efpia

European Federation of Pharmaceutical Industries and Associations

The Power of One: a commitment to collaboration

2013 Annual Review and forward look

Contents

The EFPIA Annual Review is meant to serve as an overview of hot topics currently being discussed in the pharmaceutical industry. As EFPIA launches its Health & Growth Strategy for an integrated life sciences strategy for Europe, this year's Annual Review examines these topics in context of the three aims underlying this vision: Better Health Outcomes; Sustainable Healthcare Systems; and a Thriving Innovative Life Sciences Sector. You will find each colour-coded section prefaced by relevant facts, figures and statistics to start the conversation on how we can achieve these goals, together.

A Commitment to Collaboration and The Power of One:

A Foreword from EFPIA Director General **Richard Bergström**

Richard Bergström
Director General of EFPIA

Collaboration is key to a more successful, healthier Europe. Looking at events of the past year, I am increasingly confident of this fact. Our greatest success stories – and biggest learning opportunities – have come from our collaborative efforts with others.

Our strategy towards an integrated life sciences strategy in Europe, launched this year, looks to unleash the power of collaboration. Working together, with a renewed focus, we will be able to improve health outcomes and remove inequalities; support predictable healthcare systems to speed access to medicines; and build a thriving innovative life sciences sector to promote European competitiveness.

The Innovative Medicines Initiative (IMI) exemplifies the positive results when we collaborate. This is one of the pillars that will help build a thriving innovative life sciences sector in the EU – something that will benefit European economies and European patients. A healthy innovative research sector is one part of a healthier future for the EU – and something worth championing.

IMI2, launched this year, will help encourage industry investment in Europe, playing a key role in stimulating collaboration with other healthcare groups, including diagnostics, IT, and imaging. This open approach will help ensure all elements of the biosciences ecosystem – major pharmaceutical companies, SMEs and academia alike – work together more effectively, and help the EU maintain its status as an attractive centre of innovation capable of enacting real world change.

IMI not only delivers results but also works to put in place mechanisms to exploit these results in broad research practice, going beyond single project results. Thanks to continued dialogue with regulators from Europe and beyond, and goal-specific projects and programmes designed with public health priorities in mind, IMI is able to turn the intangible into tangible results with real benefits for patients.

Healthcare professionals (HCPs) and healthcare organisations (HCOs) have valuable working relationships with the industry necessary to advance medicines research and development. Doctors and healthcare organisations offer invaluable insights into patient behaviour and disease management, which can help inform the pharmaceutical industry's efforts to improve patient care and treatment options.

By continuing in a spirit of partnership and collaboration, we can better understand a new discovery's role in society and how it can best play its part in delivering real benefits.

Of course, doctors should be compensated for their time and the expertise they share – but this could become clearer. That's the aim of the *EFPIA Code on Disclosure of Transfers of Value from Pharmaceutical Companies to Healthcare Professionals and Healthcare Organisations* which launched this year, requiring EFPIA member companies to disclose financial and other transfers of value (i.e. speaking fees for a congress) made to HCPs and HCOs. The aim is to illuminate the relationship between industry and HCPs/HCOs so patients can have full confidence in the system.

This is just one part of EFPIA's Responsible Transparency initiative. I am proud to see the progress my member companies have made in implementing the EFPIA-PhRMA Principles for Responsible Clinical Trials Data Sharing, which formally came into effect on 1 January of this year. I had the opportunity to highlight some of the concrete examples of progress made at the DIA (the Global Forum for Therapeutic Innovation & Regulatory Science) Euro Meeting in Vienna in March.

Above all, the most profound change needed in my industry is to take the next step to involve patients in the development and evaluation of new medicines. Nobody knows the disease better than the patient. They understand the real benefit of a new therapy, and what side effects can be tolerated. Beyond those suffering from a disease, we need to acknowledge that we serve society at large and involve all citizens. How do we make sure our research priorities are right? This is one of the key priorities to take up in the coming years.

These challenges can't be solved by the pharmaceutical industry alone; just developing a new medicine won't do the trick. By continuing in a spirit of partnership and collaboration, we can better understand a new discovery's role in society and how it can best play its part in delivering real benefits.

This document explains how the power of one collaborative effort is already being realised and helping patients. I hope you enjoy reading the content and it inspires you to get involved and get connected with our mission.

Growing Together Towards a Healthier EU:

An Introduction from EFPIA President **Christopher Viehbacher**

Christopher Viehbacher
President of EFPIA

Access to healthcare is a right but is something we often do not appreciate until our own health or that of a loved one is in danger. Over the past five years, the value of health and the healthcare systems designed to support good health, have come to the forefront of the conversation in Europe. Austerity measures and budget cuts have taken a toll, not only on European economies, but also on the health of European citizens.

The economic downturn has had a dramatic effect beyond finances. We have seen increases in HIV and other infectious diseases that are more closely linked to the scaling back of public budgets. In one region of Greece, a 29% increase in the rate of heart attacks from 2008-2011 has been reported.[1] Countries whose health systems are showing the most strain – Greece, Portugal, Spain – are those where austerity has cut deepest – while countries like Iceland, whose government rejected cutbacks as a way through the crisis, are seeing a minimal impact on health[2].

There is not only bad news: We have learned from the hard times. Healthcare stakeholders, public policy actors and everyday European citizens recognise the problems existing in today's European healthcare systems. They have come together to discuss how to solve those problems. I'm proud to be part of this conversation which highlights a common goal that should drive all of us: Building a better future, both in terms of health and economy, for Europe. How do we achieve a healthier EU?

We need to **improve health outcomes. One way is by increasing prevention and chronic disease management**. Chronic diseases are an area of increasing concern in Europe – in fact this past March, the EU held its first Summit on Chronic Diseases acknowledging the seriousness of the issue. The discussion was timely: Chronic diseases account for 75% (over €700billion) of Europe's healthcare bill and are responsible for up to a 7% GDP loss in some EU countries[3]. We also need to consider that key risk factors for chronic diseases, such as age and adult obesity, are projected to increase. If we do not take action immediately, we can only expect further prevalence and a more severe impact of chronic conditions.

[1]http://www.newstatesman.com/world-affairs/2013/04/heart-attacks-maternal-care-human-cost-austerity-greece
[2]http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)60102-6/abstract
[3]European Commission (2010): Projecting future healthcare expenditure at European level Economic Papers 417 / July 2010

A thriving life sciences sector is good news for Europe and European citizens. Efforts made to nurture the life sciences in Europe will pay off, both in terms of health outcomes and economies.

Another step towards a healthier EU requires **addressing the deepening disparities across Europe in access to healthcare and innovative solutions**. Consider, for instance, the fact that life expectancy in Romania is nine years less than in Spain[4]. Eliminating differences in access to healthcare and medicines between (and within) countries is essential if we are to ensure equal care for all.

Finally, **we need to build an environment in Europe that will nurture a thriving innovative life sciences sector**. In the 1960s, Europe was the hub of pharmaceutical discovery, accounting for nearly 60% of all new chemical entities. While the US has since caught and overtaken Europe, the continent remains a medicines powerhouse. Europe has many of the required components for leading in the life sciences sector, including boasting the highest number of the world's research scientists and a large proportion of its biotechnology patents. However, it faces increasingly tough competition from other areas in the world.

Across the board, we are seeing greater acceptance of the **need to connect science to health needs, by strategically consolidating research agendas between public and private actors - and among European Member States**. R&D is what drives the pharmaceutical industry. It's what allows us to deliver new and improved medicines to patients. Increasingly, the conversation is turning to the other ways R&D contributes to society, beyond creating medicines. A thriving life sciences sector is good news for Europe and European citizens. Efforts made to nurture the life sciences in Europe will pay off, both in terms of health outcomes and economies.

These goals are admittedly ambitious – but they are feasible. As EFPIA Director General Richard Begström notes in his introduction: Collaboration is the key to success. We are already seeing the positive outcomes (some of them highlighted in this Review) of more open conversation and collaboration. We can also see a path towards a more positive future – for European patients, citizens and society as a whole.

[4]The World Bank: Database on life expectancy http://data.worldbank.org/indicator/SP.DYN.LE00.IN

Better Health Outcomes:

Facts and Figures

In recent decades, we have made huge improvements in health outcomes and life expectancy. In Europe alone, men and women can expect to live a decade longer than they would have in the 1950s[1]. Medicines have played a key role in this achievement, notably in areas of infectious disease and chronic conditions – even cancer.[2] Once seen as a major killer with poor prognosis for survival, cancer is in many cases now considered treatable, particularly with early diagnosis.

Such advances in healthcare have moved society beyond the concern of simply extending life. We also must concern ourselves with improving life in later years, especially as age-related diseases become more prevalent. A person's life isn't just about quantity, but quality. Every European lives on average 18.4 years with disability or illness.[3] This is set to rise as the share of disability life-years, as a percentage of total life-years, increased in all but two EU-28 countries from 1990-2010.[4]

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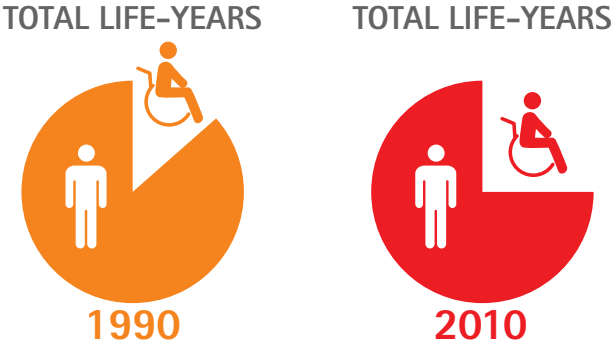


[1]United Nations, Department of Economic and Social Affairs (2011): World Population Prospects – The 2010 Revision; released on 3 May 2011 http://esa.un.org/wpp/index.htm

[2]Lichtenberg, F. (2012): Pharmaceutical Innovation and Longevity Growth in 30 Developing and High- income Countries, 2000-2009 NBER Working Papers 18235, National Bureau of Economic Research, Inc. (2012); Smith, B (2011): The Future of Pharma, Gower Publishing Limited (2011)

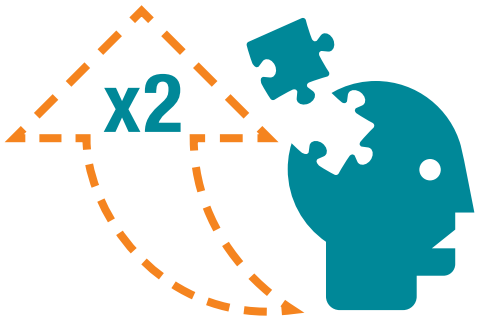
[3]Eurostat: variousdatabases(accessed 2013); A.T. Kearney analysis

[4]Lancet: Healthy life expectancy for 187 countries, 1990–2010 (2010); A.T. Kearney analysis

[5]Eurostat: variousdatabases(accessed 2013); A.T. Kearney analysis

Additionally, despite progress, inequalities persist across Europe, both between and within countries. The pharmaceutical industry is dedicated to reducing healthcare inequalities – but it cannot accomplish this alone. Greater equilibrium will require a collaborative effort bringing together policy-makers and healthcare stakeholders.

