Pharmaceutical Industry & Compliance, Here Comes the Sun?

What is the role of the compliance function in pharmaceutical companies in the Netherlands in the disclosure of financial relations with HCPs and health institutions

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CONTENT

1. Introduction

1.1 General

The Dutch national "Ombudsman" spoke in the second "Montesquieu Lezing"[1] in The Hague about transparency and mentioned transparency as one of the most important demands for our modern society. Transparency as an important means against corruption, and transparency as an essential asset for building trust.

In the pharmaceutical world, in the last years transparency has become an important new development, as expressed in the "List of Guiding Principles Promoting Good Governance in the Pharmaceutical Sector"[2], following the EU Commission initiative on Ethics & Transparency in the pharmaceutical sector. Transparency was already implemented for clinical trials, see e.g. ClinicalTrials.gov (a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world). Since 2012 financial relations in the Netherlands between pharmaceutical companies and health care professionals and institutions, are to be disclosed in a registry, published at www.transparantieregister.nl.

The Dutch self-regulation organization (CGR – Code GeneesmiddelenReclame) has adopted a code of conduct concerning the disclosure of these financial relations[3], that has come into force on 01 January 2012, the first round of disclosure was done in April 2013 (over the year 2012). The code of conduct was agreed upon by the pharmaceutical industry, the doctor's association, and pharmacists association, after pressure from politicians and the public opinion.

1.2 Promotion and pharma

Pharmaceutical industry plays an important role in the health care environment. Pharmaceutical companies develop medicinal products, manufacture them, and sell the products to the market. This makes their role a specific one, because of the commercial background of these companies, next to the fact that they have a social responsibility. The Dutch 'Raad voor de Volksgezondheid en Zorg' (RVZ) acknowledges this specific role and responsibility[4].

The RVZ mentions the danger that there would be no proper balance between business and public interest within a pharmaceutical company. This can directly affect the trust of the patient in health care, the ethics of a health care professional (HCP), and eventually damage public health. HCPs need to be able to oppose commercial pressure of the pharmaceutical industry, and deliver countervailing power. In pharmaceutical companies, countervailing power needs to be expressed too, so the public interest is not set aside. The role of a compliance officer within a company needs to be investigated.

The business interest of a pharmaceutical company is especially seen in the marketing and sales activities. By these activities, health care professionals are persuaded or convinced to prescribe a medicinal product. In this thesis a more in-depth analyzes will be given of the influence of pharmaceutical companies through their marketing and sales activities (see 3.3.2.2 *Influencing techniques and strategies in general*). Within the pharmaceutical market and for the Dutch situation in particular, activities by the industry towards prescribers are deployed. Examples are sponsored medical education, professional gifts, and free support[5]. The influence has effect on prescription behavior, especially because of the mechanism of reciprocity. Prescribers feel somehow obliged to

[1] Nationale ombudsman, Tweede Montesquieu Lezing, Den Haag, 03-09-2013
[2] Platform on Transparency and Ethics, List of Guiding Principles Promoting Good Governance in the Pharmaceutical Sector, 2012
[3] CGR, Gedragsregels openbaarmaking financiële relaties, Code Geneesmiddelenreclame, in force since 01-01-2012
[4] Raad voor Volksgezondheid en Zorg, Farmaceutische industrie en geneesmiddelengebruik, RVZ, Den Haag 2008
[5] Damen-van Beek Z, Van Eijk MEC, Beïnvloeding door farmaceutische bedrijven, Huisarts Wet 2013;56(4):166-9

return a favor as described in the publication (see 3.3.2.2 *Influencing techniques and strategies in general*), the mechanism works with health care professionals, although they will state they are immune for the influence. A publication has been made regarding the effect of small gifts[6].
The specific marketing and sales activities of Dutch companies are limited by the guidelines for allowed promotion activities of the Dutch self-regulating body CGR (Code Geneesmiddelen-reclame)[7]. The CGR is the self-regulating body, with the aim to guide promotion for medicinal products in the right direction. Next to the Code, CGR published more specific guidance. From the Code, the specific influencing instruments can be derived, CGR mentions: medical representatives, advertising (for HCPs or for the public), sponsoring of specific projects, hospitality, sponsoring for manifestations and scientific meetings, medical education, providing samples, gifts, non-interventional (phase IV) clinical research, engagements with HCPs for specific services provided to companies.
A definition for promotion in the pharmaceutical market includes[8] any activity undertaken, organized or sponsored by a pharmaceutical company, or with its authority, which promotes the prescription, supply, sale, administration or consumption of its medicinal product(s). This definition will be used throughout this thesis. This EFPIA definition is used too in the Dutch Medicines Act[9].

1.3 Transparency and pharma

Promotion for medicinal products has been criticized for years. In the Netherlands a well-known publication about marketing practices of the pharmaceutical industry is 'Slikken: Hoe ziek is de farmaceutische industrie?'[10]. A more recent, international publication[11] also describes activities from companies towards doctors. There are discussions ongoing how prescribers should protect themselves for the influencing techniques of companies[12]. Next to that, authorities and regulators monitor activities of companies, investigate on complaints and act against offences of the Medicines Act. In the last years, the Dutch Health Inspectorate (IGZ – Inspectie voor de Gezondheidszorg) has performed theme research concerning activities of pharmaceutical companies in the Netherlands. Investigations have been done concerning medical education activities and advisory boards organized by pharmaceutical companies. IGZ published the outcomes[13].
In literature, there has been a call for transparency, to counter the undesirable influence by companies, e.g. the RVZ sees this as a relevant contribution. Offerhaus mentions the lack of transparency as a difference with the Anglo-Saxon countries[14].
In 2009 the Dutch Minister of Health referred to a development in the US, where Congress was discussing the Physicians Payments Sunshine Act[15]. The CGR introduced this transparency guideline, with an obligation for pharmaceutical companies, members of the association of innovative pharmaceutical companies, and for HCPs to disclose financial relations in a specific transparency register, starting from January 2012[16]. In April 2013 the Minister of Health reported to Parliament

[6] Kerst AJFA, De invloed van kleine geschenken van de farmaceutische industrie, GEBU 46, 3, 35 (2012)
[7] http://www.cgr.nl/Home
[8] EFPIA, **C**ode of Practice on the Promotion of Medicines, as amended by the Statutory General Assembly on 24 June 2013
[9] Geneesmiddelenwet (2007) art. 86
[10] Bouma J. Slikken: Hoe ziek is de farmaceutische industrie? Amsterdam: Veen, 2006
[11] Goldacre B. Bad Pharma, London: HarperCollins, 2012
[12] Dinant GJ, Mansfield PR. Van zoete koek naar gezonde scepsis. De houding van huisartsen tegenover geneesmiddelenreclame. Huisarts Wet 2005;48(6):304-6
[13] IGZ, Adviesraden farmaceutische industrie getoetst aan reclameregels, Utrecht, December 2012
[14] Offerhaus L. Ned Tijdschr Geneeskd. 2006; 150 (15)
[15] Bouma J. Klink wil alle bedragen zien, Trouw, 04-05-2009
[16] http://www.cgr.nl/Transparantie

that the Transparency register had become public, and the disclosure of financial relations between HCPs and companies over 2012 had become a fact[17].
CGR decided to limit the level of transparency, by setting a lower limit of 500 EUR on yearly basis per HCP or health institution, and by only requiring disclosure of payments concerning service agreements and sponsoring. Not disclosed are hospitality, gifts, prices and discounts, and amounts (cumulative) lower than 500 EUR per year. Also payments for clinical trials are not disclosed in the transparency register[18].
In the whole of Europe, in the last year, transparency has become an important new development, as expressed in the "List of Guiding Principles Promoting Good Governance in the Pharmaceutical Sector"[19]. Transparency was already implemented for clinical trials, see e.g. ClinicalTrials.gov[20] (a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world). As clinical trials are not part of the Dutch transparency guideline, they are out of scope for this project.

1.4 Compliance and pharma

In 2003 the OIG (Office of Inspector General – Department of Health and Human Services) issued a 'Compliance Program Guidance for Pharmaceutical Manufacturers'[21]. The program provides elements for an effective compliance program. When you look closely, the elements in this program, follow the principles of the U.S. Foreign Corrupt Practices Act[22]: implemented policies and procedures, an operative compliance officer, effective training and education, lines of communication, internal monitoring and auditing, disciplinary guidelines and responding accurately on detected problems.
The OIG emphasizes the mutual goals of the public and private sector: reducing fraud and abuse; enhancing health care provider operational functions; improving the quality of health care services; and reducing the cost of health care. The OIG also recognizes the complexity of the pharmaceutical industry. According to the OIG there should be a compliance program focused on Marketing and Sales activities, next to other focus areas as pricing and rebate information, as these are specific areas of potential fraud and abuse. In general risk areas are identified, that are specific for the pharmaceutical industry by OIG: Integrity of Data used to Establish Government Reimbursement (linked to drug pricing), Relationships with Purchasers and their Agents (linked to discounts), Relationships with Physicians and Other Referral Sources (linked to drug prescriptions), Relationships with Sales Agents (linked to sales activities), Drug Samples (linked to illegal sale of free samples). The OIG also comments on disclosure of any potential conflicts of interest and of industry sponsorship or affiliation and concludes that disclosure may reduce the risk of abuse, it doesn't eliminate the risk.
In the meanwhile, all big pharmaceutical companies have established a compliance function. This can be seen on the public websites of the companies, and certainly in the US companies refer to the OIG Compliance Program. In a search of corporate pharmaceutical websites[23] (top 10 global companies), the compliance activities can be found. The set-up of the information about the program seems to

[17] Minister van Volksgezondheid, Brief aan De Voorzitter van de Tweede Kamer der Staten-Generaal, Start Transparantieregister Zorg, 25 april 2013
[18] Bos K. Niks te verbergen, Medisch Contact, nr. 51/52 - 21 december 2012
[19] EFPIA, **C**ode of Practice on the Promotion of Medicines, as amended by the Statutory General Assembly on 24 June 2013
[20] http://clinicaltrials.gov/
[21] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003
[22] A Resource Guide to the U.S. Foreign Corrupt Practices Act, By the Criminal Division of the U.S. Department of Justice and the Enforcement Division of the U.S. Securities and Exchange Commission, November 14, 2012
[23] Global websites: Pfizer, AstraZeneca, Merck & Co, GlaxoSmithKline, Abbott, Amgen, Sanofi-Aventis, Novartis (check 22-2-2014)

follow the elements as described by the OIG. The description differs between the companies: Sales & Marketing Compliance; Ethics and Compliance; Ethical Interactions; and Business Ethics can be found. Most of the companies refer to their Code of Conduct and governance structures. The same search on the local Dutch website of these companies[24], does not give any information about compliance programs. There is a link to the corporate website, but the local activities are not described. In only a few of the corporate websites, specific information can be found about transparency or disclosure of financial relationships with HCPs and/or health institutions. There are references made to e.g. EFPIA (European Federation of Pharmaceutical Industries and Associations) guidelines, or US guidelines, but there is hardly information about transparency.

[24] Dutch websites of: Pfizer, AstraZeneca, Merck & Co, GlaxoSmithKline, Abbott, Amgen, Sanofi-Aventis, Novartis (check 22-2-2014)

2. Research question

2.1 Main objective

This research will focus on the role of compliance in the pharmaceutical industry, especially on the compliance role in the current transparency and disclosure practices and developments in the Netherlands. In the introduction the separate topics have been described briefly, after thorough research they will give the possibility to reach conclusions and introduce recommendations about this role. The main objective of this thesis is to increase the knowledge about the role of compliance in transparency and disclosure obligations of a pharmaceutical company in the Netherlands. The general research question is:

What is the role of the compliance function in pharmaceutical companies in the Netherlands in the disclosure of financial relations with HCPs and health institutions

This thesis will be written from a Dutch compliance perspective, in the specific Dutch regulatory and transparency environment, within the setting of EU and other international developments. Dutch pharmaceutical companies are normally part of, and operating in an international corporate background, and are part of at least the EU framework of directives, guidelines and industry codes. This national and European framework sets a scope, and leads to a series of sub-questions.

2.2 Sub-questions

2.2.1 What is the role of the compliance function in a pharmaceutical company

For the research question it is essential to have insight in the role of the compliance function in a pharmaceutical company. In the Dutch Medicines Act[25] there is no obligation to have a compliance officer nominated, and also in the EU directive[26] a compliance function is not mentioned. It is relevant to look more in detail to the existence and the 'Raison d'être' of compliance in the pharmaceutical industry. The following methods will be used to get a thorough view:

General view on Compliance: based upon the postgraduate education "Compliance and Integrity management" at the Free University (Amsterdam): a general view on compliance will be described, pointing at the relevant aspects for the pharmaceutical industry (see 3.1).

Legal aspects: a review will be done of EU and Dutch regulations and guidelines, industry codes, and other documents that guide companies in legal and compliance issues (see 3.2).

Literature search: a search will be done in international scientific literature to find a description of the responsibilities of a compliance function in a pharmaceutical company. The search also will focus on the local Dutch situation, so with a search of local (scientific) literature (see 3.3).

Annual reports and other publications from pharmaceutical companies: to be able to know if and how companies have organized compliance, the annual reports concerning the organizational structure will be reviewed of leading pharmaceutical companies. These reports can be found on the internet. Next to that the same information will be retrieved for Dutch companies, the local affiliates, also via the websites of these companies (see 4.1).

Questionnaire: a questionnaire will be set-up with relevant questions about how the role of compliance is set up, and is perceived in Dutch pharmaceutical companies. The population will

[25] Geneesmiddelenwet (2007)

[26] DIRECTIVE 2001/83/EC OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 6 November 2001 on the Community code relating to medicinal products for human use

consist of compliance and legal officers, business professionals (sales and marketing), and general managers of companies that are member of Nefarma[27], the association for innovative pharmaceutical industry in The Netherlands. The questionnaire will be send via the tool 'SurveyMonkey'[28] (see 4.3).
Interviews: to get a better understanding of the role of compliance within a pharmaceutical company, and the perception of compliance, interviews will be performed with the legal manager of Nefarma, and with the legal officer of the Dutch self-regulating body concerning promotion of medicinal products (CGR). There will be an interview with an inspector of the Dutch Health Inspectorate (IGZ), and with an independent lawyer specialized in pharmaceutical law (see 4.4).

2.2.2 What kind of relations exist between pharmaceutical companies and HCPs and health institutions, and what are the financial relations

The business model of pharmaceutical companies is a very specific one; it is a combination of the commercial set-up of these companies, next to the fact that they have a social responsibility in the health care system (see 1.2 *Promotion and pharma*). This sub-question aims to have a clear perspective on the marketing and sales techniques and strategies of companies, the effect of influencing on prescribers, and the relationships involved. The sub-question also offers a view on the extent of the budgets used by (Dutch) companies for marketing and sales activities. The following methods will be applied:
Legal aspects: a review will be done of EU and Dutch regulations and guidelines, industry codes, and other documents concerning marketing and sales activities by pharmaceutical companies (see 3.2).
Literature review: a search will be done in international scientific literature to get a general view on pharmaceutical influencing techniques and strategies. What are the techniques used, what is the effect on prescribers, and how do pharmaceutical companies build relationships. Next to that, the perception of the marketing and sales activities by prescribers, patients and authorities will be investigated. Also data will be searched to know more about the budgets involved (see 3.3).
Questionnaire: a questionnaire will be set-up with relevant questions about the kind of relations between companies and prescribers and health institutions in the Dutch setting. The population will consist of compliance and legal officers, business professionals (sales and marketing), and general managers of companies that are member of Nefarma, the association for innovative medicines in The Netherlands. The questionnaire will be send via the tool 'SurveyMonkey' (see 4.3).
Review of the Dutch "Transparantieregister": the register (www.transparantieregister.nl) contains data about payments of pharmaceutical companies in the Netherlands to prescribers and health institutions. The available data are from the years 2012 and 2013. By an analysis of the data (high level) there will be more insight in the payments of companies to prescribers and health institutions, and information available about the numbers of companies, prescribers and health institutions involved (see 4.2).
Interviews: to get a better understanding of the relations with HCPs and health institutions, interviews will be performed with the legal manager of the Dutch association of innovative pharmaceutical manufacturers (Nefarma), and with the legal officer of the Dutch self-regulating body concerning promotion of medicinal products (CGR). There will be an interview with an inspector of the Dutch Health Inspectorate (IGZ), and with an independent lawyer specialized in pharmaceutical law (see 4.4).

[27] http://www.nefarma.nl/english/homepage
[28] https://nl.surveymonkey.com/

2.2.3 What are the transparency obligations and practices of pharmaceutical companies

In recent years there have been developments in the disclosure of financial relations between pharmaceutical companies and prescribers and health institutions. In this section information will be retrieved about the current regulations (laws and codes), and there also will be a focus on the history of transparency practices, especially in the pharmaceutical industry. As there has been experience with disclosure of these data, it is necessary to have a view on the current transparency practice, especially in the Dutch situation. Methods that will be applied:

Legal aspects: a review will be done of EU and Dutch regulations and guidelines, industry codes, and other documents concerning transparency obligations (see 3.2).

Literature review: a search will be done in international scientific literature concerning transparency/disclosure of financial relations. The focus will be on the current situation, but also the history of transparency will be discussed, and the general view of disclosure of financial relations by stakeholders. Next to that, the costs of transparency will be investigated (see 3.3).

Questionnaire: a questionnaire will be set-up with relevant questions about the obligations and practices, including perception, of companies concerning transparency in the Netherlands. The population will consist of compliance and legal officers, business professionals (sales and marketing), and general managers of companies that are member of Nefarma, the association for innovative medicines in The Netherlands. The questionnaire will be send via the tool 'SurveyMonkey'(see 4.3).

Review of the Dutch "Transparantieregister": the register (www.transparantieregister.nl) contains data about payments of pharmaceutical companies in the Netherlands to prescribers and health institutions. The available data are from the years 2012 and 2013. By an analysis of the data (high level) there will be more insight in the transparency practices of companies in the Netherlands (see 4.2).

Interviews: to get more insight in the transparency practice of the relations with HCPs and health institutions in the Netherlands, interviews will be performed with the legal manager of the Dutch association of innovative pharmaceutical manufacturers (Nefarma), and with the legal officer of the Dutch self-regulating body concerning promotion of medicinal products (CGR). There will be an interview with an inspector of the Dutch Health Inspectorate (IGZ), and with an independent lawyer specialized in pharmaceutical law (see 4.4).

2.2.4 What is the role of the compliance function in transparency in pharmaceutical companies in the Netherlands

In this section the focus will be on the role of compliance in transparency obligations, practices and developments. Has compliance an added value in decisions about disclosure, is compliance involved in the practical implications of transparency. Has compliance a role in the ethical discussion concerning transparency? The following methods will be applied:

Legal aspects: a review will be done of EU and Dutch regulations and guidelines, industry codes, and other documents concerning the role of compliance in transparency obligations (see 3.2).

Literature review: a search will be done in international scientific literature concerning the role of compliance in transparency/disclosure of financial relations. Including the ethical aspects (see 3.3).

Questionnaire: a questionnaire will be set-up with relevant questions about the (perceived) role of compliancy in transparency within Dutch companies. The population will consist of compliance and legal officers, business professionals (sales and marketing), and general managers of companies that

are member of Nefarma, the association for innovative medicines in The Netherlands. The questionnaire will be send via the tool 'SurveyMonkey'(see 4.3).
Interviews: to get a better understanding of the role of compliance in transparency, interviews will be performed with the legal manager of the Dutch association of innovative pharmaceutical manufacturers (Nefarma), and with the legal officer of the Dutch self-regulating body concerning promotion of medicinal products (CGR). There will be an interview with an inspector of the Dutch Health Inspectorate (IGZ), and with an independent lawyer specialized in pharmaceutical law (see 4.4).

