students in local businesses to explore realistic career options, while gaining vocational experience and developing social skills. The donation also purchased adjustable desks that can comfortably accommodate students in wheelchairs or with disabilities.
- An enlarged internship program. We now offer four internships in Shire's mailroom to upper school students.
- A donation of excess office supplies for use in writing and arts classes.



£15,000

We made a £15,000 grant to the Sick Children's Trust in the UK, which will provide accommodations for around 50 families with sick children in the hospital.

Supporting patient and local communities continued

Other activities from across Shire

Since 2010, our Massachusetts sites have donated more than \$900,000 worth of surplus equipment, such as microscopes and laptops, to local schools and non-profit organizations. We also made a \$25,000 donation to the Community Therapeutic Day School in Lexington, to celebrate the opening of a new building for Shire's U.S. Commercial operations.

In the UK, we made a £15,000 grant to the Sick Children's Trust, which operates 10 houses that provide accommodations for parents with sick children in the hospital. The Trust also provides emotional and practical support, and was established on the belief that having parents on hand during hospital treatment benefited a child's recovery. Our donation will provide accommodations for around 50 families over an 18-month period.

We continue to invest in local projects designed to make a difference to disadvantaged young people and their families, from financial donations to the donation of equipment such as microscopes and laptops.



\$71,000

We donated \$71,000 to the relief effort following an earthquake near our plant in Rieti, Italy.

Disaster relief

We understand the need to react to and support unforeseen crises globally. In significant disasters, local communities still require support long after the crisis has passed. We continue in our role as a board member of the Partnership for Quality Medical Donations (PQMD), a global alliance of non-profit and corporate organizations, that aims to enhance access to healthcare in underserved communities and areas affected by disaster.

In 2016, we supported the relief effort following an earthquake in central Italy, just 60 kilometers from Shire's manufacturing plant in Rieti. The earthquake resulted in more than 290 fatalities and largely destroyed many small towns. We

were very fortunate that all of our employees were unharmed. We donated approximately \$71,000 to the relief effort — a \$60,000 corporate donation and \$11,000 raised by our employees.

In December 2016, a massive fire in Cambridge, Massachusetts, close to our Kendall Square office, destroyed 15 buildings and displaced 89 people. In response to the tragic incident, we supported the Mayor's Fire Relief Fund with a \$25,000 donation, which was established to assist the families and individuals directly affected by the devastating fire.

What we will do in 2017

- » Launch an updated community relations strategy and program guidelines for our sites around the world.
- » Provide opportunities for 30 employees to volunteer as a counselor or family pal at a SeriousFun Children's Network camp around the world.
- » Donate over 6,000 volunteer hours to SeriousFun Children's Network camps and programs through a variety of activities throughout the year.
- » Raise awareness of the ACMG Foundation genetic fellowship program and its accomplishments.
- » Refine our strategic disaster relief approach for the newly combined Company.
- » Continue providing disaster and emergency relief support where it has the greatest impact, especially in our local communities.



24,000

We now have approximately 24,000 employees. Their efforts and commitment continue to support people with rare diseases through every step of their journey.

2

People and culture

Our employees come to work every day with a common purpose: to develop and deliver breakthrough therapies that enable people with life-altering conditions to live their lives to the fullest. But we can only be truly successful if we attract, develop, and retain world-class people. By investing in training and development, we aim to create a high-performing, healthy, and inclusive workplace where everyone is encouraged to excel.

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People and culture

Why it matters

At Shire, we know our people are fundamental to our success and our future as the leading global biotechnology company in rare diseases. We strive to maintain a motivated workforce that brings a diversity of experiences, skills, and perspectives. To do so, it is crucial we create a safe and engaging environment where talent is nurtured and achievements are rewarded.

Our approach

2016 was an exciting year for Shire. Our combination with Baxalta means we now have approximately 24,000 employees across the organization, over 300 percent more than the 5,500 employees in Shire the previous year. We are excited about the varied perspectives and experiences this new talent brings to the organization.

Throughout 2016, we focused on integrating and reinforcing our combined cultures. Our rapid growth in a short timeframe means the emphasis on supporting and developing our people is more important than ever. Within our newly combined Company, we continue to focus our approach in key areas — working to attract and develop the best talent, creating a diverse and inclusive workforce, providing a safe and healthy workplace for our people, and encouraging our employees to volunteer.



In today's talent marketplace, employees want to be associated with a company that helps them feel good about their contributions — and those of the Company — to address society's issues and problems. They want to know that they are making a positive difference. Paychecks and vacation time are not enough anymore.



Beth Cliff

Head of Talent and Organizational Development

People and culture

Talent attraction and development

Our long-term success requires the right people, with the right skills, in the right roles. To achieve this, we work hard to ensure we can attract the best people to Shire, actively recruiting entrepreneurial and imaginative people who engage with our culture and values. To retain our talent, we invest in training and development, identify and nurture top performers, and help all employees to realize their full potential. Our policy is to fill vacant roles with internal candidates where possible, which helps develop our people and keeps valuable knowledge and skills within Shire.

We aim to foster a culture that inspires, motivates, and rewards our people for performance. This helps us build an engaged workforce that generates ideas and innovations, and encourages stronger performance so that we may better serve our patients.



4,500+

Since its launch, 4,500+ employees have used the ShireLearns Hub, a new online training platform.

What we did in 2016

Talent and organizational development

We want to support our employees to learn and grow continuously while doing their best work. We believe that everyone at Shire — regardless of role or seniority — has the opportunity to demonstrate leadership every day. In 2016, we developed and rolled out a number of new initiatives to support our employees in the development of essential workplace skills and enhance engagement. These included:

- Developing a new employee engagement pulse survey, which will be rolled out across Shire in 2017.
- Launching the ShireLearns Hub, a new online platform that provides employees with access to training, webinars, reading material, and links to partner sites. Since launch, 4,500+ employees have used the resource.
- Delivering the 'Manager 101' program, which provides managers with training to engage their teams, develop capabilities, and define goals. During the year, 335 managers completed the two-day course and 84 completed the one-day course.
- Introducing the Leading Beyond program, designed to facilitate efficient collaboration and increased productivity among management in our newly integrated Company.
- Facilitating our second annual Leadership Masterclass, an opportunity for individually selected, highly-performing individuals to explore specialized topics with internal Senior Leadership.

Talent attraction and development continued



Expanding our onboarding programs

In 2016, we developed a global onboarding process for the newly combined Company that includes:

- Updated onboarding resources for managers and new employees, easily accessible on our employee portal.
- An enhanced orientation program for new employees that provides a consistent onboarding experience.

Designed to be simple and accessible, this manager-led process aims to engage new employees and enable them to be productive from the start.

Recognizing outstanding performance

A strong performance culture supports continuous improvement and helps us to achieve our goals. Our pay-for-performance philosophy provides managers with a variety of programs to recognize and reward outstanding employee contributions. Examples include:

- CEO Award: Awarded to colleagues who have truly distinguished themselves with outstanding performance, making a significant difference to our stakeholders and colleagues, and, most importantly, in the lives of our patients. In 2016, 164 employees received an individual or team CEO Award, representing nine countries and nine of our 13 global functions.
- Employee Recognition Awards: Awarded to colleagues for actions both small and large that make a difference to Shire and the lives of our patients. In 2016, 60,000 awards were distributed to employees, recognizing them for many different activities.



60,000

Employee Recognition Awards were given to 60,000 employees for positive actions that have made a difference across the organization.