Advances in science and technology have allowed for great strides in medicines research and development, benefitting patients around the world. But with progress come new hurdles. As an industry, we are now facing two distinct challenges: Improving quality of life, not just quantity of life years; and ensuring that all patients have equal access to healthcare advances. Medicine and healthcare are not just about extending lives, but making lives better. This is a challenge that goes beyond R&D – it requires a collaborative effort among policy-makers, payers, and industry.

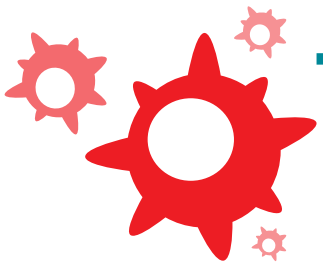


There is a predicted two-fold increase in late-stage Alzheimer's to

7.5M BY 2050[6]

Demographic and lifestyle changes

are predicted to result in an increased incidence of cancer



+400,000 NEW CASES 2010 → 2020

LIFE EXPECTANCY

ROMANIA

9 YEARS < THAN

SPAIN

the vast differences in access to healthcare and medicines between these two countries is a contributing factor.[7]

[6]Brookmeyer R et al. (2007)
[7]The World Bank: Database on life expectancy http://data.worldbank.org/indicator/SP.DYN.LE00.IN

Moving Ahead on Global Health Issues

The EU is a major player in global health issues, not only through the research and development it supports, but also as a supporter of development. The recent approval of the 2nd phase of European & Developing Countries Clinical Trials Partnership (EDCTP) is a strong signal of the EU's continuing commitment. Increasingly, the conversation is turning towards sustainable development and the status of many developing nations as up-and-coming power players on the global scene.

A compelling example of the shifting tone in the conversation around global development was evident in the roundtable event which took place during the April 2014 EU-Africa Business Summit[1]. The roundtable brought together diverse participants from the healthcare and pharmaceutical industries to discuss and determine recommendations aimed to improve healthcare in Africa. The conclusions of the meeting were summarised in a series of recommendations and presented to the heads of state at the EU-Africa Summit.

The event brought together diverse participants, from public policy actors to pharmaceutical industry representatives and NGOs. Following the roundtable, EFPIA hosted an EU-Africa debate on non-communicable diseases, under the patronage of Rebecca Taylor MEP. The debate featured speakers from the NCD Alliance, the International Association of Patient Organisations and the European pharmaceutical industry. This was a continuation of previous debates held as part of EFPIA's Global Health Initiative (GHI).

The final report from the first part of the Global Health Initiative was published in December 2013. "The Global Health Initiative: Recommendations from Public Debates" summarises the recommendations gleaned from the project. The GHI was established with the aim of exploring collaborative, dialogue-driven solutions to global health issues. This was accomplished through a series of public debates, each bringing together diverse stakeholders to discuss global health issues. The final report covers the outcomes of these debates – which ranged from topics such as clinical trials in developing countries to supply chain and delivery issues impacting access to medicines – and provides recommendations for next steps.

[1] 'Health and Pharmaceutical; promoting growth, innovation and access to healthcare and pharmaceuticals through EU-Africa Business Cooperation, including local production of generic medicines in Africa'

It is clear that my companies have to deliver profits to the people that invest in risky projects, but all the professionals in the companies are driven by the idea that the results of our research reach patients all around the world – whether rich or poor.

EFPIA DG Richard Bergstrom
blogs on Global Health (5 December 2013)

In the year ahead, EFPIA will continue its efforts surrounding the GHI. The point of this endeavour thus far has been to spark debate and conversation on complex global health issues. By offering recommendations gathered from a consensus among diverse stakeholders, EFPIA does not propose a "silver bullet" solution. By moving the discussion ahead, however, we can start to lay the groundwork for concrete actions.

One of the most significant international debates of the coming year will concern the part that health will play in international development objectives after 2015. EFPIA will continue to advocate constructive dialogue with key stakeholders from both developing and developed areas. The engagement of governments is central to the success of such initiatives. As the source of new and improved medicines, the research-based pharmaceutical industry has a responsibility to engage in the dialogue surrounding global health issues – after all, these medicines serve patients around the world, not just in Europe.

An initial set of industry proposals can be found at: http://www.ifpma.org/fileadmin/content/Publication/2014/EFPIA_IFPMA_JPMA_PhRMA_Perspectives_on_UHC_March2014.pdf

Global health is an area which concerns all of us.

Commissioner Tonio Borg.
Introducing the Global Health Initiatives final report

Fighting Counterfeiting, Protecting Patients

Counterfeiting is a crime with very real consequences: it presents a major threat to patient safety and we have seen the devastating evidence of this. Factors like an increase of unlicensed online "pharmacies" have amplified the risk and called increasing attention to the issue – pushing governments, security officials, and the pharmaceutical industry to act.

Just this past spring, some 2.4 million counterfeit drugs were seized at the French port of Le Havre. According to a statement issued by French Customs Authorities, some of the counterfeit medicines contained no active ingredients – while others had different levels of the appropriate active ingredient, presenting a serious potential health risk[1]. In 2011 alone, approximately 30 million fake medicines were seized at EU borders.[2] What is especially troubling is the fact that it's impossible to know what the real numbers are – they are very likely higher than what is reported. Counterfeiters are criminals. They don't report their earnings and sales, or release quarterly reports. We can't know for sure just how big the problem is. Statistics aside, there is no doubt that action is required – because it only takes a single counterfeit pill to impact the wellbeing of one patient.

Knowing this, EFPIA has teamed up with PGEU (Pharmaceutical Group of the European Union), GIRP (Groupement International de la Repartition Pharmaceutique) and EAEPC (the European Association of the Euro-Pharmaceutical Companies) to develop an anti-counterfeiting model for Europe. These organisations – representing pharmacists, wholesalers, and parallel traders, respectively – came together with the aim of developing a system that will provide a high level of security for patients while being cost-effective, pan-European and interoperable – and capable of being effectively integrated into existing structures and practices in the distribution chain. The result is the European Medicines Verification System (EMVS), a system designed to ensure that medicines are making it safely from the point of manufacture to the point of sale – to the patient.

The proposed ESM verification system comprises the European Hub and the National Blueprint Systems (nBPS). The European central hub is connected to a series of single-country or multi-country data repositories that serve as verification platforms. Pharmacies and other registered parties can use these to check a product's authenticity. The system will be interoperable between EU countries and will allow for the reconciliation of products traded between EU member states (known as parallel traded products) through the European central hub. It will also offer those countries that do not want to set up their own national system the opportunity to join an existing product verification infrastructure. These components are to be managed by the European Medicines Verification Organisation (EMVO), which is to be founded in the course of 2014 and foresees participation of authorities and other relevant stakeholders in the overall governance.

2014 is a big year for the venture, as the Hub will be connected to the German securPharm system[3]. This is the first time the Hub has linked with a national system covering the full information chain at European level – from manufacturer to pharmacy. Meanwhile, development and implementation of the European Hub is well under way.

Fighting Fakes: A Look at the Numbers

30 million – Number of fake medicines seized at EU borders in 2011 alone. **2.4 million** – Number of counterfeit drugs seized at French port of Le Havre in Spring 2014. **1.2 million** – Number of doses of counterfeit Aspirin seized by French custom officers in May 2013. **1 million** – Number of fake Xanax pills seized at Zurich airport in October 2013. **1** – One dangerous counterfeit pill is all it takes to endanger a person's wellbeing.

The EMVS is in line with the Falsified Medicines Directive (FMD - 2011/62/EU), an initiative of the EU to fight back against counterfeiters and the dangerous goods they bring across EU borders. The FMD asserts that all prescription-only medicines will have to bear safety features (i.e. a unique serial number placed on each pack, together with tamper-evident packaging).[4] The FMD also requires the establishment and management of a repository system that will store the unique identifiers of the serial packs, and contain information on the safety features. The European Commission will determine the specifications of the serial number to be placed on packs when it sets out the rules for implementation in the "Delegated Acts". Once the Delegated Acts are published – anticipated in the first quarter 2015 – EU Member States and pharmaceutical companies supplying the EU market will have three years to take the necessary steps and ensure they are in compliance. These specify that the composition, format and carrier of the unique identifier will be fully harmonised across the EU; medicine authenticity will be guaranteed by an end-to-end verification system supplemented by risk-based verifications by wholesale distributors; and that the repository containing the unique identifiers will be set up and managed by stakeholders, with national competent authorities having the ability to access and supervise the database.

In Europe, the FMD is an important step towards better protecting patients from counterfeit medicines. EFPIA welcomes this initiative as another step towards protecting patient safety in the EU. The pharmaceutical industry has a vested interest in fighting counterfeiting: developing new medicines is only one part of providing healthcare treatments for patients – we also have to ensure that people benefit from those medicines. The sooner we can implement measures like the European Stakeholder Model and the Falsified Medicines Directive, the sooner we will be making patients that much safer.

In January 2014 EFPIA signed the Memorandum of Understanding (MoU) on the sale of Counterfeit Goods via the Internet, already signed by some 33 e-commerce platforms and major brand owners. The MoU aims at establishing a code of practice in the fight against the sale of counterfeit goods over the Internet while enhancing collaboration among its signatories. In addition EFPIA participates as an observer in the Alliance for Safe Online Pharmacy (ASOP EU) initiative at European level, an informal multi-stakeholder patient safety coalition whose objective is to make buying medicines online safer by encouraging voluntary and collaborative action against illegal online pharmacies.

EFPIA also continues its outreach efforts towards Council of Europe members to ensure they ratify the MEDICRIME Convention (Convention on counterfeiting of medical products and similar crimes involving threats to public health). This would result in the adoption in each country of a common definition of counterfeit medical products, the criminalisation of the manufacture and supply of counterfeit medicines, and the introduction of effective, proportionate and dissuasive sanctions and measures against counterfeiters.