3. Theoretical framework

3.1 General view on Compliance

In this section, based upon the course "Compliance and Integrity Management" (VU Amsterdam) a general view on compliance will be described with the relevant aspects for the pharmaceutical industry. The definition that is used by the course is (translated):

> "With a broad scope, promote and enforce the applicable laws and (internal) regulations, and the protection of the integrity of the organization as well as the integrity of its managers and employees, with the objective to manage risks and prevent the related possible damage"[29]

This definition implies that the compliance unit or officer has a thorough knowledge of the relevant laws, codes and regulations for the company or industry sector in scope. Next to that integrity is a focus of compliance, looking at the organization as a whole, and to all individual managers and employees. Compliance management should be risk based and, therefore, risk management is the third important aspect of the tasks of a responsible compliance officer.

The landscape of legal environment of the industry sector that a company operates in, including the regulators, has to be known. The 'license to operate' is essential for a company to survive. In the pharmaceutical business in the Netherlands, a license from the authorities is necessary to be able to operate, operate in that sense that medicinal products can be sold to customers (foremost wholesalers and hospitals). This can be a 'wholesaler license' as issued by the ministry of Health (Ministerie van VWS). Linked to the Medicines Act[30], there are several regulators involved that operate especially in the medical and pharmaceutical market, a market where the quality and safety of patient care plays an essential role. The most important regulators are (including scope):

IGZ	Inspectie voor de Gezondheidszorg	Quality and safety of care, including pharmaceutical products
CCMO	Centrale Commissie Mensgebonden Onderzoek	Clinical studies
CBG	College ter beoordeling van geneesmiddelen	Product licenses (Netherlands)
EMA	European Medicines Agency	Product licenses (European Union)
Farmatec	Farmatec (CIBG – ministry of Health)	Pharmaceutical licenses
CGR	Code Geneesmiddelenreclame	Self-regulation for promotional rules pharmaceutical products
ZI	Zorginstituut Nederland (formerly CVZ)	Reimbursement of a.o. pharmaceutical products
NZa	Nederlandse Zorgautoriteit	Control healthcare markets

table 1: most important regulators in Dutch pharmaceutical landscape

The requirements of the Act, and the specific industry codes (like CGR in the Netherlands) must be well known, and applied. Next to these specific pharmaceutical regulations, there are also more general laws and requirements in scope, including the related regulators. Examples are the Data Privacy Law (WBP)[31] and the working conditions of employees (ARBO)[32]. The scope of compliance

[29] Dr. Sylvie C. Bleker-van Eyk, Intern Toezicht in relatie tot de 1e lijn, Compliance & Integriteit | nr.1 jaargang 4 | april 2013
[30] Geneesmiddelenwet (2007)
[31] Wet Bescherming Persoonsgegevens (2001)
[32] Arbeidsomstandighedenwet (2005)

should be the fields that are essential for the 'license to operate' of the company. The scope should also be based on risks (risk based compliance)[33].
The rules from the Act, and the specific industry codes need to be applied by the business. In the pharmaceutical industry especially by marketing and sales employees that are having direct interactions with HCPs and HCOs. They need to know the requirements, and the risks of non-compliant behavior, including the consequences of non-compliant behavior for the company and for them personally. In that sense is the business the first line of defense, see figure 1.

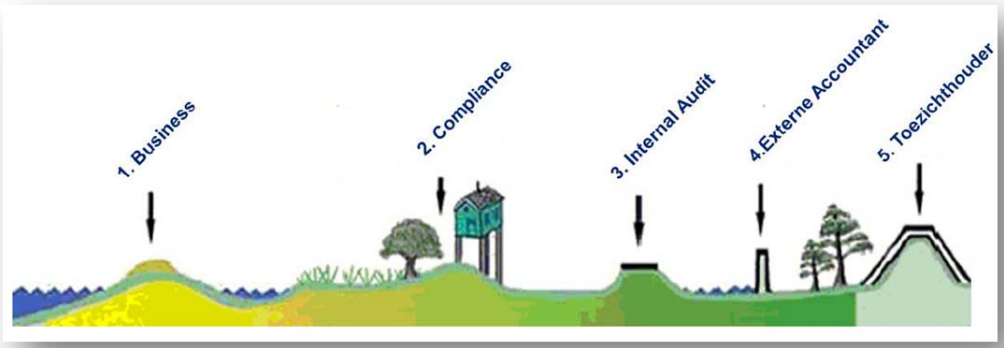

figure 1: Five Lines of defense (ref. Compliance & Integriteit | nr.1 jaargang 4 | april 2013)

The Compliance function can be seen as the second line of defense, and can support the business. The OIG[34] has described the requirements for a compliance program for pharmaceutical companies. All the different elements build an effective second line of defense (e.g. policies and procedures, training and education, and disciplinary guidelines, see 1.4 *Compliance and pharma*). Essential for compliance is to have knowledge of the business, and being close to the business to be able to assist, explain, train, correct, re-train, and to apply preventive actions if necessary. The next internal line of defense is the internal audit (an internal check of the functioning of the own organization by the internal audit function, followed by corrective and preventive actions). The next line, the external accountant, is certainly a logical line of defense in the financial world but is less evident in the pharmaceutical sector. The pharmaceutical industry has such specific laws and guidance, that external accountants will focus on the financial aspects of the organization, the more specific pharmaceutical aspects could be underexposed during a check as knowledge about the 'license to operate' is mostly not available, unless the accountant company has hired specific knowledge to perform a proper investigation. The last line of defense is the external regulator. As mentioned before, there are several active in the pharmaceutical market. Looking at promotional legislation, the IGZ (see before) is the most involved authority. Next to that the self-regulatory body CGR (see 1.2 *Promotion and pharma*) can play an important role. The IGZ can impose fines, the ultimate measure is the deletion of the pharmaceutical license, with the result that the products can't be sold anymore, and the business has to stop.

Integrity (ethics) starts on a personal level, in an organization compliance doesn't have a direct grip on personal integrity of employees; still the recruitment process should, next to competences, knowledge and experience, also focus on the integrity of a possible new employee. Compliance can play an essential role of the integrity of an organization. In an article[35] in the Harvard Business Review, organizational integrity is based on the 'concept of self-governance in accordance with a set of guiding principles'. The authors clearly place the responsibility for ethical behavior with the management of an organization. They give some directions for an effective implementation of an

[33] Compliance landscaping (college 9-12-2013, Sylvie Bleker-van Eyk)
[34] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003
[35] Lynn Sharp Paine, Managing for Organizational Integrity, Harvard Business Review, March-April 1994:106-117

integrity strategy; this strategy should be 'broader, deeper, and more demanding that a legal compliance initiative'. The values of a company should play an important role. The authors seem to follow the by the OIG[36], almost 10 years later, described elements for an effective compliance system, to 'insure that laws and company standards are being met'. It is obvious that integrity and compliance are closely linked, both concern the behavior of management and employees. One could make a division between desired behavior (integrity) and demanded behavior (compliance). Bakkers described this too in a column by writing: compliance is not a department, it is a mindset[37].

Organizations need to be aware of the 'integrity triangle', also known as the 'fraud triangle' described by Schimmel[38]. Pressure, rationalization, and opportunity can influence the behavior of employees, and need to be managed. Organizations and especially the management should be aware that the compliance function could play an essential role.
Another kind of integrity is systemic integrity. This could apply on a system like the pharmaceutical industry. Within the pharmaceutical system, transparency can be an important aspect in further increasing the integrity of the system.

The Dutch national bank (De Nederlandsche Bank - DNB) provides keys to come to an integer company culture, a system also described as the 'culture house'[39]. The key elements are: openness for discussion, exemplary behavior, practicality, transparency, and enforcement. The objective is that in organizations, employees (including management), take responsibility and are accountable. Also in (pharmaceutical) companies it is necessary to work with the expected integrity. DNB is actively assessing the culture within Dutch banks, also by performing audits focused on culture and behavior. DNB is especially interested in the sustainability of business models[40]. With an integer culture and business, banks will survive.

3.2 Legal aspects

3.2.1 What is the role of the compliance function in a pharmaceutical company

The Dutch Medicines Act[41] contains no obligation to have a compliance officer nominated, and also in the Pharmaceutical EU directive[42] a compliance function is not a requirement. In all other Dutch legislation, a compliance officer is not a necessity either for organizations. Formally a compliance officer is not necessary according to Dutch law.

In US law there is the requirement for organizations to have an adequate systems of internal accounting controls[43]. In the Federal Sentencing Guidelines for Organizations (FSGO), as composed by the United States Sentencing Commission (USSC) and amended in 2010, it is described that organizations are responsible for prevention and detection of criminal conduct. These guidelines describe the elements of an organization's compliance and ethics program, and the introduction may have been helping to create a new job description: the Ethics and Compliance Officer[44]. In the

[36] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003
[37] Richard Bakkers, Compliance is geen afdeling, het is een mentaliteit, Compliance & Integriteit | nr 2 juli 2010:4
[38] Schimmel, P.J., Fraudebeheersing, hoe doe je dat?, Kluwer, Deventer, 2004
[39] De Nederlandse Bank, Het DNB Cultuurhuis, 2009
[40] A.J. Kellermannn, Gedrag en cultuur: hype but here to stay, Compliance & Integriteit | nr 2 juli 2010:7
[41] Geneesmiddelenwet (2007)
[42] Directive 2001/83/ec of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use
[43] Foreign Corrupt Practices Act of 1977 (FCPA) (15 U.S.C. § 78dd-1, *et seq.*)
[44] Diana E. Murphy, The Federal Sentencing Guidelines for Organizations: A Decade of Promoting Compliance and Ethics, 87 IOWA LAW REVIEW(2002), 697-719

guidelines there is a description of a minimum requirements for an effective compliance and ethics program[45]. The USSC document from 2005 is seen as the standard concerning compliance guidance, it sets a clear obligation for organizations to prevent and detect criminal behavior.

In 2003 the OIG in the US (Office of Inspector General – Department of Health and Human Services) issued a 'Compliance Program Guidance for Pharmaceutical Manufacturers'[46]. The program provides elements for an effective compliance program. When looking closely, the elements in this program, follow the principles of the U.S. Foreign Corrupt Practices Act[47]: implemented policies and procedures; an operative compliance officer; effective training and education; lines of communication; internal monitoring and auditing; disciplinary guidelines and responding accurately on detected problems.

General risk areas are identified by the OIG that are specific for the pharmaceutical industry: integrity of data used to establish government reimbursement (linked to drug pricing); relationships with purchasers and their agents (linked to discounts); relationships with physicians and other referral sources (linked to drug prescriptions); relationships with sales agents (linked to sales activities); drug samples (linked to illegal sale of free samples). The purpose of the compliance program guidance is to encourage the use of internal controls to efficiently monitor adherence to applicable statutes, regulations and program requirements[48]. Among these is the designation of a compliance officer. OIG elaborates on this element by describing the compliance officer's responsibilities, including 'developing, operating, and monitoring the compliance program, and with authority to report directly to the board of directors and/or the president or CEO'.

Professional skepticism is a behavior that can help compliance officers in with maintaining integrity. Professional skepticism has its origin in the auditing literature, Nelson[49] has done research on it. The concept is based on countervailing power as first described by Galbraith[50]. Within companies the compliance function is the function that can express professional skepticism, as a natural behavior. This is not specifically described in literature, but as compliance has knowledge of laws, regulation and industry codes, is aware of the business and the competitor environment of a company, and has a relatively independent position without any sales incentives, compliance is in the position to exert firm countervailing power.

The ethical basis for compliance in business can be found in the UN Global Compact. The UN Global Impact is a 'strategic policy initiative for businesses that are committed to aligning their operations and strategies with ten universally accepted principles in the areas of human rights, labor, environment and anti-corruption'[51]. In principle 10 it is ordered that 'Businesses should work against corruption in all its forms, including extortion and bribery'. Organizations are encouraged to introduce anti-corruption policies and programs.

[45] Federal Sentencing Guidelines Manual, Chapter Eeight - Sentencing of organizations, part b - Remedying harm from criminal conduct, and effective compliance and ethics program, 01, November 2010
[46] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003
[47] A Resource Guide to the U.S. Foreign Corrupt Practices Act, By the Criminal Division of the U.S. Department of Justice and the Enforcement Division of the U.S. Securities and Exchange Commission, November 14, 2012
[48] http://oig.hhs.gov/compliance/compliance-guidance/index.asp
[49] Nelson, M. 2009, A Model and Literature Review of Professional Skepticism in Auditing, Auditing: A Journal of Practice & Theory, Volume 28, No. 2, pages 1-34
[50] John Kenneth Galbraith, American Capitalism - The Concept of Countervailing Power. Boston: Houghton Mifflin, 1952
[51] http://www.unglobalcompact.org/AboutTheGC/index.html

The EFPIA code 'lays down a set of fundamental rules covering a range of activities such as medicines advertising in medical publications, contacts with sales representatives, and the supply of samples, gifts and hospitality'[52]. The code mentions that each company must have a senior employee that is responsible for the standards of the Applicable Code(s) are met (section 18.02.b). It doesn't specifically mention a compliance function.

In the Dutch CGR (Code Geneesmiddelenreclame) code specific guidelines are provided concerning interactions of pharmaceutical companies with health care professionals. Also in this code there is no mention of a compliance officer or function. Still there is a requirement in article 14 for a 'scientific service department' that is responsible for the 'internal content review of promotion'.
Meanwhile an ISO norm is in development. In January 2014 the ISO Draft International Standard 19600 'Compliance management systems - Guidelines' has been published. In this guideline the management of compliance will be defined, and the roles and responsibilities of the board, management, line managers and employees of a company will be described, and the independence of the compliance function[53].

3.2.2 What are the financial relations between pharmaceutical companies and HCPs & HCOs
In the Dutch Medicines Act ('Geneesmiddelenwet' from 01-07-2007), chapter 9 regulates the promotion of medicinal products. It is stated that promotion is only allowed according the specific articles of the Act. Essential in the Act is that promotion of a product should promote its rational use, and promotion should be objective (art. 84.3). An extra demand is that there is control on all promotion by a scientific department (art. 95.1), and administrative obligations need to be taken into account (art. 95.2). There is no specific need for a compliance officer, but the law explicitly requires companies to be compliant, and this is subject to potentially high penalties, but does (with some specific exceptions) not explicitly require organizations to include particular roles or functions that ensure and monitor that the company is compliant. The Act also describes promotion to the general public, but this is out of scope of this research.

All the data in promotional documents should be exact, up-to-date, verifiable and complete, so an HCP is able to judge the therapeutic value of a medicinal product. All used citations, tables and other figures should have an accurate reference. As these interactions don't imply a financial relationship, they are out of scope of this subject. Samples can't be handed over, except under specific conditions. More relevant for the subject of this research are the inducements described in art. 94 of the Act. In principle inducements are allowed, namely the following ones: money or services representing a certain amount of money, for services provided by HPCs (written agreement necessary), and hospitality provided during a meeting or a manifestation.

The Medicines Act is not comprehensive about (on)acceptable financial relationships between HCPs/HCOs and pharmaceutical companies, but gives a clear direction. The Dutch legislation follows the Council Directive 2001/83/EC[54].

[52] http://www.efpia.eu/topics/building-trust/codes-of-practice
[53] Betekenis van een ISO-norm voor compliance management, KAMNieuwsbrief 4 / 2013
[54] Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidated version: 16/11/2012)

In the US in 2003 the OIG (Office of Inspector General - Department of Health and Human Services) issued a 'Compliance Program Guidance for Pharmaceutical Manufacturers'[55]. The Office of the Inspector General (OIG) is an office that is part of Cabinet departments and independent agencies of the United States federal government, as well as some state and local governments. Each office includes an Inspector General and employees charged with identifying, auditing, and investigating fraud, waste, abuse, and mismanagement within their specific territory[56]. The guidance gives a clear focus on risk areas for the pharmaceutical industry: '(1) integrity of data used by state and federal governments to establish payment amounts; (2) kickbacks and other illegal remuneration; and (3) compliance with laws regulating drug samples'[57]. The risk area that is especially relevant for the research question concerns the remunerative relationships. In the US constellation this is linked to 'entities or persons in a position to generate federal health care business', such as e.g. purchasing organizations, and physicians. In scope are clinical decision-makers, potential increased costs, risks of overutilization or inappropriate use of medicinal products, and patient's safety or quality of care. The guidance also offers 'safe harbor' for specific situations that are not deemed violations against the guidance.

The OIG looks closely at the interactions with health care providers, and the risk involved with pharmaceutical companies. Important questions are, if a physician has influence on generation of business for the company, if the remuneration is in line with fair market value, if there is a potential increase of costs for healthcare spending or overutilization/unnecessary services, and if the payment affects the integrity of the professional judgment of the physician. The OIG also refers to the code of conduct of the Pharmaceutical Research and Manufacturers of America (PhRMA), not as a safe harbor, but as a reduction of risk if the code is followed. The PHRMA code[58] gives directions for gifts and gratuities. The OIG acknowledges that the support of (independent) continuing education is less of a risk, as there is an independent accreditation of the medical content. The guidance for free drug samples is very restricted too.

In the EU, the EFPIA issued a Code of Practice on the promotion of medicines[59]. EFPIA is the association of European national innovative pharmaceutical industry societies, in the Netherlands Nefarma[60] is the involved national association. In the Code the principle is followed that accurate, fair and objective information needs to be provided, so prescribers can make rational decisions about the use of medicinal products in healthcare. Potential conflicts of interest with healthcare professionals should be avoided, according to EFPIA. Next to guidance about promotional material, the Code also covers interactions with healthcare professionals concerning contractual arrangements (including non-interventional studies, and consultancy and advisory board work). The EFPIA requires the member associations to establish adequate procedures, so there will be compliance with the Code of Practice. In the Netherlands Nefarma is obliged to impose these rules to its members.

[55] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003
[56] http://en.wikipedia.org/wiki/Office_of_the_Inspector_General
[57] Rebecca L. Burke and Robert J. Saner II, OIG's Compliance Program Guidance for Pharmaceutical Manufacturers, May 2003
[58] PhRMA, Code on Interactions with Healthcare Professionals, revised January 2009
[59] EFPIA, Code of Practice on the Promotion of Medicines, as amended by the Statutory General Assembly on 24 June 2013
[60] http://www.nefarma.nl/nefarma/organisatie

In the Code there are interactions mentioned that imply a financial relation, they are: events and hospitality, donations and grants that support healthcare or research, fees for service, sponsorship of healthcare professionals, the use of consultants, non-interventional studies of marketed medicines, and medical samples. Other activities have no direct financial impact, like issuing promotional materials. All the activities that will influence prescribers, are allowed as long as the conditions are met. Since the last version of the EFPIA code (June 2013), there is a prohibition on gifts (art. 17). Next to EFPIA, there is the IFPMA, the International Federation of Pharmaceutical Manufacturers & Associations, with their own Code of Practice[61]. The code doesn't differentiate much from the one from EFPIA. For this research it is essential to focus on the Dutch guidelines about interactions between pharmaceutical companies and HCPs and HCOs.