People and culture

Diversity
and inclusion

At Shire, we are committed to people of all races, genders and sexual orientations. We believe our collective differences provide a solid foundation for our sector-leading position. Harnessing our differences provides a wealth of ideas and innovations that allow us to be more responsive to customer needs.

We do not have diversity targets or quotas and we do not focus exclusively on one group of employees over another. We do, however, make sure we foster a positive and inclusive culture, and we aim to provide all employees with a supportive work environment that values diverse opinions and experiences.

Shire currently has eight employee-led BRGs: B-Equal (LGBTQ+), EnAble (disability), Black Leadership Council, Building Asian Leaders, Impacto (Latinx employees), VETS (veterans), Early Career Professionals, and Women@Shire.



What we did in 2016

In 2016, we reinforced our commitment to diversity and inclusion by extending our employee-led Business Resource Groups (BRGs) across the entire organization. An active part of legacy Baxalta, we are pleased to have introduced BRGs across all of Shire this year.

These networks play an important role in ensuring Shire is as diverse as the patients we serve. Dedicated websites and information about each of our BRGs were also created or updated throughout 2016, to raise awareness of BRGs and provide insight to any employees interested in participating.

Throughout June, we celebrated Pride Month, globally. Led by B-Equal, Shire's LGBTQ+ Business Resource Group, colleagues from across the business joined together in numerous events to show support for the LGBTQ+ community and value the diverse contributions of all. In Northern Illinois, for example, colleagues celebrated Pride Month at a screening of award-winning documentary filmmaker Yoruba Richen's film, "The New Black", which focuses on the intersection of the Black and LGBTQ+ civil rights movements.



A diverse and inclusive workforce enables us to bring different ideas to the table, innovate more quickly and truly serve the patients who count on us.



Courtney Denitzio

Organizational Effectiveness Consultant

People and culture

Employee health, safety, and wellness

We want our employees to be healthy and safe at work. We believe that all safety incidents are preventable and we are determined to create a work environment free from injury or harm. In order to achieve this goal, we work to identify potential hazards in our operations and take measures to mitigate them.

Alongside injury statistics, we track a range of leading indicators to monitor and measure our safety performance. These performance indicators help to focus our safety, occupational health, and industrial hygiene efforts.

We also aim to promote healthy lifestyles and behaviors with our people. Engagement on health and safety provides opportunities to educate, counsel, or coach employees, with information that encourages healthy living and raises awareness of safety.



In developing our EHS policy for the newly combined Company, we have been focused by our new vision for excellence in this area: Enabling a safe and healthier world.

Safety indicators



Total Recordable Incident Rate (TRIR)

1.01

Lost Time Incident Rate (LTIR)

0.16

Note: 2015 data is not comparable to 2016 data, due to the combination with Baxalta during 2016. The 2016 data includes all Shire operations within the newly combined Company.

What we did in 2016

Occupational Safety

In 2016, we continued to focus on improving Shire's safety culture and performance. In November, we launched a new Environment, Health, and Safety (EHS) policy for the newly combined Company. We also created focused injury- and illness-reduction strategies and developed a new Safety Leadership program that will be launched in 2017.

It is essential that the behavior and actions of our leaders contribute to our goal of an incident- and injury-free workplace. Senior leaders are in a unique position to influence health and safety in the workplace and to help establish the conditions that create a safe working culture. The new Safety Leadership program, therefore, aims to influence our leaders' behavior and help them make a personal commitment to safety.

Across Shire, our safety management systems are based on the internationally applied, British standard Occupational Health and Safety Assessment Series (OHSAS) 18001. Currently 12 sites are independently certified to this standard. Our management approach continues to ensure that all environment, health, and safety (EHS) incidents are recorded and categorized according to potential severity, and that we devote appropriate resources to discovering the root causes of incidents, correcting them, sharing learnings, and preventing recurrence.

To increase our safety capability, we allocated additional resources in 2016 to create a new, global safety team. We have increased our emphasis on managing specific risks, such as contractor and construction activities, which is an essential focus as our Company grows. We also maintained our focus on identifying, assessing and mitigating high hazard risks, such as exposure to hazardous materials, falls from height, and release of flammable materials.

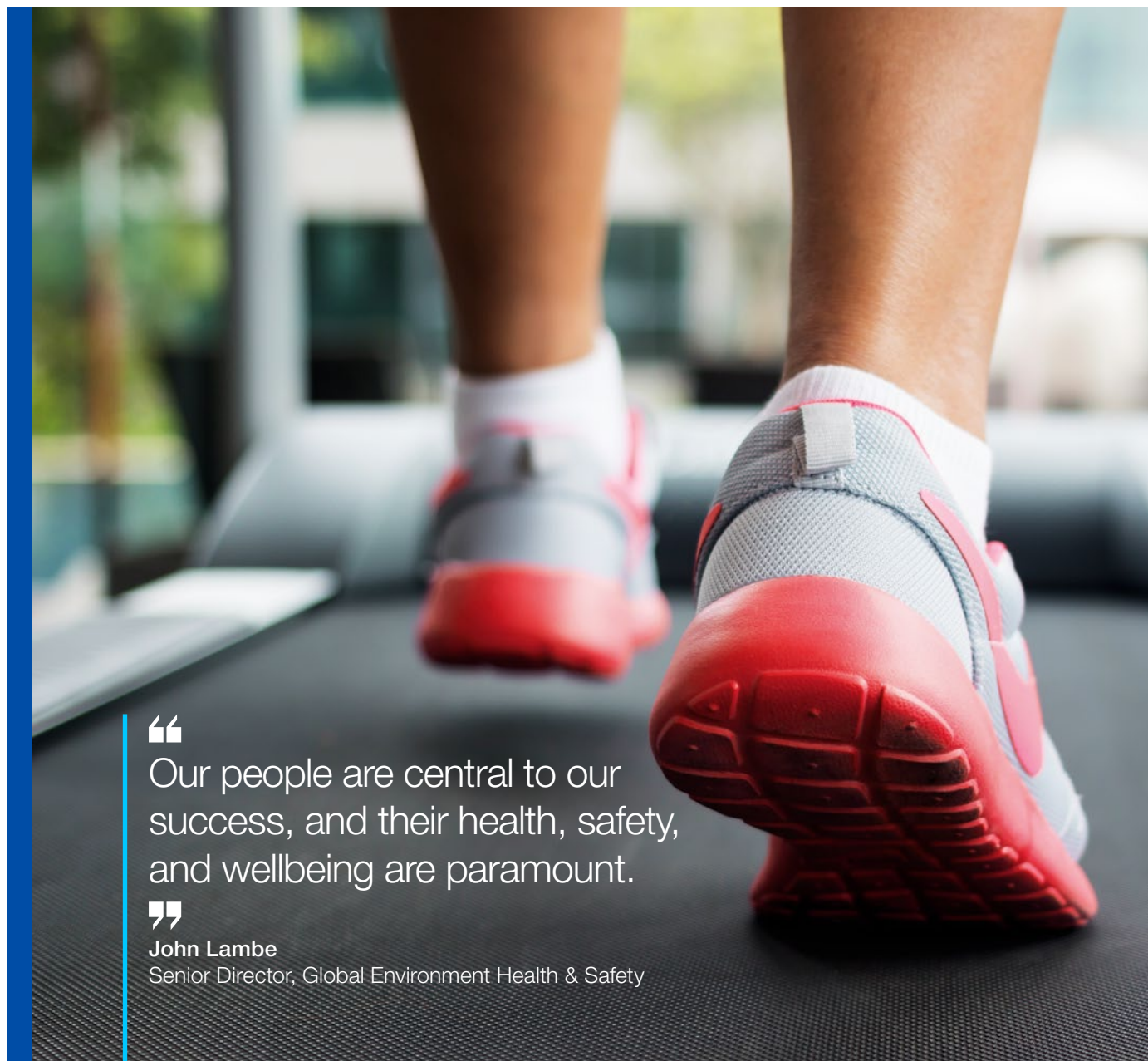
Employee health, safety and wellness continued

Health and wellness

We continue to provide our employees with tools to help them maintain good health. We operate health clinics across our major sites and we provide health screenings and educational programs for employees at our principal locations. For example:

- We continued our successful flu vaccination program at all major sites. In Vienna, we provided additional vaccinations free of charge, such as diphtheria, tetanus, polio, pertussis, and TBE.
- We constructed a new fitness space for employees at our Bannockburn, Illinois, site and provided activities at our wellness centers across a number of sites.
- Eight blood pressure kiosks and three body composition scales were installed in different locations, to allow employees to check their blood pressure, weight, and body fat percentage, and we continued our cardiovascular screening at selected U.S. facilities.
- We hosted a number of courses and demonstrations on topics such as healthy cooking, stress reduction, and nutrition counseling.