[1]http://www.pharmatimes.com/Article/14-04-10/Huge_haul_of_fake_drugs_seized_in_France.aspx#ixzz2yr4h9sBy
[2]EC Customs Report, July 2012.
[3]Securpharm is a national anti-counterfeiting initiative. Launched by German pharmaceutical manufacturing, pharmacist, and wholesaler associations, it is designed to test whether medicinal products are genuine or not and is intended to comply with the EU Falsified Medicines Directive.
[4]Certain products or product categories of prescription-only medicines might be exempted according to a risk assessment. Over-the-counter medicines, for instance, are excluded – unless there is a risk of falsification

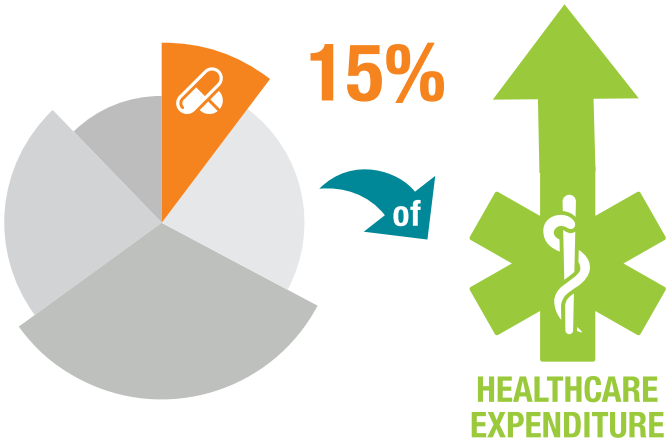
Supporting Sustainable Healthcare Systems:

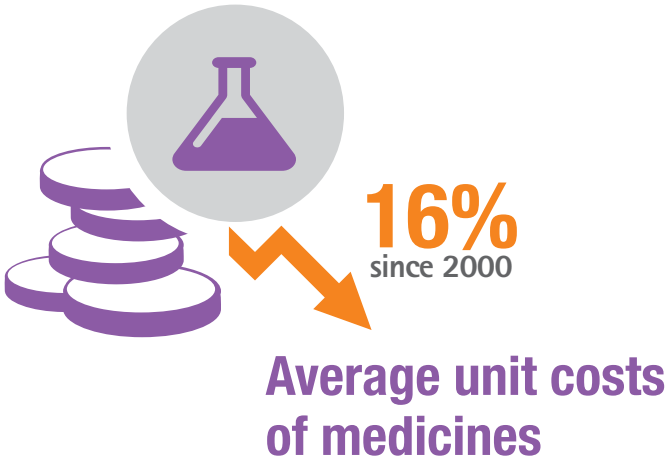
Facts and Figures

While there is a perception that medicines are the cause of rising healthcare costs in Europe, this is not the case. In Europe, medicines expenditure accounts for less than 15% of total healthcare expenditure[1] – far behind other interventions, e.g. inpatient care and long-term nursing care. Medicines prices are actually down, thanks largely to both price control measures and the highly competitive market that exists for medicines post-expiry.

Medicines accounted

for less that 15% of the growth in healthcare expenditure across OECD-countries in the period 2004–2010.



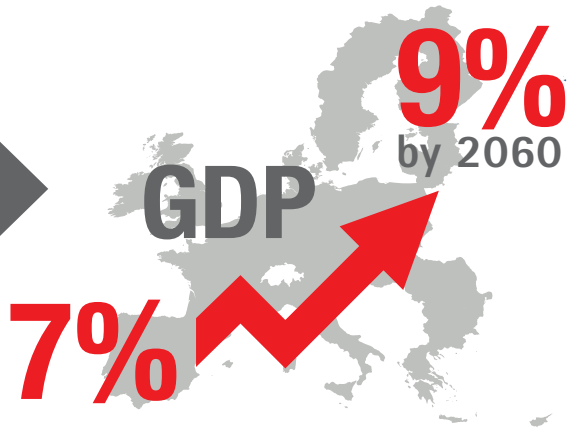


[1]OECD: Health Statistics Database

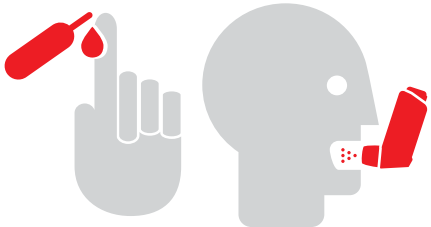
Ensuring sustainable healthcare systems is essential to ensuring a vibrant future for the EU. A recent study by the European Commission projects that, without new approaches, average healthcare spending could rise from just under 7% of GDP to almost 9% of GDP by 2060.[2] Such an increase is only justified if it is positively reflected in the state of our healthcare systems. We need to consider issues that will arise in the future, and how to tackle them. For instance, risk factors for chronic diseases (age, adult obesity) are projected to increase; meaning that we can expect increasing incidence and impact of chronic conditions.

A recent study by the European Commission

PROJECTS THAT
(without new approaches)



Average healthcare spending



Already, chronic diseases

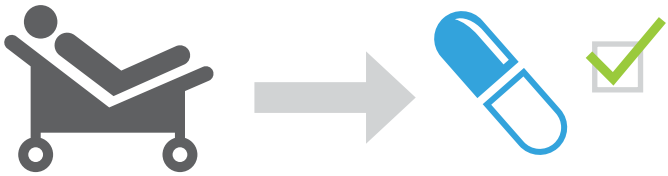
account for **75%** (over €700billion) **of Europe's healthcare bill**

resulting in

[2]European Commission (2010): Projecting future healthcare expenditure at European level Economic Papers 417 / July 2010
[3]The Economist Intelligence Unit (2012)

Early, appropriate use of medicines is one of the most effective interventions a health system can make. A patient who takes their medicines costs the system anywhere between 50% less (e.g. in dyslipidaemia) and 90% less (e.g. in hypertension) than a patient who does not stay on pharmaceutical treatment[4]. Medicines help keep costs down. In the case of chronic disease pathways, medicines play a key role in many areas. In cardiovascular disease, respiratory disease and diabetes, some of the lowest cost pathways have a pharmacological approach at their heart. Even in these cases, the cost of medicines comprises a relatively small proportion of the total costs of the condition. For example, medicines account for just 5% of the cost of treating coronary heart failure in Germany.[5]

Only a significant improvement in health outcomes, supported by an increase in innovation, can keep healthcare expenditure under control. This requires collaboration and a change in perception, underscored by a better understanding of where healthcare spending is going, and the value of investment in different areas. If we want sustainable systems, we can't revamp just one area; we need to address the system as a whole.



A patient who takes their medicine

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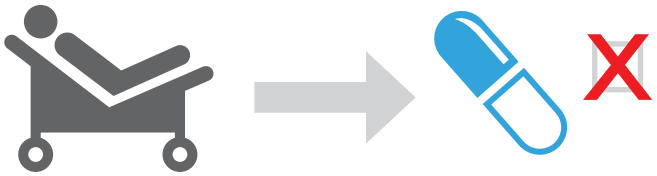
Dyslipidaemia Hypertension

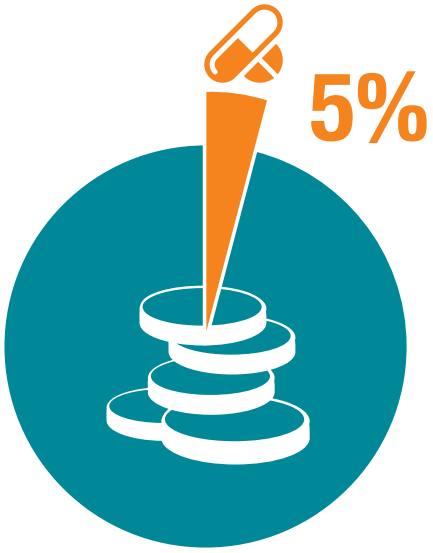
than



than a patient who does not take their medicine

Even in these cases,

the cost of medicines comprises a relatively small proportion of the total costs of the condition



Total costs for treatment of coronary heart failure in Germany

[4]Roebuck, C. et al. (2011): Medication Adherence Leads To Lower Health Care Use And Costs Despite Increased Drug Spending Health Affairs, 30, no.1 (2011): 91-99 doi: 10.1377/hlthaff.2009.1087

[5]A.T. Kearney Analysis

Advancing Opportunities Through Trade

Over the course of the last year the EU has continued its ambitious trade agenda, focusing on ongoing and new Free Trade Agreements (FTAs), as well as bilateral dialogues with third countries. EFPIA continued its advocacy actions towards key EU stakeholders, leveraging the interests of the European pharmaceutical industry.

EFPIA has been one of the key supporters of the launch of the Transatlantic Trade and Investment Partnership (TTIP) between the EU and the US. The aim of the agreement is to create what would be the largest area of free trade globally and would further strengthen what is already the world's most dynamic trading relationship. We believe the agreement could be a key driver of economic growth and job creation on both sides of the Atlantic, and most importantly, serve to strengthen the transatlantic pharmaceutical market. EFPIA has strongly advocated for an ambitious and comprehensive agreement, addressing our industry priorities in the fields of regulatory compatibility initiatives, intellectual property and market access. A conclusion to this agreement is only expected at the end of 2015, but an intense agenda of negotiating rounds will take place in 2014 to ensure that the timetable is respected.

EFPIA has also continued to support the EU-Japan Economic Partnership Agreement. The two sides have made headway in addressing key non-tariff barriers laid out in the roadmap established after the scoping exercise, including on pharmaceutical issues. EFPIA has, together with other industry sectors, publicly supported the continuation of th ese important negotiations.

One of the key outcomes of the past year has been the signing, by the EU and Canada, of the political agreement on the Comprehensive Economic and Trade Agreement (CETA) following four years of intensive negotiations. While some issues remain under discussion, the general framework and various sectoral matters are already solved, including our industry's requests regarding intellectual property (IP). We understand that satisfactory outcomes were achieved on all three of our objectives, namely the introduction of a PTR/SPC system, an effective Right of Appeal for Originators and the upholding of the eight-year coverage of Regulatory Data Protection. EFPIA and the Canadian pharmaceutical association Rx&D have been working hand-in hand in order to obtain clarification on the agreement's content and to conduct outreach activities to key stakeholders.

EFPIA continued to engage with the European Commission in order to keep the industry's priorities high on the agenda in bilateral dialogues with China and Russia in the areas of intellectual property, public health and regulatory matters.

Towards this end, EFPIA contributed to, and participated in, the EU-China High-Level Regulatory Dialogue, and kept its active engagement with the IP Dialogue and supported the EU's IP Key Project in Beijing.

EFPIA stepped up efforts in raising awareness of the industry's challenges in entering the Indian market. A series of advocacy actions were conducted to reach out to key policymakers and stakeholders. These efforts have already yielded results, as IP challenges were registered in the EU's key trade barriers list for India.

EFPIA has also continued dialogues and engagement with other important trading partners, as well as continuing to monitor the developments of the EU's FTAs with Vietnam and Thailand.

There is still much to come in the year ahead and we look forward to having a continued dialogue with all our stakeholders in order to continue creating greater opportunities for our industry in key international markets.

IP: Facilitating R&D, Fostering Innovation

The EU's intellectual property (IP) system is a work in progress. However developments during 2013 highlighted how important IP is to the EU's economic future and underline the commitment to continue building the system.

