SUSTAINALYTICS

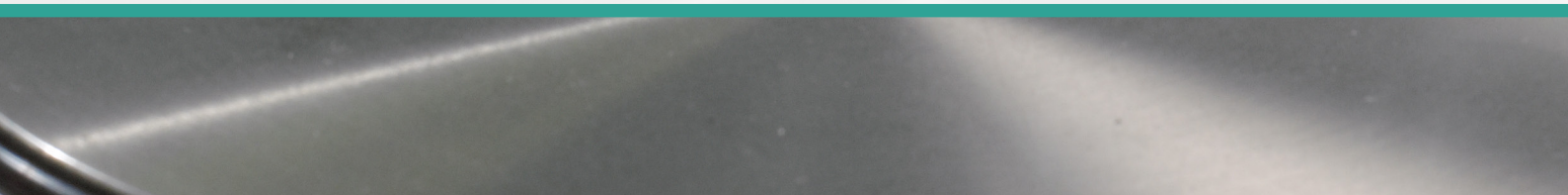
From Policy to Practice

Ethical conduct and consumer protection in the pharmaceutical industry

Hazel Goedhart and Sonja Siewerth

Report commissioned by ASN Bank

February 2016



About Sustainalytics

Sustainalytics supports investors around the world with the development and implementation of responsible investment strategies. The firm partners with institutional investors that integrate environmental, social and governance information and assessments into their investment decisions.

Headquartered in Amsterdam, Sustainalytics has offices in Boston, Bucharest, Frankfurt, London, New York City, Paris, Singapore, Sydney, Timisoara and Toronto, and representatives in Brussels, and Washington D.C.. The firm has over 250 staff members, including more than 120 analysts with varied multidisciplinary expertise and thorough understanding of more than 40 industries. In 2012, 2013 and 2014, Sustainalytics was voted best independent sustainable and responsible investment research firm in the **Extel IRRI survey.**

Sustainalytics
www.sustainalytics.com

For general enquiries:
contact@sustainalytics.com

Preface by ASN Bank: Towards a Consumer-Focused Pharmaceutical Industry

Almost everybody takes medicine at some point in their lives. Therefore, the pharmaceutical industry plays a very significant role when it comes to people's health and their access to health. By developing medicines, cures, vaccines, over the counter drugs and medical products, pharmaceutical companies help people from becoming ill and help them to get better. Or, in the case of people who live with chronic diseases or pain, to improve their quality of life.

Sustainable society

ASN Bank believes that healthcare and access to healthcare are important elements of a sustainable society. While we believe that pharmaceutical companies play an important role in this respect, we are confronted with ongoing ethical controversies in the daily practices of pharmaceutical companies.

Unethical behaviour by company representatives not only affects companies' own reputations, but it also leads to financial risks such as costly fines, (legal) procedures and settlements and dissatisfied investors. More importantly, however, unethical behaviour negatively impacts the health of people. Promoting medicine for different uses than what it is intended for (called off-label marketing) and not publishing negative test results can result in injuries and potentially lead to deaths. These issues are alarming and warrant action.

While we could have decided to withdraw as an investor, we decided not to, preferring a course of engagement. We believe access to health, and the significant role pharmaceutical companies play, are an important part of a sustainable society. Therefore, by choosing a constructive route and by being a well-informed active investor, we believe we have the potential to change behaviour. For this reason, we asked Sustainalytics to develop this report as an independent basis for dialogue and engagement.

Policy versus practice

In the pharmaceutical industry we note stringent policies on the one hand, and repetitive controversies on the other. The reason pharmaceutical companies are established seem at odds with their business models and cultures.

This indicates to us that commitment to ethical behaviour does not always correlate to good ethical performance. In other words, there seems to be a gap between what is preached on the one and practiced on the other hand. In our practice, we also noted that discussions with pharmaceutical companies about individual (or grouped) controversies rarely lead to results. For this reason, we decided to focus on the implementation and enforcement procedures that companies have in place.

Focus

We decided to take a consumer centred approach: how do we make sure in the end a consumer has access to the right medicines and safe products? We decided not to focus

on access to medicine, as we believe this subject is well taken care off by the Access to Medicine Foundation, which is an organisation we wholeheartedly support. Instead, we focus on ethical conduct throughout the product cycle: from R&D, to manufacturing and distribution, to marketing and sales, and post-marketing.

Dialogue

This report will serve as the basis for dialogue we have started with several pharmaceutical companies in 2015. ASN Bank has decided to mark the ethical performance of the pharmaceutical industry as a top priority in our engagement strategy in the forthcoming years. Our goal is, together with pharmaceutical companies, to achieve better consumer protection, which also positively impacts the risk profile and reputation of pharmaceutical companies.

We invite anyone, from pharmaceutical companies, investors to civil society organisations to join us and use this report to their advantage to make sure ethical conduct will become widespread. So in the end we can all benefit from a healthy pharmaceutical industry in a sustainable society.

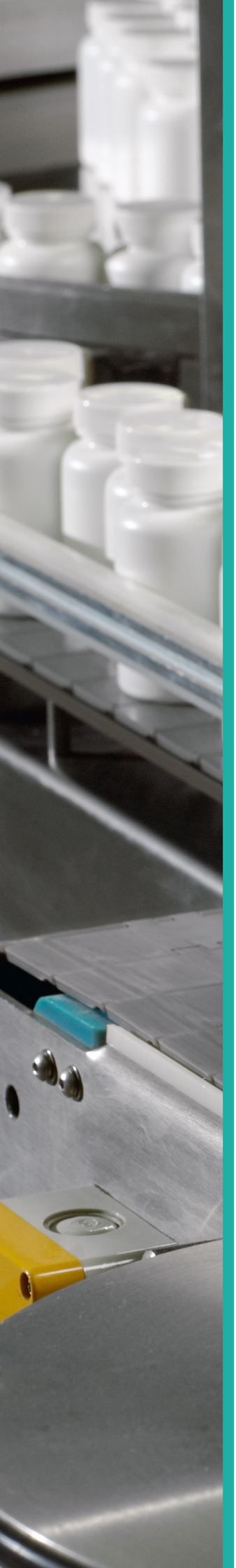


Table of Contents

Introduction

Ethical behaviour and consumer protection are of paramount importance in the pharmaceutical industry. In no other industry do the quality and safety of products have such significant and widespread impact on consumers as in the pharmaceutical industry; the stakes are literally those of life and death. This is illustrated by the numerous grave scandals over drug safety and effectiveness of the past decade, which have harmed hundreds of thousands of consumers.

What does product quality and safety mean for the purposes of this report? Generally, it means that medicines should deliver the health effects that companies promise and be of pure, stable and consistent composition (quality), and that they should not cause undue harm to patients, i.e. any health risks must be outweighed by the benefits (safety); these two dimensions are closely intertwined.

Ensuring product quality and safety does not start and end in the factories where drugs are manufactured. Rather, the way that drugs are designed and tested to a great degree determines their effectiveness and can also entail inherent risks for patients, such as severe side effects. Furthermore, the way that drugs are marketed can in some cases lead to misinformed doctors and patients, and thus cause inappropriate drug use. The potential impact on consumers of faulty design, testing, manufacturing or marketing includes: illness, hospitalization and death caused by, for instance, adverse reactions to a drug, an improper dose, or inappropriately chosen treatment.[1] The European Commission estimates that about five percent of hospital admissions are due to an adverse drug reaction and that this is the fifth most common cause of hospital death.[2] While adverse drug reactions can likely never be completely eliminated, the pharmaceutical industry can be held responsible when for instance companies deliberately hide side effects, as has happened on numerous occasions.

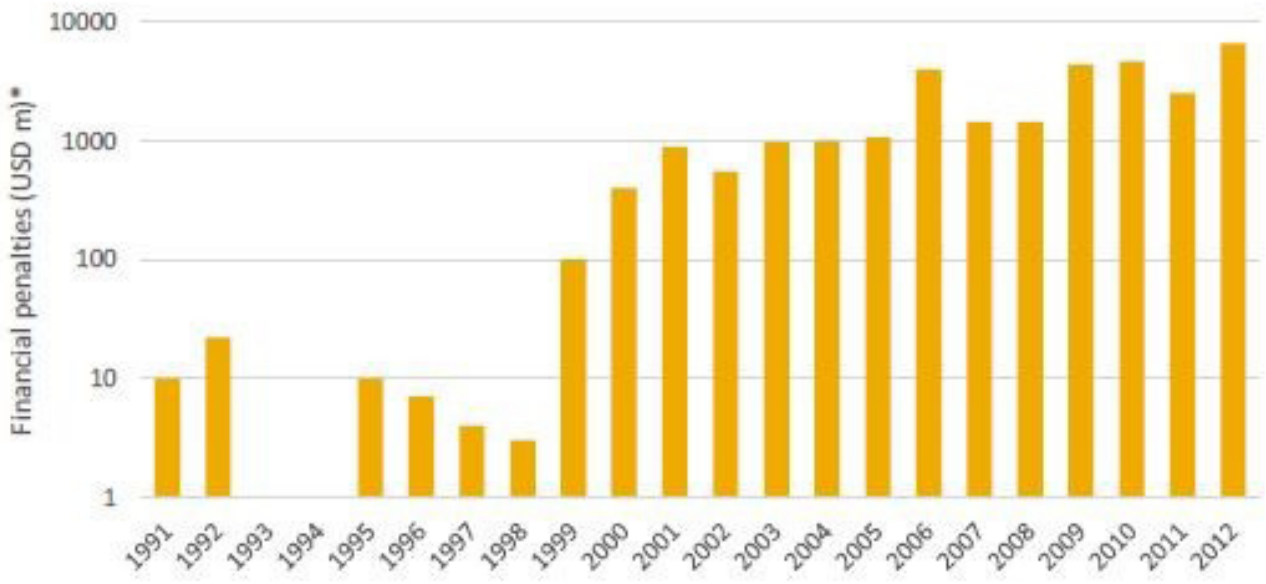
As such, there are grave risks to be dealt with, for which the industry bears at least a partial responsibility. This report will uncover the implications of (un)ethical business practices in the pharmaceutical industry in relation to product quality and safety. Because there is gap between policy and practice, the focus will be on what companies can and should do to avoid harming consumers, while zooming in on the area between policy and practice: the internal mechanisms and structures that companies have in place to ensure consumer protection. In other words, this report looks beyond the commitments that pharmaceutical companies make with regard to product quality and safety towards what they are doing to implement and integrate those commitments into their day-to-day business, for instance in terms of managerial responsibility, training staff on ethical conduct, voluntary auditing, etc. These kinds of internal checks and balances allow companies to bridge the gap between their commitments and their actual impact on consumers.