We can see that these programs have an impact. Over time, our wellness programs have helped employees discover unknown diabetes, elevated blood pressure, cardiac arrhythmias, unhealthy cholesterol levels, and other health issues.



Our people are central to our success, and their health, safety, and wellbeing are paramount.



John Lambe

Senior Director, Global Environment Health & Safety

People and culture

Employee volunteering

We understand that our impact and reach extends beyond our Company into the local communities in which we live and work, as well as to the therapeutic communities and groups that represent our patients and their families. We want to ensure we achieve a positive impact outside our Company by encouraging our dedicated employees to engage in volunteering throughout the year.



25,000 hrs

Employee volunteers gave over 25,000 hours to community organizations during our Global Day of Service.



What we did in 2016

On October 7, Shire hosted its second annual Global Day of Service. More than one-third of our newly expanded workforce participated in volunteer projects worldwide. Employee volunteers dedicated over 25,000 hours of their time in more than 150 locations. Many projects focused on helping children to “overcome odds.” They included employees helping prepare the SeriousFun Children’s Network camp in Ireland for fall programs, and others developing activity booklets for sick children in Switzerland. You can watch our video to learn more about the day on [Shire’s YouTube channel](#).

In order to better capture, analyze, and promote employee volunteering globally, we launched a new portal — VolunteerMatch. This connects employees with volunteer opportunities and allows them to track their volunteering hours. To date, more than 2,500 employees have logged over 14,000 volunteer hours into the system. This does not yet represent all volunteering hours across Shire and we will continue to roll out the system in 2017, encouraging employees to track their hours so that we may better capture the impact of volunteering across the Company.



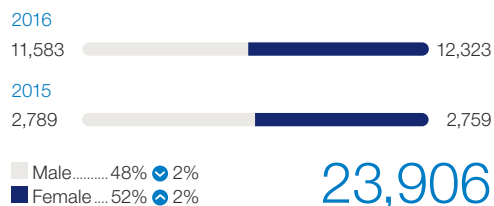
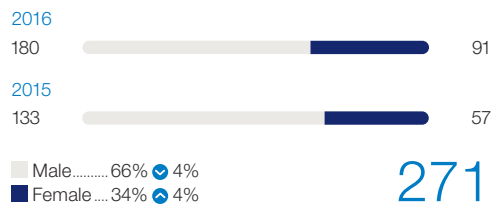
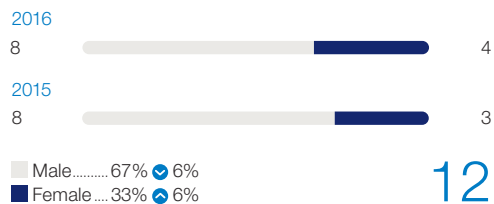
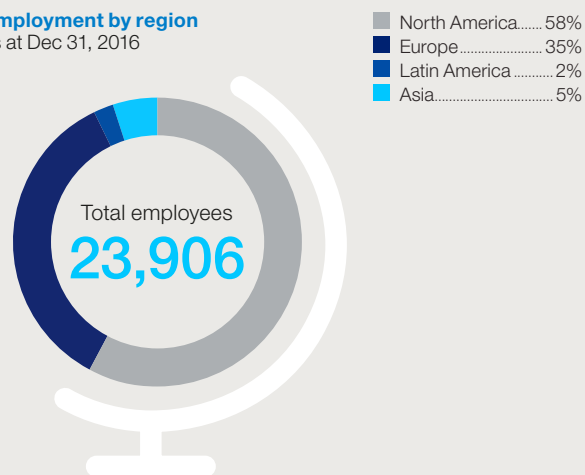
2,500

More than 2,500 employees have accessed our VolunteerMatch portal, logging over 14,000 volunteer hours.

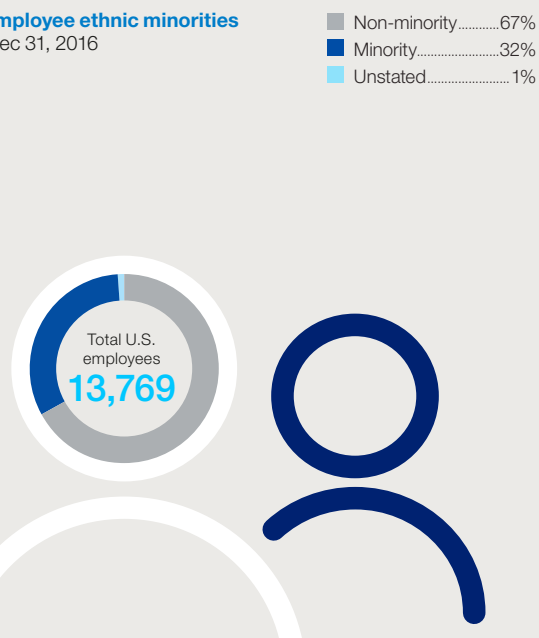
People and culture

People indicators

Employee gender statistics

Shire global employees gender split
as at Dec 31, 2016Shire senior managers gender split
as at Dec 31, 2016Shire plc Directors gender split
as at Dec 31, 2016Employment by region
as at Dec 31, 2016

Employee ethnicity

U.S. employee ethnic minorities
as at Dec 31, 2016

What we will do in 2017

- » Continue to expand the catalogue of talent and organizational development tools used across Shire to promote continuous growth for employees of all levels.
- » Roll out an employee pulse survey to the entire organization, as the first step in developing employee engagement as a critical performance driver.
- » Establish a cross-functional "Learning Council" to discuss and develop Shire's learning and development agenda.
- » Continue to integrate diversity and inclusion into recruitment and development activities.
- » Develop and roll out the Safety Leadership program to senior managers.
- » Strengthen our focus on identifying, assessing and mitigating high hazard risks.
- » Develop a comprehensive wellness strategy.
- » Run another Global Day of Service with the goal of expanding the reach and success of the program.

66%

We promote the sustainable and efficient use of natural resources, waste minimization, recycling, energy efficiency, and responsible product stewardship. This year, we diverted 66 percent of total waste from landfill.

3

Sustainable operations

Managing the environmental and social impacts of our operations, products, and sourcing is fundamental to our success. We work to ensure the products we deliver are safe, effective, and of the highest quality. Operating responsibly and using resources efficiently means living up to exacting standards, and supporting our partners and suppliers to do the same.

- 37 Environmental management and compliance
- 40 Product stewardship
- 41 Product quality and safety
- 42 Responsible manufacturing and sourcing



Sustainable operations

Why it matters

At Shire, we believe there is a clear relationship between operating sustainably and being a global leader in developing breakthrough therapies.