A joint study[1] by the European Patient Office (EPO) and the Office for Harmonization in the Internal Market (OHIM) highlighted the value of IP to European citizens and to the EU, underpinning its general economic performance. For instance, about 39% of total economic activity in the EU (worth some €4.7 trillion annually) is generated by IPR-intensive industries, while approximately 26% of all employment in the EU (56 million jobs) is provided directly by these industries, and a further 9% of jobs in the EU stems indirectly from IPR-intensive industries.

OHIM also carried out an IP perception study, which highlighted that despite the importance of IP to the EU economy, it remains poorly understood by many people. A lack of knowledge and wrongful perceptions surrounding IP[2], particularly in the field of medicines development, has been cause for concern. Change is ahead, however, as the value of IP is being communicated more clearly, in a way that not only IP lawyers, but also everyday citizens, can understand.

The positive momentum surrounding IP seen in the past year doesn't stop there. From last autumn, EFPIA, the European Generic Medicines Association and other organisations in the business community joined forces in supporting the European Commission's Proposal to review the European Union trademark legislation. The proposal aims to make trademark registration systems more accessible and efficient across the EU, and to introduce robust measures to fight the transit of trademark counterfeit goods in the EU, including medicines. In February 2014, the European Parliament's vote in that direction was particularly welcomed: the capacity of European customs to act is essential in this global fight against the trade of counterfeits.

The decision to create a unitary patent and a Unified Patent Court (UPC) was reached in 2013. EFPIA welcomed this development: until now, patentees in the EU could only obtain a bundle of national patents and enforce them nationally, i.e. via potentially 28 separate litigations. This is an expensive process and poses the risk of different outcomes in different countries. The UP and UPC offer the prospect that a single expert court can decide on the status of a single pan-EU patent and that protection against further infringement will also be available on a pan-EU basis. To that end, the UPC Rules of Procedure, whose 16th draft was released in spring 2014 after an extensive public consultation, will be critical. EFPIA will continue to work to ensure that the new Court is a success.

Finally, EFPIA welcomed the Commission's Proposal for a Trade Secrets Directive, which will strongly foster investments and cross-border R&D collaborations, thereby ultimately benefiting innovation and competitiveness of EU research industries.

EFPIA hopes that discussions surrounding IP will continue to grow, at all levels – not just among industry and policymakers, but also at civil society level. By maintaining the current momentum underpinning and demonstrated by the initiatives above, the new institutions can continue to foster a positive environment for IP that will best serve the interests of the EU and its citizens.

[1]EPO-OHIM, IPRs intensive industries: contribution to economic performance and employment in the EU. Industry-Level analysis report, September 2013. https://oami.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/resources/home/joint_report_epo_ohim_en.pdf

[2]OHIM, EU citizens and Intellectual Property: Perception, Awareness and Behaviour", November 2013. https://oami.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/documents/IPContributionStudy/25-11-2013/european_public_opinion_study_web.pdf

[3]OHIM, EU citizens and Intellectual Property: Perception, Awareness and Behaviour", November 2013. https://oami.europa.eu/tunnel-web/secure/webdav/guest/document_library/observatory/documents/IPContributionStudy/25-11-2013/european_public_opinion_study_web.pdf

Demystifying IP for Everyday Europeans

"All these words are not familiar to me,
they make me think of multinationals,
they belong to a reality that is not mine."

"I have heard about this [Intellectual Property]
but it still feels like something far away.
This is not relevant to my daily life."

These quotes are from a report examining European Citizens' relationship to Intellectual Property, which was released in November 2013[3]. It highlights a major problem in the lack of awareness surrounding IP in Europe. It's understandable: IP is a complex topic, the nuances of which are difficult to capture, especially as it's certainly not something people think about every day.

IP has a major impact on the everyday lives of Europeans, however, and it's important that people are aware of this. With its communications around IP, EFPIA hopes to demystify the topic.

Check out:
- **EFPIA's IP website: http://www.efpia.eu/topics/innovation/intellectual-property**
- **EFPIA Video explaining IP: http://www.efpia.eu/blog/151/51/New-Video-on-World-IP-Day-Introducing-Marty-the-Medicine**

Avoiding duplication in HTA

Health Technology Assessment (HTA) is a general concept that reflects a wide range of methods used by policymakers to support their health policy decisions. HTA is used to measure the medical, economic, social and ethical implications of the use of all health technologies, e.g. medicines, as well as diagnostic and treatment methods, medical equipment, rehabilitation and prevention methods, and organisational and support systems used to deliver healthcare. The overall goal of HTA is to support decision-making that is patient-focused and achieves optimal value. Unfortunately, this is not the case in many countries. HTA is often used as a way to contain cost without taking into account the broader benefits outside the health care budget – such as whether people can stay in the work force longer or stay in nursing homes, costs often carried by society.

In Europe, national decision-makers are increasingly making use of HTAs to support decisions on the allocation of healthcare resources, including expenditure on medicines. National budget holders are interested in understanding the added value of new medicines compared to existing treatments. The evidence required to prove this added value needs to be generated by the developers of medicines during drug development, and comes in addition to the requirements from regulatory agencies for regulatory approval.

Over the past few years, regulatory and HTA agencies have been increasingly willing to jointly discuss appropriate evidence requirements along the life cycle of products. Industry welcomes this development. EFPIA calls for a formal framework of a joint scientific advice process between regulatory and HTA/payer authorities to align evidence requirements both pre-launch (Phase II) and post-launch. Such a joint process should be coordinated and consistent, involving regulatory and HTA/payer authorities and company representatives in shared discussions, and lead to two separate advice documents (a formal CHMP scientific advice letter and a separate HTA scientific advice report). The advice documents must ensure that participants can rely on its content in subsequent national processes.

These principles should be reflected in the EMA guidelines on parallel scientific advice (2014)[1], the SEED project guidelines for a permanent process (expected in 2015)[2]; and the HTA Network discussion paper on HTA-regulatory interactions (also expected in 2015)[3], and be translated into any necessary legislative and process change at the national and European levels.

As elements of HTA in the EU come under review, it is essential that all relevant stakeholders – including patients, healthcare professionals and industry – are active in the conversation.

Despite having one regulatory system for the approval of new medicines, inequalities in access to medicines remain, since decisions on pricing and reimbursement of medicines are more fragmented than ever and are taking longer. HTA in EU Member States has been established with a variety of objectives and methodologies, resulting in different HTA evidence requirements for industry across Member States. This has led to inconsistencies in findings on the added value of the same innovative medicines from one country to the next[4].

In the interest of a more streamlined process, and more equal access to innovative medicines for European patients, the European Commission is supporting EU-wide collaboration between HTA agencies. Industry supports European collaboration on HTA as a way to tackle unnecessary duplication and to enable greater clarity, higher methodological standards in HTA, and improved predictability, along with better and timelier access to medicines. In particular, industry calls on the European collaboration on HTA to recognise the role that HTA plays in fostering innovation in Europe.

In addition to a joint scientific advice process, the HTA Network is looking at the opportunity to conduct joint multi-country assessments of relative effectiveness (the clinical aspects of HTA excluding cost-effectiveness) at the time of launch. EFPIA considers that joint relative effectiveness assessments (REAs) can improve efficiencies in HTA if the joint rapid REA provides a factual report from which Member States take relevant information to support and speed up their local appraisal processes. Any joint rapid REA should replace some elements of national assessment, so that it does not result in an additional European layer and ultimately speeds up patient access to innovation. Context-specific elements of HTA should remain at the national level. Towards this end, industry is calling on the HTA Network to discuss and clarify how joint REA will be useful and used at national level, and to secure political commitment from Member States to incorporate REA assessments in their national decision-making process. They should also discuss ways to ensure that joint REA reports are of consistent high quality and put in place relevant quality control mechanisms. Joint rapid REA could be particularly useful for countries with limited HTA capacity, which could refer to these factual reports as the basis of their national decisions, rather than referencing existing single country systems.

In some countries, HTA has evolved contrary to its objective of supporting patient-focused decision-making and has been misused as a rationing tool. In particular, models focusing only on binary decisions based on fixed cost-effectiveness thresholds fail to recognise innovation and do not give sufficient considerations to patient-relevant outcomes. Industry considers that HTA should primarily build on assessment of medical added value of health technologies taking into account health outcomes relevant to patients. Where economic evaluation is used, it should be one of the information elements of HTA but should not mandate decisions. EFPIA is concerned about activities of some HTA agencies in Europe to advance models based on fixed cost-effectiveness thresholds beyond their borders which goes against the principles put forward in European collaboration.

Moving forward, HTA and the assessment of medicines more generally will need to adapt to the new science. Advances in science and technology have allowed us to refine the way we develop medicines. For instance, personalised medicines for cancer offer targeted treatments based on a specific cancer subgroup's unique molecular makeup. Because cancer cells are heterogenous and genetically unstable, the cancer subgroup may develop resistance to a pharmaceutical agent during treatment. This has encouraged a move away from traditional trial models, towards adaptive methodologies. Such shifts represent significant changes in the sphere of medicines research and development, and need to be considered when reviewing HTA systems. The regulatory environment surrounding medicines research and development – including HTA – must acknowledge and reflect these changes.

The aim is an HTA process that is comprehensive, transparent, robust and systematic. An HTA system based on these principles can help healthcare decision-makers in effectively reaching decisions and determining allocation of resources, and can also facilitate informed updates and diffusion of health technology. As elements of HTA in the EU come under review, it is essential that all relevant stakeholders – including patients, healthcare professionals and industry – are active in the conversation.

[1]http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2014/05/news_detail_002097.jsp&mid=WC0b01ac058004d5c1
[2]http://www.earlydialogues.eu/has/
[3]http://ec.europa.eu/health/technology_assessment/policy/network/index_en.htm
[4]See latest comparisons presented at LASER Workshop in February 2014 between IQWIG/GBA and HAS assessments, reference to be added

Advancing Pharmacovigilance to Keep Patients Safe

As the process that monitors medicines to ensure they reduce risks and increase benefit, pharmacovigilance is essential to ensuring the safety of medicines for patients.

In 2010 the European institutions adopted a new Directive and Regulation dedicated to pharmacovigilance, amending the community code for pharmaceutical products, which became applicable from July 2012 onwards. EFPIA has been working with relevant stakeholders towards its implementation in an efficient and cost-effective manner.

The main challenge for industry is the complexity of the changes as well as availability of the details of implementation. The industry will therefore need time to fully adapt to the new requirements. EFPIA's pharmacovigilance committee has facilitated pragmatic, consistent implementation of the 2010 pharmacovigilance legislation and subsequent guidance directly relevant to patient safety, transparency and provision of benefit-risk information.

EFPIA experts also actively contribute their technical expertise to shape the future development of innovative and scientifically-based pharmacovigilance methods, such as benefit-risk assessment. These assessments are used to compare the benefits of a medicine with any potentially risky side effects, and help determine whether a medicine makes it to market. In this area, EFPIA contributed to the ICH E2C guideline, which gives standards for Periodic Benefit-Risk Evaluation Reports.