In the Netherlands the EFPIA code is reflected in the code of practice of the self-regulating society CGR (Code Geneesmiddelenreclame). The CGR was established in 1998 by stakeholders in the Dutch healthcare system and the pharmaceutical industry. The Code refers to promotion of medicinal products towards HCPs. The definition of promotion, as described in the Medicines Act is broad: 'any kind of influencing, with the apparent intent to promote the prescription, supply, sale, administration or consumption of a medicinal product'. c. The code includes guidance about advertising (verbal, in writing and audio-visual), hospitality (at scientific conferences, symposia and other meetings), service providers (HCPs as speakers, advisory board members, consultants), gifts, samples and other benefits and requirements to certain types of research. The general rules require responsible behavior, taking into account the interest of the patient and public healthcare, and to costs for medicinal products paid from the public healthcare budget. The Code mentions companies and HCPs as equally responsible for proper behavior.

The self-regulation Code results directly from the EU Directive as the Medicines Act was only published in 2007. It has been established in close cooperation with the Dutch Health Inspectorate, the national competent authority and regulator.
The Code forbids companies to offer gifts or gratuities, discharges of invoices, price dependency of the number of products bought, or any obligation for an HCP to prescribe medicinal products after any interaction. Payments for services can be done, but should be reasonable, and there has to be a direct link between the service provided, and the payment offered. No other obligations can be linked to the payments. In an explanation by CGR of the standard for payments to HCPs[62], a background can be found for the rules concerning financial relationships with companies. The pharmaceutical industry should be aware of the political charge of the situation, especially if payments to prescribers are involved. The CGR Code aims to secure the integrity of information and free choice, the independence of HCPs, the health of patients and the ethics of the whole pharmaceutical sector. The explanation emphasizes the reciprocity, as both parties need to take their responsibilities. This is laid down in a legal policy: 'it is not allowed to accept or solicit for forbidden inducements'[63].

[61] IFPMA, IFPMA Code of Practice, 2012
[62] Stichting CGR, Toelichting bij de Gedragscode Geneesmiddelenreclame, hoofdstuk 6 – Gunstbetoon en andere financiële relaties, laatstelijk gewijzigd m.i.v. 16 mei 2014
[63] Beleidsregels gunstbetoon Geneesmiddelenwet

CGR has issued several specific guidelines and in general the following activities of companies are allowed. A distinction can be made between activities:

- that lead to a financial relationship: sponsoring of specific projects, hospitality, sponsoring for manifestations and scientific meetings, non-interventional (phase IV) clinical research, engagements with HCPs for specific services provided to companies
- and that do not establish a direct financial relationship: medical representatives, advertising (for HCPs or for the public), medical education, providing samples, gifts.

For this research we will focus on the interactions that lead to a financial relationship. To get a better understanding of the involved interactions, it is necessary to describe them, and give an example from daily practice.

Sponsoring of specific projects

The general rule is that financial support is allowed, as long the conditions that are set by CGR are fulfilled[64]. These conditions of sponsoring are: intact integrity (the independency and reputation of both parties must be secured), a clear and legitimate objective of the sponsoring (scientific and/or quality improving activity, direct or indirect improvement of care to patients, no other regular budgeting possible), and transparency (a written agreement).

Examples of sponsoring can be found on the website of CGR (www.cgr.nl), as advices about projects are published there (anonymously). One example (advice AA13.037) is concerning the sponsoring of a training institute and a working group of a medical society to organize a tropics internship for Dutch physicians in training in Ghana. Another example (A10.052) concerns a project for improvement of gathering and management of study data in a hospital in Utrecht. The data handling was done manually and that was an inefficient way of working. CGR refers to the code of conduct for sponsoring in the health sector in the Netherlands[65], as a general code, CGR has elaborated on this for the pharmaceutical sector.

Hospitality

The guideline concerning inducements (Normen Gunstbetoon[66]), allows that the costs of hospitality can be (partly) paid by a company for a HCP. Hospitality according to the guideline means travel, lodging and registration costs for a meeting. Conditions are that the hospitality is reasonable, that it is secondary to the objective of the meeting, and that the hospitality is only offered to the attendants of the meeting. The location of the meeting needs to be suitable for the occasion (no undue luxury). 'Reasonable' is defined by CGR, as maximum € 500 per meeting per therapeutic class, with a maximum of € 1500 per year, or maximum 50%; the rest is paid by the HCP him/her self. An extra demand is that the hospitality can only be granted for scientific meetings. Examples are taking doctors to international scientific congresses, organized by the international societies of doctors, e.g. the European Society of Cardiology[67] and the American Society of Clinical Oncology[68]. The CGR can provide advice about the scientific level of (international) meetings.

[64] Stichting CGR, Gedragscode Geneesmiddelenreclame, hoofdstuk 6.5- Sponsoring van projecten, laatstelijk gewijzigd m.i.v. 16 mei 2014
[65] Gedragsregels voor fondsenwerving in de zorgsector, opgesteld onder verantwoordelijkheid van het ISFG, juni 1999
[66] Stichting CGR, Toelichting bij de Gedragscode Geneesmiddelenreclame, hoofdstuk 6.4 - Bijeenkomsten en manifestaties, laatstelijk gewijzigd m.i.v. 16 mei 2014
[67] http://www.escardio.org/congresses/esc-2014/Pages/welcome.aspx

Sponsoring for manifestations and scientific meetings

Next to sponsoring of HCPs who visit scientific congresses, CGR provides guidance about the sponsoring of congresses. There is no direct interaction with an individual HCP, but with an HCO or scientific medical society. In these cases there needs to be a written agreement with a description of the rights and obligations of the organizing committee and the sponsor. The benefit of the sponsor needs to be described clearly, e.g. the use of a booth on the exhibition space, the mentioning of the company in the program booklet. The examples of congresses mentioned in the previous section are also applicable here.

Non-interventional (phase IV) clinical research

A different category of financial relations is the support of specific studies[69] that are not covered by the law concerning medical scientific trials (in the Netherlands: Wet Mensgebonden Onderzoek - WMO). In the past, these kind of trials were set-up by companies too, next to the gathering of relevant scientific data about new medicinal products, to directly influence the prescription behavior of doctors. Examples have been written about extensively[70]. The CGR acknowledges the scientific relevance of these kind of trials, as long as the conditions are met. These trials look to find real-life experience from prescribers about new products. The studies are observational and non-interventional trials. The work of the doctors in these trials is qualified as providing services, that can be paid for (see next section), as long as the study has clear scientific value.

Engagements with HCPs for specific services provided to companies

HCPs provide services to pharmaceutical companies, e.g. in case of non-interventional research (see above), acting as a speaker, or as an adviser. Another example is taking part in advisory boards of companies. CGR allows this, if there is a reasonable balance between services provided and the remuneration. The independency of the HCP must be secured. The hourly fee (fair market value) for HCPs has recently been published by CGR[71].

Next to CGR, there is the Code of Conduct for the pharmaceutical industry in the Netherlands, the GFB[72] (Gedragscode Farmaceutische Bedrijfstak). This code is less detailed and describes the social responsibility of companies, and the respect that is necessary for the professional independency and integrity of HCPs, referring to the codes of EFPIA and IFPMA.

3.2.3 What are the transparency obligations and practices

The Dutch Medicines Act contains no requirements regarding disclosure or reporting . The same is true for the Pharmaceutical EU Directive. An example of transparency in other Dutch law is the Act concerning the subsidization of and control on political parties[73]. All donations over € 1.000 need to be registered, and amounts above € 4.500 will be disclosed by the government. Discussions have been ongoing about the basis for transparency in the pharmaceutical sector in the Netherlands. The

[68] http://am.asco.org/

[69] Stichting CGR, Toelichting bij de Gedragscode Geneesmiddelenreclame, hoofdstuk 6.3 - Dienstverlening en onderzoek, laatstelijk gewijzigd m.i.v. 16 mei 2014

[70] Bouma J. Slikken: Hoe ziek is de farmaceutische industrie? Amsterdam: Veen, 2006

[71] Stichting CGR, nieuwsbrief 1, februari 2014, Redelijke vergoeding

[72] Stichting GFB, Gedragscode Farmaceutische Bedrijfstak, November 2002

[73] Wet van 7 maart 2013, houdende regels inzake de subsidiëring en het toezicht op de financiën van politieke partijen (Wet financiering politieke partijen)

former minister of Health preferred a legal basis[74], but invited the sector to come up with a self-regulation solution via CGR.

In France[75] a transparency Act has come into force. The Act is applicable for pharmaceutical companies, medical device producers and cosmetic manufacturers. Benefits for HCPs and HCOs (in-kind or in cash) need to be disclosed, also all kinds of agreementsas well as invitations to visit scientific meetings like congresses. All payments above € 10 need to be disclosed[76].

In the United States, the Sunshine Act (Physician Payment Sunshine Act - PPSA) is part of the Patient Protection and Affordable Care Act from 2010. Companies need 'to disclose, on an annual basis, gifts and payments provided to covered recipients, as well as covered recipients' ownership and investment interests in the company'[77]. The actual filing of disclosure reports will be done, starting in 2014. The following payments need to be reported:

> consulting fees; compensation for services other than consulting; honoraria; gift; entertainment; food; travel; education; research; charitable contribution; royalty or license; current or prospective ownership or investment interest; direct compensation for serving as faculty or as a speaker for a medical education program; grant; or other.

There are some exclusions:

> payments less than $10 (unless the aggregate amount for the covered recipient exceeds $100 in the calendar year); product samples; educational materials that directly benefit patients or are intended for patient use; in-kind items for the provision of charity care; and payments through a third-party when the manufacturer is unaware of the covered recipient's identity.

The US Act also describes penalties for failure to comply with its requirements. Failure can be a mistake in reporting (with less high fines) or failure can be a knowing failure to report (with high fines, with a maximum of $100.000). In several States of the US there were existing State laws (e.g. Columbia, Massachusetts, Minnesota); these remain in effect, so that companies must comply with both the US Sunshine Act and the State reporting requirements.
A special website[78] was set up to inform the public: 'The Official Website for Open Payments (the Sunshine Act)'.

In June 2013 EFPIA has adopted a specific disclosure code[79] requiring implementation in national guidelines by 31 December 2013. EFPIA underlines the 'valuable, independent and expert knowledge derived from their clinical and management experience' that HCPs and HCOs can provide to pharmaceutical companies. They see an important advantage of these interactions for patient care and for research & development of novel treatments. But the interactions need to be conducted with integrity and have to be transparent. Therefore a specific disclosure guideline has been adopted to

[74] Dagblad Trouw, Klink: Farmasector moet zelf transparantie regelen, May 29, 2009
[75] LOI n 2011-2012 du 29 décembre 2011 relative au renforcement de la sécurité sanitaire du médicament et des produits de santé" ("French Sunshine Act")
[76] D. Jeffrey Campbell, Brian P. Sharkey, Porzio, Bromberg & Newman, P.C., The Trend Towards Global Transparency: A Challenging New World for the Life Sciences Industry, Washington, D.C., 2012
[77] D. Jeffrey Campbell, Brian P. Sharkey, Porzio, Bromberg & Newman, P.C., The Trend Towards Global Transparency: A Challenging New World for the Life Sciences Industry, Washington, D.C., 2012
[78] http://www.cms.gov/Regulations-and-Guidance/Legislation/National-Physician-Payment-Transparency-Program/index.html
[79] EFPIA code on disclosure of transfers of value from pharmaceutical companies to healthcare professionals and healthcare organizations, Adopted by the EFPIA Statutory General Assembly of 24 June 2013

'enable public scrutiny and understanding of these relationships and thus contribute to the confidence of stakeholders in the pharmaceutical industry'. EFPIA also takes into account the data privacy aspects for HCPs, but EFPIA doesn't restrict the disclosure possibilities. EFPIA refers to the EU Commission initiative on Ethics & Transparency in the pharmaceutical sector[80]. EFPIA opened a specific disclosure website[81], where a lot of information is found concerning transparency, and initiatives taken.

The Code describes the disclosure obligations for member companies of the Federation: 'each Member Company shall document and disclose Transfers of Value it makes, directly or indirectly, to or for the benefit of a Recipient' (art. 1). There will be an annual disclosure covering a full calendar year, starting with reporting over the year 2015. Within 6 months reporting has to be done, and the data will need to be available for 3 years. There are different possibilities suggested for the platform of disclosure, it can be a website of a company, or a central platform of a relevant government of local industry association (art. 2), this is up to the national association. The code makes a distinction in disclosure between financial relationships to HCOs and HCPs:

- HCOs: donations and grants (that support healthcare), contribution to costs related to events (organizing an medical or scientific event), fees for service and consultancy (fees & related expenses)
- HCPs: contribution to costs related to events (registration fees, costs for travel and accommodation), fees for service and consultancy (fees & related expenses)

This concerns individual disclosure by companies, there is also an aggregate disclosure requirement, e.g. concerning research & development (art. 3). The methodology of preparing the disclosures and identifying the financial interaction for each category has to be published too by companies. The Code requires member associations to impose sanctions for violations of the locally implemented code. The sanctions should be proportionate, and a combination of publication and fines is advised. The sanctions will be against companies not compliant with the local disclosure codes, like the CGR disclosure code, or the comparable Belgium guideline[82].

In the Netherlands, CGR considers pharmaceutical companies and HCPs/HCOs as natural partners, pharmacotherapy can benefit from a responsible cooperation between both parties. For example the development of new medicinal products and the exchange of knowledge about the proper use. A financial relationship can be part of this cooperation. This is regulated in the Dutch Code of Conduct (CGR[83]). In 2011 a specific guideline was adopted for the disclosure of financial relationships[84]. CGR refers to the established requirement for HCPs to disclose anyhow relationships with pharmaceutical industry. Also the Royal Dutch Academy of Science has a disclosure requirement for scientists in their scientific independency statement[85].

The first year the disclosure code was applicable was 2012. Within 3 months after the end of a calendar year, the data need to be published. There is an obligation to disclose aggregated amounts

[80] Platform on Ethics & Transparency, List of Guiding Principles Promoting Good Governance in the Pharmaceutical Sector, European Commission, Enterprise and Industry
[81] http://pharmadisclosure.eu/
[82] pharma.be, Code voor deontologie, Gewijzigd door de Algemene Vergadering van 28 maart 2014, Hoofdstuk 5bis Transparantie
[83] Code Geneesmiddelenreclame
[84] Stichting CGR, Gedragscode Geneesmiddelenreclame, hoofdstuk 7 – Transparantie, laatstelijk gewijzigd m.i.v. 16 mei 2014
[85] Nederlandse Academie van Wetenschappen, Verklaring van Wetenschappelijke Onafhankelijkheid

per year per HCP and HCO of €500, EFPIA doesn't have a limit in its code. CGR has considered, with using this lower limit, the proportionality between the administrative burden and the importance of the disclosure.
The following relationships need to be published in the Netherlands:

- Service agreements (for general consultancy, advisory board member, speaker arrangement, non-interventional research, and other services)
- Sponsoring (of meetings, and of other projects – innovative or quality improving activities that imply a direct or indirect improvement of patient care, promotion of medical science; these activities can only be sponsored if they can't be financed within the regular healthcare framework).

Data that need to be disclosed are:

> the name (or chamber of commerce number) of the company, the year of payment, name and work address of the involved HCP (or official registry number) or HCO (or chamber of commerce number); and only if the amount per year per HCP/HCO exceeds € 500.

The data need to remain available for three years, the first publication was foreseen for the first quarter of 2013[86]. In the Netherlands the data are published on a centralized website[87], developed by CGR and the 'Stichting Transparantieregister Zorg'.

3.3 Literature search

3.3.1 What is the role of the compliance function in a pharmaceutical company **(version 04-05-2014)**

For the role of a compliance officer in a pharmaceutical company, the 'Compliance Program Guidance for Pharmaceutical Manufacturers'[88] of the OIG is the most important reference. The program provides elements for an effective compliance program for pharmaceutical companies. Companies should designate a compliance officer 'and other appropriate bodies (e.g., a corporate compliance committee) charged with the responsibility for developing, operating, and monitoring the compliance program'. Some prerequisites are described, like 'an effective line of communication between the compliance officer and all employees' including a whistleblower process. The guidance points out that policies and procedures are not only developed by compliance, but also by the compliance committee and the operational managers. Compliance needs to be owned by business operations too, but the compliance officer needs 'to serve as the focal point for compliance activities'.

The OIG states that the organization of compliance within a company depends on the size and resources of a company and the complexity of the tasks (depending on the operations of the company). Anyhow, the function needs to be high-level within the company, with direct access to 'the company's president or CEO, board of directors, all other senior management, and legal counsel'. The document mentions the specific primary responsibilities of a compliance officer, these tasks are (short summary):

> Set up an appropriate compliance program; reporting to senior management; setting up and handling an educational and training program; review of business partners; coordinating specific personnel issues in cooperation with Human Resources; managing internal

[86] Stichting CGR, Toelichting bij de Gedragscode Geneesmiddelenreclame, hoofdstuk 6 – Gunstbetoon en andere financiële relaties, laatstelijk gewijzigd m.i.v. 16 mei 2014
[87] www.transparantieregister.nl
[88] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003

compliance review and monitoring activities including handling reports of noncompliance (independently)

As a last responsibility, OIG mentions 'Continuing the momentum', meaning a regular review of the compliance program, and revival of the culture of compliance that has been initiated by the implementation of compliance in a company. This culture of compliance 'begins at the executive level and permeates throughout the organization'.

In the Netherlands there is no comparable guidance document available. The Dutch Association of the Innovative Pharmaceutical Industry (Nefarma) has no specific working group for compliance[89]. There are several other working groups that relate to activities and responsibilities of companies as laid down in the Medicines Act. As the Act sets the requirements for companies for their trade license, these activities can be seen as essential and could be part of the responsibilities for a compliance function (see chapter *3.1 General view on Compliance*). Activities related to the trade license of companies (wholesaler license or manufacturers license, see Farmatec[90]) are reflected in the working groups of Nefarma, like: Medical Directors consultation, Project Group Clinical Operations, Project Group Observational studies, Registration managers, Working Group Pharmaceutical Affairs. Maybe in the US the tasks of a Compliance function are broader than in the Netherlands, there is no literature found on this subject.

In January 2014 Chris Fonteijn, the chairman of the Board of the Netherlands Authority for Consumers and Markets (ACM), discussed compliance programs at the 'seminar Compliance', organized by the International Chamber of Commerce[91]. He made several interesting statements about compliance and compliance programs, and the value of these programs for the ACM. The advice was clear: install and maintain an operating compliance program. This program can be an accelerator for innovation in a company. The program by the way is conscious self-interest, and every company needs a customized set-up, as business models, risks, culture and values differ. Risk description and risk rating are the start of the set-up, goal is to decrease risks, and an evaluation step is necessary. A well operating compliance program can decrease possible fines after infringements of the competition law, anyhow a well operating program anyhow limits the impact of the infringement to the company.
During an internal meeting of Nefarma, Frederik Schutte of CGR (see paragraph 4.4 *Interviews*) referred to this seminar and the statements of the chairman of the ACM. He posted the question if a compliance program could be part of the monitoring policy of the Dutch healthcare regulator (IGZ). This could be part of risk-based monitoring of IGZ, based upon 'high trust, high penalty'. The idea is that companies with a well operating compliance program would get low priority in the monitoring system of IGZ, and the program could decrease the amount of a possible fine. It is not yet defined how a compliance program in the pharmaceutical industry in the Netherlands should look like. Visibility of compliance in pharmaceutical companies seems to be an issue.

[89] http://www.nefarma.nl/ledennet/werkgroepen (not public)
[90] http://www.farmatec.nl/geneesmiddelen/vergunningen/farmacie/
[91] https://www.acm.nl/nl/publicaties/publicatie/12571/Toespraak-Chris-Fonteijn-bij-International-Chamber-of-Commerce-over-compliance/

3.3.2 What kind of relations between pharmaceutical companies & HCPs and health institutions exist, and what are the financial relations

3.3.2.1 Definition promotion

In the pharmaceutical world the definition of promotion that is used is from EFPIA[92], and looks at any activity undertaken, organized or sponsored by a pharmaceutical company, or with its authority, which promotes the prescription, supply, sale, administration or consumption of its medicinal product(s). In general promotion refers to raising customer awareness and especially to generating sales.