For consumers, the pharmaceutical industry's ethical conduct clearly requires improvement. Consumers want to know that their health and wellbeing come first. They want to know that any drug prescribed to them is really the most appropriate treatment available, and that any potential risks are outweighed by the benefits. Doctors and other healthcare professionals have similar concerns. Overall, trust in the industry is at an all-time low. This report will explore what needs to be done and what (some) companies are already doing.

The costs of unethical business practices

Apart from the moral obligation of companies to minimise risks for consumers, there are also very significant financial implications for not applying the highest standards towards ethical behaviour and consumer protection. Product quality and safety incidents have cost the pharmaceutical industry over USD 13 billion in fines and settlements between 2009 and 2012 in the U.S. alone[3] (see also Figure 1). Many of these fines are not intended merely to penalise companies for the health risks inherent in the design of their products (e.g. side effects) but to penalise companies for attempting to conceal these risks or knowingly providing false information about their products, in violation of drug marketing regulations. This illustrates how improper marketing of drugs is a huge factor that aggravates health risks to consumers, in addition to drugs that are poorly designed, tested or manufactured (each of these factors will be explored separately in chapters 1.2 to 1.4).

Figure 1:
Trend in financial penalties for product quality and safety issues in the U.S.



* logarithmic scale

Source: Almashat, S. and Wolfe, S., 2012

Although fines in the U.S. tend to be higher, a similar pattern of fines can be observed in Europe. For instance, U.K. regulators, between 2004 and 2012, imposed on average EUR 765,000 per year in fines for improper pharmaceutical marketing practices.[4] And in the Netherlands, a record total of EUR 836,123 was imposed in 2014.[5]

The above figures exemplify that companies seem to focus on the short term commercial gains of introducing new products to the markets quickly, versus focusing on the medium- and long-term business benefits of ensuring that medicines are safe and of high quality. It is expected that consumer and regulatory pressure to ensure consumer protection will increase further. Therefore, reaching minimal legal requirements will no longer suffice. Companies that go above and beyond minimum legal standards will not only remain ahead of the regulatory curve but will also be better placed to mitigate potential adverse impacts on society and patients.

Impact on consumers of unethical business practices

The potentially severe adverse impacts on consumers of poor product quality and safety management are showcased in Table 1 below. The events are categorised according to where in the product life cycle a lack of risk management occurred:

- Research & Development: poor design of products and/or insufficient testing before products are launched in the market
- Manufacturing & Distribution: lack of quality control in the factory or during transportation and storage leads to products that have been potentially compromised
- Marketing & Sales: provision of false and/or deceptive information on products, off-label marketing, and aggressive marketing tactics such as bribery of doctors

As the example of Vioxx (see Table 1) shows, poor risk management at the Research & Development stage often goes hand in hand with unethical practices during Marketing & Sales. In other words, when products entail safety risks because of design flaws or lack of rigorous testing, companies will sometimes try to cover up these risks by providing false or deceptive product information during their marketing interactions with health professionals, in order to boost sales.

Table 1: Examples of adverse consumer impacts from unethical business practices

Company	Stage of Risk Management Failure	Description of Event	Consumer Impacts
Johnson & Johnson (J&J)	**Research & Development**	**Hip replacement product scandal** Johnson & Johnson has faced tens of thousands of lawsuits brought by hip replacement patients who accused the company of knowingly selling faulty implants. The implants were launched without sufficiently rigorous safety testing, which led to injuries and additional surgeries.	• Over 90,000 people worldwide used the product, with an estimated one in eight to one in three patients being affected by a faulty implant. • Affected patients experienced severe pain and debilitating injuries, and were forced to undergo additional surgeries to remove or replace the implants.
Sanofi	**Manufacturing & Distribution**	**Toronto production halted** In 2012, Sanofi received a warning from the FDA, after an inspection of Sanofi's Toronto plant. The letter listed about two dozen quality issues related to the production process at the plant, including mold and contamination problems. The company was forced to stop production of bladder cancer drug ImmuCyst/TheraCys and Sanofi's BCG vaccine for tuberculosis. Operations were only fully resumed as of 2015.	• The global supply of ImmuCyst and the BCG vaccine was severely restricted from 2012 to 2015, which may have impacted thousands of patients' access to treatment. • Before operations were suspended, patients may have been exposed to potentially defective products.
GlaxoSmithKline plc (GSK)	**Marketing & Sales**	**Bribery scandal in China** In 2014, a Chinese court found GSK and four of its executives guilty of widespread bribery of non-government personnel to boost drug sales, and the company was fined nearly USD 500 million.	• Structural bribery has increased drug prices and jeopardised access to affordable medicines for tens of thousands of patients. • Doctors were encouraged to prescribe drugs indiscriminately. As such, patients were denied reliable information on safe drug use and prescribed inappropriate drugs.

Merck & Co. (Merck)	**Research & Development & Marketing & Sales**	**Vioxx scandal** Merck has paid over USD 5 billion in settlements and still faces consumer claims over its painkiller Vioxx. The lawsuits accuse the company of providing unreliable product information, applying deceptive promotional practices and fabricating medical journal studies to enhance Vioxx's credibility.	• Studies found significantly increased likelihood of fatal heart attack or stroke from taking Vioxx. • Up to 38,000 people died from heart attacks or strokes after taking Vioxx, with a total of about 160,000 patients injured. [6]

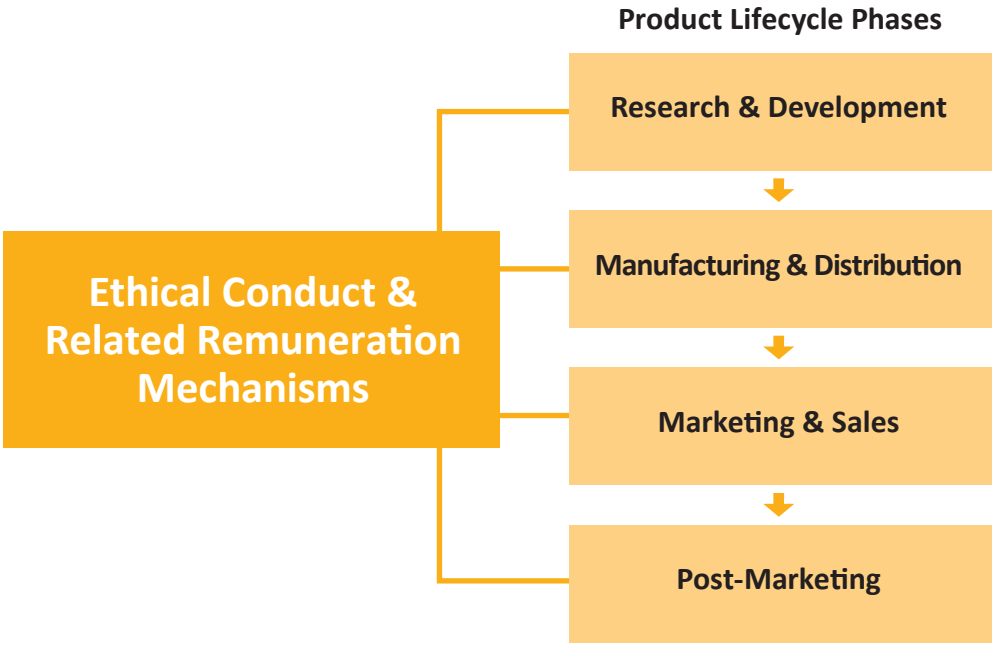
The structure of this report

This report analyses the adverse effects of unethical business practices and poor quality and safety management on consumers and society at large and is structured as follows. First, an overview of the product life cycle is provided to make clear in which stages ethical behaviour and consumer protection are particularly important. Second, the concept of ethical conduct and related remuneration mechanisms are discussed. Third, the report reflects on the main topics, risks and best practices at each stage of the product life cycle. Finally, industry performance is analysed, including examples of individual companies' performance in the area of product quality and safety across the product life cycle. In this last section, concrete insights are drawn from a sample of the 15 largest pharmaceutical companies globally based on market capitalization (excluding biotechnology companies).

1. Product Life Cycle

Product quality and safety in medicines is paramount at all phases of the product life cycle. A typical product life cycle is depicted in Figure 2. Research and development (R&D) refers to the design and testing of new products before they are marketed. Manufacturing and distribution refers to drug production and delivery to the end user. Marketing and sales entails all business activities that are focused on promoting and selling (more) products. Finally, post-marketing refers to the monitoring of products' health effects over the long term. A deeper understanding of the issues will result from analysing the associated risks and best practices along the product life cycle (see chapters 1.2 - 1.5). Ethical conduct (chapter 1.1) is seen as an overarching topic, of importance throughout the product life cycle and throughout a company's operations.

Figure 2: Ethical conduct and consumer protection in the product life cycle



1.1 Ethical Conduct & Related Remuneration Mechanisms

What is ethical conduct, and why is it an issue for product quality and safety?

Ethical conduct includes adherence to ethical standards and compliance with local, national and international laws in all business dealings and is therefore crucial to guarantee product quality and safety. Effective ethical conduct management entails strong management of ethical issues, in particular corruption, fraud, and conflict of interest. Such management should go, where necessary, beyond what is required by regulatory standards, and apply to all operations worldwide. Poor ethical conduct is a threat to consumers in myriad different ways, many of which will also be explored in subsequent chapters. But perhaps the most significant effect of unethical conduct is that it compromises the integrity and dependability of health systems and erodes trust in the industry.