EFPIA has also contributed to two relevant projects of the Innovative Medicines Initiative: PROTECT and WEB-RADR. PROTECT (Pharmacoepidemiological Research on Outcomes of Therapeutics by a European Consortium) aims to address limitations of current methods in the field of pharmacoepidemiology and pharmacovigilance. Coordinated by the European Medicines Agency (EMA), the project will develop a set of innovative tools and methods that will enhance the early detection and assessment of adverse drug reactions from different data sources, and enable the integration and presentation of data on benefits and risks. WEBRADR, expected to start in the third quarter of 2014, will develop a smartphone app for reporting ADRs and outcomes by patients and healthcare professionals. The objective is that the app will allow two-way information flow for transmission of important information and safety messages.

In the past year, EFPIA also initiated a discussion with regulatory stakeholders such as the EMA and its Pharmacovigilance Risk Assessment Committee (PRAC) on how to improve collaboration with PRAC and how to better implement PRAC decisions. An agreement was reached with the EMA on the maintenance process surrounding the Article 57(2) database and how to improve data quality in the database. Article 57(2) of Regulation (EC) No 1235/2010 requires marketing authorisation holders (MAHs) to electronically submit information on all medicinal products for human use authorised in the EU by 2 July 2012. For its part, PRAC aims to improve data quality and maintenance of the database.

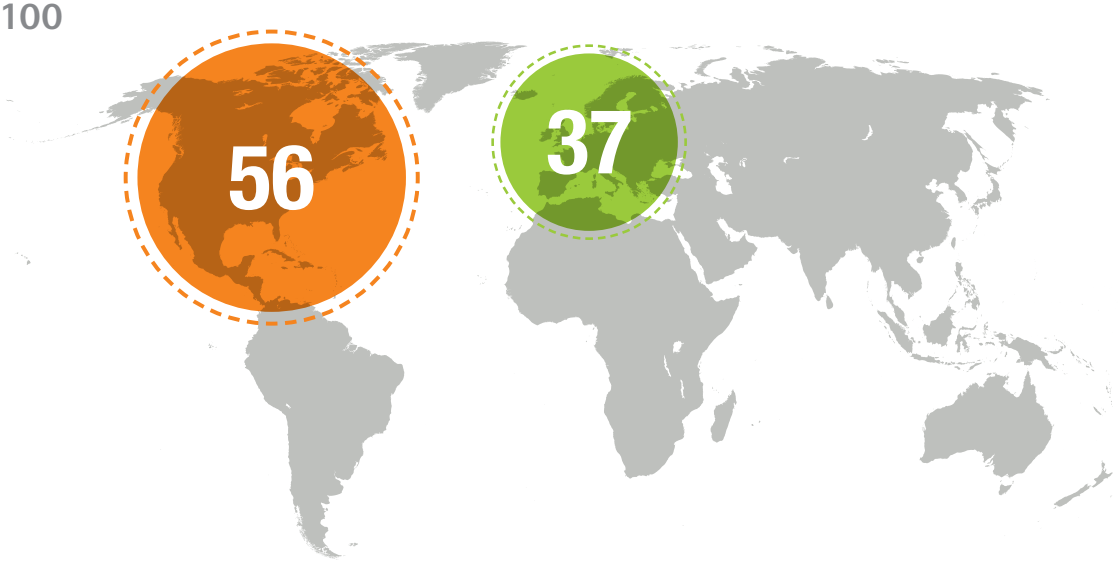
Building a Thriving Innovative Life Sciences Sector:

Facts and Figures

The EU is facing increasingly tough competition, with Europe consistently lagging behind the US as the place where innovators want to test and launch their products first.[1] In the 1960s, Europe was the pharmacy capital of the world, accounting for nearly 60% of all new chemical entities.[2] Out of the Top 100 centres for medical research, 56 are American and only 37 are European. 8 of the Top 10 academic centres are American, and Asia is catching-up fast.

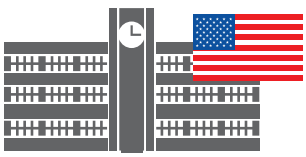
Top centres for medical research in the world

Out of 100



Top academic centres

Out of 10



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[1]PAREXEL Biopharmaceutical R&D Statistical Sourcebook 2012/2013 (eStats); Hard copy

[2]Daemmrich, A (2009): Where is the Pharmacy to the Word? International Regulatory Variation and Pharmaceutical Industry Location http://www.hbs.edu/faculty/Publication%20Files/09-118.pdf

The pharmaceutical industry is one of the highest value-added sectors, with a footprint that connects some of the brightest start-up ventures in Europe, academic centres, diverse health networks, and a whole infrastructure of high-value technology and science services. These workforce advantages translated to a wider, positive impact during the recent financial crisis, with the pharmaceutical sector proving more resilient than other industries between 2008-2010, largely maintaining employment at a time when other manufacturing sectors contracted by between 10% and 15%.[4] The pharmaceutical industry employs over 700,000 people in Europe, contributing 17% of total business enterprise R&D employment[5] .

From 2008-2010

PHARMACEUTICAL INDUSTRY

EMPLOYMENT MAINTAINED

MANUFACTURING SECTORS

EMPLOYMENT CONTRACTED

The pharmaceutical industry employs over

in Europe, contributing

17% of total business enterprise R&D employment.

In 2013 Europe's pharmaceutical trade surplus was estimated at

€90 BILLION

[4]EFPIA (2013): The pharmaceutical Industry in Figures: Key Data (2013)
[5]EFPIA (2013): The pharmaceutical Industry in Figures: Key Data (2013)

IMI: Delivering High Quality Research from Science to Patients, Together

Innovative Medicines Initiative

The Innovative Medicines Initiative (IMI) was established in recognition of the fact that the most pressing healthcare problems societies are facing today – from neurodegenerative diseases to anti-microbial resistance – will only be successfully conquered through a collaborative effort. Today IMI is the world's largest public-private partnership in the healthcare sector, with a budget of €2 billion – €1 billion each from the European Union and EFPIA. IMI. The second Innovative Medicines Initiative will carry on this mission towards delivering new and improved medicines to patients.

The second Innovative Medicines Initiative will take the collaborative vision of IMI even further in its service to patients and the public health agenda. The IMI2 concept relied heavily on the World Health Organization's *Report on Priority Medicines for Europe and the World* in determining its Strategic Research Agenda (SRA). The SRA, an essential element of the evolution from IMI to IMI2, was determined with input from more than 80 organisations, including regulators, patients, academia and learned societies. The first five big questions to be addressed by IMI2 include neurodegeneration, metabolic disorders, immune-mediated diseases, infections and translational safety.

What makes IMI2 notable is its shift in focus, as it strives not only to advance medicines research and development (R&D) but also the delivery of the results of that R&D to patients, particularly in the field of targeted therapies. This vision is encapsulated in the SRA tagline: *The right prevention and treatment for the right patient at the right time*.

The IMI2 legal package was released for legislative process in July and the European Council position was taken in November 2013. With inter-institutional negotiations concluded and endorsed in spring 2014 and launch of IMI2 planned in July 2014, it would take less than a year to complete this legislative process. The results are expected to offer the necessary framework that will allow IMI to remain the largest public-private partnership (PPP) in biopharmaceutical research worldwide.

As IMI2 gets under way, IMI1 has continued to carry on with its mission, launching five new calls for research project proposals covering key public health challenges: vaccines, antibiotics, pharmacovigilance, and personalised tumour therapies, among others. IMI Call 11 came with

IMI and Anti-Microbial Resistance (AMR)

Anti-microbial resistance has been described as being "as big a risk as terrorism" by UK Chief Medical Officer Dame Sallie Davies, while the World Health Organization has called the hunt for new antibiotics a "race against time". In the EU alone, we are seeing some 25,000 deaths per year related to AMR, costing the European economy more than €1.5 billion annually. IMI has a number of projects devoted to this growing public health threat through its New Drugs for Bad Bugs (ND4BB) programme. These include COMBACTE (Combatting Bacterial Resistance in Europe) and TRANSLOCATION (Molecular basis of the bacterial cell wall permeability).

a total budget of €340 million and covers essential areas of healthcare including Alzheimer's Disease, osteoarthritis, and antimicrobial resistance – all areas that are of growing concern to societies around the world.

We have already seen some great success stories from IMI and more are expected. For example, take U-BIOPRED, which explores personalised approaches to severe asthma, or the NEWMEDS project, which has created the largest known database of studies on schizophrenia, making it possible to improve clinical trials. More inspiration can be found from the DIRECT project, which is advancing personalised therapies in diabetes, and PharmaCog, a project devoted to developing new tools to test candidate drugs for Alzheimer's.

IMI projects are contributing in many ways to addressing patient, public health and medicines research needs. By promoting a better understanding of disease, IMI is paving the way for accelerated pathways towards new or improved treatments in areas of unmet medical need. Most IMI projects address questions in fields of emerging and innovative sciences and are intended to result in novel tools, methodologies and standards that can make medicines development more efficient as well as improving regulatory standards, guidance and practice for the benefit of public health. Some projects have been instrumental in triggering the development of regulatory guidelines, and many results have already been implemented in the internal processes and decision making of pharmaceutical companies, therefore speeding up the development of new medicines for a number of diseases.

Looking at the anticipated impact of IMI2, there is more progress to come. IMI2 expands on the vision of the first IMI, and will further support activities of strategic importance to the European Union's competitiveness and industrial leadership, addressing specific societal challenges of the Horizon 2020 Programme with the ultimate aim of improving European citizens' health and wellbeing. How is this to be done? Some anticipated areas of impact outlined in IMI2's plans include an increased success rate in clinical trials; where possible, a reduction in the time to reach clinical proof of concept in medicines development; the development of new therapies for disease areas of high unmet medical need; and the provision of support for the development of tools, standards and approaches to assess efficacy, safety and quality of regulated health products.