Our commitment to sustainable operations incorporates environmental sustainability and delivering products of the highest quality and safety. We're also committed to making positive changes along our value chain by encouraging our business partners, suppliers, and contractors to adopt responsible and sustainable practices.

Our approach

We focus on four main areas to manage the impacts of our operations, products, and manufacturing and sourcing activities:

- Environment, health, and safety (EHS) management and compliance¹.
- Product stewardship.
- Product quality and safety.
- Responsible manufacturing and sourcing.

In this section we outline our approach in these areas, highlighting action and progress in 2016.

¹ Health and safety is covered in the People and culture section (page 31).



As our Company grows, it is important that we remain good stewards of natural resources. We are committed to managing our EHS impacts across the value chain.



Deborah Donovan
VP, Environment, Health & Safety

Sustainable operations

Environmental management and compliance

Across our business, we strive to minimize the adverse environmental impacts and risks associated with our products and operations. We promote sustainable and efficient resource use, waste minimization, recycling, and energy efficiency. Compliance with environmental regulations is the baseline at all of our operations.

We follow one approach and apply one set of policies wherever we work. But we also recognize that local circumstances require local action, so all facilities develop projects and initiatives that reduce our local environmental impact.

Our management systems are based on international standards, including the ISO 14001 Environmental Management System standard and Occupational Health and Safety Assessment Series (OHSAS) 18001 standard. We use independent, third party auditors to certify our management systems to these standards. Twelve Shire locations are currently certified to ISO 14001, with additional sites recommended for certification in 2017.

What we did in 2016



Total GHG emissions

23.3

metric tons/revenue (US\$m)

A new global EHS policy and performance index

One of our most important tasks in 2016 was to develop [a new global EHS](#) policy for our recently combined Company. Published in November 2016, the global policy outlines our commitments within our own operations and across the value chain.

We also re-established our internal EHS index — a scorecard of multiple key metrics to track, evaluate, and communicate monthly performance to senior leaders. The metrics are a combination of leading and lagging indicators, and we aim to expand the scorecard in 2017. See the People and culture section to read about our efforts in health and safety (see page 31).

Environmental management and compliance continued

Energy and greenhouse gas (GHG) emissions

Energy is one of Shire's most significant manufacturing costs. Reducing its use improves business efficiency and enhances our environmental performance by conserving natural resources and reducing GHG emissions.

One of the realities of our newly combined Company is the increase in our operational and environmental footprint. With this in mind, we embarked on several initiatives during the year to deliver future savings. These include developing a program to share across the business our experience of integrating new, energy-efficient technologies into our manufacturing. The program will help replicate and amplify our energy reduction efforts worldwide.

An example is at our facility in Vienna, Austria, where we implemented multiple energy conservation projects in 2016, such as converting to LED lighting, installing variable speed motor systems, and optimizing cooling and ventilation. These efforts resulted in annualized savings of over \$100,000 and reduced energy consumption by 1,680,000 kWh.

We also established new baselines for organization-wide energy use and GHG emissions to help us track and manage our performance as a newly combined Company. In 2016, we consumed 3,890 trillion joules of energy and emitted 266,000 metric tons of GHG emissions².



Scope 1 emissions
148,000
Metric tons/CO₂e.



Scope 2 emissions
118,000
Metric tons/CO₂e
(market-based methods).

We also made headway in sourcing renewable energy. In Italy, we signed an agreement to purchase renewable energy, beginning in 2017, that will reduce GHG emissions at our two Italian manufacturing sites. In recent years, manufacturing facilities in Belgium, Switzerland, and Austria, have entered into similar agreements to purchase electricity generated from solar, hydro, and geothermal sources.

Our Company-wide focus on reducing Shire's climate change impact helped us achieve a climate score of "B" in CDP's latest performance evaluation.

² Scope 2 emissions based on market-based methodology.



Environmental management and compliance continued

Water and waste management

Our focus on how we use resources improves efficiency, creates less waste, and reduces risks and impacts on the environment and our local communities.

Water is particularly important, given its essential role in manufacturing and link to energy use. Throughout 2016, we continued to explore and implement water conservation projects, Company-wide.

Southern California recently experienced a major and prolonged drought, which led to water becoming more expensive and less accessible over time. In this region, we completed two major water conservation projects. The first was in our Los Angeles manufacturing facility, where we saved approximately 19,000m³ of water, delivering financial savings of nearly \$320,000 in 2016. We achieved this by reducing water flushing within the Central Utility Building from 20 to five minutes, and developing a water-tracking tool that helps identify additional reduction opportunities by showing how and where water is used.

Secondly, at our Thousand Oaks facility, we upgraded our reverse osmosis water treatment system to improve efficiency, and introduced drought-tolerant plants around the site. Over a two-year period, these and other water-saving efforts have reduced the site's annual water consumption from 352,000m³ to 201,000m³, a 43 percent reduction.

Overall, in 2016 we consumed 4,216,000m³ of water in our operations — 3,949,000m³ from municipal supplies and 267,000m³ from on-site sources.



We continue to look for waste-reduction opportunities, prioritizing our efforts on high-volume waste streams and facilities that produce the most waste or have particularly strong improvement potential.

Since 2014, our BioLife team has actively engaged with a key supplier to address their packaging waste. Through this partnership, the supplier has committed to replace a non-recyclable plastic tray with a cardboard insert in early 2017. This material substitution will eliminate near 50 metric tons (108,000lbs) of waste from going to landfill and increase the amount of corrugated material recycled by our BioLife operations.

In 2016, we generated 23,210 metric tons of waste and our landfill diversion rate was 66 percent. In total, we recycled approximately 13,830 metric tons of waste that would have otherwise been sent to landfill.

Environmental compliance

Across our organization, we had eight environmental incidents that required notification to regulatory agencies, none of which resulted in a Notice of Violation.



Total waste

23,210

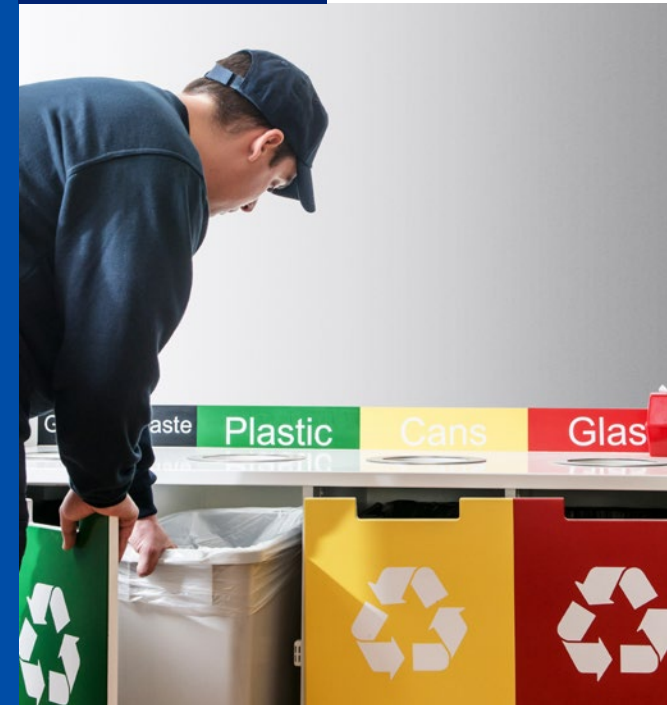
metric tons.



Total water consumption

4,216,000

cubic meters.



