

# **Background Study on the Influence of Three Industrial Sectors on Knowledge Development in Biomedical Research**

Dr. Samantha A. Adams  
Rik Wehrens, MPhil  
Prof. Dr. Roland Bal

Instituut Beleid and Management Gezondheidszorg  
Erasmus Medisch Centrum, Rotterdam

## **1. Introduction**

Public health and health care are situated within a hybrid environment, where diverse economic, social and political forces are at play. Innovations necessary to improving health emerge from a complex institutional interplay involving diverse stakeholders with differing perceptions of value. (WHO, 2006) Academic research groups must interact with, and establish their place in, this hybrid environment with multiple actors, where various factors influence the nature of research being done. Groups simultaneously shape the environment and are shaped by it, relying upon the different actors for resources such as funding, legitimacy, information, instruments and know-how. (Van der Weijden, 2007)

The Dutch Advisory Council on Health Research (RGO, 2007) distinguishes between two types of factors (intrinsic and extrinsic) that influence biomedical and other health-related research programs. They suggest that push (intrinsic) factors are inherent to the research world, such as the available infrastructure, national and international trends within a specific research field and a given medical center's research policy. Extrinsic, or pull factors, by contrast, include influences stemming from external financing, international trends and explicit societal needs (and in the case of university medical centers, patient care). (RGO, 2007) Among the pull factors is the increasing presence of external financing coming from a mix of government, charitable and industry funds. Van der Weijden (2007) explains the well-known four-flow funding structure for research in the Netherlands: first flow of funding is provided for in university budgets, the second flow stems from (intermediary) government and EU research programs, the third flow, from charitable organizations and the fourth flow, from industry. The work of van der Weijden (2007) reflects that, despite variations at the departmental level, medical and health research groups generally rely to a large extent on external financial resources

Given the increasing dependence of academic research groups in the Netherlands on external sources for funding research, there has been an increase in national attention for what these different financial pull factors mean for the nature of research being done. International publications, such as Callahan's (2003) book entitled "What price better health?" have only contributed to growing national concerns about conflicts of interest in various phases of knowledge development. Callahan traces the history of biomedical research in the United States and the gradual development of what he calls the research imperative. He argues that there is a failure in the current system that is attributable to how funding practices influence academic research. Although Callahan criticizes the roles of both public and private sector funding in this failure, it is the issue of private sector funding that receives the most attention.

One dominant line of thought regarding health- and medicine-related R&D, correct or not, assumes that industrial players (most especially, the pharmaceutical industry) determine what progress in innovation is made by controlling where research investments go and what research lines are stifled in the process. Various authors (see, e.g.: Kleinman, 2003; Metlay 2006) have explored how industry connections shape academic cultures, and what this

means for the publication of research results and wider dissemination of knowledge (Sismondo, forthcoming). A collection of essays and interviews put together by Health Action International (HAI, 2006), repeatedly points to the dominance of pharmaceutical commercial interests over public health interests in health-care agenda-setting, as well as to the need for a counterweight to this industrial influence, most especially a voice that advocates for patients and consumers and their specific health needs. Nestlé (2002) makes similar claims in her book on the different ways that the food industry influences nutrition and health.

Hopkins (2004), however, challenges this line of thought by making an important distinction between what he calls artefact-led change and technique-led change. Artefact-led change, according to Hopkins is the well-known development structure wherein networks of firms and professionals develop novel services through traditional R&D processes. Where this type of research and development is done, there is room for the industry to influence knowledge development and distribution in different phases of the research process. Technique-led change, in contrast, is a lesser-known form of research and development whereby new technologies are developed within networks of non-commercial groups. With this type of research, diffusion and change take place largely in an ad hoc, 'bottom-up' manner and industrial groups play little to no part in the earliest phases of research. Commercial actors, Hopkins argues, only become relevant in later phases, once a new product or process is well-established and non-commercial groups need help specializing products or automating production. Hopkins further argues that for both types of research it is not just financial resources, but also other factors, such as the tacit knowledge and professional norms, which influence knowledge and product development and diffusion.