3.3.2.2 Influencing techniques and strategies in general

In pharmaceutical marketing, or medico-marketing, the regular marketing theories are applied. There is no specific pharmaceutical marketing theory, the strategies and techniques applied in other markets are relevant for medico-marketing, this is confirmed by pharmaceutical marketing professionals. Important aspects of strategic marketing planning (including looking at customer demands, and customer satisfaction) are[93]:

- market research (for segmentation and targeting, positioning, customer satisfaction, competition)
- industry analysis and market developments (to plan investments)
- competitor analysis (strength and weaknesses, strategies, market data)
- distribution (sales channels)
- internal analysis (own organization strong and weak spots, benchmarking)
- methods of analysis (SWOT, marketing information systems)
- marketing objectives (sales numbers or market share)
- marketing instruments (especially communication methods)
- implementation (including human resources)

In the marketing handbook of Anselm[94] the established communication methods are explained. Most of the instruments are applied in the pharmaceutical marketing practice, some methods are not used due to legal boundaries. The communication that is generally used, and is allowed in pharmaceutical promotion are:

- brand elements, especially the brand name, packaging is less relevant, as the EU Directive[95] and the Dutch Medicines Act[96] restrict communication on the package; also free samples
- advertisements in medical journals, these can be on a national level in the Netherlands like the NTVG[97] "Nederlands Tijdschrijft voor Geneeskunde', or on an international level like well-known peer-reviewed journals e.g. 'The New England Journal of Medicines[98]' or 'The Lancet[99]'

[92] EFPIA, **C**ode of Practice on the Promotion of Medicines, as amended by the Statutory General Assembly on 24 June 2013
[93] K.J. Alsem, Strategische marketing planning, theorie, technieken, toepassingen, 5e druk, Noordhoff Uitgevers B.V. | 2009
[94] K.J. Alsem, Strategische marketing planning, theorie, technieken, toepassingen, 5e druk, Noordhoff Uitgevers B.V. | 2009
[95] Directive 2001/83/ec of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use
[96] Geneesmiddelenwet (2007)
[97] http://www.ntvg.nl/
[98] http://www.nejm.org/
[99] http://www.thelancet.com/

- personal selling and direct- marketing, done by sales representatives or key account managers
- sponsoring, companies sponsor specific medical and or scientific projects that without external funding can't be established
- events, companies can organize their own events, e.g. to present a new product, and it is usual to sponsor HCPs to go to scientific congresses or other meetings, sponsoring is limited to travel and lodging costs, meals and the registration fee.

All of these marketing activities are limited in use to the rules that are set in the Medicines Act and the CGR[100] guidelines. In chapter 3.2.2 the specific restrictions are described.

3.3.2.3 Focus on pharma, effect on prescription behavior

The pharmaceutical industry plays a specific role in the health care system. Companies develop medicinal products, manufacture them, and introduce them to the market. Next to a clear commercial role, they have a social responsibility. The Dutch 'Raad voor de Volksgezondheid en Zorg' (RVZ) describes this specific role and responsibility[101].

In a review[102] (2000) in the peer-reviewed Journal of the American Medical Association (JAMA) the effect was investigated of interactions between pharmaceutical companies and physicians that prescribe medicinal products. The interactions that were investigated were:

> pharmaceutical representatives, gifts, samples, industry-paid meals, funding for travel or lodging to attend educational symposia, pharmaceutical representative speakers, continuous medical education sponsorship, and honoraria, research funding, employment.

In total 538 studies were included in the review by searching in MEDLINE with the subjects 'conflict of interest' and 'drug industry'. As outcome of the interactions was found impact on knowledge (accepting wrong claims), attitude (positive attitude toward a company and new drugs), and prescribing behavior (increased prescription of the product of a company). The association was statistically significant and even dose-response was demonstrated. Effects that were witnessed were preference for, and rapid prescribing of new drugs, request to add medicines to the hospital formulary, influence (decrease) on prescription of generic drugs. These outcomes are supported by other authors mentioned in the review; interesting is that the outcomes were not linked to recollection of the name of the sponsor, or the belief that the physician could not be influenced. An older study[103] gave the same direction.

In the pharmaceutical market there has been a shift from product lifecycle to industry lifecycle[104]. The market is maturing as is obvious from the declined growth rates and the low number of new product launches. To be successful as a company it is essential to excel in marketing. In the pharmaceutical sector inquiry[105] from the European Commission, it is shown that the number of new

[100] Stichting CGR, GedragscodeGeneesmiddelenreclame
[101] Raad voor Volksgezondheid en Zorg, Farmaceutische industrie en geneesmiddelengebruik, RVZ, Den Haag 2008
[102] Ashley Wazana, Physicians and the Pharmaceutical IndustryIs a Gift Ever Just a Gift? JAMA. 2000;283(3):373-380
[103] J P Orlowski and L Wateska, The effects of pharmaceutical firm enticements on physician prescribing patterns. There's no such thing as a free lunch. Chest 1992;102; 270-273
[104] Brian D Smith, Excellence in medical marketing: Origins, definition and precursors, Journal of Medical Marketing (2007) 7, 25 – 32
[105] European Commission, Final Report on its competition inquiry into the pharmaceutical sector - Final Report (8 July 2009) - Commission Staff Working Document (Technical annex to the Commission Communication) part 1

molecular entities decreases through the years (51 in 1991 – 21 in 2007). Companies can't keep their pipelines of products in development filled, the increasing requirements for safety and efficacy increase the costs for R&D, and there is an increasing control over prices and reimbursement levels by governments. The pharmaceutical market has clearly changed in the last decades.

In his article B.D. Smith[106] provides an overview of the current view on, and the elements of medico-marketing. Marketing can be defined as the entire process of understanding and satisfying customer needs. The strategy is built by defining market segments and the value proposition. For the implementation, actions need to be set and adequate resources deployed, so the appropriate marketing mix can be utilized, consisting of product and promotion, channels to the market, human resources, and customer experience. After the implementation, monitoring is necessary of the development of the value, the utilized resources, checking of defined performance indicators, and the performance relative to competitors.

In another study[107] (2010) research has been done concerning the influence on pharmaceutical promotion by the changed pharmaceutical market, the industry lifecycle instead of product lifecycle as mentioned before. New drug introductions have slowed down in comparison with the other study, the old successful products have gone out of patent and generic versions are available. The newer drugs (biologics) have some other characteristics: a smaller number of patients (specialized drugs), often administered by injection, and with higher prices. The marketing instruments investigated are: free samples, office based detailing, hospital-based detailing, journal advertising, e-promotion and conferences and meetings. The research was done with older drugs and with biologics. In the years until 2010 the absolute value of spending on promotion, and the share of sales used for promotion decreased significantly. Still the sales increased. The reason is especially that the newer drugs are more expensive, and promotion can be more targeted as these medicinal products are prescribed by a smaller specialized group of physicians. Some have even unique distribution channels. Conclusion of the authors is that there is no shift in the expenditures on promotion, the authors still say that with an increasing role for biologics, a more substantial shift in promotional patterns is to be expected, without commenting what the shift will be.

One of the established marketing tools in pharmaceutical business is relationship marketing, so-called sales management, often now referred to as key account management (KAM). Brian D. Smith describes[108] the theory of key account management in the pharmaceutical industry is described. Key are the different stages of KAM development: explanatory, basic, cooperative, interdependent, and integrated. Important aspects are longevity providing for long-term mutual value, willingness to enter in a relationship associated with services (price reductions are not sufficient in a mature market), and knowledge sharing.

In a study concerning the effect of marketing efforts of pharmaceutical companies, it is shown that companies especially apply detailing, advertisements, medical education and mailings. Companies in the Netherlands are not allowed to direct marketing at patients. There is a clear relationship between the budget for marketing expenses and the prescription of medicinal products that are

[106] http://en.wikipedia.org/wiki/Brian_David_Smith
[107] Kornfield R, Donohue J et al, Promotion of Prescription Drugs to Comsumers and Providers, 2001-2010, PLoS ONE 8(3):e55504
[108] Brian D Smith, Myth, reality and requirements in pharmaceutical Key Account Management, Journal of Medical Marketing (2009) 9, 2, 89-95

introduced to the market; the same is the case for frequent prescriptions. So the introduction of a new product can be accelerated by the use of marketing instruments[109]. The effects are only seen on brand level, as marketing efforts are made on product level, and not focused on the involved company .

The marketing of new medicinal products is put in perspective in a study by ECRi (Erasmus Competition and Regulation institute). Marketing consists of information coming from medical representatives, brochures, and advertisements in medical journals, free samples, and financial inducements. Marketing will lead to faster market penetration, asdescribed above (see previous paragraph). The authors[110] state that new medicines can lead to lower costs for public health care (in cases where new products lower costs for other treatments). They see informative marketing (medical information provided by companies) as an important source of information for physicians, as companies own the scientific data about new products that they have developed. Marketing can also be manipulative, as there is an asymmetry of information, as physicians don't have the scientific overview of these products. The authors don't see manipulative marketing as a big problem, because in the Dutch market there are countervailing powers available. They even state that because of that, no new strict regulations are necessary. The expertise of the prescribers should be raised, so they can judge the information provided by companies themselves. In a report[111] of the CPB (Centraal Planbureau) the asymmetric information situation is described too, as companies have the research information of new drug available, and the prescribers don't have access to all data.

In a perspective in the NEJM[112], the effects of physician-industry relationships are mentioned: prescription of brand-name drugs instead of a cheaper generic version, free samples stimulate off-label use (use that is not medically proven), premature adoption of new products, reduced adherence to evidence-based treatments, and a limited ability to acknowledge and manage the effects of physician-industry relationships.

3.3.2.4 Perception of pharmaceutical marketing and financial relations

The Dutch 'Raad voor de Volksgezondheid en Zorg' (RVZ) has described[113] the specific role of the pharmaceutical industry in society. Companies can have a desirable influence, when a new cost effective drug is introduced that has an added value in treating patients; the influence can also be highly undesirable when it concerns aggressive (or manipulating) marketing activities for products that don't have an added value and/or lead to increased costs for public health. Pharmaceutical companies have a commercial interest and clear influence on public health care. In different publications the perception of this role is documented, and especially the more undesirable effects of medico-marketing are described.

[109] P.S.H. Leeflang et al. Onderzoek naar de effecten van marketinginspanningen op de afleverhoeveelheden van receptgeneesmiddelen, RUG, Faculteit der Economische Wetenschappen, 17 mei 2004
[110] SEOR-ECRi, Marketing van innovatieve geneesmiddelen, de voor- en nadelen, eindrapport 13 september 2006
[111] CPB How does pharmaceutical marketing influence doctors' prescribing behaviour? CPB Netherlands' Bureau for Economic Policy Analysis, The Hague, March 2002
[112] Eric G Campbell, Doctors and Drug Companies – Scrutinizing Influential Relationships, N Engl J Med 367;18: 1796-1797
[113] Raad voor Volksgezondheid en Zorg, Farmaceutische industrie en geneesmiddelengebruik, RVZ, Den Haag 2008

A publication about activities of companies is written by journalist Joop Bouma: 'Slikken: Hoe ziek is de farmaceutische industrie?'[114]. In the Dutch newspaper Trouw, Bouma has written about medico-marketing practices for years. Another well-known criticizer of pharmaceutical companies in the Netherlands is the GP Hans van der Linde. In an opinion article[115], he provides his view on marketing activities, like deception (manipulative information about new products); paying key opinion leaders as advisors to speak about products; decreasing academic freedom (universities that are depending on companies to be able to do research); medical education, partly paid by pharmaceutical companies. He pleads for less influence of industry on prescribers, and more independent information and scientific research.

In a press release[116] of the scientific journal of Dutch GPs (H&W - Huisarts & Wetenschap), H&W states that companies have influence on the prescription behavior of GPs. Again the asymmetric information level is referred to, and it is claimed that the information that is provided by companies is manipulative. The statements are based on a scientific publication[117] in H&W. The publication mentions that half of the Dutch GPs, and an unknown part of practice assistants, are visited by sales representatives, and accept gifts and invitations for industry-sponsored refresher or postgraduate courses. The writers advice that GPs no longer should talk with representatives of the pharmaceutical industry. This statement is supported by the Dutch Institute for Rational Use of Medicine (Instituut voor Verantwoord Medicijngebruik; IVM).

IVM publishes regularly reports about marketing activities of pharmaceutical companies. IVM is 'specialized in the distribution of information and solutions for the proper, safe, affordable and effective use of medicine. The IVM provides information from an unbiased perspective'[118].
In one report[119] they investigate 'if sponsoring leads to unbalanced information or subliminal advertising'. Research has been done at Dutch e-learning courses for GPs that are sponsored, directly or indirectly, by pharmaceutical companies. The most important conclusion is that during these courses unbalanced representation of information has been provided, and that authors of both sponsored and unsponsored courses don't always disclose ties with pharmaceutical industry.

In a recent publication[120] in a Dutch weekly journal, the general opinion about the pharmaceutical industry was extremely negative, companies don't deliver real innovations, are risk-averse and depend completely on patents. Companies just want to make as much money as possible, and are not interested in their social responsibilities.

In a newsletter of CGR[121] the minister of Health in the Netherlands, states that pharmaceutical self-regulation has set a trend and she would like other sectors (like Medical Devices) to follow the trend. In the same Newsletter, there is a report about a symposium of CGR with opinions about the self-regulation Code. It is mentioned that CGR is not very visible, that possible infractions of the Code are

[114] Bouma J. Slikken: Hoe ziek is de farmaceutische industrie? Amsterdam: Veen, 2006
[115] Hans van der Linde - Het pillenbedrog - Gezondheid – TROUW - 18-5-13
[116] H&W Farmaceutische industrie heeft helft dokters in de tang, persbericht, Utrecht, 4 april 2013, Huisarts & Wetenschap
[117] Damen-van Beek Z, Van Eijk MEC, Beïnvloeding door farmaceutische bedrijven, Huisarts Wet 2013;56(4):166-9
[118] http://www.medicijngebruik.nl/english/about-us
[119] Gezonde Scepsis, E-learning nascholingen huisartsen leidt sponsoring tot reclame? Instituut voor Verantwoord Medicijngebruik, november 2010
[120] Jesse Frederiks, Dure Pillen, De Groene Amsterdammer, 09-04-2014
[121] Stichting CGR, nieuwsbrief 8, mei 2014, Nieuwe integrale Code

not published (especially concerning inducements and medical education), and that there should be more communication about the codes and compliance programs of the different companies.

3.3.2.5 Costs of pharmaceutical marketing

In an older publication[122] of the Dutch CPB (Centraal Planbureau) it is stated that pharmaceutical companies spend 20% of their sales on marketing activities. Instruments used are: sales representatives, advertisements and direct mail, post-marketing studies, medical education, and sponsoring of research. The CPB concluded that a permanent increase in marketing with 10%, results in a 3% increased demand for the product involved in due time.

In an US publication[123] concerning influence of pharmaceutical industry marketing, data are collected concerning pharmaceutical company promotion spending. In 2012 in the US, $27 billion was spend by companies on drug promotion, of this amount $24 billion was spend on marketing to physicians, the rest was for advertising to consumers (based upon Cegedim Strategic Data 2012).
A subdivision was made between the types of marketing:

Detailing	In this study over 60% of the expenditure of marketing is spend on detailing, so face-to-face promotion to physicians, part of this is meals with doctors, and gifts. This shows that sales representatives are a very important part of medico-marketing.
Samples	Free samples are handed over to enable doctors to 'try' new medicines, when they have patients eligible for the treatment. It could be said that this also benefits patients, but normally patients are insured. In this study it is shown that almost 30% of the expenditure is used for sampling.
Educational and Promotional Meetings	This concerns meetings organized and sponsored by companies, for these manifestations speakers are hired (often HCPs), and meals are provided. Treatments and products are the common topic of these meetings. Almost 9% is spend.
Promotional Mailings	This concerns unsolicited materials with promotional content, as it concerns promotion; this doesn't concern scientific information. Still the promotional regulations apply to these publication. 5% of the total expenditure is spend on these items.
Journal and Web Advertisements	These concern the classical advertisements for products in medical journals. For the scientific journals (often organized by medical societies) this is an important source of revenue. Advertisements (also on the internet) are regulated by strict promotion rules. Of the total expenditure, this is a very limited part.

table 2: types of medico-marketing and costs (based upon Pewhealth, Persuading the Prescribers, 2013)

[122] CPB How does pharmaceutical marketing influence doctors' prescribing behaviour? CPB Netherlands' Bureau for Economic Policy Analysis, The Hague, March 2002
[123] Pewhealth, Persuading the Prescribers: Pharmaceutical Industry Marketing and its Influence on Physicians and Patients, Nov 11, 2013

Next to the direct activities, companies also apply indirect marketing; the study mentions as instrument: Continuing Medical Education (CME). This kind of medical education is considered independent, still 32% ($752 million) of the funding of these training is provided by the pharmaceutical industry.

Leeflang[124] mentions that in the US about three times more is spent on marketing than on R&D, the marketing budget is not purely promotional activities, as also general costs and administrative costs are part of this. In the sector inquiry of the European Commission[125], relevant information can be found about the European pharmaceutical market. Including information about spending on marketing by pharmaceutical companies (based upon information of 31 originator companies). In 2007 companies spent €15,7 billion on marketing activities, and €13,3 billion on research and development. The report also mentions that on average, there are two times as many employees in the marketing and sales department than in R&D. In some companies the ratio is even 3:1.

Data about marketing budgets are not public, companies don't make them public, only limited data can be found. Recently a report[126] was published by SEO Economisch Onderzoek concerning the pharmaceutical industry in the Netherlands. The report describes that it is difficult to retrieve the amount that is spend on marketing, as companies are not obliged to mention the marketing costs in their annual reports, they are accounted under 'selling, general and administration'. A reference is made to the sector inquiry of the European Commission (see above), the writers state that the number of sales representatives in the last years has decreased. SEO did an investigation concerning marketing costs, but they don't mention an amount. A clear conclusion is that costs for medical activities and market access have increased. This can be found in the shift in personnel from 2007 until 2012: marketing 73 → 63%, market access 5 → 9%, medical 23 → 29%.

3.3.3 What are the transparency obligations and practices of pharmaceutical companies

In literature, there has been a call for transparency for several years. In a US perspective[127] several aspects of transparency have been discussed, with a focus on the benefits for patients. It is acknowledged that for the development of treatments, relationships between industry and physicians are necessary. The author emphasizes that especially doctors themselves are responsible for the positive effects for patients and the risks with their own industry relationships.
In the Netherlands also pleas[128] have been made for more transparency. The news concerning the development of regulations for disclosure has been published[129] regularly. After the adoption of the Dutch transparency guideline, a medical journal[130] reported about the main features of the disclosure responsibilities. The coordinator of the CGR (see 4.4 *Interviews*) expresses his fear that the register could be seen as a 'black list'; but the background is to end any secrecy, as he says, 'there is nothing to hide'. The choice has been made for self-regulation, as there was support from both sides, industry and physicians.