Sustainable operations

Product stewardship

A significant part of our environmental footprint comes from the products we design, manufacture, and sell. Reducing impact in these areas is a key focus. We use lifecycle management tools to identify where our biggest product impacts arise cradle-to-grave.

Our Product Stewardship Program is a partnership between our research and development (R&D), technical, marketing, and supply chain groups. It plays a vital role in ensuring product compliance and meeting product stewardship objectives.

Within the program, internal working groups execute our stewardship plans. The Packaging Committee, for example, meets regularly to improve how our products are packaged and transported in the most transparent, safe, and environmentally-efficient way.

What we did in 2016

Product carbon footprinting

In 2016, we worked with third party partner, The Carbon Trust, on a lifecycle assessment to recertify the product carbon footprints of three different bags of Flexbumin 25% [Albumin (Human)] sold in the U.S., Europe, Latin America, and Asia.



From plasma collection, to manufacturing, distribution, and end-of-life, the assessment looked at the whole product lifecycle to understand where the biggest carbon impacts arose. The results show that product distribution has the greatest carbon impact,

because the bags are typically airfreighted and require refrigeration during transport. Understanding these results helps us to focus on strategies for product distribution and route optimization, which will deliver the greatest environmental benefits.

Packaging

In 2016, we made a number of improvements to our packaging, delivering tangible environmental benefits.

In Europe, we worked with a local partner to reduce the shipping weight of our Elvanse® product by 77 percent and the number of airfreight shipments by 74 percent. We also optimized pallet packing to increase the number of units per pallet and the number of pallets that can be carried per truck. This means we make fewer journeys with our products, reducing the environmental footprint of our product transportation.

Another example was changing to a more environmentally friendly ink to print the scale on our Natpara® cartridge holders. The new ink uses fewer additives and is halogen and aromatic compound free.

Product compliance

Throughout 2016, we continued to address regulatory requirements, including, but not limited to, packaging and batteries, the use of biocides, and use of substances of very high concern (SVHC).

As a newly combined Company, we began to develop a more cohesive plan for evaluating the sustainability requirements of the materials we use to make our devices. The resulting "New Device Development-EHS Plan" outlines how we will support our Device Engineering teams to review and evaluate sustainability requirements before selecting materials to be used in manufacturing.



▼77%

We reduced the shipping weight of our Elvanse® product by 77 percent and the number of airfreight shipments by 74 percent.

Sustainable operations

Product quality and safety

Product quality, safety, and efficacy are some of the most important aspects of our work. Applying our expertise and technical know-how ensures we maintain the highest levels of performance in these areas.

We apply a comprehensive set of measures and controls to meet quality and safety regulations, and other national and international standards. Through these safeguards, we identify and minimize any potential risk of harm from our products to our patients, employees, communities, and local environment. In the event we suspect issues with our products, we swiftly employ our recall management systems to protect our patients and the public.



I get up every day knowing that our sharp focus on product safety will improve the quality of our products and minimize any risk of harm to our products. And that makes me proud to be part of the Shire team.



Shawn Fitzpatrick
Associate Director – Bioreactor Manufacturing

What we did in 2016

Quality risk assessments

To comply with new European Medicines Agency (EMA) guidelines, we launched a new Quality Risk Management process to assess and control cross-contamination risks in manufacturing. Under the new process, we completed potency and toxicology evaluations of our commercial products and those in clinical testing to determine health-based exposure limits and identify any risks.

We also continued using Environmental Risk Assessments (ERAs) for our marketed drugs. In 2016, this included Xiidra® 5%, a prescription eye drop used to treat Dry Eye Disease. ERAs provide a systematic procedure to investigate if the chemicals used in our products pose risks to human health or the environment, and if they can be used as intended without causing detrimental effects.



Sustainable operations

Responsible manufacturing and sourcing

We are keenly aware of how important it is to work closely with our manufacturing and sourcing partners to build a responsible supply chain. We start by considering Responsibility alongside more traditional functional, quality, and financial aspects when selecting partners and suppliers, and making purchasing decisions. All partners and suppliers we work with are required to commit to and uphold our policies on social, environmental, and ethical Responsibility.



In Cell Culture, when I have a good day, it means a great day for many more patients. That's wonderful.



Alex Wilson
Manufacturing Technician 2

What we did in 2016



\$254m

In 2016, we spent \$254 million on small businesses in the U.S. as part of our Supplier Diversity Program.

Working with our partners and suppliers

To further promote our Responsibility standards with current and prospective suppliers, we enhanced our processes for responsible and ethical procurement decisions.

Firstly, we modified our standard Request for Proposal to include references to Shire's Code of Ethics and Conflicts of Interest policies. Secondly, we established a new process for analyzing the financial health of suppliers to mitigate risk, ensure supply continuity, and ultimately, increase stakeholder and patient confidence.

We also worked directly with key suppliers to improve working conditions for employees and use more environmentally-friendly chemicals in the workplace. For example, we led an initiative to eliminate the highly corrosive solutions used in histology staining (using chemicals to color microscope samples). Our procurement team worked closely with suppliers producing these solutions to develop two new pre-mixed solutions that replace the more corrosive ammonium hydroxide and sulfuric and ethanol mixes. The new solutions are helping to provide a safer process that is less prone to errors and delivers consistent results for histology staining.

Supplier diversity

Supplier diversity is a key part of our responsible sourcing program. In the U.S., our Supplier Diversity Program provides opportunities to small, minority, and women-, disabled- or veteran-owned businesses. In 2016, we spent approximately nine percent of our U.S. procurement with companies in our Supplier Diversity Program, equating to about \$254 million.

Working with the wider industry is vital to making a large-scale difference to the issues and challenges we jointly face. This year, we became a member of The Diversity Alliance for Science (DA4S). This organization provides companies like ours with a platform to identify, attract, and develop small and diverse businesses. In doing so, we collectively progress inclusive procurement practices within the life science and healthcare industries.

Responsible manufacturing and sourcing continued

Conflict minerals

The illegal exploitation of natural resources fuels corruption, violence, and human rights violations in many places around the world. The issue is particularly pressing in the eastern Democratic Republic of Congo and adjoining countries, where conflict minerals — primarily cassiterite (for tin), wolframite (for tungsten), coltan (for tantalum), and gold ore — are financing armed conflict.

New legislation in the U.S. and Europe is helping guide companies on how to start addressing this severe human rights issue. In 2016, we worked to meet due diligence and disclosure requirements, including requesting and evaluating conflict minerals-related data from our Contract Manufacturing Organizations to ensure compliance with new conflict minerals rules throughout our extended supply chain.

We also took steps to identify and evaluate Shire products and devices that have a higher risk of containing conflict minerals in their materials or components. This has helped us define what is in scope and out-of-scope for exercising due diligence measures.

In 2016, we filed Form SD to meet our conflict minerals reporting requirements. We also updated our conflict minerals policy for the newly combined Company, which will be published in 2017.



Natural unusual gray-black stone cassiterite

What we will do in 2017

- » Update our global EHS management system for the combined Company, including how it translates to site operations.
- » Expand our Energy Management Program across the newly combined Company.
- » Establish a GHG management strategy for the newly combined Company, including scope 3 emissions.
- » Establish a governance structure for our product stewardship program and communication processes for compliance and performance, especially around water and chemicals management.
- » Integrate EHS requirements within the whole product life cycle, from pre-clinical to launch.
- » Use leading environmental building standards to assess the environmental sustainability of our offices and manufacturing facilities.
- » Develop a responsible supply chain working group to develop and implement programs and policies for the newly combined Company.
- » Publish our updated conflict minerals policy and report on the country of origin for our minerals, smelters, and refiners using the reporting template from the Conflict-Free Sourcing Initiative.