### 1.1 Project background

Meeting the demands of different groups in various phases of research and development (R&D) processes often presents seemingly insurmountable challenges and it has been suggested that there are simply too many organizations involved in certain innovative processes, such as pharmaceutical development. (RGO, 2005) Despite the fact that the conflict between commercial and social interests is widely acknowledged (Permanand and Altenstetter, 2004), the influence of industry on research remains a socially sensitive topic (Steenhoek, 2008). Nonetheless, the willingness of different actors involved in innovation policy and processes to address specific R&D challenges is changing. ('t Hoen in HAI, 2006) Neither traditional policy techniques nor traditional market techniques have proven sufficient for handling complex issues related to the innovation processes that lead to demonstrable health gains. Not only is there increasing recognition that assumptions about the corrective power of market forces are not proving true (Trouiller et al, 2001), leading to the need for alternative development structures, but also many policy areas have felt the need, in some way or another, to revise their traditional steering mechanisms and have developed new policy instruments to that effect.

With an eye on these issues, the Health Council of the Netherlands (Gezondheidsraad) is working under the Center for Ethics and Health (CEG) on a policy description report that addresses the issue of the influence of three health-related industry areas (pharmaceuticals, diagnostics, and food/nutrition) on the production of bio-medical knowledge. One question receiving special attention is: what necessary and beneficial research is not being done and why? Gaps in research may appear to be easily identifiable, simple issues at first, but have proven to be difficult and complex problems that are related to a spectrum of other ethical, institutional, economical and political issues. For this reason, it is important to understand how bio-medical knowledge is developed and disseminated, what values govern these processes, and what this means not only for medical care but also for public health.

At the outset of this project, the process of knowledge production was divided into four phases: agenda-setting, development of knowledge, dissemination of knowledge and practical application of knowledge. The Department of Health Policy and Management

(iBMG) of the Erasmus MC was asked to provide a background document on the first phase of knowledge development - how research agendas are created. While we agreed to conduct research on the first phase mentioned above, we also indicated that, because research is often cyclical, rather than linear (WHO, 2006), the distinction between the four phases is not black and white. Different phases can be blended in practice, where both informal and formal aspects play a role, such that agendas for research may be changed during the development, dissemination, or even application, of knowledge gained from specific research and development processes.

This background document gives an overview of research conducted between June and September, 2008. We begin with an overview of the research questions specific to this background study and the methodology used. In the results section, we first give a general overview of results that cross all three categories, followed by category-specific information. In the discussion we first answer the research questions and then reflect on these issues in light of further research and public health interventions.

## **2. Research Questions and Methodology**

In order to address the general question of how the pharmaceutical, diagnostic and food industries influence the development of biomedical knowledge, we formulated the following research questions:

1. What are the most important groups in the Netherlands involved in pharmaceutical, diagnostic and food research?
2. How are research agendas developed within these groups?
3. Where is the influence of different industrial sectors evident in the agenda-setting processes of these groups?

The research consisted of two phases: desk research and interviews. We began with a literature study of currently published articles in order to gain an overview of both national and international perspectives on the topic. We used Scopus, an Elsevier abstract and citation index that delivers results from all academic disciplines, as well as news resources, patent office reports and websites. It searches existing databases, such as Medline, cutting out redundancy in the search process. Due to time limits, we were unable to search the Cochrane database, despite this being suggested by several interviewees. To supplement out literature search, we then reviewed websites, which provided not only an overview of specific research groups and institutions within the Netherlands, but also access to pre-publications or other research-related information from well-known authors who focus on the topics at hand. We then used a snowball method to gather further articles and names for potential interviewees.