Pharmaceutical companies' operations are highly regulated by governments.[7] However, as companies constantly interact with government officials, they are confronted with an "ever present temptation to cut corners, bend rules and influence decision makers."[8]

Unethical business practices include providing financial inducements (e.g., gifts, hospitality, meals, fees and grants) as part of interactions with government officials and healthcare professionals. Such practices are pervasive throughout the industry, in both developed and emerging markets. Some pharmaceutical companies even claim that business practices in certain overseas countries require bribery and companies that do not participate in such practices would lose most of their business to competitors.[9] But recent accusations in developed markets demonstrate that these markets are certainly not immune to unethical behaviour either. For instance, U.K. health officials allegedly enjoyed lavish trips and events paid for by pharmaceutical companies hoping to boost their sales.[10]

According to Pharmaceutical Business Research Associates (2014), a research and consulting firm, pharmaceutical companies continue to practice systematic corruption since fines are too small and the penalties are too superficial to serve as real deterrents.[11] The 2013/14 Kroll Global Fraud report survey (2014) shows that less than half of the healthcare and pharmaceutical firms are planning to invest in due diligence and staff background checks to control bribery and corruption globally.[12] However, changing regulations - in developed and emerging markets - call on companies to implement new compliance mechanisms.

Ethical conduct goes beyond corruption however. Fraud for instance is also a recurring problem in the industry. **Novartis**, for example, is being investigated by Japanese authorities for allegedly tampering with the results of clinical trials for a leukaemia drug. This allegation points to poor ethical conduct at the Research & Development stage of the product life cycle. Similarly, corruption points to a lack of ethical conduct at the Marketing & Sales stage. Hence, ethical conduct is seen as an overarching requirement that spans all phases of the product life cycle and all aspects of companies' operations (see Figure 2).

Implementation and enforcement procedures

A company's implementation of anti-bribery and corruption policies can demonstrate how well it is mitigating risks related to unethical conduct. Pharmaceutical companies are challenged to understand local corruption risks, including local industry codes, and consider all people on the ground, including employees, partners and third-parties. Furthermore, the implementation of one global standard that applies to all operations worldwide and goes beyond compliance with local standards is challenging, but nevertheless a prerequisite for ethical conduct.

Companies that want to change their internal culture tend to implement their policies through regular training, audits, reporting mechanisms for violations and procedures for corrective action. Compliance training should take place on a frequent basis (i.e. annually) and apply to employees, partners and third-parties. Effective training should teach behavioural skills and compliance with industry standards, such as the Pharmaceutical Research and Manufacturers of America (PhRMA) Code, provide training feedback, reinforce successful application, and measure training application in the field.[13] Pharmaceutical companies should regularly engage in both internal and external audits to examine compliance with ethical standards. Finally, companies need to implement formal mechanisms to collect and investigate complaints by adopting a whistleblower system that entails a global anonymous compliance hotline and a non-retaliation clause against reporters. The adoption of whistleblower mechanisms supports good ethical conduct, permitting disclosure and investigation of unethical practices.

Finally, companies can integrate ethical standards and sustainability practices into their culture by linking part of executive remuneration to environmental, social and governance (ESG) performance targets, such as ethical or product quality and safety standards.

Relevant Indicators to Measure Individual Company's Performance

The following sub-chapters provide a reflection on the main topics, risks and best practices in product quality and safety management across the product life cycle. As stated previously, ethical conduct should be seen as overarching to all of the life cycle stages.

1.2 Phase I: Research & Development

What does this stage entail and why is product quality and safety an issue at this stage?

The research and development (R&D) stage basically refers to all the steps that take place before a new product receives marketing approval, i.e. before it can be widely sold in the market place. In the R&D stage, companies need to conduct extensive scientific testing to determine the efficacy of a new product, whilst at the same time ensuring that potential side effects and other complications are uncovered. Ultimately, the benefits of a new product should outweigh the risks.

Unfortunately, the results of an estimated half of all clinical trials are withheld from regulators and the public, and the results that are disclosed are frequently incomplete or misleading.[14] Selective disclosure of test results makes it hard to substantiate companies' health claims about their products and poses various health risks. Specifically, doctors and patients might not be informed of side effects that could outweigh the benefits of pharmaceutical products, they might not be sufficiently aware of the conditions under which a product is (in)effective, or they might mistakenly believe the product to be more safe or effective than alternative treatments.

Implementation and enforcement procedures

Quality standards that govern product development include Good Laboratory Practice (GLP) and Good Clinical Practice (GCP). GLP and GCP standards entail numerous guidelines to ensure that pharmaceutical studies are scientifically accurate and that the clinical properties of new products are properly documented. Adherence to these standards is enforced through frequent inspections by regulatory authorities, and typically a requirement to gain marketing approval for new products. However, due to the low transparency of clinical research, regulators and doctors are only getting part of the picture. Hence, companies should provide full transparency of all their clinical trial data. Although regulators in developed markets in the past few years have enacted stricter requirements to improve disclosure of clinical trial data, companies should go beyond minimum legal requirements by proactively disclosing the results of all their clinical trials, regardless of whether their

outcome is favourable to the company or not, and disclosure should include results from terminated and historical trials.

In addition to transparency of R&D activities, the R&D intensity of companies (i.e. the percentage of revenues invested in R&D activities) can also be seen as a proxy indicator for the extent to which companies are focussed on delivering new high quality products that meet public health needs. One should be careful however when directly comparing companies according to their R&D intensity, as differences can also be explained by variations in business models, types of R&D conducted, and accounting standards.

Relevant Indicators to Measure Individual Company's Performance

1.3 Phase II: Manufacturing & Distribution

What does this stage entail and why is product quality and safety an issue at this stage?

The manufacturing and distribution stage covers all business activities that take place in production plants or in delivering drugs from the factory to the end user. At this stage, it is key to ensure that each batch of product that leaves the factory is of the right composition. At the production plant, contamination, incorrect dosages or an improper manufacturing climate are just a few of the risks that could render a product defective. Subsequently, during distribution, products might be further exposed to either the penetration of counterfeit medicines or to improper handling during storage or transportation. For instance, to preserve a medication's properties, some vaccines might require cold storage. The potential health impact of products that have been compromised varies from ineffectiveness to severe adverse reactions.

Although the most severe cases of poor quality management during manufacturing or distribution tend to occur in emerging markets, developed markets are certainly not immune either. For instance, between 2006 and 2011, the annual number of U.S. Food and Drug Administration (FDA)-regulated product recalls more than doubled from 4,266 to 9,288; these product batches were recalled due to for instance lack of sterility or potential contamination during the production process.[15]

Product quality and safety during manufacturing and distribution is heavily regulated through for instance inspections at factories and storage facilities. However, this is not always sufficient to prevent incidents, as illustrated by the increased number of recalls. Therefore, companies should take their own measures, beyond legal requirements, to provide an additional level of quality assurance.

Implementation and enforcement procedures

Best practices to uphold product quality and safety at the manufacturing stage include implementing quality management systems that consist of regular employee training

on product safety, external product safety audits, incident investigation and monitoring of product safety performance. Companies also need to implement standard operating procedures for product recalls in situations where a product may be defective. These procedures should include clear steps to revoke products from the markets and to warn doctors, pharmacies and patients. Additional assurance could be provided by seeking external certification of the company's quality management system, beyond the assurance provided by regulatory inspections. Examples of internationally acknowledged standards include ISO 9001, Good Manufacturing Practice (GMP) or ISO 13485.

Relevant Indicators to Measure Individual Company's Performance

1.4 Phase III: Marketing & Sales

What does this stage entail, and why is product quality and safety an issue at this stage?

This stage entails all business activities that are focused on promoting and selling (more) products. Industry spending on product promotion generally outpaces spending on research and development of new treatments. Pharmaceutical companies use a variety of tactics to increase prescription and sales volumes for their products. All of these tactics entail inherent risks of misinformation, conflict of interest and sometimes outright corruption, which may negatively impact customers' health. Although bribery is arguably the worst form of improper marketing, and illegal in most markets, some of the other forms are particularly problematic because they take place in a legal grey area. This concerns most notably inviting healthcare professionals to lavish events whilst paying for their transportation and accommodation, or paying fees to healthcare professionals for "services" as a financial incentive to boost sales for a certain product.

Improper marketing practices can harm society and patients in several ways, such as:

- Over-prescription of expensive patented products when cheaper and equally effective generic products are available;
- Prescription of products for which the health risks outweigh the benefits;
- Prescription of products that are not suitable for certain diseases or patient groups;
- Provision of biased and unreliable product information to patients; and
- Insufficient patient awareness of potential health risks, including side effects.

Implementation and enforcement procedures

To mitigate the aforementioned risks, companies could implement voluntary industry marketing codes which have been in existence for decades, such as the Code of Pharmaceutical Marketing Practices of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA). However, these industry codes are not as strong as they could be. For instance, the IFPMA code does not cover advertisements and communication to the general public, nor does it address conduct of pharmaceutical sales representatives. Conversely,

the WHO's Ethical Criteria for Medicinal Drug Promotion do cover these issues and generally promote higher standards. Additionally, companies could follow ethical medicine promotion by implementing restrictions on direct payments and other more common forms of unethical promotion such as providing samples, gifts and hospitality to doctors and patients. Ethical marketing training programmes for sales representatives, mitigation practices such as ethical review of promotional materials and sales incentives to reward compliance should also be encouraged [see also sub-chapter on Sales Incentives].

Relevant Indicators to Measure Individual Company's Performance

1.4.1 Sales Incentives

What do sales incentives entail, and why are they an issue for product quality and safety?
Traditionally, pharmaceutical companies have employed a sales volume-based system to establish rewards for high performing sales staff and consequences for low performing sales staff. Sales commissions and bonuses often tie to sales quotas. These sales-volume based systems have been a driving force for pharmaceutical sales representatives to engage in inappropriate behaviours such as overly aggressive marketing, including the following:

- Providing financial inducements (e.g., gifts, hospitality, meals, fees and grants) and non-financial inducements (e.g., career opportunities), as part of promotional interactions with healthcare professionals;[16]
- Providing product information that is unreliable, incomplete or misleading; and
- Promoting drugs for unapproved uses or target groups, a practice known as "off-label marketing."