No.1

We disclose all applicable clinical trial data on [shiretrials.com](https://www.shiretrials.com) and other websites. We have been recognized by AllTrials as the number one pharmaceutical company for clinical disclosure.

4

Ethics and transparency

Upholding high standards of ethics and transparency is fundamental to everything we do. We hold ourselves accountable for operating ethically and responsibly, and ensure we are transparent with our stakeholders. This includes implementing the right policies and procedures so that we meet the highest standards of integrity across all parts of our business and in all our business relationships.

46 Ethical business conduct
49 Clinical trial transparency



Ethics and transparency

Why it matters

Shire is now the leading global biotech serving patients with rare diseases. We strive to deliver strong results in order to maintain our leadership position and bring greater benefits to our patients. How we achieve these results is of equal, if not greater, importance than the results themselves, creating a need for us to behave ethically, transparently, and with integrity at all times. It is absolutely fundamental that everyone working at or on behalf of Shire understands our focus on this commitment.



Our approach

We are committed to the highest standards of ethics and integrity. This means ensuring we have the right policies and procedures in place and helping all of our employees, especially our managers, understand how to foster a culture based on ethics, Responsibility, and transparency.



Our commitment to doing business with high standards of ethics and integrity helps us earn and maintain the trust of the patients and communities we serve.



Jennie Orrico
Chief Compliance and Risk Officer

Ethics and transparency

Ethical business conduct

There are key areas of ethical business conduct that remain at the forefront of our Company and the work we do year on year. These areas require constant monitoring and development and are outlined in this section.

Ethical conduct

[Our Code of Ethics](#) outlines our expectations for doing business with integrity. It highlights where employees may need to be alert to situations that pose ethical questions and provides guidance on how to make the right decisions. New employees are required to read and commit to the Code of Ethics when joining Shire, and all employees must review and renew their commitment every year. During 2016, we worked to ensure that all employees of our newly combined Company have read the Code of Ethics and understand the implications for them.

Anti-bribery and corruption

We do not tolerate bribery or corruption. Everyone working for or with Shire, including partners and suppliers, must ensure they work without engaging in any form of bribery or corruption. Employees have access to our Anti-Bribery and Corruption (ABC) policy and receive training on the policy when they join the Company and annually thereafter. Additional training is provided to employees working in areas with a higher risk of bribery and corruption.

Ethical marketing, selling, and professional support

Given our commitment to developing treatments for rare diseases, we focus our scientific and commercial efforts toward specialty physicians. In addition to our medicines, we also provide these physicians with information and data relating to our therapeutic areas. We want to develop strong and transparent relationships with physicians, as well as with patient groups, to build trust and raise awareness of rare diseases, in order to improve access to medicines for patients.

We adhere to the most stringent commercial and medical regulatory requirements and obey industry promotional and non-promotional guidelines for each country in which we operate. We do this by training our Sales, Marketing, and Medical Science Liaison (MSL) professionals so that they have a thorough understanding of these guidelines and requirements. [Read more on our approach to ethical conduct.](#)

Our code of ethics outlines our expectations for doing business with integrity. We make sure all employees have read the code and understand its implications.



Ethical business conduct continued

Bioethics and animal welfare

We are committed to researching and developing new, well-differentiated medicines that provide meaningful patient benefits, but we must comply with the rules and regulations that govern our industry. Great progress has been made in recent years to reduce and improve the use of animals in pharmaceutical research and development. Until validated alternatives become available, however, health and drug regulatory authorities around the world continue to require animal testing to support the clinical development and registration of new medical products.

We have clear ethical standards, principles, and processes governing the necessary use of animals during research, development, and registration of new medicines at Shire. Our facilities that work with animals are accredited by the Association for Assessment and Accreditation of Laboratory Animal Care (AALAC), reinforcing our commitment to responsible animal research. We also practice the “3R” guiding principles for the ethical use of animals in testing:

- **REDUCE** the number of animals used to the minimum necessary for scientific validity.
- **REPLACE** the use of animals as scientifically-validated alternatives become available.
- **REFINE** the methods and techniques applied to improve the wellbeing of the animals used.



We recognize the importance of respecting the human rights and fundamental freedoms of all.

Since our combination with Baxalta, we have been developing our Global Animal Welfare policy. This will outline the principles, processes, and ethical standards governing the necessary use of animals in our work, and describe the overall process for justifying and tracking internal and external animal studies at Shire.

Human rights

We recognize the importance of observing the human rights and fundamental freedoms of all. We support the UN Universal Declaration of Human Rights and commit to the principles of the International Labor Organization's Declaration on Fundamental Principles and Rights at Work. It is particularly important that we safeguard the rights of those taking part in our clinical trials. We do this through the informed consent of trial participants and adhering to the International Conference on Harmonization of Good Clinical Practice Guidelines.

What we did in 2016

Responding to the Modern Slavery Act

As our Company continues to grow, our compliance programs must evolve to support our growth and continue to add value. This year, we have prepared our statement in response to Section 54 of the Modern Slavery Act 2015, outlining our policies and action to identify and tackle the risks of modern slavery throughout our business and supply chain. It covers Shire's financial year from January 1 to December 31, 2016 and is published on our website, shire.com.

We have prepared our statement on Modern Day Slavery, outlining our policies and actions to tackle the risks of modern slavery across our business and supply chain.



Ethical business conduct

continued

Enhancing the transparency of our political engagement

We support and contribute to political candidates in the United States who share Shire's commitment to patient access and innovation.

We respect all local, federal and national political customs everywhere we operate and comply with applicable laws, regulations and industry standards governing these contributions.

Following the merger with Baxalta, Shire created a unified Political Action Committee (PAC), integrating our political engagement activities and policies. PAC funds are generated from voluntary contributions from eligible Shire employees.

Shire's Public Affairs team maintains clear rules and procedures governing the activities of our PAC, which conducts our political engagement.

In 2016, Shire's PAC made political contributions totaling \$32,500 to candidates in the United States.



Training employees and third parties

We are committed to providing effective compliance training for all of our employees, including through our online e-learning modules, which were updated this year. These modules cover our Code of Ethics, anti-bribery principles, transparency requirements, and global healthcare guidelines, which enables our business to operate compliantly in our industry.

In many countries, third party partners work on our behalf to deliver, market, and sell our products. We hold them to the same standards we apply to ourselves. To help them understand our requirements, we ran an online training course for partners around the world on our Anti-Bribery and Corruption (ABC) policy and Code of Ethics.

Monitoring compliance

We use internal auditing and monitoring programs to assess the effectiveness of our compliance programs and help us make adjustments where appropriate. In 2016, we added real-time analytics to our compliance monitoring program to increase awareness and potential identification of compliance risk.

Ethics and transparency

Clinical trial transparency

Across Shire, we follow the [Principles for Responsible Clinical Trial Data Sharing](#) that were jointly adopted by the Pharmaceutical Research and Manufacturers of America (PhRMA) and the European Federation of Pharmaceutical Industries Association (EFPIA) in 2014.

We pledge to share clinical trial data in a responsible manner, consistent with the following principles:

- Safeguarding the privacy of patients.
- Preserving scientific rigor and trust in regulatory systems.
- Maintaining incentive for investments in biomedical research.