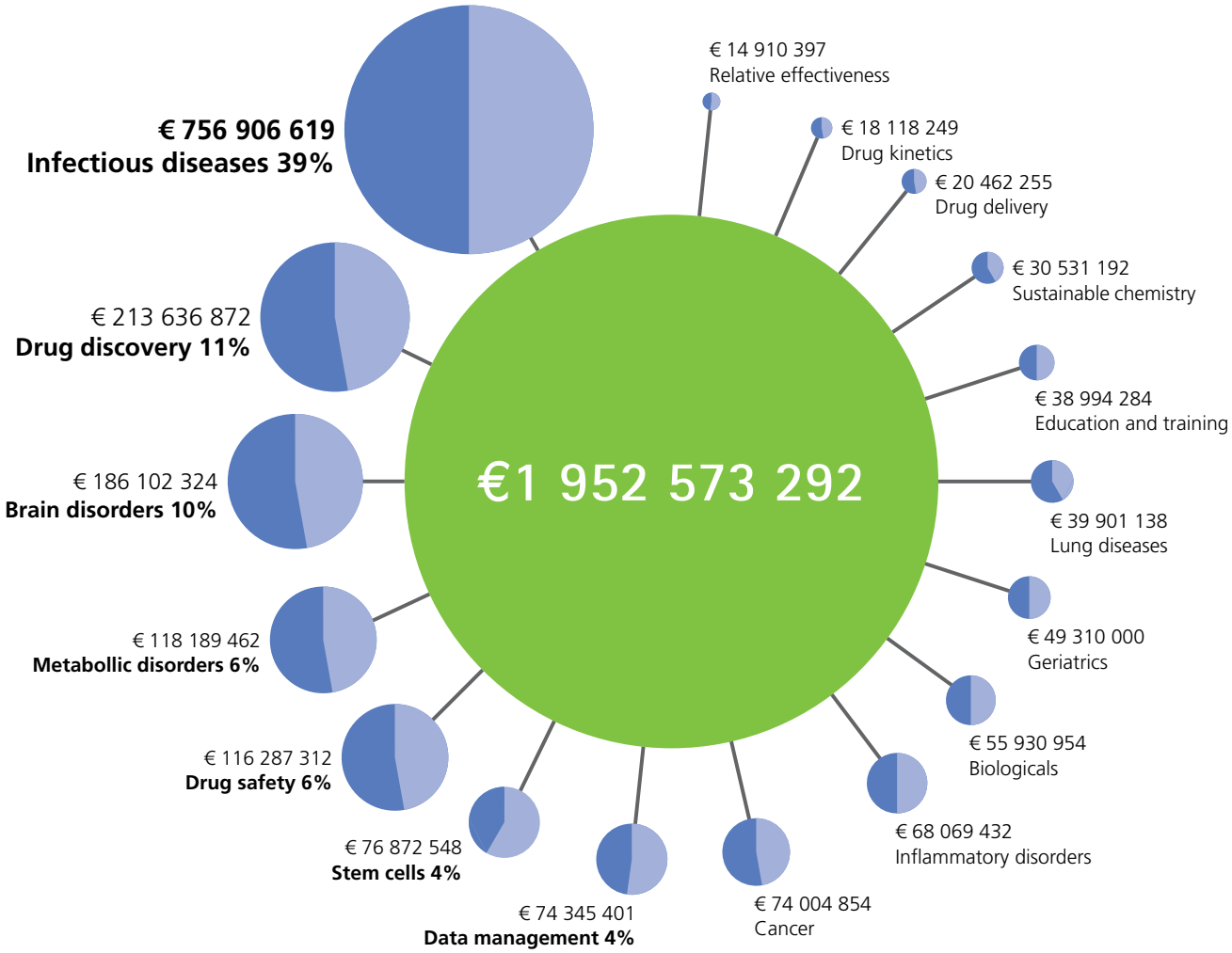
IMI not only delivers results but also works to put in place mechanisms to exploit this knowledge in broad research practice, going beyond single project results. Thanks to a favourable intellectual property policy, good regulatory practice arising from continued dialogue with regulators from Europe and beyond, and a specific platform on the exploitation of results, IMI is focused on producing tangible outcomes.

IMI in Numbers

23 patient organisations. **14** regulators. **714** academic & research teams. **410** EFPIA teams. **135** SMEs. More than **6,000** researchers. **61%** of projects reported some form of patient involvement. **12** regulators on boards of projects. **50%** of projects have representatives of regulatory authorities on scientific advisory boards.

IMI in Numbers

IMI delivers tangible results from science to patients, together. This is possible thanks to its collaborative spirit. Society is evolving and we are facing increasingly complex health challenges that are impossible for any one party to solve alone. IMI invests in areas important to society and health systems:



Supporting New Regulatory Pathways

As the science and technology surrounding innovation progress, the regulatory process supporting innovation likewise needs to advance. Further progress in gene therapies, diagnostic technologies and targeted therapies requires regulatory and access pathways that support the most efficient delivery of treatment to patients. Cost-effective systems that promote innovation and enhance the transfer of innovation to patients will benefit all stakeholders.

> ***Strategies for adapting the clinical trials to allow fast availability of new medicines to patients and to incorporate effectiveness parameters are being explored to promote personalised medicine attuned to public health needs and constraints.***
>
> European Commission, "Use of '-omics' technologies in the development of personalised medicine", SWD(2013) 436 final, Pg 12.

This is not an issue exclusive to the EU. Around the world, regions are competing to update regulatory processes so as to keep pace with the evolution of research & development (R&D). It is important that Europe does not fall behind. Lagging R&D investment also impacts job creation, and can result in a 'brain drain' from Europe. Consider, for instance, the fact that out of the top 100 centres for medical research, 56 are American and only 37 are European. Digging deeper, eight of the top 10 academic centres are American – and Asia is catching-up fast. By getting ahead of the game by developing new regulatory pathways, the EU can establish itself as a leader in the life sciences now and into the future.

Progress is already being made. This spring, the European Medicines Agency (EMA) announced an adaptive pathway pilot project with real medicines in development – a bold step in improving the way innovative and much-needed new therapies reach patients. This signals an exciting new direction for Europe. The US and UK have been focused on accelerating the existing process of approving medicines via "breakthrough designations" which aim to dedicate greater focus and attention to areas of unmet medical need. EMA has been the first to come forward with an actual adaptive pathway to test this approach in situ, placing Europe, EFPIA, and the Innovative Medicines Initiative 2 (IMI2) at the centre of a potential global leap forward.

This approach, the Medicine's Adaptive Pathways to Patients (MAPPs), builds on advances in medical science, genomics, and personalised medicine to facilitate an approval process that adapts quickly to a given patient's response to therapies. It will launch with a clearly defined patient population with unmet medical needs. This will be followed by continued evidence-gathering in support of expanding the pool of recipients of the new therapy as the knowledge base of MAPPs grows. Ultimately, MAPPs is about bringing better, new therapies to patients who need them.

Despite this promise, challenges remain. In order for a MAPP to be implemented, all stakeholders must be aligned and agree on the evidence package for early approval and re-assessments at the design phase. This is

Getting a medicine to patients eight years earlier than is possible under the traditional drug development cycle – with the support of payers – is not as inconceivable as some might imagine.

Hans-Georg Eichler, M.D., Frank Pétavy, M.Sc., Francesco Pignatti, M.D., and Guido Rasi:Informa UK 2013, Scrip Regulatory Affairs, "New Medicines Eight Years Faster to Patients"

a particular challenge in Europe, as it requires 'buy-in' from the Member States and multiple Health Technology Assessment (HTA) authorities. In addition, reimbursement discussions are already taking many years in some countries, and simply moving more new medicines faster to a bottleneck at the national level will ultimately not help patients. These however, are both problems that the EMA pilot can help to solve.

In order to better understand hurdles like these, EFPIA has asked the Escher Project to perform a regulatory review. The aim of the project is to identify deficiencies and inefficiencies within the regulatory system, and to generate scientific evidence to identify opportunities to improve it. A report is expected by September of this year.

Following this, in October of this year, EFPIA plans to organise an international conference on new clinical trial models that will take place at the Royal College of Physicians in London – another step towards solidifying Europe's position as the global thought leader in adaptive pathways.

The Innovative Medicines Initiative (IMI), a public-private partnership between EFPIA and the EU, is another opportunity to push ahead with the exploration of MAPPs. IMI2 can serve as a valuable tool to test such new ideas in a safe environment, and address questions that patients, doctors, payers and regulators may have. The tools to advance new regulatory pathways are at our disposal. Now is the time to move forward in exploring actions; to ensure that regulatory systems are keeping up with the new sciences in a way that will ensure patients benefit.

Adaptive licensing is characterised as an acknowledgement that evidence development is a continuum – regulatory approval would come in stages... evidence development would continue in parallel with marketing.

Lynn G. Baird, Mark R. Trusheim, Hans-Georg Eichler, Ernst R. Berndt and Gigi Hirsch, www.diahome.org, Therapeutic Innovation & Regulatory Science published online 9 May 2013, "Comparison of Stakeholder Metrics for Traditional and Adaptive Development and Licensing Approaches to Drug Development"

Clinical Trials Data Sharing: Moving Towards Transparency Together

In the past year, EFPIA and its member companies have made great strides towards enhancing responsible sharing of clinical trial data. The year 2014 started off with big news, as implementation of the EFPIA-PhRMA joint Principles for Clinical Trials Data Sharing began on 1 January 2014.

The EFPIA-PhRMA Principles were established with the intent of creating a common baseline for data sharing that all EFPIA and PhRMA member companies can agree to. As a result of these new measures, researchers are now able to submit proposals to receive access to patient-level data, protocols, and clinical study reports for new medicines approved in the US and EU after January 1, 2014. The biopharmaceutical sector's commitment to data sharing provides new avenues for the scientific community and patients to benefit from clinical research, while maintaining patient privacy, the integrity of national regulators, and incentives for companies to make long-term investments in biomedical research.

Great progress has already been seen since the 1 January launch date, with a number of EFPIA and PhRMA member companies sharing their expanded data-sharing measures publicly. Prior to the launch, EFPIA held a public webinar, featuring three member companies sharing the steps they have taken toward implementing the Principles. Such efforts underscore the fact that the key to success will be collaboration and sharing of best practices. In line with this belief, EFPIA, PhRMA and their member companies have been working to promote awareness of progress and of means of data sharing.

EFPIA is committed to, and delivering, increased sharing of its clinical trials data to advance public health goals and achieve the best end results for patients. This needs to be a collaborative conversation, however. This should include industry, as well as regulators, academia, researchers, and the individuals that all of these groups serve – patients.

EFPIA has actively contributed to calls to comment on the European Medicines Agency's draft policy on publication and access to clinical trial data. EFPIA made a formal submission on the draft policy in September 2013, and participated in a final consultation on the draft policy in May 2014. The final policy and an implementation plan are expected to be presented to the EMA Management Board for endorsement at its June 2014 meeting, and EFPIA looks forward to seeing the end result.

The EFPIA–PhRMA Principles – What do they include?

- **Patient-level clinical trial data, study-level clinical trial data, full clinical study reports, and protocols from clinical trials in patients for medicines approved in the United States and EU beginning this year will be shared with qualified scientific and medical researchers upon request and subject to terms necessary to protect patient privacy and confidential commercial information. Researchers who obtain such clinical trial data will be expected to publish their findings.**

- **Companies will work with regulators toward a mechanism to provide factual summaries of clinical trial results to patients who participate in clinical trials.**

- **The synopses of clinical study reports for clinical trials in patients submitted to the Food and Drug Administration, European Medicines Agency, or national authorities of EU Member States will be made publicly available upon the approval of a new medicine or new indication.**

- **Biopharmaceutical companies also reaffirm their commitment to publish clinical trial results regardless of the outcome of the trials. At a minimum, results from all phase 3 clinical trials and clinical trial results of significant medical importance should be submitted for publication.**

Promoting Understanding of Stem Cell Research

Stem cell research continues to be one of the most promising fields of biomedical research and offers huge potential to greatly improve the health of European citizens. However, a desire to keep budgets in check has threatened the future of this innovative research in the EU. In the past year, a number of individuals and organisations have come out to voice their support for this invaluable research – which EFPIA believes is vital to finding treatments for a number of diseases.