While a volume-based sales model is of little to no concern in many other industries, the principle of "selling as many drugs to as many patients as possible" neglects that a particular treatment might not necessarily be in the best interest of all patients. The provision of incentives to doctors can lead them to prescribe products that are not appropriate for certain patient groups, for which the health risks outweigh the benefits, or for which equally effective (and cheaper) generic versions are available. It has been shown that even when doctors believe they cannot be influenced, marketing tactics do change their behaviour and prescription habits.[17]

Implementation and enforcement procures

A company's shift away from a "volume-based" sales approach to a more "value-based" sales approach (focused on value creation as the customer defines it) can mitigate product quality and safety concerns. Best practices include establishing sales personnel remuneration programmes based on technical knowledge (including expertise on pharmaceutical products, symptoms, and diseases) and quality of service/consumer engagement.

Relevant Indicator to Measure Individual Company's Performance

Sales Personnel Remuneration Programme

1.5 Phase IV: Post-Marketing (Pharmacovigilance)

Why is product quality and safety an issue at this stage?

Once a medicine is sold in the market place, the responsibility of a pharmaceutical company does not end. If companies do not monitor how their products perform in the wider market place, potential problems (such as side effects inherent in the design of the product, or defects related to faulty manufacturing) cannot be signalled early. Such monitoring of products' health effects is referred to in the industry as pharmacovigilance (PhV), defined by the World Health Organisation as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem."[18]

In other words, PhV entails the monitoring of a product's medium-and long-term effects on consumers. Of course, some of the effects that are inherent in the product design are already known from the clinical trials that are conducted prior to receiving marketing authorisation, i.e. during the R&D process. Yet, certain health effects may only become evident during large-scale and long-term use — that is, several years after a product has been launched in the market.

Pharmaceutical companies are largely responsible for collecting and reporting adverse drug events to authorities, an important aspect of PhV. However, recent reports show that pharmaceutical companies are doing a substandard job in reporting adverse drug events to authorities.[19] This is alarming for public health, since it leaves doctors and patients with inadequate information on the risks of certain products. It also means that precious time may be lost before certain (negative) health effects become widely known and corrective measures can be taken.

Implementation and enforcement procedures

Companies should implement post-marketing surveillance to detect and respond to potential product safety concerns. Best practices include tracking (unanticipated) side effects of all new products, providing a mechanisms for adverse events reporting, as well as investigating incidents and taking corrective actions, such as product recalls.

Relevant Indicator to Measure Individual Company's Performance

Product & Service Safety Programme

2. Reflection on Company Performance

The internal mechanisms & structures companies have in place

From the large number and significant impact of controversies in the pharmaceutical industry, it is clear that the quality and safety of today's pharmaceutical products are under threat. Companies attempting to hide information related to poorly designed drugs, contamination and falsification of drugs, or aggressive marketing to boost sales – all of these practices are still too frequent in the industry. The most salient question that therefore arises is: What are companies doing to avoid future controversies?

The first chapter of this report provided an overview of the main topics, risks and best practices in product quality and safety management across the product life cycle. This chapter subsequently analyses industry performance on the various topics identified above, including individual companies' performance in the area of product quality and safety across the product life cycle. Analysis has been done on the entire group of 132 pharmaceutical companies that are part of the Sustainalytics research universe. Furthermore, specific insights are drawn from additional research on a sample consisting of the 15 largest pharmaceutical companies globally, based on market capitalization (excluding biotechnology companies).

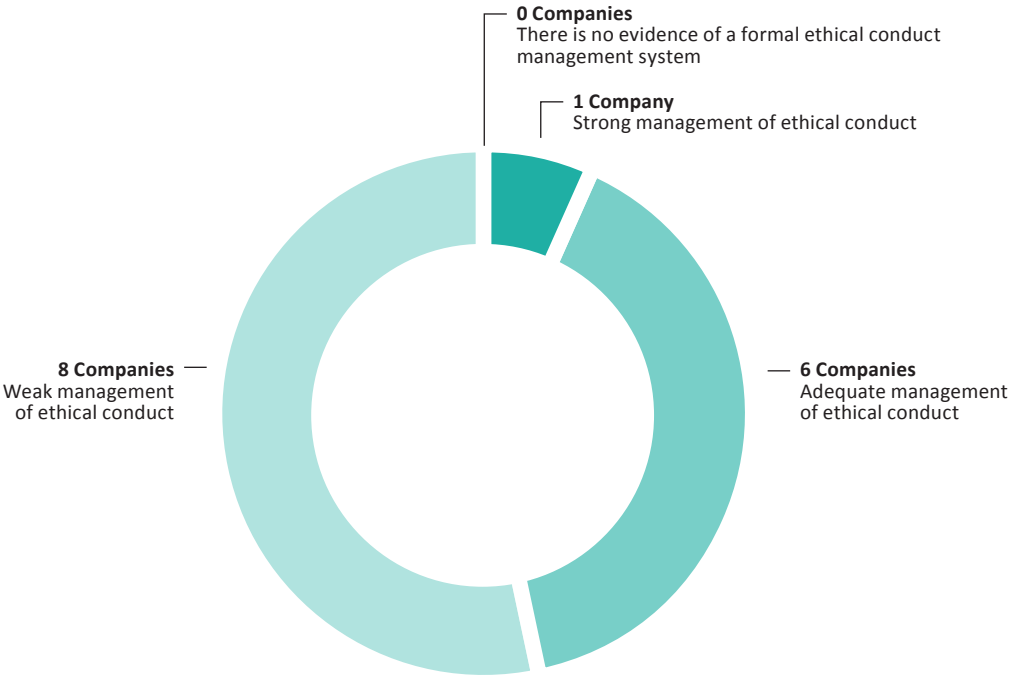
In analysing performance, companies are assessed mainly based on the strength of their internal mechanisms to ensure consumer protection, rather than the strength of their policies. In other words, performance assessments are not based on commitments but rather on what companies are doing to mitigate product quality and safety risks, i.e. how do they manage these risks in their day-to-day operations? Involvement in controversies or scandals is not taken into account, since the aim of this exercise is rather to identify to what extent the selected companies are prepared to avoid future involvement in controversies. Finally, in assessing performance, only those elements that go beyond legal compliance are taken into account. For instance, in assessing whether companies undergo external auditing of their quality management systems, points were awarded only for voluntary auditing and not for audits imposed by regulatory agencies.

2.1 Ethical Conduct & Remuneration

General Performance Insights

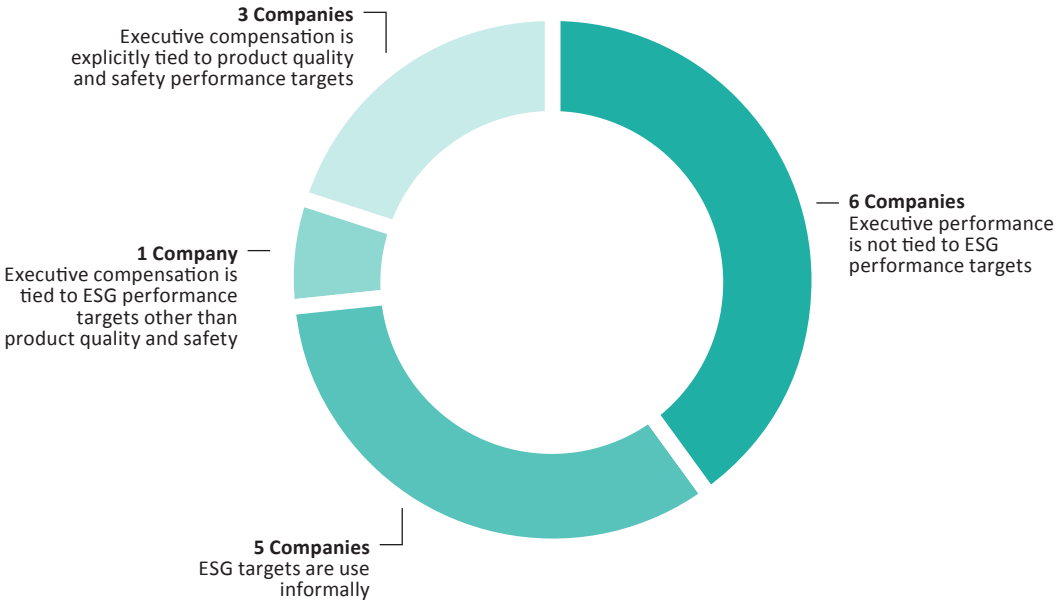
Sustainalytics' data shows that only 10% of the 132 researched pharmaceutical companies demonstrate leading practice when it comes to whistleblowing mechanisms, including policies on non-retaliation against whistleblowers and permitting whistleblowing by external parties. Leading companies in this area publicly report on performance data; that is, types of violations and how misconduct is addressed. Over half (58%) of the 132 pharmaceutical companies tracked implement whistleblower programmes assessed as adequate; that is, compared to strong programmes, they lack a performance reporting component. Approximately one-third of all companies report limited or no activities in this regard. Whilst it is encouraging to see that the majority of the industry has adopted some form of whistleblower mechanism, significant room for improvement remains regarding the scope of such programmes.

Figure 3: Ethical Conduct Management



Regarding ethical conduct management, the findings from the 15 largest pharmaceutical companies (see Figure 3) indicate that there is still significant room for improvement. Only one of the companies, **GlaxoSmithKline (GSK)** has implemented strong mechanisms to manage ethical conduct. These mechanisms entail board and managerial oversight on this topic, formal ethics trainings for all levels, internal and external compliance audits, corrective action procedures, and extending the same standards to third parties. However, it is expected that at least several years might be needed to demonstrate the real world effects of improvements that GSK has recently implemented. Of the other companies, six can be considered to have adequate systems to manage ethical conduct, but tend to lack external audits, procedures for corrective action and/or ethics training at the executive level. Finally, the remaining eight companies are considered to have weak mechanisms to manage ethical conduct, showing deficiencies in more than a few of the above-mentioned areas. Roche scores poorest on ethical conduct management. The company outlines commitments to promote ethical behaviour and compliance with laws and regulations and has installed board and managerial oversight of ethical conduct, but provides no disclosure on additional details that would point towards a formal system to manage ethical conduct.