[124] P.S.H. Leeflang et al. Onderzoek naar de effecten van marketinginspanningen op de afleverhoeveelheden van receptgeneesmiddelen, RUG, Faculteit der Economische Wetenschappen, 17 mei 2004
[125] European Commission, Final Report on its competition inquiry into the pharmaceutical sector - Final Report (8 July 2009) - Commission Staff Working Document (Technical annex to the Commission Communication) part 1
[126] SEO Economisch Onderzoek, De farmaceutische industrie in het maatschappelijk debat, Een feitelijke beschrijving van de markt voor innovatieve geneesmiddelen in Nederland, In opdracht van Nefarma en Amcham, Amsterdam, mei 2014
[127] G Campbell, Doctors and Drug Companies - Scrutinizing Influential Relationships, N Engl J Med 367;18: 1796-1797
[128] Offerhaus L. Ned Tijdschr Geneeskd. 2006; 150 (15)
[129] Bouma J. Klink wil alle bedragen zien, Trouw, 04-05-2009
[130] Bos K. Niks te verbergen, Medisch Contact, nr. 51/52 - 21 december 2012

In a white paper[131], looking at financial relationships between pharmaceutical and medical device manufacturers on the one side, and HPCs and HCOs on the other side, the focus was on clinical research. This is outside the scope of this research, but the authors also elaborate about the 'Right to Know'. In several studies participants of clinical research projects were asked about if they wanted to be informed about financial conflicts of interest of the investigator, who was performing the study. The clear trend is that a 'large minority' wanted to know, but that most of the patients didn't think that the information would affect their decision to participate in a study. The authors link the right to know to the availability of choice. Weinburg[132] et al. emphasize that there should be genuine choice. Not a 'naked' need to know in the heat of politics. In his research he finds that most participants in clinical trials can't judge the risks of financial relations. He poses the question, if 'simple disclosure to prospective research participants is an effective strategy, standing alone'. On the other hand, he finds that disclosure of financial interests is important to patients to preserve trust in doctors. The research was done with participants in clinical trials, so there is no direct conclusion to be made for payments to HCPs and HCOs by pharmaceutical companies in a non-research setting. Still the raised issues can be relevant.

Rosenthal *et al*[133] describe the effects of implementing the Physician Payments Sunshine Act. The rules will 'inject a welcome dose of sunshine'. In September 2014 posts will be made on a publicly accessible website, goal is to 'influence the behavior' of companies, prescribers and patients. The authors express skepticism concerning the effect on patients and their view of prescribers, and their response to the disclosed data. The effect could be limited. Therefore they propose to work with 'learned intermediaries' to assess and analyze disclosed financial relationship data. These intermediaries could be e.g. health insurance companies; researchers and watchdog organizations can also serve as valuable intermediaries. A link is made to the financial world, where the Securities and Exchange Commission (SEC) makes their filings public, institutional investors and financial analysts have the expertise, time, and incentive to go carefully through the information, and bring discipline to the reporting companies. Conclusion of the authors is: 'this sunlight must be filtered through the lens of a capable, motivated intermediary'.

Agrawal *et al* provide an overview of the Reporting Requirements of the Physician Payments Sunshine Act[134]. In the US 'Data collection begins in August 2013, with public reporting starting in 2014, under the National Physician Payment Transparency Program (NPPTP) of the Centers for Medicare and Medicaid Services (CMS)'. Part of the disclosure are the research payments, also ownership and investment interest are part of the reporting obligations. The requirements are for companies, not for physicians. It gives patients the possibility to choose their doctors, based upon these data. Not just these data, also based on 'publicly available quality and resource-utilization data'. According to the authors, the Transparency Program (NPPTP) will improve understanding of the relations between industry and physicians.

[131] Seton Hall University School of Law, The Limits of Disclosure as a Response to Financial Conflicts of Interest in Clinical Research, A White Paper by The Center for Health & Pharmaceutical Law & Policy, Newark, December 2010
[132] Kevin P. Weinfurt et al. Views of Potential Research Participants on Financial Conflicts of Interest, Barriers and Opportunities for Effective Disclosure, J Gen Intern Med 2006; 21:901–906
[133] Meredith B. Rosenthal et al. Sunlight as Disinfectant — New Rules on Disclosure of Industry Payments to Physicians, N Engl J Med 368;22: 2052-2054
[134] Shantanu Agrawal et al. The Sunshine Act — Effects on Physicians, N Engl J Med 368;22: 2054- 2057

There is also uncertainty about the behavior of industry. Firms could reduce gifts and payments related to marketing. On the other hand companies could, because of the new transparency obligations, under-report, or misclassifying payments into a non-reportable category[135]. The authors also point out that new in the regulations are the reports for clinical research, these payments were not part of the existing State requirements. There can be a negative effect on the public, as the average patient can't make a distinction between pure scientific medical research, and low quality medical trials (marketing initiated). Again here it is mentioned that the patient isn't always able to judge payments to physicians. There is at the moment no evidence that disclosure affects the marketing practices of the industry, although there is disclosure in a number of States since several years. The article provides a good overview of the State regulations, and a comparison with the PPSA.

In an article in the BMJ[136] it is stated that there has always been a US lead in aggressive marketing. . Companies claim an important role in drug development, and in improvements of treatments of patients. Still companies only disclose data after legal requirements are enforced. The author refers to efforts of external organizations to compare disclosure data. ProPublica is such an organization that in the project 'Dollars for Docs'[137] publishes payment data per State and per company, and per doctor: 'Has Your Health Professional Received Drug Company Money?'. They have used the data from 15 companies that have published information (mostly because of legal settlements). Through the last years, it seems that companies have decreased their financial support, probably also because of the financial pressure on the pharmaceutical market, and tougher ethical codes. One of the big pharmaceutical companies even stopped paying for hospitality for doctors during scientific congresses. Also under the pressure of the FCPA the pressure on the industry is getting stronger. Still, transparency has been the result of legal requirements, hardly of voluntary actions according to the author.

The cost of transparency is not described. Rosenthal *et al*, mention that the Centers for Medicare and Medicaid Services estimate the disclosure compliance cost will be nearly $1 billion over 5 years. Gorlach et al. make the statement that the new regulatory transparency requirements increase the compliance cost for manufacturers. For the Dutch situation, there is no information available. Except that the Stichting Transparantieregister and CGR have announced that the cost for companies will be €10 per line in the register per year. The number of contracted relationships in the register is in 2013 7.500, this would mean a cost for all companies of €75.000. There are over 50 companies involved, which would mean an average of less than €1.500 per company. Of course there are a lot of other costs involved, like the tracking of payments to HCPs and HCOs, the gathering of the specific requested information per relationship (e.g. the kind of relationship, registry number, exact amount), and the preparation of the lists to upload to the register.

[135] Igor Gorlach and Genevieve Pham-Kanter, Brightening Up: The Effect of the Physician Payment Sunshine Act on Existing Regulation of Pharmaceutical Marketing, Global Health and the Law, Spring 2013, 315-322
[136] Andrew Jack, Letting the sunshine in on doctor-pharma relationships, *BMJ* 2011; 343
[137] ProPublica. Dollars for Docs. 2014. http://projects.propublica.org/docdollars/

3.3.4 What is the role of the compliance function in transparency in pharmaceutical companies in the Netherlands

A literature search on 'pharmaceutical industry', 'compliance', and 'transparency' or 'disclosure' doesn't produce relevant references. Inglehart[138] is referred to, he describes the obligations of companies (Medicare providers) to create internal compliance programs to be more vigilant against fraud. There is a certain link with public reporting of payments to health care providers. It is obvious that manufacturers need to have a compliance system, to 'police their own activities'. A specific role of a compliance function in disclosure activities isn't given. In Dutch literature this isn't mentioned at all. The role of compliance in transparency is not reported.

[138] John K. Iglehart, The ACA's New Weapons against Health Care Fraud, n engl j med 363;4: 304-306

4. Analysis and results

4.1 Annual reports review

To get more insight about the organization of the compliance function in pharmaceutical companies, the most recent annual reports of leading pharmaceutical companies have been searched to get information about the existence of a compliance officer or function, and the reporting lines for compliance. Next to that, also some general information is added, see table 3. The reports of these companies were found in the internet, every company has made their annual reports accessible.

Company	Origin	Employees	Sales	CO	CO report to	Reference	Part of report
Abbott	US	appr. 70,000	$21.8bn	Kathryn S. Collins Chief Ethics and Compliance Officer	Chairman of the Board and CEO	2013 Annual Report & Website Global Citizenship	Global Citizenship, Ethics and Compliance
Amgen	US		$18.2bn	Cynthia M. Patton Chief Compliance Officer			
AstraZeneca	UK (British-Swedish)	51,700	$27.97bn	Katarina Ageborg Chief Compliance Officer	Audit Committee	AstraZeneca Annual Report and Form 20-F Information 2012 "Delivering value through innovation"	Performance (p. 47) / Corporate governance
Bayer	Germany	110,500 Healthcare: 55,300	€39.76bn Healthcare: €18,612bn	Group Compliance Officer	Audit Committee of the Supervisory Board	Annual Report 2012	Corporate Governance Report
BMS	US	> 24,000	$ 16.39bn	Anne Nielsen Chief Compliance and Ethics Officer	Board of Directors	2013 Annual Report	2013 Form 10-K
GSK	UK	99,488	£26.4bn	Simon Bicknell Corporate Compliance Officer	Governance, Ethics and Assurance	Annual Report 2012	Governance & remuneration
J&J	US	128,100	Pharmaceutical Segment: $28.1bn	Chief Compliance Officer	Enterprise Risk Management	Annual Report 2013 & website J&J	Website J&J: 'Managing Risks'
Lily	US	37,925	$23,113.1	Melissa Stapleton Barnes, Chief Ethics and Compliance Officer	CEO	2013 Annual Report	Highlights of the Company's Corporate Governance
MSD	US	appr. 76,000	$44.033bn	Michael J Holston Chief Ethics and Compliance Officer	Board of Directors	Annual Report on Form 10-K	Corporate Governance
Novartis	Swiss	135 696	Pharmaceuticals $32.2bn	Peter Kornicker, Chief Compliance Officer	Board of Directors	Annual Report 2013	Corporate Governance
Pfizer	US	appr. 78,000	$51.6bn	Rady Johnson Chief Compliance and Risk Officer	CEO, Audit Committee, Regulatory & Compliance Committee	Annual Review 2013, website: Corporate Compliance	Quality and Compliance
Roche	Swiss	85,080	CHF46.780bn	Dr Urs Jaisli Chief Compliance Officer	General Counsel	Annual Report 2013	Responsible Business
Sanofi	France	112,128	€32.951bn	Global Compliance Officer	CEO	Annual Report 2013, website	Compliance (website)

table 3, compliance function in big pharmaceutical companies

All the large pharmaceutical companies (the 10 companies with the highest sales in pharmaceuticals) have a comprehensive website, and annual reports can be found on their respective websites. The websites of the Dutch affiliates are linked to the sites of the mother companies (see companies in table X). None of the affiliate websites mentions a local compliance officer or compliance function. It seems the compliance function is not common, at least it is not shared publicly as no local information is provided, in contrast to the global organizations.

Looking at the list of global compliance responsible persons, the split between male and female is around 50%, not all companies mention the name of the person in the annual report. The titles differ from Global Compliance Officer to Chief Ethics and Compliance Officer to Chief Compliance and Risk Officer. All large pharmaceutical companies have appointed a responsible Compliance Officer, and most of the companies refer to local compliance officers in the organization. The global Compliance Officer reports to the CEO, the Board of Directors, or the Audit Committee. The OIG[139] requires for the function 'with authority to report directly to the board of directors and/or the president or CEO'.

[139] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003

4.2 Analysis Transparency register

In the Netherlands disclosure obligations exist since 01 January 2012. In April 2013 for the first time financial relations have been published on the website www.transparantieregister.nl. In April 2014 the data have published over 2013. The register makes public different kinds of cooperation between HCPs and pharmaceutical companies.

The 'Stichting Code Geneesmiddelen Reclame' (CGR) initiated the founding of the disclosure society: 'Stichting Transparantieregister Zorg' and has set-up the disclosure guideline[140]. The disclosure society has build the central database with webportal in 2012 with the financial support of the Ministry of Health (Ministerie van Volksgezondheid, Welzijn en Sport). All relevant organizations[141] of the pharmaceutical industry and HCPs were involved, and support the disclosure obligations.
The guideline requires that physicians, pharmacists, nurses and physician assistants, and pharmaceutical companies publish financial relations. So there is not just a requirement for companies, but also for HCPs. The obligations exist for service agreements (e.g. speaker arrangements, or medical scientific authorship), and for sponsoring (e.g. financial support for a specific project in a hospital); a total amount per HCP or HCO per year below 500 EUR doesn't have to be disclosed. Other relationship don't have to be disclosed, like sponsoring of clinical trials, business relations (e.g. discounts), free samples, and financial relations without a benefit for the company (like small gifts, and hospitality). For clinical trials there is a separate disclosure obligation and website (http://clinicaltrials.gov).

Meanwhile there is a separate disclosure guideline[142] for veterinarians and companies manufacturing and distributing medicinal products for animals.

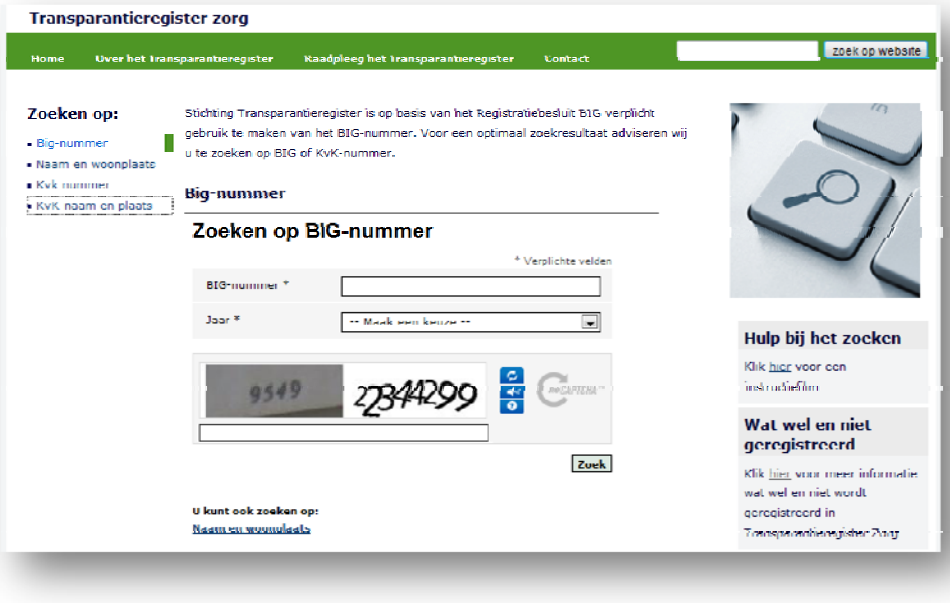

figure 2 screenshot of search function www.transparantieregister.nl

[140] Stichting CGR, Gedragscode Geneesmiddelenreclame, hoofdstuk 7 – Transparantie, laatstelijk gewijzigd m.i.v. 16 mei 2014
[141] Nefarma, Bogin, Neprofarm, FIDIN, KNMG, KNMP, KNMvD, V&VN, NAPA, NVZ, NFU, OMS, LHV
[142] http://www.fidin.nl/Beleid/Aanprijzing

In the register searches can be done in two ways: information can be found with the HCP registry code (BIG number, the number can be found on the website with these registry numbers www.bigregister.nl); or the registry number (KvK number from the Chamber of Commerce). It is not possible to search on pharmaceutical company to have an overview of the aggregated payments of a company (see figure 2).

In a Dutch Medical journal[143] the information about the disclosure obligations was published in 2012. The coordinator of the CGR commented that he hoped that the register wouldn't be considered as a 'black list', the intention is to end the mystery of payments from companies to doctors. But in a 'Dutch way', without the impossible obligations that are linked to the US Sunshine act, where every 10 dollar needs to be justified and published. HCPs in the article comment that they don't have any objections against transparency.

In local journals there were negative reactions too after the first publication of the financial interactions, even the comment[144] that transparency doesn't prevent conflict of interest happening. The expalantion of the complainer: 'Transparency is a smokescreen to hide conflict of interest, as the problem is handed over to the patient. The patient needs to investigate in the use-unfriendly register where the big amounts, like money for research, aren't reported'.

In table 4 below, are the compiled data distilled from the transparency register over the years 2012 and 2013.

table 4: Overview data Transparency register

Year	2012	2013
Companies involved	> 50	> 50
Total budget	€ 30M	€ 33M
Number of contracted relationships	7.600	7.500
HCPs	2.100	2.000
average amount per HCP	€ 2.000	€ 2.250
number of hours spent	15-25 h	16-23 h
budget	€ 4M	€ 5M
HCOs	1.200	1.200
average amount per HCO	€ 25.000	€ 25.000
budget	€ 26M	€ 28M
Visitors website	55.000	na

Source: Stichting CGR, Nieuwsbrief nummer 4, april 2014, and www.transparantieregister.nl

It is necessary to put these figures into perspective. The register is somewhat vague about the number of companies, more than 50 is stated (Nefarma has 38 members, status 06-06-2014), there is no possibility to check this in the register. When you check the number of pharmaceutical license holders in the Netherlands at Farmatec[145] (Ministry of Health, responsible for the issue of pharmaceutical licenses), there are in total over 400 current licenses[146]. Most important group are the holders of a wholesaler license and a manufacturers license, these companies can distribute, sell

[143] Karin Bos, Niks te verbergen, Banden met farmaceuten onthuld voor publiek, Medisch Contact Nr. 51/52 - 21 december 2012, 2954-2956
[144] http://www.artsennet.nl/Nieuws/Nieuws-uit-de-media/Artikel/131648/Psychiater-transparantieregister-werkt-niet.htm
[145] http://www.farmatec.nl/geneesmiddelen/vergunningen/farmacie/
[146] Farmatec - Overzicht farmaceutische-vergunninghouders d.d. 15-04-2014 Ministerie van VWS

products to the customers the wholesalers). It could mean that only a minority of the Dutch license holders is having financial relationships with HCPs and HCOs, or the reporting is limited. Probably the most active companies are part of the disclosure, as Nefarma members are obliged to publish the data in the register.

The total budget disclosed in the register indicates that per company on average about € 600.000 is spent on services from HPCs and HCOs. In average a company pays for services to HCPs € 80.000, and € 520.000 on services and sponsoring to HCOs. As this is the first time this is disclosed, it is not possible to draw any conclusion from these amounts.

In the register there are professional relationships mentioned with a bit more than 2.000 HCPs. The HCPs have all a registry in the Dutch BIG-register. In the registry there are in total 453.074 HCPs registered (2014[147]). The biggest group are nurses, followed by physicals. As the big majority of nurses are legally not allowed to prescribe medicinal products, the most important group of HCPs for pharmaceutical companies are physicians. From the group of physicians, the most relevant segments are the general practitioners and the specialists. In the overview of the general Dutch Society of physicians[148], the number of GPs mentioned is 11.912, and the number of specialists is 21.750 over the year 2012. The total group of most relevant HCPs is around 33.000. It would mean that about 6% of the HCPs are having financial interactions with pharmaceutical companies there are no data to verify this. Companies in general work with key opinion leaders (KOLs), per definition this is a limited group of HCPs.

Patients need the BIG-registration number of the HCP to be able to retrieve the financial relationships of their physician. The BIG registry allows to find the BIG-number in different ways, at least the name is necessary, but also the profession (physician, pharmacist, nurse etc.) of the HCP, and the specialism (e.g. internal medicine, cardiology, psychiatry). With the BIG-number, the data can be found on the Transparency register site. The site mentions the activities for which the HCP is paid, and the name(s) of the involved companies.