The second part of this study comprised a number of semi-structured interviews with key stakeholders in the field. In the context of this study, a total of 21 interviews with 23 respondents were conducted, whereby 11 interviews (including 2 duo interviews) were conducted by iBMG and we used 10 interviews conducted by the Gezondheidsraad. Of these interviews, 11 interviews focused solely on the pharmaceutical industry, 4 focused solely on the food industry, 1 focused solely on the diagnostic industry and 5 were cross-category. Because there is interest in what the conclusions of this study mean not only for biomedical research but also for medical practice and public health, we also interviewed persons that could link the industrial areas to these fields.<sup>1</sup> All interviews were summarized from written

---

<sup>1</sup> One drawback to the study was the inability, for practical scheduling reasons, to schedule interviews with researchers at the Top Institute for Food and Nutrition (TIFN, see the sub-section on Food in the Results section below). They have indicated willingness to participate in an interview, but were unable

notes and two interviews were transcribed from recordings. For thirteen interviews, a member check was done. The remaining five must still be completed. The transcripts were divided according to relevant industry topic prior to analysis. Cross-category interviews were reviewed as a separate category, in order to establish links/themes that cut across all categories.

### **3. Results**

#### **3.1 General Results**

The first thing we noticed in this research project is that the overarching question is problematic, not so much because of the scope of what it tries to cover, but because it presupposes “an industry” in each of the three areas. However, it is impossible to view industry in any of these areas as a homogeneous structure. As our interviews within the food industry reflected – talking to 4 persons from 4 different departments within one company (that is situated in one branch of the food industry) reveals very different relationships with the public sector, depending on departmental research needs. The same is true of the pharmaceutical and diagnostic industries, where the problem is further complicated by the rise of smaller biotechnology and niche firms, which may not be major players, but are nonetheless commercial enterprises. (Schmid and Smith, 2004; Light, 2006; WHO, 2006; PWC, 2007) This point will be further illustrated in discussions of industry in each of the three sections below.

A second result is that it is difficult to explicate how agendas are set and research decisions are made in the relationship between public research groups and all three industrial sectors. Public research in the Netherlands is a large, broad-sweeping field and research activities are diverse. (Gezondheidsraad, 2008) Allocation of resources for research is complex and divided between multiple agencies. (van der Weijden, 2007) Outside of specified fourth-flow research funding, where and when links between universities or public research institutions and the private sector are made is not always clear. Such fourth-flow funding varies greatly between different biomedical sub-disciplines. (van der Weijden, 2007) Further still, despite calls for more transparency in e.g., the pharmaceutical industry, we know very little about concrete processes (Permanand and Altenstetter, 2004) and there is a lack of feedback on which research strategies produce which outcomes. (Schmid and Smith, 2004) Out and Broekmans (2007) suggest that many criticisms levied at the pharmaceutical industry are a direct symptom of insufficient knowledge about the processes in place there. They further argue that these misconceptions inhibit positive collaboration with universities. Similarly, Frantz (2006) argues that an air of mystery continues to surround the field, consequently leading to the trivialization of many problems related to R&D strategies. Knowledge of the issues at stake and daily practices in the pharmaceutical arena are far greater than in the other two areas of study, although attention for the food industry is on the rise. Nonetheless, we still see recognition for the lack of concrete descriptions of how agenda-related decision-making processes work. Consequently, insights into cross-sector collaborative practices are also often lacking. This is especially evident in sections 3.2.3 and 3.4.2, which address Public-Private Partnerships in the pharmaceutical and food industries, respectively.

All of these authors suggest the need for more research, but few of them point to what type of research is necessary. If we consider the point by Schmid and Smith (2004), that hundreds of R&D decisions must be made to get one product to the market, as well as the aforementioned point about feed-back loops, then we realize that sufficient knowledge on these processes can not be gained through short-term research. There is a dearth of detailed description in the literature, and interviews within industry also do not provide answers that

---

to do this prior to the end of September. We recommend that the Gezondheidsraad consider supplementing the current interviews with an interview with members of TIFN.

tell us more than, “we follow the market” or “we respond to public criticisms.” As Zuiderent and van der Grinten (forthcoming) point out, for medical technology industries, the market is ill-defined and actually comprised of multiple markets, depending on the technology and targeted user-group in question. What a market is and how it is shaped in what circumstances becomes a new empirical sub-question specific to a given product and/or social group. (Callon, 1998) Getting into the politics of scientific cooperation between different parties (both public and private) requires longer-term, ethnographic research, which provides an in-depth and situated study of multiple sites. (Penders, 2008)