The debate around stem cell research remains heated, however, with a number of ideological arguments shrouding the benefits this unique type of research can offer. What makes stem cells so unique for medical research? For one, stem cells can divide indefinitely and produce identical copies of themselves. They can also divide and produce more specialised types of cells.

Of special interest are embryonic stem cells, which have the unique ability to differentiate into all types of cells. This gives scientists access to types of cells that would otherwise be difficult to obtain. Embryonic stem cells are, unfortunately, also among the most controversial. In fact, embryonic stem cells are isolated from an embryo only four or five days after fertilisation, at which point the embryo is in blastocyst stage, consisting of a ball of about 100 cells – each with the potential to develop into different cell types that would make up a human body.

While there are other types of stem cells, no other type can replace embryonic stem cells. There are two other types of stem cells of interest to scientific research: tissue stem cells, derived from foetal or adult tissue, and genetically engineered induced pluripotent stem cells (iPS). However, iPS cells are poorly understood and not yet ready for clinical research at this time. Tissue and iPS cells lack the unique capability of embryonic stem cells to differentiate into all types of cells.

Stem cells offer the potential to address challenging areas of unmet in Parkinson's Disease and type II diabetes, for example. The potential benefits of stem cell research are undeniable. Recognising this, there has been a groundswell of support from a number of EU organisations voicing support for stem cell research - evidence of the growing recognition of just how valuable this research can be.

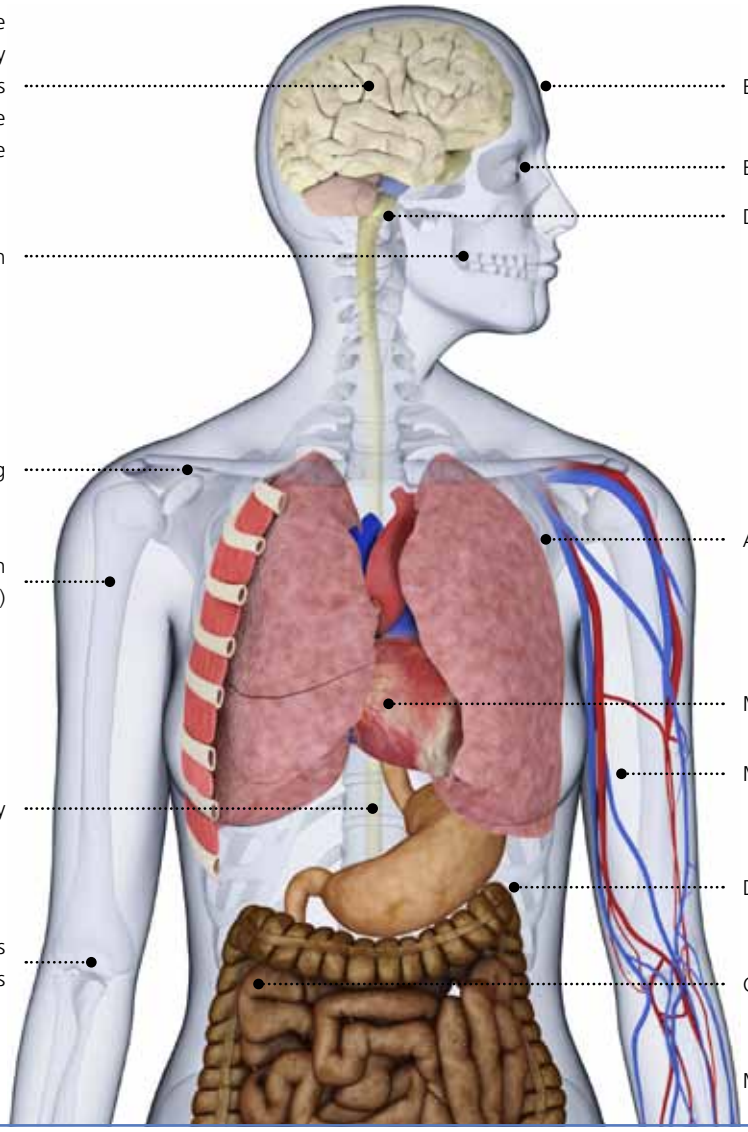
In spring 2014, more than 30 organisations banded together to call on the European Parliament and European Commission to oppose the 'One of Us' Citizens' Initiative, which seeks a ban on all financing of activities that presuppose the destruction of human embryos, including stem cell research. Such a ban would have a negative impact on research involving human embryos for regenerative medicine, reproductive health and genetic diseases. Current European Union research funding rules do not mandate such research but rather enable it in countries where it is not excluded by law – and after in-depth ethical scrutiny has been conducted. While the political debate continues, research moves ahead to enhance iPS cells' development, storage and use in R&D and medicine.

Europe is currently a leader in this field of research, and clinical trials resulting from stem cell research are already under way. To protect this R&D in Europe, and the benefits it promises for patients around the world, the funding framework supporting such research (including all types of stem cells) needs to be protected.

Advancing iPS cell Research with IMI's StemBANCC

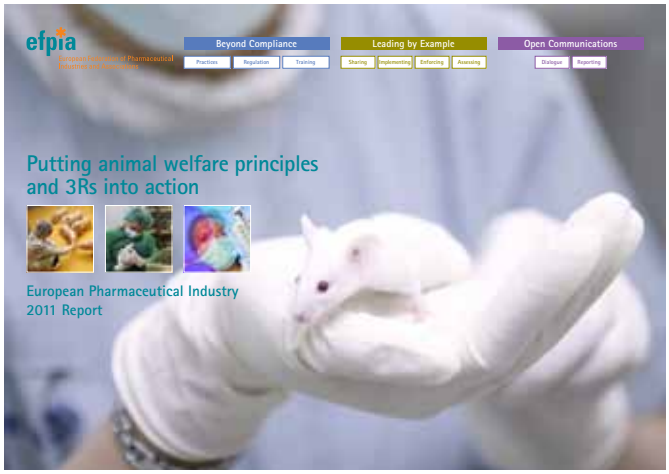
StemBANCC is an academic-industry partnership uniting 23 academic institutions and ten pharmaceutical companies. It is one of the largest ventures of the Innovative Medicines Initiative, with a budget of €55.6 million. Currently, many drugs fail rather late in the drug development process because the tests used in the earlier stages of drug development are not precise enough. StemBANCC aims to generate and characterise 1500 high quality human induced pluripotent stem (iPS) cell lines derived from 500 patients as research tools for drug discovery. iPS cells are adult cells that have been genetically reprogrammed to lose their tissue-specific qualities and become pluripotent. The iPS cells will be used to develop human disease models in vitro, in order to enhance early stage drug development. The project will investigate the use of human iPS cells for toxicology testing by generating liver, heart, nerve and kidney cells.

What could we accomplish with stem cell research?



Animal Welfare Principles: Putting the 3Rs into Action

Promoting good science and animal welfare, while increasing understanding of how the two are intertwined, is essential to ensuring high-quality research and development (R&D). It is also an integral part of successfully achieving the 3Rs: systematically replace animals with alternative methods where possible; reduce and refine the use of laboratory animals (3Rs); and improve standards of care throughout the supply chain and during research.



Currently, animal research remains an indispensable element in the research, development and production of new medicines. Living systems are extremely complex. For example the nervous system, blood and brain chemistry, and immunological responses are all interrelated, making it impossible to explore, explain, or predict the course of diseases or the effects of possible treatments without observing and testing the entire living system of a whole body (animal or human). In such cases, animals are indispensable in research.

In the meantime, scientists continue to look for ways to reduce the number of animals needed to obtain valid results, refine experimental techniques and enhance animal welfare, and replace animals with other research methods whenever feasible – the 3Rs principles.

These principles are an integral part of both European and worldwide legislation. Directive 2010/63 is among the most progressive legislative measures in the world. Others regions may have similar wording – however, what the EU mandates is in many other countries merely a recommendation. Now, the European Commission – with support from experts – is putting together detailed guidelines to facilitate the application of this Directive. To enhance knowledge surrounding the topic, EFPIA continues to promote information about 3Rs, through education and training of personnel, inspections, and ethical evaluation of projects.

In the late 1980s, EFPIA established an expert group in charge of fostering the exchange of information and good practice within and across sectors, and promoting development and uptake of 3Rs approaches. Today, EFPIA continues to enhance the knowledge base surrounding the 3 Rs. The publication of the 2012 report "Putting Animal Welfare Principles and 3 Rs into Action" provides current updates on achievements in reaching the 3 Rs. Of note is the addition of a section on science, demonstrating how the implementation of 3Rs strategies can be viewed as an integral part of continuously evolving science that will benefit the development of new medicines and animal welfare – evidence of the link between science and welfare. At a time when research challenges impose more cross-sector and international collaboration, there is also momentum to enhance scientific innovation globally – across companies, sectors and borders alike.

The Innovative Medicines Initiative (IMI) offers the opportunity for continued progress and scientific research that promotes collaboration and delivers positive 3Rs results. The EUROPAIN project aims to improve the treatment of patients with chronic pain by establishing translational models in animals and humans. Such improvements in human pain modelling may lead to improved animal models or a decrease in their use. OrBiTo aims to enhance our understanding of how orally administered drugs are taken up from the gastrointestinal tract into the body, and apply this knowledge to create new non-animal laboratory tests and computer models that will better predict the performance of these drugs in patients. This will further reduce the need to carry out such studies in animals.

As research paradigms evolve and industry continues its efforts, more dramatic improvements can be expected in the future.

Animal Research Part of Nobel Prize Winning Research

The 2013 Nobel Prize for Medicine/Physiology went to three scientists who discovered how cells in the body transport material – research with major potential implications for progress in areas like diabetes and brain disorders. As with most Nobel Prize research, animal studies were integral to the researchers' success. In this case, yeast, cows and genetically modified mice were involved in the research process. Looking back, nearly all Nobel Prizes in Physiology or Medicine have required some form of animal research. According to Americans for Medical Progress, in the past 34 years, all awards but one have been dependent on animal research.

Annexes: Glossary of Terms

Clinical trials Set of procedures in medical research and medicine development that are conducted in humans intended to discover or verify the effects of one or more investigational health interventions (e.g., medicines, diagnostics, devices, therapy protocols).

Differential Pricing Adapting medicine prices to the purchasing power of consumers and epidemiological conditions in different geographical or socio-economic segments.