4.3 Survey on Compliance and the Transparency register

4.3.1 General

A questionnaire has been set-up with relevant questions about:

- how the role of compliance is set up, and is perceived in Dutch pharmaceutical companies
- the kind of relations between companies and prescribers and health institutions in the Dutch setting
- the obligations and practices, including perception, of companies concerning transparency in the Netherlands
- the (perceived) role of compliancy in transparency within Dutch companies

The population consists of compliance and legal officers, business professionals (sales and marketing), medical employees and general managers of companies that are member of Nefarma,

[147] https://www.bigregister.nl/overbigregister/cijfers/
[148] http://knmg.artsennet.nl/Opleiding-en-herregistratie/RGS-1/Aantallen/89908/Overzicht-aantal-geregistreerde-specialistenprofielartsen.htm

the association for innovative medicines in The Netherlands. The questionnaire has been send via the tool 'SurveyMonkey'. The questionnaire was done anonymously, although Nefarma has a big database of relevant professionals, only a minority did cooperate. In the end (after some special requests in specific interest groups like Legal and Compliance working groups, a total of 33 persons answered the questions of the survey). Below the different answers are summarized.

4.3.2 Company and Function Information

In total 34 of around 120 surveys were returned . All respondents were from pharmaceutical companies and these companies are Nefarma members (members of the legal and communication working groups, and Merck BV employees), as a result a certain knowledge of CGR and disclosure is to be expected.
From the 33, 11 respondents had a Marketing and sales function, 7 (21%) had a Compliance function. The rest (45%) is divided over other departments like Medical, Legal, Management and others. The majority of the respondents (55%) work for a company with 21 – 50 employees, also the bigger companies (> 50 employees) are well represented. Especially companies with a German headquarter take part in the survey, followed by US based companies. Of the companies involved, 85% was a local affiliate of an international company.

4.3.3 Compliance Function

In 66% of the cases, there is a global compliance officer, in the local situation over 70% of the respondents mention that there is a local compliance officer. Still 25% of the respondents haveskipped this question.

It seems that in most cases, compliance is part of the legal function, the same in local and global settings. But more than half of the respondents skipped the question (almost 60%), so this answer doesn't give much clarity about the position of compliance officers in Dutch pharmaceutical companies.

The purpose of the global compliance function is especially defined as providing compliance policies, behavioral rules and ensuring monitoring, and oversight of implementation level of internal codes in all affiliates of the global company. Also mentioned is the support of local compliance, a gatekeeper role for local/international projects above a certain threshold. Risk management is also an aspect that is seen as a global compliance role, including anti-corruption measures. Trust and reliability of the company is another purpose, including ethical business conduct.
The purpose of the local compliance function is seen as translating global policies according to the local legal framework and ensuring implementation. Also the support of the global function is mentioned, next to support of local marketing and medical, including compliance training. Also being a gatekeeper for local projects within a certain budget, next to responsibility for local risk management. A specific opinion from a respondent (working in the legal department of a big affiliate of a German company) stated: 'Build a sustainable competitive advantage by aligning compliance with business needs and fully integrating compliance risk management in daily business activities and strategic planning'.

From the 21 (out of 33) respondents who answered this question, 85% is satisfied or very satisfied with the global compliance function, 24 answered this question concerning the local function, and all were satisfied or very satisfied with the local function.

4.3.4 Marketing & Sales activities of your company

The survey is done especially by coworkers of companies (80%) with maximum 30 persons in marketing and sales functions. From the respondents , 100% confirmed that their companies were involved in hospitality activities with HCPs, sponsoring of projects in health institutions and of sponsoring of scientific meetings and manifestations. Also 100% said that their company was

involved in service agreements with HCPs (e.g. consultants, advisory board members, speakers). Free samples and gifts seem done less, still observational studies is apparently done by a majority of the involved companies (over 85%).
Concerning the effectiveness of the marketing activities, one third of the respondents didn't answer. Of the activities mentioned, as effective and very effective are judged hospitality activities with HCPs, sponsoring of projects and of scientific meetings and manifestations, and service agreements with HCPs. Free samples and gifts are hardly seen as effective.

4.3.5 Disclosure requirements

All respondents confirm they know the CGR Code of Conduct and are aware of the guideline on disclosure of financial relationships. All involved companies (Nefarma members) work according to the CGR rules.

As strong points of the code are mentioned: it creates a fair competitive paying field, that it protects patients and HCPs; effective self-regulation imposed by industry and other stakeholders; the Code provides for transparency, pragmatism and clear guidance. The weak points mentioned: the code is not always clear and open for interpretation and can be stretched a little; some principles are narrow minded; HCPs don't know the rules; the Code doesn't apply to Medical Device manufacturers; there are no rules concerning interactions with non-HCPs , like hospital boards/buyers, insurance companies and (partly) patient advocates (these groups play an increasing role in the new pharmaceutical society); in the Code there is no concern for the patient.

In most of the companies it seems that compliance is responsible for transparency activities, at least in two times more of the cases compared to the legal, finance, medical and marketing departments. It is for the respondents difficult to judge what the workload is for these activities, the majority says they don't know, for the rest they think it to be 0 - 0,5% fte. It seems that companies work with a simple excel sheet as tool to handle transparency data, also there are companies with an automated system. It is for the respondents not know how many financial relations their companies have, neither with HCPs, nor with HCOs.

4.3.6 Transparency register

All involved stated to be familiar with the transparency register, except one. The respondents deem the register useful (around 50%), a minority says the register is hardly useful, but it has to be noted the 33% didn't answer this question.
The register is seen as an important and necessary step in regulating financial relationships between HCPs and the industry, an increase in transparency is considered a good development. Still there are doubts about the data, are these all data? Are these data the exact data of the company? Is transparency guaranteed? Next to that, there are questions about how often the information is consulted, and there is a remark about the fact that it is hard to find data. It is noted that it is for companies a comprehensive administrative exercise to provide the data, it is a administrative hurdle and burden. One respondent mentions that the reason for the existence of the register is to satisfy a political hype (on a national, EU and global level). 'Nobody looks anymore, until a journalist will start digging in it'.

As strong points of the register are mentioned transparency itself, so the financial relations between doctors, hospitals and companies are clear. This has also a positive influence on the bad reputation of companies, as it is clarified that companies comply to the rules, next to that, the register satisfies political demands. It is seen as strong point that only the relationships of physician is disclosed, so you can check your treating physician. One respondent mentioned that you can have an oversight of the different pharmaceutical companies, but that is not correct. The register is supported by HCPs, HCOs, and the pharmaceutical industry.

Many perceived weaknesses are mentioned by the respondents, these can be divided in two categories:

> Scope: the scope is too small, not everything is transparent, the register is not completely up-to-date, financial relations for clinical research projects are missing, there are ways to pay specialists money without a publication in the register, there is no check on the disclosure data provided to the register, no search can be done on companies, it's difficult to find a specific HCP, it's a lot of work for companies to provide the data for the register
> Information behind the data: there are too many data in the register, the data leave room for interpretation, HCPs don't have enough knowledge about the register and the disclosure code, the data in the register don't provide the 'why' behind the amounts, so misinterpretation is possible, and it's unclear which actual conclusions regarding influencing can be made.

Several suggestions are made to improve the register. Respondents want to add clinical projects, and to especially increase the search possibilities in the register (separate countries and doctors, add a description of the sponsored project, easier look up of physician, search by company – linked to professional address instead of residence, to make the register broader available), the workload for companies (make it automated and more simple to work with, make it a user friendly system where you can add data on a daily or monthly base, help doctors to be involved, give better feedback to companies and monitor reporting of HCPs, it should be enforced rigorously). Also the suggestions is made to add clinical research projects.

Apparently, companies do not (regularly) check the register. Only 20% of the respondents say they have checked the register, but comments are added that it was out of curiosity, or to see how it works. Only two respondents add that they actually use it to check certain HCPs for financial relations. The same is true for HCOs, there is one remark that the register is actually used to make a risk-based decision per HCO before payments. The register is not used to check activities of other companies, also for this question a minority (33%) mentions the use to monitor competitors.

A majority confirms that the compliance role should play in transparency activities (60%), remarks are made that compliance is needed to comply with the rules, e.g. checking amounts, compliance should provide guidance for transparency activities, it should play a consultancy role, and perform sample checks. The possible role is described in different remarks: documentation of payments is mentioned, coordination and transfer of the data to the register so complete transparency is ensured, including the implementing of effective systems and technology, training of personnel concerning transparency and the local systems, risk assessment (including a monthly update about commercial activities from competition), and monitoring of the system.
A clear majority of the respondents recognize an added value of compliance in transparency activities (40% agree and 40% strongly agree). There is clearly no agreement about a positive effect of the Transparency register on marketing and sales activities; over 40% of the respondents didn't answer the question, and the rest of the answers were almost equally divided between agree (36%), somewhat agree (32%), and disagree (26%). There seems a tendency to see a slight positive effect of the register on the reputation of the pharmaceutical industry; still 36% didn't answer the question, but of the rest 18 out of 21 strongly agree (19%), agree (19%), or somewhat agree (48%) on the positive effect on the reputation.

4.4 Interviews

4.4.1 Interviewer & Interviewees

Interviewer: Albert van Maaren

Interviewees:

❶ Federik Schutte, Secretary General Foundation of the Code of Conduct for Pharmaceutical Advertisements (ambtelijk secretaris Stichting CGR)
Date: 30-04-2014; location: office Brabers, Den Haag

❶ Björn Eussen, Coordinator Dutch Transparency Register
(voormalig coördinator Stichting Transparantieregister Zorg)
Date: 30-04-2014; location: office Brabers, Den Haag

❷ Kirsten Gussinklo, Policy advisor Legal Affairs Nefarma
(beleidsadviseur juridische zaken)
Date: 01-05-2014; location: office Nefarma, Den Haag

❸ Anke Heezius, lawyer / owner Life Sciences Legal, Amsterdam
Date: 13-05-2014; location: restaurant WTC, Amsterdam

❹ ir. B. (Bas) van der Heide, coordinating/specialist senior inspector IGZ,
ministry of Health (VWS)
Date: 19-05-2014, telephone call

4.4.2 Introduction

The interviews were done to get an expert opinion about compliance, financial relations, disclosure, and the possible role of compliance in transparency activities. Especially to add to the information that can be retrieved from the survey (see 4.3 *Survey on Compliance and the Transparency register*). Essential is to have information from the initiator of the Transparency register (CGR), and Federik Schutte, secretary of CGR, is the person involved in the development and implementation of the register from the start. Next to the CGR input, it is necessary to have the view of the 'Stichting Transparantieregister Zorg'. Björn Eussen, was coordinator of the register during the development and implementation phase.

As the pharmaceutical industry was one of the major stakeholders during the set-up of the register, there was an interview with the legal advisor of the industry association, Kirsten Gussinklo. Nefarma is one of the members of CGR. It should be noted that Kirsten is in her current position for 5 months at the moment of the interview, she wasn't involved before in the disclosure developments, of the industry association (note: meanwhile Kirsten has left Nefarma). The regulator in the pharmaceutical market, IGZ, has a limited role in disclosure activities, as the Law doesn't require disclosure. Still IGZ sees the disclosure of financial relations as an important development, as it is closely linked to promotional activities. The interview with Bas van der Heide, senior health inspector, adds the view of the regulator. To have a more independent view too, there was an interview with Anke Heezius, lawyer and specialized in a.o. pharmaceutical law and promotional guidelines.

4.4.3 Opinion table

Code of Conduct (CGR): strong points	
❶	• Self-regulation: on the one hand non-binding, but on the other hand does provide legal certainty, because of cooperation/working arrangements with IGZ • Level playing field: same rules apply for all Nefarma members, and members are able to address possible violations of these rules to other companies • Knowledge platform: advice can be obtained from CGR, advices offer legal certainty (IGZ will not disagree with the advices)
❷	• The code gives more details than the Dutch Medicines Act, but it doesn't give full legal certainty. • CGR is also the contact point for questions about the Code and the guidelines.
❸	• CGR was more a court function, nowadays self-regulation has become successful. This is a great achievement of the CGR. It seems there is more willingness between companies to solve their issues. • It seems the CGR code is getting stricter, following the changes by EFPIA, e.g. the ban on gifts.
❹	• The Code is linked to transparency, advices from CGR are made public, and also the verdicts are published. In comparison, the work of IGZ is much less transparent, as official warnings and administrative fines cannot be published.

Code of Conduct (CGR): weak points	
❶	• No sanctions • Possible free rider behavior dilemma
❷	• Some room for interpretation possible of the Code and guidelines, this can cause legal uncertainty (see remark a) • The role of IGZ is not always clear, the prospective review by CGR (advice procedure) still can lead to actions by IGZ (see remark a)
❸	-
❹	• There is a limited number of complaints at CGR concerning inducements. • There is no active monitoring by CGR. • Self-regulation shouldn't be covering up breaches for the regulator.

Financial relations industry-HCPs & HCOs	
❶	-
❷	All companies (Nefarma members) agree that there should be clear rules; the perception is that the rules are very strict.
❸	-
❹	According to the Medicines Act there is no ban on financial relations between companies and HCPs/HCOs. But undesirable influence of the prescription behavior is not allowed, the policies ('beleidsregels') set the standards for IGZ.

The role of the regulator (IGZ)	
❶	• IGZ checks the register too, and even urges companies to report in the register if they see a relation has not been put into the register. Apparently there is even a fine-procedure running initiated by IGZ, concerning a financial relation in the register with a too high payment, well above the fair market value.
❷	• IGZ has in principle no involvement with the register, as there is no legal basis. There are working arrangements between the IGZ and CGR, that should lead to more legal certainty for companies.
❸	-
❹	• There are no legal disclosure obligations, so IGZ has no formal role. • For disclosure there is a link with the policy on inducements, so IGZ checks the register now and then to verify contracts and payments that they find in regular investigations. So no formal role, but still a look at disclosure. • IGZ receives the data sources if asked for at CGR. • IGZ doesn't see the register as a tool to monitor companies and HCPs, as there are no details to be found (no solid data), still the data can provide a general picture of a HCP, or a certain signal (see remark b)

Transparency, general view & obligations and practices	
❶	• The vision behind the Transparency register is that it should serve the individual patient to be able to have a discussion with his/her patient about relations with pharmaceutical companies. The register doesn't judge the payment, but just provides information to the patient. • The proportionality principle is specific for the Dutch disclosure guideline. It was decided not to make the privacy aspect (agreement for publication) leading, but the balance of interest between the public interest and the private interest of HCPs. • It is obvious that the Netherlands are a front-runner in publication of transparency data; there is a lot of interest in the technical solutions implemented here (a central database; and a low entry level e.g. for doctors to report). • The coverage of the register is considered appropriate, there are about 30 Nefarma members, and over 50 different companies have put reports in the register. Companies have implemented the guideline well apparently. Doctors, as they need to check the data that was delivered by companies before publication, didn't have many complaints concerning the reports. • The number of HCPs is relatively low, but can be explained that industry works with the top physicians, the Key Opinion Leaders (KOLs).
❷	• The CGR disclosure guideline is not completely in line with the new EFPIA Disclosure Code. • Companies report all of their financial interactions according to the disclosure guideline in the register. • Companies think the process is working, still with some practical issues. • Patients seem to have little interest in the register. • It is not clear if physicians are completely aware of the self-regulation obligations. It seems that physicians don't report often themselves.
❸	• Transparency in general is a good development. It's clear that the vision is to disclose financial relations between HCPs and HCOs, but the disclosure is limited, the interests of pharmaceutical companies are taken into account (you can't find directly information about specific companies). • The Transparency register seems an 'image instrument': positive for companies (improvement reputation) and HCPs (improvement status: when you are asked by the industry, you must be important), but no critical issues are published.
❹	• IGZ sees disclosure as an important development, also now an international development. There will be no legal regulation soon. The expansion of the register is a good development, with the addition of the Medical Devices (also self-regulation). • Still there is no clarity about payments of international companies to HCPs, HCPs themselves are obliged to disclose these relations, it is not known if this is done, and if international fees are higher. It seems that the coverage of the register is satisfactorily. • There are informal working arrangements between IGZ and CGR about the Transparency register. IGZ can have a look at source data, and IGZ remains informed about the developments (see remark c).

Transparency register: strong points	
❶	• It seems clear that journalists are interested in the data in the register, but without the aggregated data per company, they have lost interest. In 2014 no requests came from journalists. The general opinion is soothed, the consensus seems to be 'we are transparent', and press and politics have lost interest. • HCPs see publication of a relationship in the register as a sign of status, being asked as a consultant is positive. • IGZ uses the register to check the information they find in the market. • One portal and not different websites (like from different companies).
❷	• One platform, all payments can be found on one site. The register can be found easily, the accessibility is good. • Transparency is perceived positively.
❸	• The register influences the public opinion. • The register generates awareness concerning the existence of financial relations between companies and HCPs and HCOs. Also the awareness of companies and HCPs is raised. • The register raises awareness, and can even act as an external threat, as the relations are public, so also IGZ can have a look, and if necessary, take corrective actions.

❹	• The register start-up was rather quick, and meanwhile other sectors are widening the scope of the register.

Transparency register: weak point	
❶	• After two years it seems that the public is not very much interested in the information in the register. In total in the first year there were 55.000 hits, 60% of the hits were there on day one. Currently, there are still at least 10 views per day. • CGR has no implications for health institutions, for hospitals there is no obligation to report. • The drawback of the BIG register is that you need to enter the physician's name, and residence to be able to use the BIG-number. You need the BIG number for the transparency register. • No data are published about clinical trials. • Not all interactions are included, as it concerns payments from €500 per HCP or HCO per year.
❷	• Information on the register site is too limited according to some companies. Being transparent, can influence the competition environment for companies. • Patients need to know the name and residence of the physician, to be able to find the financial relation.
❸	• Not everything is reported, especially reporting from HCPs and HCOs seem to done less • Non-Nefarma members don't need to report, e.g. generic manufacturers will not publish financial relations. Also physician don't report many relationships. • It seems that patients can't really judge the extent of the relationship • The register doesn't seem very user friendly, as patients need to find the BIG registry number of their doctor first. • There is no obligation to disclose the relations as there is not legal background. Next to that, there are no sanctions if a financial relationship is not published in the register. • The accessibility of the register is limited, and the information available is limited (no details provided).
❹	• The search function, it could even scare visitors away. • For patients the data are difficult to interpret, how many patients are really discussing the data with their HCP?

Usefulness Transparency register	
❶	• The register was set up with the purpose to give patients the possibility to check the financial relations between industry and the physicians they attend. Information can be found per individual HCP or HCO. EFPIA set up its disclosure guideline especially to build trust, aggregated data per company are requirements.
❷	• 'Is the public really interested in the information in the register?'
❸	• Transparency in healthcare is a good initiative, especially focused on the public • It seems the register is meanwhile accepted, but is doesn't raise special attention. • The register is clearly there to avoid conflicts of interest, and to disclose financial relations.
❹	• The register helps to make the topic of HCP-industry relations open for discussion, without any accusations. • It's limiting risks, as HCPs, HCOs and companies give more thought, before contracts are signed, and relations are started (awareness).

Workload transparency activities companies	
❶	• An important question is where the 'work' for the transparency register starts (writing agreements, business arrangements, reporting). Important part of the work consists of relating the actual payment data (Financial department) with the relations established in written agreements. • There is a commercial tool to store disclosure data (from Cegedim), a lot of companies work still with simple excel overviews. • Since the EFPIA Disclosure Code, there is a development that more and more companies centrally coordinate the documentation of financial relationships with HCPs and HCOs, so disclosure reporting will be relatively easy.
❷	• Around 2 hours per month according to one Nefarma member
❸	• There is a considerable workload for disclosure activities. Although meanwhile there is coming

	more standardization from the global units.
❹	• This aspect is not known, at a first glance it seems quite a lot of work. It concerns book keeping, checking the kind of interaction, setting up contracts (incl. a transparency clause). • For one person it could be months of work.