Figure 4: Executive Remuneration Tied to ESG Performance Targets



Regarding executive remuneration, among the sample of the 15 largest pharmaceutical companies (see Figure 4), only **GSK, Bayer** and **Sanofi** provide evidence that executive compensation is directly linked to product quality and safety. Specifically, the variable component of CEO or other executive salary is based on (amongst others) criteria like product safety performance or ethical marketing. Furthermore, **Novartis** mentions business ethics and sustainability as one of the principles on which executive compensation is based, without referring specifically to product quality and safety. This indicates that these companies have at least to some degree integrated ethical standards and sustainability practices into their corporate culture. Five other companies use ESG performance targets informally to compensate executives, for instance by referring to "company reputation" in relation to remuneration, or by referring to linkages between remuneration and sustainability performance outside of formal remuneration policies or annual reporting. The remaining six companies do not show any evidence of anchoring sustainability performance in executive remuneration.

2.2 Research & Development

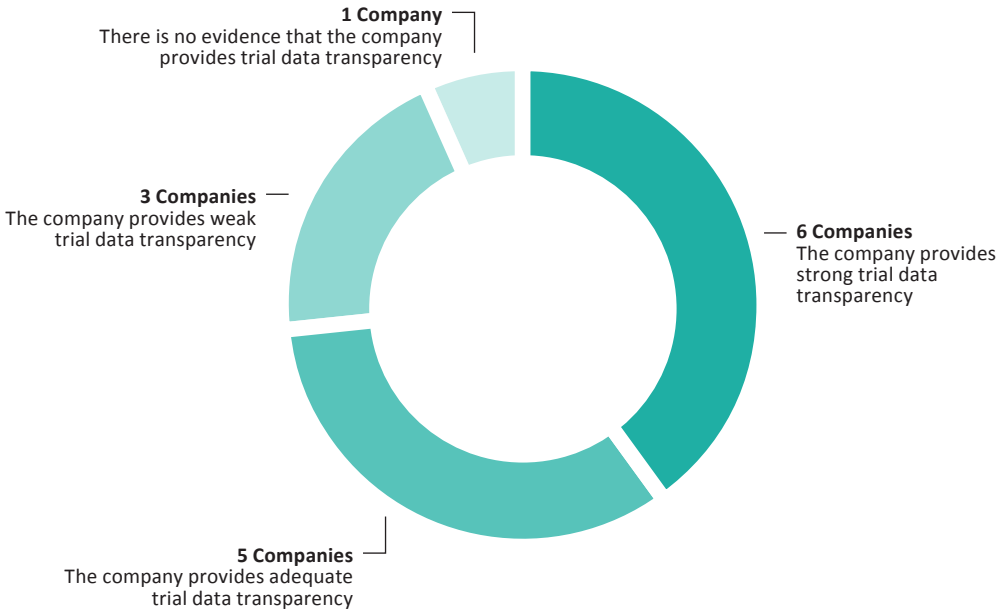
General Performance Insights

A recent study (2015) found that almost half of all trials (47%) in the pharmaceutical industry remain unpublished.[20] Notably, trials with positive findings were three times more likely to be published than those with negative results. Research funded by governments was twice as likely to be published as research funded by the industry. To increase the availability and reliability of clinical trial data, reformers have called for new policies that would require pharmaceutical companies and other clinical trial sponsors to provide outside researchers access to their data.[21]

Performance Insights from the 15 Largest Pharmaceutical Companies

Performance in this area among the 15 largest pharmaceutical companies (see Figure 5) is encouraging, with six companies, **AbbVie, AstraZeneca, Bayer, GSK, Merck & Co** and **Sanofi,** providing evidence of strong trial data transparency. This includes all of the following elements: registration of all clinical trials in recognized online registers before studies are initiated; publication of (summary) trial results in credible databases or peer reviewed journals; publication of results of terminated trials; commitment to specific timeframe for results disclosure; and having a mechanism in place to make raw data (i.e. full patient-level data that has not been aggregated or processed) available to third parties. Five additional companies provide evidence of all but one of the above-mentioned elements. Only four companies provide weak or no transparency on their clinical trials.

Figure 5: Trial Data Transparency



The overall strong performance in this area can be interpreted as a response to new regulation that has been put in place in recent years in developed markets, requiring some degree of public disclosure of trial design and outcomes. The Food and Drug Administration (FDA) in the U.S., for instance, requires companies to register certain trials and results on a government website. Furthermore, new EU Clinical Trial Regulations are expected to take force by mid-2016, requiring the registration of all drug trials conducted in Europe, as well as the publication of results summaries. However, in our assessment of the 15 largest pharmaceutical companies, points were awarded only to companies that go beyond legal requirements and proactively disclose all of their trials anywhere in the world, whether legally required or not. Furthermore, making raw data from past studies available to third-party researchers is not legally required in any jurisdiction, yet the six strong performers do have mechanisms in place for this.

It should be noted though that the above-mentioned strong performance only emerged in the past year or two, whereas the success of these measures can only be assessed in the long-term. What perhaps remains to be seen, for instance, is to what extent external researchers will in practice be able gain access to clinical trial data when it matters most,

e.g. to verify health claims made about certain products or to compare products against similar treatments from competitors.

The two generic drug producers that are among the 15 largest pharmaceutical companies, **Valeant** and **Teva**, provide either limited or no reporting on how they ensure clinical trial data transparency. While the companies' involvement in the R&D stage is more limited than for innovator companies, both **Teva** and **Valeant** also conduct clinical trials to ensure safety and efficacy of products for human use. It can therefore be reasonably expected that these companies should disclose related data.

Some companies in our sample have publicly pushed back against calls for enhanced trial disclosure. Most notably, **Pfizer**, in spite of the fact that it provides adequate trial disclosure according to our assessment, has stated that will resist demands from investors and transparency campaigners that it disclose results from all historical drug trials[22] Furthermore, **Roche** has been involved in a conflict with researchers demanding access to the raw data of its trials for the controversial influenza treatment Tamiflu; the company refused for years to hand over the requested data.[23]

Best Practices

In line with best practice, **Johnson & Johnson (J&J)'s** subsidiary, Janssen Research and Development (Janssen), entered into an agreement with Yale School of Medicine's Open Data Access (YODA) Project in 2014 to facilitate the sharing of raw data on clinical trials with third-parties. As part of the agreement, YODA reviews requests from investigators and physicians seeking access to anonymized clinical trials data from Janssen, and makes final decisions on data sharing.[24] Although some other companies also have a mechanism in place for making raw data available at the request of qualified researchers, **J&J's** data sharing mechanism is unique in the sense that an independent third-party makes decisions on who gets access to **J&J's** data.

2.3 Manufacturing & Distribution

General Performance Insights

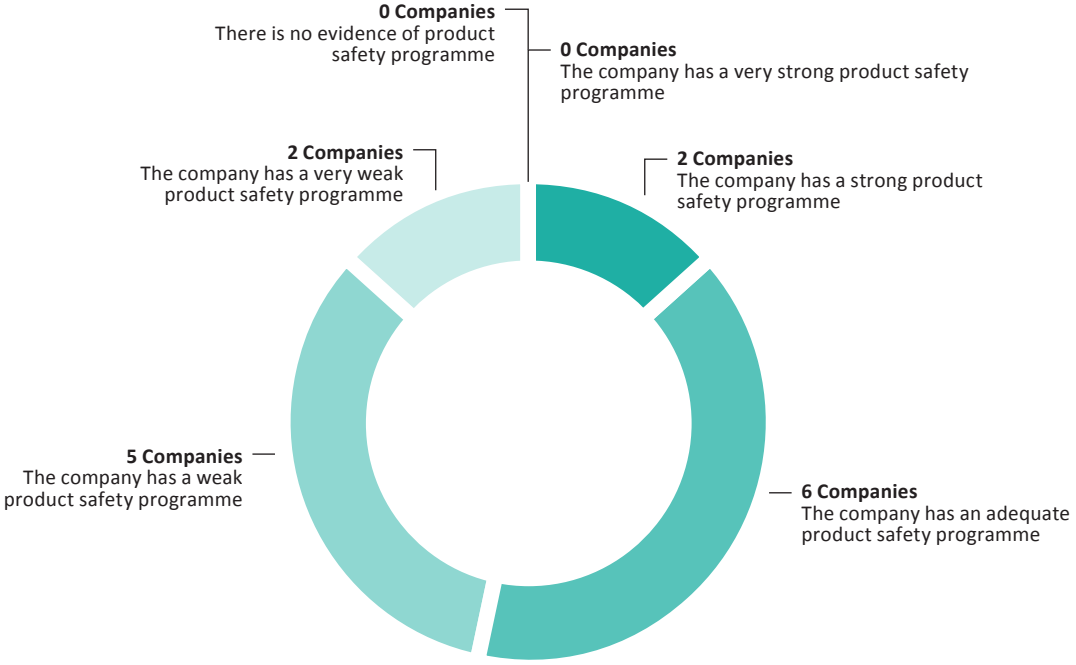
A company's implementation of quality management system (QMS) certifications can be used as an indication of how well it is mitigating product quality and safety risks. It appears that the industry is lagging behind in adopting QMS practices beyond minimum legal requirements. Nearly three-quarters of the 132 pharmaceuticals companies researched by Sustainalytics do not demonstrate evidence of external certifications to ISO 9001 or other internationally acknowledged standards, such as Good Manufacturing Practice (GMP) or ISO 13485. This contrasts with the few leading companies in this area - 5% of the 132 companies researched by Sustainalytics - which have a certified QMS for over 90% of their entire operations. Audits and inspections by regulatory authorities are not taken into account; companies are given credit only for voluntary external certifications.

The fact that the larger part of the 132 companies do not have an adequate system might be explained by the fact that the industry in general does not feel comfortable soliciting external scrutiny of their operations. The argument often used by companies is that additional scrutiny is not necessary, since the industry is already heavily regulated. The large number of product quality and safety incidents in the industry however does point out a clear need for an additional level of assurance.