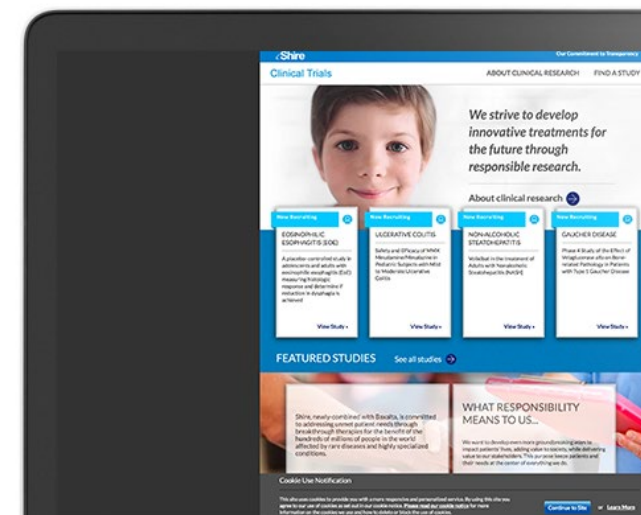
We disclose clinical trial information on public registers and websites at a number of points across the trial process, including: prior to patient recruitment; within one year after study completion; following marketing authorization; and when investigational research programs have been discontinued.

Our dedicated clinical trials website, [shiretrials.com](#), uses filters to enhance the search function, providing easy access to detailed information about our clinical trials for patients and other stakeholders. We also post Clinical Study Reports, which provide a short overview of the purpose and results of the clinical trials, for all Shire-sponsored clinical studies within 18 months of trial completion.

What we did in 2016

Improving shiretrials.com

During 2016, we incorporated the data and reports of clinical trials from Baxalta on [shiretrials.com](#). This has grown our robust resource for clinical trial information and data.



Clinical trial data transparency is vital for our credibility and to promote innovative research.



Jeremy Chadwick, PhD
Head of Clinical Development Operations

Clinical trial transparency continued



#1

We have been recognized as the number one pharmaceutical company for clinical disclosure by AllTrials.



100%

We disclosed 100% of all applicable clinical trials on public websites.

Public disclosure

As part of our commitment to transparency, we disclosed 100 percent of all of our newly combined Company's applicable clinical trials on public websites, in accordance with our policy, and specific requirements in different jurisdictions. We also posted 75 Clinical Study Report synopses on shiretrials.com. Publishing the results of all of our clinical trials has been acknowledged by AllTrials who, this year, recognized Shire as the number one pharmaceutical company for clinical disclosure.

Making disclosure accessible for patients

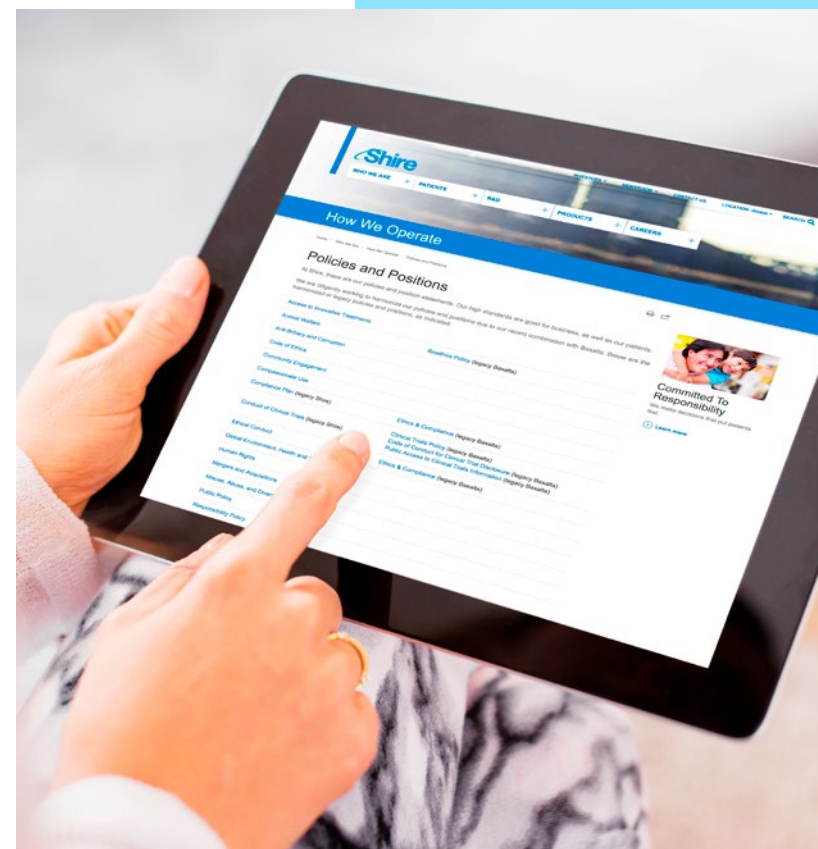
In line with the European Medicines Agency policy, we have developed plain language summaries of clinical study results for patients who participated in our trials. We did this in collaboration with the Center for Information and Study on Clinical Research Participation (CISCRP), a non-profit organization dedicated to engaging the public and patients as partners in the clinical research process. We also established a process and template for responsible data sharing that fulfill the EFPIA/PhRMA requirements and meet the expectations of the EU Clinical Trials Register.

What we will do in 2017

- » Continue to distribute our Code of Ethics to all employees and ensure all have taken the associated e-learning training modules.
- » Continue to reach the highest levels of clinical trial disclosure and commit to a target of >95 percent timely clinical trial registration/ results reporting.
- » Establish more robust disclosure standards, including providing plain language summaries for the general public via our website, which will exceed EFPIA/PhRMA transparency requirements.
- » Continue to protect patient privacy, especially in rare disease trials, by balancing trial data provision with protection of patients' personal data.