Improvement of the Transparency register	
❶	• An evaluation survey will be done with pharmaceutical companies, HCPs and with 'users' of the register, especially the more critical ones (public, and press). After the adoption of the EFPIA Disclosure Code, the Transparency register will be adapted to meet as much as possible the EFPIA requirements, especially hospitality payments (when > €500) will need to be reported, starting in 2015. Compliance with the EFPIA guidelines is subject of further discussion. From 2016 also the financial relations between industry and patient organizations will be published in the Transparency register (data from 2015). • Developments are that manufacturers of implants will report too, other Medical Device manufacturers will follow. After the evaluation, there are probably more developments to be expected. • The setup of the register can be seen as an important first step; next will be adding payments for hospitality (following the new EFPIA Disclosure Code), also Clinical Trial payments could be added. • The need for transparency is increasing, you see developments e.g. in the hospital sector, where quality indicators are published, or even indicators per HCP, health insurance companies make these efforts. • The idea is to broaden the disclosure scope, and increase the cooperation by self-regulation. The wish for after 5 or 10 years, is to have one portal for all financial relations with HCPs and HCOs (not just pharma), and the register is a well-known institute, and reporting is obvious for all involved stakeholders. • Recommendation is to actively link the Finance data with the systems that document relations with HCPs and HCOs (e.g. the Purchase Order number, very regularly used in companies, can be included in the written agreements).
❷	• The next development will be the incorporation of the EFPIA Disclosure Code, and the outcomes of the planned evaluation in May 2014. EFPIA asks for aggregated data (per company) in their guideline. There are no plans to implement that in the Netherlands for now. • An expert opinion could be interesting, e.g. analyzing the effect of financial relationships on prescription behavior. • Non-Nefarma members should report more (no formal obligation at this moment). • The Stichting should improve the communication about the register, so it will become more known to the public. • Other parties should connect to the platform, like manufacturers of Medical Devices (or the association), health insurance companies, patient organizations.
❸	• The develop is that the requirements are getting stricter following EFPIA (e.g. hospitality payments).
❹	• It should be made more complete, all kinds of relations need to be incorporated in the register. • Other financial relations should be added, like hospitality, although it will be not easy to establish the amounts to be published (complexity of different costs involved).

Compliance and disclosure activities (incl. added value)	
❶	• Compliance is there to set-up, implement and maintain a functioning compliance system as a separate department (e.g. no connection with Finance). • Every company needs procedures and processes to be able to publish the required payment data in the register. In practice this is rather complicated, as it can involve written agreements, business arrangements, medical content and payments. So at least Legal and Finance are involved and regularly business functions and the Medical department. Compliance has to have the overview and to coordinate, as it has the knowledge of the codes, concerning legal aspects and disclosure requirements. • Compliance can act as central coordination point in companies.
❷	• As you need to comply with the rules, compliance can play a role. Compliance can act as guard, at least in theory, e.g. by providing procedures.

❸	• The compliance function should be independent, and act as the conscience of the company. On global level compliance will focus especially on the company values and standards, local will deal with local legislation and codes, and will have a more legal view. • The role of compliance is not embedded in the legal framework. It can be that the function is at some points 'in between' the commercial interest and the legal obligations. • Compliance should be able to decide what relations need to be disclosed. Compliance should take care of the contracts (including disclosure clauses), this is not just an obligation for the legal function. • Next to that compliance should set up and manage the system for transparency activities, as compliance has a company-wide role, and will be able to connect legal, finance, IT, and other necessary departments. • Compliance can't be an extra task next to other responsibilities. Compliance should have a clear role description.
❹	• Compliance is a crucial function for the regulator. • Compliance could make the picture complete, procedures, processes, training, audits (monitoring). • Compliance should have a broad responsibility, not just promotional guidelines. • There is not a complete picture how the function should look like in pharmaceutical industry.

Transparency register and effect on business and industry reputation	
❶	• Yes, transparency is no longer a topic, as the financial relations are published. The interest seems to have shifted to the manufacturers of Medical Devices (they don't close the data yet).
❷	• The register doesn't improve the reputation, as the public interest is very limited.
❸	• Transparency has a positive effect, as the quality of the activities increases, there are not more activities. • In 2012 and 2013 the publication was concerning a big amount, and no scandals have come out of the disclosure by the companies. This gives the hint that there is nothing wrong, and the is nothing to hide.
❹	• After the implementation of the register, there was limited public discussion about the financial relations between HCPs and industry. • There is a positive effect, as it is made clear there is nothing to hide. • It is too early to say if there is an effect of transparency on the business. Probably independent experts should assess the effect. • There is awareness raised with the involved parties.

Role compliance in disclosure in companies in the Netherlands	
❶	• Compliance could play a coordinating role in transparency activities (combining knowledge concerning CGR guidelines, the Law on Medicines, and legal input, together with the linking of information about relationships with HCPs and HCOs and the payments done by the Finance department).
❷	• Compliance can act as guard, at least in theory, e.g. by providing procedures.
❸	• The role of a compliance function should be formalized more. In court cases it has been shown that judges take into account if companies have a compliance system (e.g. procedures, training, monitoring and sanctions).
❹	• The role of Compliance should be raising awareness, e.g. by only approving contracts for HCPs/HCOs with a clause concerning transparency. • The awareness should be broadened to the international setting, and all involved employees should be made aware too. • Everything that has to do with value (money or other), should be organized strictly, including disclosure. That should be the role of Compliance.

Remarks/recommendations	
a	• Transparency is a container concept, the word was used in the title of the register ('Transparantie Register Zorg') as for the general public it is more appealing than the word 'disclosure' (openbaarmaking) – FS
b	• AH proposed to compare compliance with a 'Qualified Person' like role (responsible for release of pharmaceutical products to the market). It should be embedded in the law, that this role is responsible for compliance, and should have the jurisdiction to decide (and is liable). It could be a role of CGR to describe such a OIG-like compliance role. Still it's not part of the Dutch culture to have too many rules.
c	• CGR could check in case of a founded complaint, if the company has an appropriate system to comply to regulations, and use of bonus-malus regulation, as an incentive to have a proper compliance program.
d	• BvdH sees the CGR as a 'first line' organization, IGZ as a 'second line' where the more severe cases (high risk public health, high risk influence prescription behavior) can be handled. CGR could do more active monitoring of compliance after issued advices, could analyze signals/patterns from the market, directly check with companies. It would make self-regulation more credible if the involved parties cooperate more (e.g. in monitoring; sanctions). IGZ itself is more involved in risk-based supervision of the market, and will monitor CGR. • When self-regulation is more active (incl. monitoring and sanctions), it could help IGZ to focus its inspections and enforcement actions. The advice function of CGR is valued by IGZ, as IGZ hardly has the possibility to give advice. There are good interactions between IGZ and CGR.
e	• Personally, BvdH is of the opinion that IGZ should provide full access to all its documents, within the legal boundaries of the Freedom of Information Act and the Privacy Protection Law. There can be more openness about the work of IGZ, at least a quicker publication of decisions of administrative fines, and the related considerations. But in order to do so the legal framework must be adapted first. There is a change of the 'Gezondheidswet' in the piperline that could make that possible. Politics plead for 'naming and shaming'. BvdH would like to be able to publish considerations of IGZ quicker (now only possible after a court decision). As long as the interests of the involved parties are not damaged (reputational damage).
f	• IGZ initially pleaded for a lower threshold amount than €500 (proportionality principle), however that would mean more reports, but the amount is arbitrary. At the moment IGZ isn't pleading for a lower amount. • IGZ doesn't see the necessity of sanctions yet, a check should be done if the register is operating well. It would improve the credibility of self-regulations if sanctions are applied for non-compliance. • There should be monitoring, like consistency checks, point checks (not possible at the moment)

4.4.4 Conclusion

The answers in the interview show little differences between the interviewees. It seems they are in agreement about the general topics, like the view on disclosure and the Transparency register, and the developments. Maybe because they meet regularly, and together discussed the Transparency guideline, and they were the key players involved in the set-up of the register.

About some topics the independent lawyer and the inspector of IGZ have more specific remarks and ideas (see 4.4.3 Remarks/recommendations, of the Opinion table). The more general outcomes of the interviews are:

Code of Conduct (CGR)

The Code is not legally binding, still self-regulation is deemed as a success. It creates a level-playing field, and CGR is transparent in its advices. Also weak points were raised, there exists no complete legal certainty, there are only a limited number of complaints at CGR, and there is no complete openness.

Financial relations industry - HCPs/HCOs
It is clear that financial relations are allowed, but there are clear rules concerning the interactions, these provide the boundaries.

Role of the regulator (IGZ)
All parties confirm that IGZ has no formal role in disclosure activities. Remarkable is that IGZ is very interested in the disclosure data, and receives source data from CGR. IGZ uses these data as an indicator concerning HCPs and HCOs, the data are monitored regularly. As these data are not more that an indication, IGZ will investigate further in case of signals.

Transparency, general view & obligations and practices
Transparency is seen as an important development, there is broad consensus over the purpose of the register providing information to patients concerning the financial relation between their HCP and pharmaceutical companies. The Netherlands is a frontrunner in this development, and has built the technical expertise. The coverage of the register is satisfactorily, especially companies have implemented the CGR guideline well; there is a relatively low number of HCP that reports their financial relations. There is general interest in more transparency, e.g. hospitals publish certain data about performance and quality indicators.

Transparency register
In the aftermath of the launch in April 2013, it seems that press and general public have lost interest; 'because we are transparent'? The register creates awareness with HCPs and industry, and influences the public opinion. There is no formal obligation for HCOs to publish financial relations.
The accessibility is limited, as first you need the BIG number/KvK number, before you can find any information. This could even scare the public away.
The register provides limited transparency, as no aggregated data on company level can be found, and no data about payments in clinical trials is provided. In that sense it could be seen that the register protects the industry, and even the register could be seen as an 'image' instrument: the reputation of companies improves, and a mention in the register can be seen as a status symbol for HCPs ('when you are in the TR, you must be important'). Still only Nefarma member companies are obliged to report, other companies don't have to report. There is no sanction if data are not published. The information is also limited, as only relations with a value per year per HCP/HCO accumulated of €500 needs to be disclosed.
All agreed that the register needs to be expanded, as there are more financial relations than only with pharmaceutical companies. A question that came up is what patients actually do with the information provided in the register.

Usefulness Transparency register
The initiative to disclose financial relations is a good one, the question comes up if the public is really interested, as not many hits are recorded at the site. Still the register gives the possibility to check the relations between individual HCPs and the industry. Anyhow awareness is raised with companies and HCPs.

Workload transparency activities companies
It is not defined what the workload for disclosure exactly consists of, it certainly concerns linking payments with agreements with HCPs and companies. More companies use nowadays central systems developed by the mother companies, as disclosure is an international demand after the adoption of the EFPIA Code. It seems the workload is considerable, especially at the moment the publication of data is coming near. The estimation differs from 2 hours per month, until months of work for one person. It is recommended to link the data concerning cooperation with HCPs and companies to the financial systems, so payments are linked to agreements.

Improvements of the Transparency register

The improvements and the development of the register are shared by all interviewees, this is linked to the general view on the register: all possible financial relations of HCPs and HCOs available for patients.

Hospitality payments over €500 per HCPs per year will be part of the register; payments to patient organizations; financial relations with medical device manufacturers, starting with manufacturers of implantations; next to that payments for clinical trials could be added; payments by non-Nefarma members. Meanwhile CGR is performing an evaluation of the register, possibly improvements follow the outcome.

Compliance and disclosure activities

There are several views on disclosure activities of the local compliance role. Especially a coordinating role is mentioned, where compliance has the overview of the whole process, as compliance has knowledge of the different aspects required for disclosure (codes and laws) and has contacts with the relevant departments (legal, finance, business, medical); a central coordination function seems appropriate. In that sense compliance could act as 'conscience' of the company, in between commercial interest and legal obligations, connecting the different functions for disclosure. For this compliance should be a separate independent function, with a clear and known role description. Compliance is considered as a crucial role for the regulator (IGZ), especially if there is a broad responsibility.

Transparency register and the effect on business and industry reputation

With the launch of the register, transparency seems no discussion topic anymore, so the register has a positive effect, there is nothing to hide. The quality of activities improves by the obligation to publish financial relations. Since the launch, no scandals came out.

Nefarma states that the register does not improve the reputation of the industry, and that the public interest is limited. For IGZ it is too early to conclude there is a positive effect on industry and their reputation.

Role compliance in disclosure in companies

As mentioned before, the role of compliance can be a coordinating one, as a guard of disclosure. Part of the role is certainly to set-up, implement and maintain a functioning system, so disclosure can be performed properly. The role for compliance should be formalized. Compliance should raise awareness within the local organization, but also in the international setting. IGZ thinks that all transfers of value with HCPs should be under the organization of compliance.

5. Conclusions and recommendations

In this section the conclusions of the different research questions are discussed. This is done per separate question, and all aspects (general view on compliance, literature search, legal aspects, research, survey and interviews) have been taken into account. The summary of the conclusions can be found in the last conclusion part, concerning the general research question (5.4). In the last part (5.5) recommendations are made.

5.1 What is the role of the compliance function in a pharmaceutical company

A Compliance function in a pharmaceutical company has to have solid knowledge of the business, and needs to be close to the business to be able to assist, explain, train, correct, re-train, and to apply preventive actions if necessary. In that sense the Compliance function can be seen as the second line of defense in the company. The directives from the Dutch Medicines Act, and the specific industry codes need to be applied primarily by the business. In the pharmaceutical industry the business is the first line of defense, especially the marketing and sales employees that are having direct interactions with HCPs and HCOs.

Personal integrity of employees, organizational integrity, ethical behavior of the management, and the ethical values of a company should play an important role. Professional skepticism is a behavior that can help organizations with maintaining integrity. The Compliance role is the function that has to express professional skepticism, as a natural behavior.

As purpose of a local Compliance functions is mentioned: 'Build a sustainable competitive advantage by aligning compliance with business needs and fully integrating compliance risk management in daily business activities and strategic planning'.

The landscape of the legal environment of the industry sector that a company operates in, including the regulators, has to be known. In the Netherlands, IGZ is the most involved authority, and is the regulator that decides about the granting and the maintenance of the pharmaceutical distribution license of Dutch companies, this 'license to operate' is essential for the existence of a company.

The essential need for compliance can be derived from the UN Global Compact, principle 10, 'Businesses should work against corruption in all its forms, including extortion and bribery'. In US law, there is a description of minimum requirements for an effective compliance and ethics program. In the OIG Compliance Program Guidance for Pharmaceutical Manufacturers[149] , an operative compliance officer is a demand. With as responsibilities, amongst others, 'developing, operating, and monitoring the compliance program, and with authority to report directly to the board of directors and/or the president or CEO'. As a specific primary responsibility of a Compliance officer 'Continuing the momentum' is mentioned, so to keep the culture of Compliance alive.

In EU legal texts for pharmaceutical companies, strict rules are provided about interactions between the pharmaceutical industry and health care professionals and health care organizations. There is no specific demand for the function of Compliance officer, it is not legally described how the regulations need to be management in an organization.

In the Netherlands there are no laws or regulations to install a compliance officer or function within pharmaceutical companies, but it is necessary to have 'scientific service department' that is

[149] Department of health and human services - Office of Inspector General - OIG Compliance Program Guidance for Pharmaceutical Manufacturers, Federal Register / Vol. 68, No. 86 / Monday, May 5, 2003

responsible for the 'internal content review of promotion'. There doesn't exist an OIG-like document. CGR in its Code of Conduct requires internal control of Compliance of the Code[150].

In corporate annual reports of the top 10 big pharmaceutical companies an operative Compliance function is described. None of the Dutch affiliate websites mentions a local Compliance officer or Compliance function. It seems a local Compliance function is not common, or it is a rather invisible function. In the survey another impression comes out: in local organizations, a majority of the involved companies seems to have a Compliance function that is part of the legal department. And the Compliance function is apparently well appreciated.

The Dutch competition authority advices to install and maintain an operating Compliance program[151]. Such a program can be considered as conscious self-interest. Every company needs a customized set-up, as business models, risks, culture and values of companies differ. Risk description and risk rating are the start of the set-up of such a program, goal is to decrease compliance risks. An operating Compliance program can decrease possible fines after infringements. Question is if a Compliance program could be part of the monitoring policy of the Dutch healthcare regulator (IGZ). The Dutch regulator is considering this possibility, it would give the regulator a tool for better control, and it would contribute to the internal relevance of the Compliance function in pharmaceutical companies.

5.2 What kind of relations exist between pharmaceutical companies & HCPs and health institutions and what are the financial relations

Medico-marketing has a direct impact on knowledge (accepting wrong claims), attitude (positive attitude toward a company and new drugs), and prescribing behavior (increased prescription of the product of a company), of HCPs. This effect is statistically significant and even dose-response was demonstrated. A clear relationship exists between the budget for marketing expenses and the use of medicinal products that are introduced to the market. Companies want to excel in marketing to be successful in the competitive market.

Pharmaceutical companies can use the asymmetric information level with prescribers, marketing can be manipulative. Some critical experts advice that doctors shouldn't talk to representatives of companies at all. The expertise of prescribers should be raised. Balanced representation of information would benefit HCPs, this is anyhow mandatory for companies following the directives for acceptable promotion of medicinal products.

According to the sector inquiry of the European Commission in 2007[152], companies spent €15,7 billion on marketing activities per year in the EU. In 2012 in the US, $27 billion was spend by companies on drug promotion[153]. Companies spend 20% of their sales on marketing activities. A permanent increase in marketing expenses with 10%, results in a 3% increased demand for the product involved in due time. Costs for medical activities and market access have increased in recent years. There is a shift in personnel between departments from 2007 until 2012: marketing (73 to 63%), market access (5 to 9%), and medical (23 to 29%)[154].

[150] Stichting CGR, Gedragscode Geneesmiddelenreclame, paragraaf 4.3 –Interne controle o correcte naleving, laatstelijk gewijzigd m.i.v. 16 mei 2014
[151] https://www.acm.nl/nl/publicaties/publicatie/12571/Toespraak-Chris-Fonteijn-bij-International-Chamber-of-Commerce-over-compliance/
[152] European Commission, Final Report on its competition inquiry into the pharmaceutical sector - Final Report (8 July 2009) - Commission Staff Working Document (Technical annex to the Commission Communication) part 1
[153] Pewhealth, Persuading the Prescribers: Pharmaceutical Industry Marketing and its Influence on Physicians and Patients, Nov 11, 2013
[154] SEO Economisch Onderzoek, De farmaceutische industrie in het maatschappelijk debat, Een feitelijke beschrijving van de markt voor innovatieve geneesmiddelen in Nederland, In opdracht van Nefarma en Amcham, Amsterdam, mei 2014

Data about marketing budgets are not made public, only limited data can be found. It is difficult to retrieve the amount that is spend on marketing, as companies are not obliged to mention the marketing costs in their annual reports, they are accounted under 'selling, general and administration'.

The perception of medico-marketing by the pharmaceutical industry is not positive. Publications have a negative trend, and manipulative marketing is seen as common practice, the tendency is to see the relationship between prescribers and companies as one of dependency.