Performance Insights from the 15 Largest Pharmaceutical Companies

Out of the 15 largest pharmaceutical companies researched by Sustainalytics (see Figure 6), only **GSK** and **Sanofi** have implemented strong programmes to manage product quality and safety. These programmes include a great number of elements, such as managerial responsibility for product quality and safety, regular employee training, and targets for improvement. Such strong programmes do not merely cover manufacturing and distribution of products but also safety risk assessments during product development (R&D) and during the post-marketing stage (the latter will be covered in chapter 2.5). Even **GSK** and **Sanofi** however lack certain elements in their programmes, namely voluntary external audits and/or reporting on such audits. Therefore, no company in our sample of 15 can be considered to have very strong programmes to manage product quality and safety.

Figure 6: Product Safety Programme



Of the remaining companies, six have adequate programmes and five have weak programmes. The latter companies have implemented product quality and safety programmes but they have a limited scope (e.g. only cover certain markets) or lack certain elements such as regularly tested procedures for product recalls. Finally, two companies, **AbbVie** and **Valeant**, stand out negatively, providing merely a policy commitment to product quality and safety but not much more.

Best Practices

Bayer deserves mention as a best-practice example. In spite of the fact that the company only has an adequate product quality and safety programme overall, it is the only company that has (nearly) all of its operations externally certified to recognised quality standards. **Bayer** reports that in FY2014 over 98% of its operations (with respect to energy consumption) received one of the following external certifications for their quality management system: ISO 9001, ISO 17025, ISO 13485 or Good Manufacturing Practice (GMP).

2.4 Marketing & Sales (including Sales Incentives)

General Performance Insights

While the WHO's Ethical Criteria for Medicinal Drug Promotion is considered a best-practice standard regarding ethical drug marketing (see Chapter 1.5), only 8% of the 132 pharmaceutical companies analysed by Sustainalytics refer to the WHO standards, and these are mostly companies from Europe. Approximately 49% of the 132 companies researched by Sustainalytics reference a regional industry association code, which is less stringent than the WHO standards, while the remaining companies provide no evidence of adhering to any drug promotion and advertising standard.

Controversial Practices

While many pharmaceutical companies include a relevant responsible marketing policy as part of their commitment to a sustainable business model, in practice, the industry has experienced major gaps between policy and performance. Some companies that have pledged their commitment to ethical marketing codes have also violated these codes' requirements on multiple occasions. The example of GSK stands out in particular as the company has a strong and elaborate bribery and corruption policy in place and still the company faced numerous allegations of bribery in product sales (see also Chapter 1.5.1). Notably, GSK has not taken this situation lightly and has announced plans to stop paying doctors to attend medical events or speak about its drugs, and to roll out this new policy globally by 2016.

Performance Insights from the 15 Largest Pharmaceutical Companies

An illustration of the significance of marketing in the pharmaceutical industry is that, on average, pharmaceutical companies spend almost a quarter of their revenues on promoting their products. When compared to the budgets available for R&D, i.e. the ratio of marketing to R&D expenditure, these numbers are even more striking (see Table 2). The figures do provide a starting point for identifying companies that might have greater or lesser exposure to the risk of improper marketing. Nonetheless, one should however take care in comparing these figures directly, as the companies involved have different business models and/or geographical focus. For instance, less marketing is needed for specialised, niche drugs, than for drugs with a broad potential patient base.[25] Furthermore, since these figures are based on the companies' own financial reporting, there could be differences in how exactly companies record or calculate their marketing expenses.

Table 2: Marketing Expenditure compared to R&D Expenditure

Company	Marketing/R&D expenditure
Bayer *	3.1
Johnson & Johnson	2.6
GlaxoSmithKline	2.3
Pfizer	1.7
AstraZeneca	2.3
AbbVie	2.3
Novartis	1.4

Sanofi	1.9
Merck & Co	1.6
Bristol-Myers Squibb	0.9
Eli Lilly	1.4
Novo Nordisk	1.7
Roche	0.9

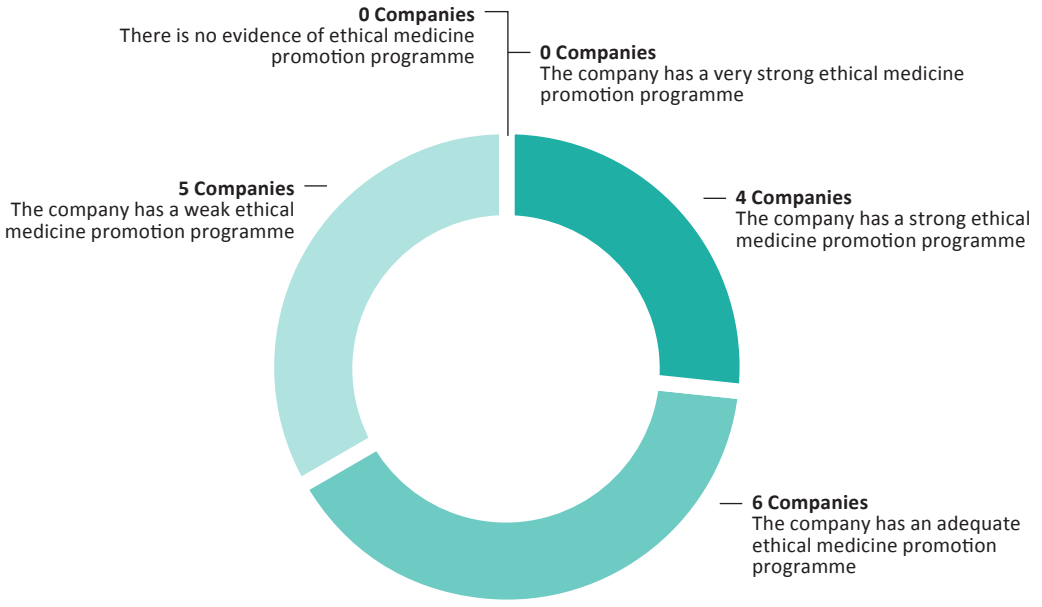
* Figures for Bayer are based on group expenses, since the company does not report its marketing expenses separately for its healthcare division;
** Valeant and Teva are excluded from this analysis, since as generics companies they are less R&D focussed.

For an industry known for its particularly high R&D intensity and the importance of R&D for the long-term viability of its businesses, it is noteworthy that almost all companies in the sample spend more on marketing than on R&D (see Table 2). This difference raises some doubts about the sustainability of the sample companies' business strategies. Investment in R&D, including the development of new products and testing their safety and efficacy, seems to play a lesser role than investment in product promotion.

The good news is that marketing expenditures in the industry have declined over the past few years, and that a steadily decreasing number of doctors is open to visits from pharmaceutical sales representatives.[26] Nonetheless, mitigating the risk of improper marketing remains key for all pharmaceutical companies.

Among the 15 biggest pharmaceutical companies (see Figure 7), there is a roughly one-third split between those that have a strong, adequate, or weak ethical marketing programme. Such a programme should include, amongst others: marketing risk assessments, regular ethical marketing training for sales staff, ethical review and approval of promotional materials, and disclosure of all payments made to healthcare professionals. **AstraZeneca** has the strongest programme, although it still lacks objectives and targets to improve its ethical marketing performance. As such, none of the companies can be considered to have a very strong ethical marketing programme. The poorest performers are **Pfizer** and **Bristol-Myers Squibb**, who provide only very scant evidence of a having an ethical marketing programme in place.

Figure 7: Ethical Medicine Promotion Programme



2.4.1 Sales Incentives

Performance Insights from the 15 Largest Pharmaceutical Companies

While a value-based sales approach can be beneficial for consumers (see chapter 1.5), only one out of the 15 largest pharmaceutical companies (**GSK**), recently implemented a sales personnel remuneration programme based on non-volume sales targets. The company stopped rewarding sales staff based on prescription volumes and instead started rewarding technical knowledge and quality of service. This new approach was implemented globally by early 2015. These new compliance strategies go beyond those adopted by any of the company's peers, and make **GSK** the undisputed leader when it comes to managing and mitigating marketing risks.

2.5 Post-Marketing (Pharmacovigilance)

General Performance Insights

In the absence of adverse drug event reporting, society and consumers are not adequately informed about medicine hazards, receive false safety signals, and cannot quantify risk in relation to benefit appropriately.[27] The FDA has stated that fewer than half of the adverse event reports submitted to the agency by pharmaceutical companies is complete.[28]

Controversial Practices

In 2012, U.K. regulators discovered that 80,000 adverse reaction reports submitted to **Roche**, including 15,000 reports of deaths, were never investigated by the company. The reports had been collected through a Roche-sponsored patient support programme but were not passed along for further investigation.[29] To prevent such cases from occurring, companies need to implement strong post-marketing control mechanisms.

Performance Insights from the 15 Largest Pharmaceutical Companies

Table 3 below depicts two key elements of a strong Pharmacovigilance system:

- Structural monitoring of product safety performance in the market place, which should include:
  - post-marketing surveillance to systematically track side effects and adverse events for several years after a new product is launched;
  - a reporting mechanism for doctors and/or patients to report product safety concerns;
- Mechanisms in place for investigating reports on drug safety issues such as (unanticipated) side effects, and procedures for corrective action.

Table 3: Post-Marketing Activities

	Post-Marketing (Pharmacovigilance)	
Company	**Monitoring of product safety performance**	**Incident investigation and corrective action**
AbbVie	1	0
AstraZeneca	1	1
Bayer	1	0
Bristol-Myers Squibb	1	1
Eli Lilly	1	0
GlaxoSmithKline	1	1

Johnson & Johnson	1	1
Merck & Co	1	1
Novartis	1	1
Novo Nordisk	1	0
Pfizer	1	1
Roche	1	1
Sanofi	1	1
Teva	1	0
Valeant	0	0

As evidenced in Table 3, nine of the 15 largest pharmaceutical companies have implemented both product safety monitoring and incident investigation and corrective action during the post-marketing stage. Furthermore, five companies do monitor product safety after products are launched, but have not implemented mechanisms to investigate incidents or take corrective actions in case of adverse events. Finally, **Valeant** is the only company that does not show evidence of either of the two Pharmacovigilance elements.

As such, it seems that in general pharmacovigilance is well embedded in companies' internal mechanisms for consumer protection. However, the example of **Roche** (see above under Controversial Practices) shows that having a pharmacovigilance system in place does not guarantee that it will always function well in practice. There are examples of products (such as **Merck's** Vioxx or **J&J's** ASR hip replacement device) that were pulled from the market years after doctors and consumers first raised safety concerns. This could perhaps have been avoided through well-functioning pharmacovigilance systems.