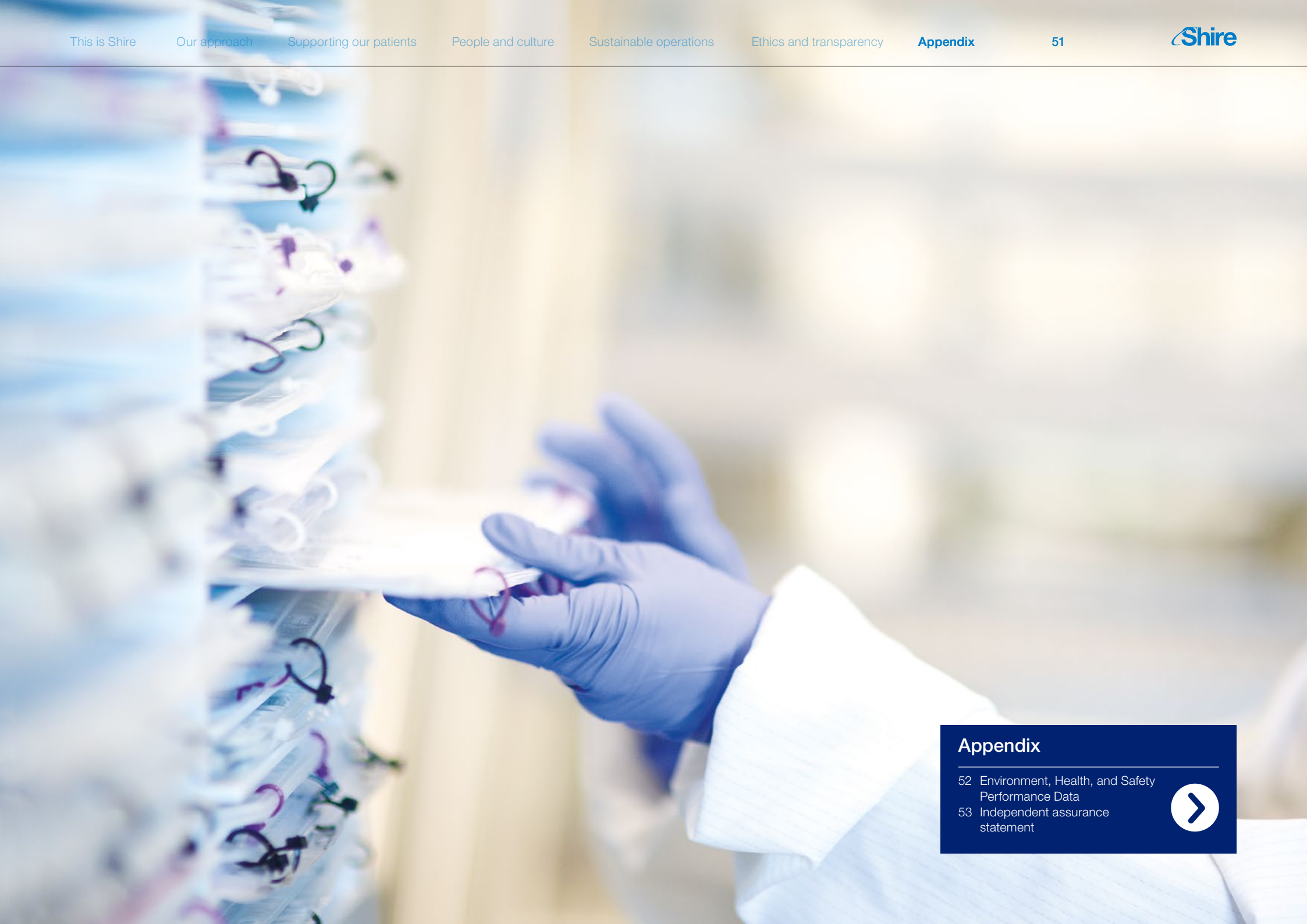


All of our Policies and Positions papers are available on our website



Read more online

[Principles for Responsible Clinical Trial Data Sharing shiretrials.com](http://shiretrials.com)
[Our commitment to transparency](#)
[AllTrials launch of Trials Tracker](#)



Appendix

- 52 Environment, Health, and Safety Performance Data
- 53 Independent assurance statement



Environment, Health, and Safety (EHS) Performance Data*

Category	Verified data
Air emissions	
NOx/SOx emissions from Company operated stationary equipment (metric tons)	45
Energy	
Energy consumption – electricity (trillion joules)	1,532
Energy consumption – fuel excluding mobile sources (trillion joules)	2,037
Energy consumption – Company operated vehicles (trillion joules)	324
Renewable energy (%), purchased + grid	40%
Renewable energy (%), purchased	28%
Greenhouse gas emissions	
Scope 1 emissions (thousand metric tons CO ₂ e)	148
Scope 2 emissions – market based methods (thousand metric tons CO ₂ e)	118
Scope 2 emissions – location based method (thousand metric tons CO ₂ e)	136
Scope 1 and 2 emissions (metric ton)/revenue (millions U.S. dollars)	23.3
Water	
Total water consumption ¹ (thousand cubic meters)	4,216
Water consumption in areas with scarce water resources	215
Water consumption in areas with stressed water resources	2,013
Water consumption in areas with sufficient water resources	1,904

Category	Verified data
Waste	
Total waste (metric tons)	23,210
Regulated waste (metric tons)	7,010
Non-regulated waste (metric tons)	16,200
Waste disposition	
Percent recycled	43%
Percent recycled with energy recovery	16%
Percent landfilled	34%
Percent incinerated	4%
Percent other disposal	3%
Reportable spills and releases	
Number of reportable spills and releases	8
Number of environmental NOV/citations	1
Total number and volume of significant spills ²	0
Health & safety	
Total recordable incident rate (TRIR)	1.01
Lost time incident rate (LTIR)	0.16

¹Water availability data were not available or determined for a number of sites with a total consumption of 84,000 cubic meters.

²GRI G4 Indicator EN24 was used as a guideline for defining a significant spill.

*Bureau Veritas North America has verified and provided limited assurance for the Environmental, Health, and Safety data in this report (see verification statement).

Independent assurance statement

Introduction and objectives of work

Bureau Veritas North America, Inc. (BVNA) was engaged to conduct an independent assurance of environmental health and safety (EHS) data to be reported by Shire for the calendar year 2016. This Assurance Statement applies to the related information included within the scope of work described below.

The determination of the EHS data is the sole responsibility of Shire. BVNA was not involved in the determination of the reported data. BVNA's sole responsibility was to provide independent assurance on the accuracy of reported data, and on the underlying systems and processes used to collect, analyze and review the information. The intended users of this assurance statement are the management and stakeholders of Shire.

Scope of work

Shire requested BVNA to conduct limited level assurance of the following:

- EHS data reported for the calendar year 2016 in the data appendix of Shire's Responsibility Review including air emissions; energy; greenhouse gas emissions; water; waste; reportable spills; and health & safety data.

Excluded from the scope of our work is any assurance of information relating to:

- Data outside the defined assurance period, the calendar year of 2016.
- Any financial data (e.g., revenues) previously audited by an external third party.

Methodology

Our work was conducted against BVNA's standard procedures and guidelines for external Assurance of Sustainability Reports, based on the requirements of the International Standard on Assurance Engagements 3000 (ISAE 3000) as the reference assurance standard and the World Resources Institute (WRI)/World Business Council for Sustainable Development (WBCSD) Greenhouse Gas Protocol and the Global Reporting Initiative (GRI) G4 Guidelines as reference reporting standards.

The work was planned and carried out to provide limited, rather than absolute, assurance and we believe it provides a sound basis for our conclusions.

As part of BVNA's limited assurance, BVNA undertook the following activities:

1. Interviews with relevant Shire personnel responsible for collecting and reporting EHS performance data. These interviews included discussions with staff members responsible for contributing data within the scope of this assurance;
2. Review of documentary evidence produced by Shire to support EHS data within the scope of this assurance;
3. Audit of performance data, including review of a sample of data to source documentation during a visit to a representative manufacturing site located in: Covington, Georgia and remote review of data from manufacturing sites located in Los Angeles, California; Lexington, Massachusetts; and Hayward, California. Consolidated data for Biolife Collection Centers was also reviewed;
4. Review of Shire data and information systems used for collection, aggregation, analysis and review of EHS data.

Our findings

On the basis of our methodology and the activities described above:

- Nothing has come to our attention to indicate that the reviewed information within the scope of our verification is not materially correct.
- Nothing has come to our attention to indicate that the reviewed information is not a fair representation of the actual environmental and health and safety data for calendar year 2016.

It is also our opinion that Shire has established appropriate systems for the collection, aggregation, analysis and review of EHS data within the scope of this assurance.

Statement of independence, impartiality and competence

The Bureau Veritas Group is an independent professional services company that specializes in Quality, Health, Safety, Social and Environmental management with over 180 years history in providing independent assurance services, and an annual 2015 revenue of 4.6 Billion Euros.

No member of the assurance team has a business relationship with Shire, its Directors or Managers beyond that required of this assignment. We have conducted this verification independently, and there has been no conflict of interest.

The Bureau Veritas Group has implemented a Code of Ethics across the business to maintain high ethical standards among staff in their day-to-day business activities.

The assurance team has extensive experience in conducting assurance over environmental, social, ethical and health and safety information, systems and processes and an excellent understanding of the Bureau Veritas Group's standard methodology for the Assurance of Sustainability Reports.

Attestation:



Lisa S. Barnes, Lead Verifier
Practice Line Leader
Sustainability and Climate Change Services
Health, Safety and Environmental Services



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