It seems that all of the Dutch innovative companies is involved in hospitality activities with HCPs, sponsoring of projects in health institutions and of sponsoring of scientific meetings and manifestations. All companies were also involved in service agreements with HCPs. These activities are linked to the financial relations that need to be reported in the Dutch Transparency register, except for hospitality (but that will follow in 2015 via EFPIA). As effective activities for companies are judged, hospitality activities with HCPs, sponsoring of projects and of scientific meetings and manifestations, and service agreements with HCPs.

In the Dutch self-regulation setting, almost everything a company undertakes can be regarded as promotion. The general rules require responsible behavior, taking into account the interest of the patient and public healthcare, and the costs for medicinal products. The Code mentions companies and HCPs as equally responsible for proper behavior. Self-regulation is deemed a success by the involved experts: it creates a level-playing field, and CGR is transparent in its advices. But there is no complete legal certainty, and no full transparency is offered. In general, persons working in pharmaceutical companies know the CGR Code of Conduct and are aware of the guideline on disclosure of financial relationships.

Involved persons in the industry mention several strong points of the Code, but there are more critical statements that can be considered as improvement points, like HCPs don't know the rules of the Code; the Code doesn't apply to Medical Device manufacturers; and in the Code there is no concern for the patient.

EFPIA issued a Code of Practice, and the principle is followed that accurate, fair and objective information needs to be provided, so prescribers can make rational decisions about the use of medicinal products.

5.3 What are the transparency obligations and practices of pharmaceutical companies

Recently in different countries around the world, disclosure guidelines have been adopted and implemented. In some countries this concerns national or federal law (France, United States), in other regions and countries self-regulation codes (EU: EFPIA, the Netherlands: CGR). Several details in the laws and codes differ (e.g. minimum amount to be published, which relationships need to be disclosed, how to publish), but it is clear the disclosure of financial relationships is part of the current standard of ethical behavior between pharmaceutical companies and HCPs/HCOs.

In the Dutch Medicines Act, no disclosure or reporting requirements are described, but since 2011 a self-regulation Transparency guideline has been adopted[155]. The first year the disclosure code was applicable was 2012. Proportionality between the administrative burden and the relevance of the disclosure was an important consideration for the set-up of the disclosure code. This resulted in a minimum amount to disclose an interaction from €500 on a yearly base, and a limited kind of interactions to be published (Service agreements, Sponsoring). Publication is done on a yearly base

[155] CGR, Gedragsregels openbaarmaking financiële relaties, Code Geneesmiddelenreclame, in force since 01-01-2012

on a centralized website. The website[156] is managed by a separate entity: the 'Stichting Transparantieregister Zorg'. CGR initiated the founding and set-up of the web portal. Purpose of the register is to make it possible for patients, to check financial relations between their HCP(s) and the pharmaceutical industry. All involved parties agree with this purpose. The Netherlands is a frontrunner in the development, and has built technical expertise during the development of the register. The current coverage of the register is considered satisfactorily, but relatively a low number of HCPs report their financial relations.

The Dutch regulator, IGZ, has no formal role in disclosure activities, as there is no legal obligation to disclose financial relations. Still IGZ is very interested in the disclosure data, and receives source data from CGR; IGZ uses data from the register as an indicator for specific financial relations. There are no data available concerning the costs of transparency in the Dutch situation. Known is that companies pay €10 per line in the register per year. Other costs involved, like the tracking of payments to HCPs and HCOs, the gathering of the specific payment data e.g. the kind of relationship, registry number, exact amount, and the preparation of the publication on the transparency website, are not known. The cost of transparency is also not internationally prescribed, there is an estimation of costs of nearly $1 billion over 5 years in the US.

Patients need the BIG-registration number of the HCP to be able to retrieve the financial relationships of their physician. The BIG registry allows to find the registry number of all Dutch HCPs. With the BIG-number, the financial relation data can be found on the Transparency register site. The site mentions the activities for which the HCP is paid, and the name(s) of the involved companies.

For HCOs the specific number can be found on the website of the Dutch Chamber of Commerce. With this number, the information on payments to the hospital can be found. The overview that is found consists of all payment to the legal entity, without any differentiation. It is not possible to see to which department of the hospital the payment has been done, neither it is clear the specific goal of the funding.

There is a general interest in more transparency, e.g. hospitals publish certain data about performance and quality indicators. Newspapers perform surveys about quality in hospitals. After the launch in April 2013 of the Transparency data, it seems that press and general public have lost interest.

The register creates awareness with HCPs and industry, and influences the public opinion.No major incidents have appeared since the existence of the register, no connection between the register and no incidents could be established. Still, the accessibility is limited. The register provides transparency aimed at patients that want to check their HCPs, there are no aggregated data of companies, no data clinical trials, and no hospitality data are provided. Only Nefarma member companies have the obligation to publish. A statement is that the register protects the industry, and even that the register could be seen as an 'image' instrument: the reputation of companies improves, and a mention in the register can be seen as a status symbol for HCPs. A question that came up is what patients actually do with the information provided in the register, and if the general public is really interested.

Meanwhile central registration systems are being developed by the corporate headquarters of pharmaceutical companies, as disclosure is an international demand after the adoption of the EFPIA Code. There is a consensus that the workload for companies is considerable, especially it is a challenge to link data for payments to HCPs/HCOs with actual agreements about financial relations.

[156] http://www.transparantieregister.nl/Home

Several improvements could be made to the transparency register, like including hospitality payments over €500 per HCPs per year; payments to patient organizations; financial relations with medical device manufacturers; next to that payments for clinical trials could be added; and payments by non-Nefarma members. Meanwhile CGR is performing an evaluation of the register possibly other improvements follow the outcome of this evaluation, CGR will decide on possible changes.

In most of the companies it seems that the Compliance function is responsible for transparency activities. Most of the pharmaceutical industry co-workers from the survey, know the transparency register and deem the register useful. It is seen as an important and necessary step in regulating financial relationships between HCPs and the industry. Still there are doubts about the data in the register: are these all relations? are these the real data? is transparency guaranteed? The co-workers find it hard to retrieve data in the register. For companies disclosure is a real administrative hurdle, and by some it is considered an action to satisfy a political hype. Some skepticism is expressed by one of the respondents of the survey: 'Nobody looks anymore, until a journalist will start digging in it'.

There are strong points of the register recognized: transparency itself, positive influence on the bad reputation of companies, you can check your treating physician, and the register is supported by HCPs, HCOs, and the pharmaceutical industry. But there are many perceived weak points mentioned by the respondents, especially about the scope of the register that is too small, no external check of the data, and about the information within the data: the data leave room for interpretation, the data in the register don't provide the 'why' behind the amounts, so misinterpretation is possible, and it's unclear which actual conclusions regarding influencing can be made. Companies don't use the register for their own data searches, to check e.g. competitors, or specific HCPs/HCOs. Within the pharmaceutical system, transparency can be an important aspect in further increasing the integrity of the industry.

Patients have a fundamental 'Right to Know', and in studies a 'large minority' wanted to know the relation between their HCP and pharmaceutical companies. Most of the patients didn't think that the information would affect their decision to participate in a study. It is concluded that most participants in clinical trials can't judge the risks of financial relations. It is unclear if transparency for patients has an added value in the relationship of the HCP and the patient, and if the trust level is increased? The effect of the right to know could be limited.

Experts would welcome a 'dose of sunshine'. Still they express skepticism concerning the effect of disclosure on patients and their view on prescribers, and their response to the disclosed data. There are pleas for 'learned intermediaries' to assess and analyze disclosed financial relationship data. 'This sunlight must be filtered through the lens of a capable, motivated intermediary'[157]. It is shown that the patient isn't always able to judge payments to physicians by pharmaceutical companies. It could be more accessible for 'ignorant' patients and gives them the possibility to choose their doctors, based upon these 'filtered' data. Uncertainty exists about the behavior of industry, e.g. because of under-reporting, or misclassifying payments into a non-reportable category.

There is no evidence that disclosure affects the marketing practices of the industry. Companies only disclose data after legal requirements are enforced. Also there are efforts of external organizations to compare disclosure data, e.g. 'Dollars for Docs', Has Your Health Professional Received Drug Company Money?[158] And under the influence of the FCPA the pressure on the industry is getting stronger.

[157] Meredith B. Rosenthal et al. Sunlight as Disinfectant — New Rules on Disclosure of Industry Payments to Physicians, N Engl J Med 368;22: 2052-2054
[158] ProPublica. Dollars for Docs. 2014. http://projects.propublica.org/docdollars/

Meanwhile transparency seems no discussion topic anymore, and the Dutch register has a positive effect on awareness of HCPs, industry, politics, and the general public. Still the impression exist that the register does not improve the reputation of the industry, and that the public interest is limited. It could be too early, after two years of disclosure, to draw any conclusions, as the data don't show any changes in financial relationships, and no increasing interest of the public or press.

5.4 What is the role of the compliance function in transparency in pharmaceutical companies in the Netherlands

A specific role of a Compliance function in disclosure activities isn't described, not in legal texts, industry guidelines or literature. From the research it is clear an added value of Compliance in transparency activities is demonstrated. Compliance should play in transparency activities, to comply with the specific disclosure requirements.

The specific role of Compliance can be a coordinating one, as a 'guard' of disclosure (set-up, implement and maintain an effective system with the optimal technology, including checks of the system), but the role for Compliance should be formalized. Next to that Compliance should raise awareness within local organizations, and also in the international setting. The regulator (IGZ) considers that all transfers of value with HCPs and HCOs should be under the organization of Compliance.

In the disclosure initiative and set up of an effective system of transparency within the pharmaceutical industry, Compliance can play a leading role. With a thorough knowledge of the legal framework and industry codes, with experience in the business and the interactions with customers, in a central and independent role in the industry and/or a company, having a broad view on how companies operate internally, including transfers of value, the Compliance function has added value, and can contribute to a more transparent business model to show that the pharmaceutical industry is a valuable and reliable stakeholder in the pharmaceutical healthcare sector.

5.5 Recommendations

Pharmaceutical companies in the Netherlands should have a full Compliance program that could follow a corporate initiative. It would benefit companies as such a program can be part of the monitoring policy of the Dutch healthcare regulator (IGZ). The principle can be followed that companies with an established operating Compliance program will get lower priority in the monitoring system of IGZ, and the program could decrease the amount of a fine in case of a possible infringement.

Improvements need to be established in the Dutch disclosure system, and the transparency register. The impression exists that not everything is transparent. Some improvements will be implemented others need to be considered: HCPs need to get more aware of their disclosure responsibilities, and the register should be more visible, the transparency awareness needs to increase. The disclosure code should be applicable for manufacturers of Medical Device manufacturers. The register is set-up for the patient, the patient needs to be involved more in the information and the accessibility of the information in the transparency register. More disclosure data can be added: hospitality payments, financial relations of companies with patient organizations, payments for investigators in clinical trials with pharmaceutical products and medical devices. It should be considered to provide the aggregated data per company.

The payments in the register are not always up-to-date. Instead of a yearly upload of the data, an upload every quarter can be considered. Technically it is no problem it would make the register more actual. A more sensitive topic is a regular check of the data in the transparency register. Stichting

Transparantieregister Zorg could provide such an independent check linking payments by companies with the publication in the register; it will give the register more credibility. Cooperation of companies, HCPs and HCOs, and the 'Stichting' needs to be intensified. If there would be cases of non-compliance, the concerned company should be sanctioned. The patient would benefit from such a development as the data will be more reliable.

The data should be more relevant for patients, at this moment it is almost impossible to interpret the amounts mentioned for HCPs and HCOs. The register needs to provide more clarity about the 'why' of the payments from companies to prescribers and health institutions, more relevant information should be provided by pharmaceutical and medical device companies about the purpose of the financial relations. It will make interpretations by patients more valuable, and patients are more able to draw conclusions from the amounts paid to their doctor. The register should provide more background information about relations between companies and prescribers and health care institutions.

The body of data in the register could be assessed and analyzed by 'learned intermediaries' to give a more general view on the aggregated data, to watch trends and give more general transparency (as there is now only transparency per HCP or HCO). Such an intermediary can even check payments on prescribers level to analyse the effect of payments on prescription on HCP level. Of course the privacy aspects need to be taken into account. As such a 'learned intermediary' a health insurance company could act, as insurers in the health care field can see prescription behavior of individual doctors. The reports of the such intermediaries can benefit patients in their interpretation of payments to their doctor.

The Transparency register will be evaluated by companies, prescribers, press and critical individuals. Also patients and patient organizations need to play a role in the evaluation and the consequences for the register.

Make the register more known to the general public. Instead of waiting for the press at the moment new data are published, the transparency register could proactively seek publicity, and even start a promotion campaign, to attract more traffic on the register website.

The regulator could be more open about the fact it uses the data of the register actively. It makes the register more credible, and can even raise awareness with companies, prescribers and patients.

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7. List of abbreviations

BMJ	British Medical Journal
ACM	Autoriteit Consument & Markt
BIG	Beroepen in de Individuele Gezondheidszorg
Bogin	Bond van de generieke geneesmiddelenindustrie Nederland
CGR	Code Geneesmiddelenreclame
CME	Continuing Medical Education
CMS	Centers for Medicare and Medicaid Services
CPB	Centraal Planbureau
EFPIA	European Federation of Pharmaceutical Industries and Associations
FCPA	Foreign Corrupt Practices Act of 1977
FIDIN	Fabrikanten en Importeurs van Diergeneesmiddelen in Nederland
FSGO	Federal Sentencing Guidelines for Organizations
GFB	Stichting Gedragscode Farmaceutische Bedrijfstak
HCO	Health Care Organization
HCP	Health Care Professional
IFPMA	International Federation of Pharmaceutical Manufacturers & Associations
IGZ	Inspectie voor de Gezondheidszorg
ISFG	Instituut voor sponsoring en fondsenwerving in de gezondheidszorg
IVM	Instituut voor Verantwoord Medicijngebruik
JAMA	Journal of the American Medical Association
KAM	Key Account Manager
KNMG	Koninklijke Nederlandsche Maatschappij tot bevordering der Geneeskunst
KNMP	Koninklijke Nederlandse maatschappij ter bevordering der Pharmacie
KNMvD	Koninklijke Nederlandse Maatschappij voor Diergeneeskunde
KOL	Key Opinion Leader
LHV	Landelijke Huisartsen Vereniging
NAPA	Nederlandse Associatie Physician Assistants
Nefarma	Vereniging innovatieve geneesmiddelen Nederland
Neprofarm	Nederlandse Vereniging van de Farmaceutische Industrie van Zelfzorggeneesmiddelen en Gezondheidsp
NFU	Nederlandse Federatie van Universitair Medische Centra
NPPTP	National Physician Payment Transparency Program
NVZ	Nederlandse Vereniging van Ziekenhuizen
OIG	Office of Inspector General
OMS	Orde van Medisch Specialisten
PhRMA	Pharmaceutical Research and Manufacturers of America
PPSA	Phycisian Payment Sunshine Act
R&D	Research and Development
UN	United Nations
US	United States
USSC	United States Sentencing Commission
V&VN	Verpleegkundigen & Verzorgenden Nederland

8. Appendices

Survey questions (see 4.3 Survey on Compliance and the Transparency register)

Company and function information

ID	Question	Selection Check or Circle best answer	Explanations and Comments
1	Your position	CEO Marketing & Sales Legal Compliance Medical	Other:
2	How many employees has your company	1-5 6-20 21-50 > 50	
3	Where is the headquarters for your company located	United States United Kingdom Germany	Other:
4	Which best describes your company?	Affiliate Independent	

Compliance function in your company

ID	Question	Selection Check or Circle best answer	Explanations and Comments
5	Does your company have a GLOBAL compliance officer?	Yes No Don't know	
6	Does your company have a LOCAL compliance officer?	Yes No Don't know	
7	The GLOBAL compliance officer is part of the following department:	Legal Medical Finance	Other (please explain):
8	The LOCAL compliance officer is part of the following department:	Legal Medical Finance	Other (please explain):
9	What is the purpose of your GLOBAL compliance function		Please explain:
10	What is the purpose of your LOCAL compliance function		Please explain:
11	Are you satisfied with your GLOBAL compliance function	very satisfied satisfied somewhat satisfied not satisfied	Comment, if necessary
12	Are you satisfied with your LOCAL compliance function	very satisfied satisfied somewhat satisfied not satisfied	Comment, if necessary

Marketing & sales activities of your company

ID	Question	Selection Check or Circle best answer	Explanations and Comments
13	How many Marketing & Sales functions (fte's) has your company worldwide		
14	How many Marketing & Sales functions (fte's) has your company in the Netherlands	1-10 11-20 21-30 31-50 > 50	
15	Which activities does your company apply (acc. to CGR code of conduct):	More options possible: o hospitality (travel, lodging and registration fees for a meeting/manifestation) o sponsoring of a meeting or manifestation o sponsoring projects of an HCO o free samples o observational (non-intervention) studies o gifts o service engagements (e.g. consultants, advisory board members, speakers)	Other (please explain):
16	Which activities of your company are effective:	o hospitality (travel, lodging and registration fees for a meeting/manifestation) o sponsoring of a meeting or manifestation o sponsoring projects of an HCO o free samples o observational (non-intervention) studies o gifts o service engagements (e.g. consultants, advisory board members, speakers)	Please rate: very effective effective somewhat effective not effective
17	Do you know the content of the CGR Code of Conduct	yes no	Comment, if necessary
18	What are in your opinion the strong parts of the Gedragscode Geneesmiddelenreclame (CGR)		Please explain:
19	What are in your opinion the weak parts of the Gedragscode Geneesmiddelenreclame (CGR)		Please explain:

Disclosure requirements

ID	Question	Selection Check or Circle best answer	Explanations and Comments
20	Are you aware of the CGR guideline concerning transparency	Yes No	
21	Is you company reporting according this CGR guideline (see previous question)	Yes No Don't know	
22	Which function in your company is responsible for the disclosure activities:	Marketing & Sales Legal Compliance Finance Medical	Other:
23	What is the workload for transparency activities (fte's):	0-0,5 0,6-1 1,1-2 > 2 Don't know	
24	With how many Health Care Professionals has your company financial relations	1-10 11-20 21-30 31-50 51-75 76-100 > 100 Don't know	
25	With how many Hospitals and Health Institutions has your company financial relations	1-10 11-20 21-30 31-50 51-75 76-100 > 100 Don't know	
26	How does you company handle the transparency data:	Excel sheets Don't know Automated system (please explain)	If you work with an automated system, please explain

Transparency register

ID	Question	Selection Check or Circle best answer	Explanations and Comments
27	Do you know the transparency register	Yes No	
28	What in your opinion is the purpose of transparency register	extremely useful very useful useful hardly useful not useful	
29	What is your impression of the transparency register		Please explain:
30	What are the STRONG parts of the transparency register		Please explain:
31	What are the WEAK parts of the transparency register		Please explain:
32	How could the transparency register be improved		Please explain:
33	Do you check the transparency register for financial relations with health care professionals	Yes No	Please explain:
34	Do you check the transparency register for financial relations with Hospitals and Health Institutions	Yes No	Please explain:
35	Do you check the transparency register for activities of other companies	Yes No	Please explain:
36	Do you think the compliance function should play a role in the transparency activities	Yes No Don't know	Please explain:
37	How can the compliance function play a role in transparency activities		Please explain:
38	The compliance function has added value in transparency activities	strongly agree agree somewhat agree disagree strongly disagree	Please explain:
39	The transparency register has a positive effect on the marketing and sales activities of my company	strongly agree agree somewhat agree disagree strongly disagree	Please explain:
40	The transparency register improves the reputation of the pharmaceutical industry	strongly agree agree somewhat agree disagree strongly disagree	Please explain:

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