Conclusion

This report reveals that it is paramount that pharmaceutical companies anchor ethical conduct management in their organisation and implement and enforce strong quality management along the product life cycle: from R&D, to manufacturing and distribution, to marketing and sales, to post-marketing. In addition, it is evident that meeting minimum legal requirements is not sufficient to mitigate adverse impacts on patients and society at large. Even a moderate adoption of product quality and safety measures, going beyond legal requirements, may not suffice to avoid future harm to consumers. Hence, the true leaders in each area of product quality and safety management should be heralded as best practice examples for all others. And since not one company shows leadership across all areas, all of them have room for improvement.

At the corporate level – where ethical conduct management (including strong management of ethical issues, in particular corruption, fraud, and conflict of interest) is crucial to guarantee product quality and safety – there is room for improvement for the majority of the 15 largest pharmaceutical companies. Most of them only implement ethical conduct management systems but do not provide evidence that executive remuneration is linked to product quality and safety or even merely to general sustainability performance targets.

At the R&D stage – where a lack of rigorous testing of new products or inadequate documentation and disclosure of clinical trial results can adversely impact society and patients – the majority of the 15 largest pharmaceutical companies implement strong or adequate trial data transparency standards, in response to increased regulation. However, major controversies are still occurring as a legacy from past years and decades. Furthermore, the commitments that companies have made to more proactive disclosure of clinical trials are too recent to draw any hard conclusions about the extent to which these new measures will really provide greater protection for consumers in the future. Therefore it is important to closely follow the developments.

At the manufacturing and distribution stage – where quality control is imperative to ensure the integrity of each batch of product – almost half of the 15 largest pharmaceutical companies have weak product quality and safety management systems, and hardly any company has gained voluntary external certification to recognised quality standards such as ISO 9001 for the majority of its operations.

At the marketing and sales stage – where aggressive marketing tactics can lead to inappropriate drug use – the 15 largest pharmaceutical companies spend 1-3 times as much on marketing as on R&D. Additionally, significant events with adverse impacts on society and patients from irresponsible marketing practices have occurred in recent years, leading to multi-billion dollar fines. Very few companies show strong mitigation mechanisms to avoid future improper marketing incidents, indicating a high probability that this will remain a controversial area for the industry in years to come.

At the post-marketing stage – where products' health effects should be structurally monitored to signal problems at an early stage – the vast majority of the 15 largest pharmaceutical companies have implemented mechanisms to monitor product safety, investigate incidents and take corrective actions in case of an adverse event. Nonetheless, we still see that often opportunities to signal certain problems at a relatively early stage are

lost. This is evidenced for instance by the many years that some products have remained on the market after initial safety concerns were raised by consumers, which could in some cases have been avoided through diligent pharmacovigilance. This raises questions over how well companies' pharmacovigilance mechanisms function in practice. More transparent communication from companies about how effective they judge their pharmacovigilance systems to be could help to further improve consistency in implementation.

Engagement with companies in the pharmaceutical sector is expected to be beneficial in closing the gaps between policies and practice that are identified in this report. It is expected that at least several years might be needed to demonstrate the real world effects of improvements that companies have recently implemented. Many of these measures were adopted in response to severe and recurring scandals that occurred over the past years and decades, or in response to tightening regulations. Rolling out new company programmes for consumer protection and instilling ethical conduct in company culture across all areas of operation requires time. And in the meantime, it is expected that new scandals will continue to emerge from the legacy of poor ethical conduct from the past. In other words, the pharmaceutical industry is currently at the brink of what could be a breakthrough towards strong ethical conduct and consumer protection. Companies that fail should expect increased pressure from the public, regulators, investors, and healthcare professionals to clean up their act. On the other hand, companies that manage this transition well can, albeit slowly, restore consumer trust and avoid regulatory backlash. Strong leaders will hopefully reform the industry by setting the bar for consumer protection ever higher. The pharmaceutical industry will then be better placed to fulfil its promise of delivering better health to those in need.

Appendix

Research Methodology – How we rate pharmaceutical companies

Sustainalytics' company research includes a thorough analysis of a set of environmental, social and governance (ESG) indicators. For the purpose of this report, Sustainalytics' focused on a sub-set of indicators related to ethical conduct and product quality and safety [see Figure 1 and Table 1]. Each indicator has a comprehensive list of underlying criteria. For every indicator, analysts evaluate the degree to which a company meets relevant best practice standards. Research is based on information disclosed by the companies themselves (such as annual reports, financial reports, sustainability reports, websites and press releases) and independent news sources such as (local) newspapers, relevant websites and NGO materials. A rigorous internal review process is implemented to ensure consistency and overall high research quality.

Figure 1: Overview of Indicators

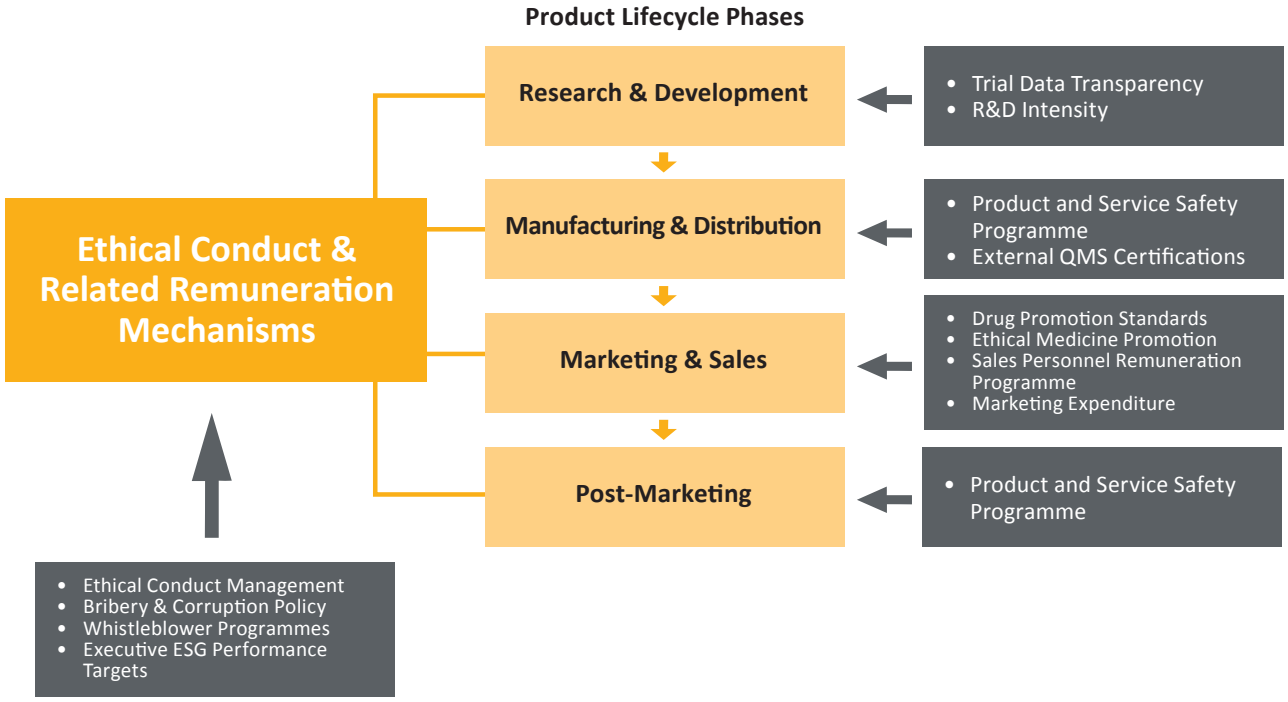


Table 1 (a) – Indicator Descriptions

Overarching Element	Indicator	Indicator Description
Ethical Conduct & Related Remuneration Mechanisms	Ethical Conduct Management	• This indicator provides an assessment of the quality of the company's overall management of ethical issues, in particular corruption, fraud, and conflict of interest.
	Bribery & Corruption Policy	• This indicator provides an assessment of the quality of the company's policy to combat bribery and corruption.
	Whistleblower Programmes	• This indicator provides an assessment of the quality of the company's reporting mechanisms and structures to detect and address ethical misconduct. A strong whistleblower programme provides a clear mechanism for reporting suspected violations and is accessible for third parties.
	Executive ESG Performance Targets	• This indicator provides an assessment of whether a part of executive remuneration is explicitly linked to sustainability performance targets, such as health and safety targets, product quality and environmental targets.

Table 1 (b) – Indicator Descriptions

Product Life Cycle Stage	Indicator	Indicator Description
Research & Development	Trial Data Transparency	This indicator measures the scope of a company's disclosure of clinical trial data. Companies are expected to register clinical trials in publicly available databases and disclose trial outcomes, regardless of whether the results are favourable to the company or not. Such disclosure promotes accountability related to product safety and efficacy claims and facilitates comparisons between similar products.
	R&D Intensity	This indicator provides an assessment of the share of R&D expenditure relative to revenues that the company generated in the most recent accounting year.
Manufacturing & Distribution	Product and Service Safety Programme	This indicator measures the strength of companies' management systems to ensure product quality and safety. In particular, the indicator assesses whether companies have clear lines of responsibility around the issue, whether they sufficiently evaluate potential health risks and benefits of products pre- and post-marketing, whether they have consistent and externally validated procedures for ensuring product quality and for responding to product safety incidents, and how companies communicate to stakeholders on product quality and safety issues.
	External QMS Certifications	This indicator provides an assessment of the percentage of ISO 9000 certified (or similarly certified) sites.

Marketing & Sales	Drug Promotion Standards	This indicator measures the strength of the company's drug promotion standards, including whether it makes reference to best practice standards, such as the WHO Ethical Criteria for medicinal drug promotion, or other codes.
	Ethical Medicine Promotion	This indicator measures the strength of the company's initiatives to avoid any improper promotional tactics, such as false or deceptive marketing and bribery of doctors. Ethical medicine promotion is key to ensuring that doctors and patients have access to complete and objective product information and facilitates the safe use of medicines.
	Sales Personnel Remuneration Programme	This indicator provides an assessment of the strength of a company's initiatives to compensate sales personnel based on non-volume sales targets, including technical knowledge and quality of service.
	Marketing Expenditure	This indicator provides an assessment of the share of marketing expenditure relative to R&D expenditure that the company made in the most recent accounting year.
Post-Marketing (Pharmacovigilance)	Product and Service Safety Programme	See Manufacturing & Distribution stage.