Epigenetics Variations in the way genetic material is packaged and read can influence gene activity without altering the sequence of DNA. These patterns of modifications in identical twins are different despite their having the same DNA.

E-health The application of Information and Communication Technologies (ICT) across a range of functions in the healthcare sector with a view to enhancing continuity of care and ensuring access to safe and high-quality healthcare.

Falsified Medicines A falsified medicine gives a false representation of its identity and/or source and/or record keeping for traceability; pretends to have been assessed and approved by the competent regulatory authority, pretending to be a genuine quality product; has an intention to deceive by a fraudulent activity; is falsified for profit motives, disregarding public health and safety; and that disputes concerning patents or trademarks must not be confused with falsification of medicines.

Free Trade Agreement An agreement between partner countries which aims to eliminate tariffs, import quotas, and preferences on most (if not all) goods and services traded between them, whilst ensuring market access (e.g. through transparency, IPR protection and enforcement, regulatory harmonisation).

Generic medicines A medicine which has the same qualitative and quantitative composition in active substances and the same pharmaceutical form as the reference medicine, and whose bioequivalence with the reference medicine has been demonstrated by appropriate bioavailability studies.

Genome A genome contains all of the information needed to build and maintain that organism, it contains the entirety of an organism's hereditary information.

Health Technology Assessment is a multidisciplinary process that summarises information about the medical, social, economic and ethical issues related to the use of a health technology in a systematic, transparent, unbiased, robust manner. Its aim is to inform the formulation of safe, effective, health policies that are patient focused and seek to achieve best value.

Human Genome The entirety of a human's hereditary information.

International Reference Pricing The practice of using the price(s) of a medicine in one or several countries in order to derive a benchmark or reference price for the purposes of setting or negotiating the price of the product in a given country. In some countries, the referencing pricing system is applied rigidly, while in other countries, it is simply one of many elements of information used to inform the pricing decision. The basket of countries chosen varies, based on a range of criteria used to justify the selection of countries.

Neurodegenerative diseases An umbrella term for diseases, which result in the progressive loss of structure or function of neurons, including Parkinson's, Alzheimer's, and Huntington's.

New Science A general term used for, biotechnological advances in the pharmaceutical industry, including personalised medicines, epigenetics, diagnostic tools such as biomarkers and nanotechnology.

Non-durables Consumable medical supplies are non-durable medical supplies that are usually disposable in nature, cannot withstand repeated use and are primarily and customarily used to serve a medical purpose.

Off-Patent Pharmaceuticals A medicine that has come to the end of its patent term and is open to generic competition.

Omics A short-hand term used to refer to a field of study in biology. For example, genomics is the study of genomes.

Patient adherence The degree to which patients adhere to medical advice and take medicines as directed.

Personalised medicines Tailored treatment to patient subgroups based on their biological characteristics.

Therapeutic Reference Pricing A method of comparing the prices for a range of different medicines, which are deemed by the founder to be similar in as much as they are part of the same therapeutic area and in some circumstances, are interchangeable. However, they are not the same medicine.

Annexes: EFPIA Governance

The European Federation of Pharmaceutical Industries and Associations (EFPIA) represents the pharmaceutical industry operating in Europe. Through its direct membership of 33 national associations and 40 leading pharmaceutical companies, EFPIA is the voice on the EU scene of 1,900 companies committed to researching, developing and bringing to patients new medicines that will improve health and quality of life around the world.

The EFPIA General Assembly comprises all members and meets once a year to define the Association's general policy. Board delegates are the CEOs or persons in charge of the pharmaceutical operations at global / international level in their company; the Executive Committee is composed of delegates from member companies and associations, elected for a period of two years. The Board/Executive Committee carries out the tasks and duties determined by the General Assembly, and ensures that these are implemented by the General Management.

EFPIA Board & Executive Committee

The role of the Board is decision making on strategy setting, priorities and governance. The role of the Executive Committee is the implementation and operation of the priorities set by the Board to which it is accountable.

Board members

President
Chris Viehbacher
Sanofi (France)

Vice-President
Ulf Wiinberg
Lundbeck (Denmark)

Vice-President
Joe Jimenez
Novartis (Switzerland)

Carlos Alban (AbbVie)
Lucia Aleotti (Menarini)
Giovanni Caforio (BMS)
Alberto Chiesi (Chiesi)
Marc De Garidel (Ipsen)
Ruud Dobber (AstraZeneca)
Roch Doliveux (UCB)
Juaquin Duato Boix (J&J)
David Ebsworth (Vifor Pharma)
Antoni Esteve (Esteve)
Jorge Gallardo (Almirall)
Allan Hillgrove (Boehringer Ingelheim)
Anthony Hooper (Amgen)
Robert Hugin (Celgene)

Carlo Incerti (Genzyme)
Lise Kingo (NovoNordisk)
Tony Kingsley (Biogen Idec)
Daniel O'Day (Roche)
Stefan Oschmann (Merck)
Eric-Paul Paques (Grünenthal)
David Ricks (Eli Lilly)
Adam Schechter (MSD)
Mike Warmuth (Abbott)
Dieter Weinand (Bayer)
Andrew Witty (GSK)
John Young (Pfizer)

Ex Officio (EFPIA Board)
Jane Griffiths – ExCom Chair (Johnson & Johnson)
Pascale Richetta, ExCom Vice-Chair (AbbVie)

Humberto Arnes (Farmaindustria)
Birgit Fischer (vfa)

Roberto Gradnik, EBE President, (Stallergènes)

EFPIA Executive Committee

The role of the Executive Committee is the implementation and operation of the priorities set by the Board to which it is accountable. The corporate heads of European operations of the member companies and heads of national associations sit on the Executive Board which agrees on the steps necessary to implement strategy and priorities set by the Board and oversight of the implementation.

Chair

Jane Griffiths (Johnson & Johnson)

Vice-Chair Corporate Members

Pascale Richetta (Abbvie)

Vice-Chair Member Associations (MA)

Humberto Arnes (Farmaindustria)
Second MA delegate to the Board:
Birgit Fischer (vfa)

Corporate Members Delegates

Khoso Baluch (UCB)
Pierre Boulud (Ipsen)
Ole Chrintz (Lundbeck)
Søren Bo Christiansen (MSD)
Jennifer Cook (Roche)
Ron Cooper (BMS)
Ugo Di Francesco (Chiesi)
Reinhard Franzen (Bayer)
Johanna Friedl-Naderer (Biogen Idec)
Alberto Grua (Grünenthal)
Jerzy Gruhn (Novo Nordisk)
Guido Guidi (Novartis)
Gary Hendler (Eisai)
Andrew Hotchkiss (Eli Lilly)
Tim Kneen (Merck)
David Loew (Sanofi)
Pio Mei (Menarini)
Tuomo Patsi (Celgene)
Jean-Yves Pavee (Abbott)
Andreas Penk (Pfizer)
Hugues Renaut (Servier)
Jean Scheftsik De Szolnok (Boehringer Ingelheim)
Joris Silon (AstraZeneca)
Trevor Smith (Takeda)
Kim Stratton (Shire)
Carsten Thiel (Amgen)
Ole Vahlgren (Otsuka)
Erik Van Snippenberg (GSK)
Paul Vibert (Baxter)
Patrick Vink (Cubist)
Thierry Volle (Vifor Pharma)

Member Associations Delegates

Anders Blanck (LIF – Sweden)
Heitor Costa (Apifarma – Portugal)
Thomas Cueni (Science Industries – Switzerland)
Erica Giorgetti (Farmindustria – Italy)
Ida Sofie Jensen (LIF – Denmark)
Philippe Lamoureux (Leem – France)
Anne Nolan (IPHA – Ireland)
Catherine Rutten (AGIM – Belgium)
Stephen Whitehead (ABPI – UK)

General Management

Richard Bergström (EFPIA Director General)
Marie-Claire Pickaert (EFPIA Deputy Director General)

Guest

Rod Hunter (P*h*RMA)

EFPIA Policy Committees

For each main field – scientific, regulatory & manufacturing; economic and social policy; intellectual property; trade & external market; research and trust, reputation and compliance – a policy committee to develop the public policy line to be taken.

Policy committees may set up Committees or working groups (WGs) in order to tackle specific issues or areas.

There are six main EFPIA Policy Committees:

Economic and Social Policy Committee (ESPC)	Chair - **Thomas Cueni**, Interpharma Vice-Chair - **Chris Strutt**, GlaxoSmithKline
External Trade Policy Committee (ETPC)	Chair - **Pius Hornstein**, Sanofi Vice-Chair - **Gisela Payeras**, GlaxoSmithKline
Intellectual Property Policy Committee (IPPC)	Chair - **David Rosenberg**, GlaxoSmithKline Vice-Chairs - **Stephane Drouin**, UCB; **Lise Ryberg**, Lundbeck
Research Directors Group (RDG)	Chair - **Paul-Peter Tak**, GSK
Scientific, Regulatory and Manufacturing Policy Committee (SRMPC)	Chair - **Sue Forda**, Eli Lilly and Company

EFPIA Executive Team

The Director General heads up the EFPIA team and is appointed by the Board to manage EFPIA.

Richard Bergström
Director General

Marie-Claire Pickaert
Deputy Director General

EFPIA would like to thank its members for their valuable contributions to this Annual Review.

Commissioned by EFPIA.
The Annual Review was researched and written by EFPIA staff, edited by Gary Finnegan and designed by Morris & Chapman.

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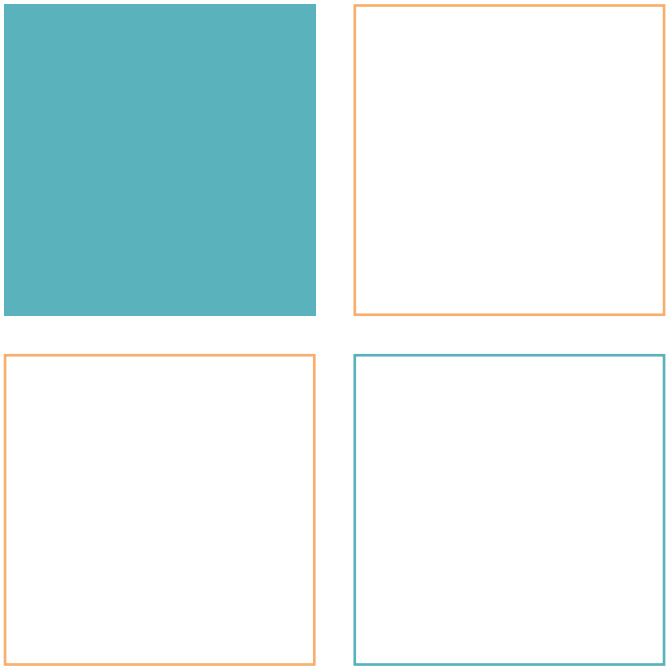
European Federation of Pharmaceutical Industries and Associations



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