Table 2 - List of Companies Covered

Company Name	Region	Country	FF Market cap. (m USD)	ISIN Code
Johnson & Johnson	North America	United States	273,782	US4781601046
Roche Holding AG	Europe	Switzerland	241,085	CH0012032048
Pfizer Inc.	North America	United States	209,237	US7170811035
Novartis AG	Europe	Switzerland	241,366	CH0012005267
Merck & Co. Inc.	North America	United States	163,608	US58933Y1055
Sanofi	Europe	France	126,827	FR0000120578
GlaxoSmithKline plc	Europe	United Kingdom	103,152	GB0009252882
Novo Nordisk A/S	Europe	Denmark	138,939	DK0060534915
Bayer AG	Europe	Germany	115,602	DE000BAY0017
Bristol-Myers Squibb Company	North America	United States	110,520	US1101221083
AstraZeneca PLC	Europe	United Kingdom	82,536	GB0009895292
AbbVie Inc.	North America	United States	107,962	US00287Y1091
Eli Lilly & Co.	North America	United States	88,594	US5324571083
Valeant Pharmaceuticals International, Inc.	North America	Canada	78,423	CA91911K1021
Teva Pharmaceutical Industries Limited	Asia-Pacific	Israel	51,007	US8816242098

Glossary of Terms

Clinical trials are studies to evaluate the effectiveness and safety of medications or medical devices by monitoring their effects on people. Clinical trials are typically conducted in various phases (I, II and III) on increasingly large groups of people. Successful completion of clinical trials is required to gain marketing approval for new drugs.

Counterfeit medicines are drugs that are deliberately and fraudulently mislabelled with respect to identity and/or source. Counterfeiting can apply to both branded and generic products and counterfeit products may include products with the correct ingredients or with the wrong ingredients, without active ingredients, with insufficient active ingredients or with fake packaging.

Good Laboratory Practice (GLP) and Good Clinical Practice (GCP) standards are both international quality standards developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). These standards include numerous guidelines to ensure that pharmaceutical studies are scientifically authentic and that the clinical properties of the investigated product are properly documented.

Good Manufacturing Practice (GMP) standards are international quality standards developed by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). GMP includes guidelines for quality assurance during drug manufacturing in order to ensure that a drug product is safe for human consumption.

Product recall is defined as the removal of a product or certain batches of a product from the market, based on suspicions that the product may be defective.

Pharmacovigilance refers to the monitoring of drug safety (mainly concerning adverse effects) after a product is sold in the marketplace.

Off-label marketing refers to the marketing of a product for unapproved uses or patient groups. For instance, a medicine that has been approved by regulatory authorities as an anti-depressant cannot be marketed as treatment for any other afflictions. Similarly, a drug approved for use in adults cannot be marketed for use in children.

Volume-based selling focuses on increasing prescription and sales volumes for products.

Value-based selling focuses on value creation as the customer defines (i.e. by providing technical knowledge, including expertise on pharmaceutical products, symptoms, and diseases, and high quality service/consumer engagement).

List of References

- Almashat, S. and Wolfe, S. (2012), "Pharmaceutical Industry Criminal and Civil Penalties: An Update", available in April 2015 at: **http://www.citizen.org/hrg2073**
- AdverseEvents (2015), "A Drug Safety Call to Arms", accessed in April 2015 at: **http://rxview.adverseevents.com/a-drug-safety-call-to-arms**
- All Trials (2015), "Half of all trials remain unpublished", accessed in April 2015 at: **http://www.alltrials.net/news/half-of-all-trials-remain-unpublished/**
- British Columbia Medical Journal (2006), "Drug Safety: Side effects and mistakes or adverse reactions and deadly errors?", accessed in April 2015, at: **http://www.bcmj.org/article/drug-safety-side-effects-and-mistakes-or-adverse-reactions-and-deadly-errors**
- BJCP (1996), "Pharmacovigilance in the pharmaceutical industry", accessed in April 2015 at: **http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1873545/**
- DrugWatch (2014), "Vioxx" accessed in April 2015 at: **http://www.drugwatch.com/vioxx/lawsuit/**
- Ernst & Young (2013), "Beyond Borders, Matters of Evidence: Biotechnology Industry Report", accessed in April 2015 at: **http://www.ey.com/Publication/vwLUAssets/Beyond_borders/$FILE/Beyond_borders.pdf**
- European Commission (2008), "Strengthening pharmacovigilance to reduce adverse effects of medicines", accessed in November 2015 at: **http://europa.eu/rapid/press-release_MEMO-08-782_en.htm?locale=en**
- FiercePharma (2014), "New numbers back old meme: Pharma does spend more on marketing than R&D", accessed in November 2015 at: **http://www.fiercepharma.com/story/new-numbers-back-meme-pharma-does-spend-more-marketing-rd/2014-11-06**
- FiercePharma (2015), "FDA study spanks drugmakers for poor adverse events reporting", accessed in April 2015 at: **http://www.fiercepharma.com/story/fda-study-spanks-drugmakers-poor-adverse-reporting/2015-02-03**
- Forbes (2015), "Buried Clinical Trial Data: The Dam Is About To Burst", accessed in April 2015 at: **http://www.forbes.com/sites/larryhusten/2015/01/14/hidden-clinical-trial-data-the-dam-is-about-to-burst/**
- Groger, L. (2014), "Big Pharma's Big Fines", accessed in April 2015 at: **http://projects.propublica.org/graphics/bigpharma**
- Johnson & Johnson (2014), "J&J Announces Clinical Trial Data Sharing Agreement with Yale School of Medicine", accessed in April 2015 at: **http://www.jnj.com/news/all/johnson-and-johnson-announces-clinical-trial-data-sharing-agreement-with-yale-school-of-medicine**
- Karu, K.R. (2013), "Global Product Recalls and the Role of Quality", accessed in April 2015 at: **http://www.pharmacompliancemonitor.com/global-product-recalls-and-the-role-of-quality/5364/**
- Kroll (2014), "The 2013/14 Kroll Global Fraud Report", accessed in April 2015 at: **http://fraud.kroll.com/wp-content/uploads/2013/10/GlobalFraudReport_2013-14_WEB.pdf**
- PLOS Medicine (2015), "Complaints, Complainants, and Rulings Regarding Drug Promotion in the United Kingdom and Sweden 2004–2012: A Quantitative and Qualitative Study of Pharmaceutical Industry Self-Regulation", accessed in November 2015 at: **http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1001785**
- Practical Law (2014), "Drivers, roadblocks and challenges in the pharmaceutical industry: Thailand", accessed in April 2014 at: **http://uk.practicallaw.com/4-574-2706**
- Sah, S. and Fugh-Berman, A. (2013), "Physicians Under the Influence: Social Psychology and Industry Marketing Strategies", accessed in April 2015 at: **http://papers.ssrn.com/sol3/papers.cfm?abstract_id=2286433**
- The Guardian (2014), "What the Tamiflu saga tells us about drug trials and big pharma", accessed in November 2015 at: **http://www.theguardian.com/business/2014/apr/10/tamiflu-saga-drug-trials-big-pharma**
- The Guardian (2015), "Pfizer resists calls for greater clinical trial transparency", accessed in November 2015 at: **http://www.theguardian.com/business/2015/aug/31/pfizer-resists-calls-for-greater-clincal-trial-transparency-medicine-drugs**
- The Inquirer (2014), "What's driving Pharma's international bribery scandals?", accessed in April 2015 at: **http://www.philly.com/philly/blogs/healthcare/Whats-driving-Pharmas-international-bribery-scandals.html**
- The Telegraph (2015), "Lavish trips laid on by drugs firms to 'sway' NHS staff", accessed in November 2015 at: **http://www.telegraph.co.uk/news/nhs/11755884/Lavish-trips-laid-on-by-drugs-firms-to-sway-NHS-staff.html**
- Volkskrant (2015), "Recordboetes voor verboden reclame farmaceuten", accessed in November 2015 at: **http://www.volkskrant.nl/binnenland/recordboetes-voor-verboden-reclame-farmaceuten~a4189837/**

- WLH Consulting (2015), "The Changing Pharmaceutical Sales Landscape: Recommendations for Achieving Compliance and Sales Excellence", accessed in April 2015 at: **http://www.wlhconsulting.com/pdf/iglass-whitepaper.pdf**
- World Health Organization (WHO) (2015), "Pharmacovigilance", accessed in April 2015 at: **http://www.who.int/medicines/areas/quality_safety/safety_efficacy/pharmvigi/en/**
- ZS Associates (2015), "Crossing the threshold: More than half of physicians restrict access to sales reps", accessed in November 2015 at: **http://www.zsassociates.com/about/news-and-events/crossing-the-threshold-more-than-half-of-physicians-restrict-access-to-sales-reps.aspx**

Endnotes

[1] BJCP, 2006
[2] European Commission, 2008
[3] Groger, 2014
[4] PLOS Medicine, 2015
[5] Volkskrant, 2015
[6] DrugWatch, 2014
[7] Ernst & Young, 2013
[8] Practical Law, 2014
[9] The Inquirer, 2014
[10] The Telegraph, 2015
[11] The Inquirer, 2014
[12] Kroll, 2014
[13] WLH Consulting, 2015
[14] All Trials, 2015
[15] Karu, 2013
[16] Sah and Fugh-Berman, 2013
[17] Sah and Fugh-Berman, 2013
[18] World Health Organization (WHO), 2015
[19] AdverseEvents, 2015
[20] All Trials, 2015
[21] Forbes, 2015
[22] The Guardian, 2015
[23] The Guardian, 2014
[24] J&J, 2014
[25] FiercePharma, 2014
[26] ZS Associates, 2015
[27] BJCP, 1996
[28] FiercePharma, 2015
[29] FiercePharma, 2015

SUSTAINALYTICS