A third finding is that the research gaps most frequently pointed to in the interviews and literature, for all three industrial areas, is not on the level of *basic* biomedical research (which largely falls under public sector), but on level of *applied* research (which generally belongs to the private sector). Gaps in the research agenda arise at the point of (pre-) clinical trials, public health interventions, post-market surveillance, and comparing the therapeutic value of new medicines. (Mossialos et al, 2004; Pecoul et al, 2004; Weely and Leufkens, 2004; Out and Broekmans, 2007) Knowledge gaps arise, thus, in the transition from public to private research phases and in those phases that largely fall under the discretion of industry. We return to this point in sections 3.2.2, 3.3.2, 3.4.3, where we discuss research gaps in each of the three industrial areas, as well as in the discussion.

### 3.2: Pharmaceutical R&D

Research conducted on pharmaceutical development has historically been understood as falling under the domain of “Big Pharma”, the large companies that are major players in the international arena. However, more recently, this understanding has been changing. This is due in part to changes in (supra-)national regulatory structures, which have trickled down to create change in research, funding and care structures. A catalyst in the already changing system was the groundbreaking report from the World Health Organization on Priority Medicines (Kaplan and Laing, 2004) that led not only to renewed political interest in agenda-setting for so-called “Orphan and Neglected Diseases” but also to renewed research interest in Public-Private Partnerships. In this section, we first examine changes in research structures over the past 20-30 years, followed by a discussion of research agenda-setting strategies. We then point to developments in Public-Private Partnerships and reflect on the influence of the pharmaceutical industry on agenda-setting for biomedical research that we see in these changes.

#### *3.2.1 Changes in Research Structures*

Pharmaceutical research and development take place at the intersection of three (often competing) inputs:

1. The free, but regulated, market (where economic considerations play a strong role),
2. The (bio-)medical sciences (where strict demands are placed on knowledge and practice)
3. National and supranational governments (which carry the responsibility for regulating products, promoting public health and making health care accessible). (Permanand and Altenstetter, 2004; WHO, 2006)

Competing within the market is a multitude of players who can be considered part of the “industry”. The obvious players are the large pharmaceutical companies as mentioned above that have longer-standing status in the field. These include names such as GlaxoSmithKline, Bristo-Myers Squibb, Pfizer, Merck, etc. Smaller companies and companies in other countries have different commercial imperatives than those that govern research in pharmaceutical companies. Advances in molecular biology over the last 30 years have given rise to the biotechnology industry, which often comprises companies that are spun-off from university laboratories. (WHO, 2006) These labs have become key drivers of R&D methods in the pharmaceutical industry, offering additional opportunities for the discovery of new

medications and drug application forms, as well as new combinations of the two. Appropriate application forms for medications are crucial to enabling further clinical research. (Steenhoek, 2008) Perhaps the best known biotech company of this sort is Genzyme. However, what began as a small break-off start-up has grown to a major competitor. Most biomedical companies are not this large, with 100-200 employees. Examples of such companies in the Netherlands include Prosensa, Pharming, OctoPlus, and Crucell. Other types of small firms with important roles in pharmaceutical research are Clinical Research Organizations (CROs)<sup>2</sup>, which generally employs experts on toxicology, chemistry and medicine metabolism, and Drug Delivery Companies (DDCs). Most sponsored clinical trials are handled by CROs (Sismondo, forthcoming), which currently manage 40-45% of “big pharma’s” volume. (SustainAbility, 2007) One example of a CRO is Quintiles, which advertises itself as the world's largest CRO. (Simondo)

Attention for the current commercial pharmaceutical R&D structure has pointed to a system that is not sustainable. Changes in policy at an EU level and differences in state regulatory policies trickle down to the industry by influencing the market. On the one hand, the process of pharmaceutical development has become more predictable. There are, for example, similarities between assessment procedures in the different member states. On the other hand, it carries more risks – that is, the chance of working on a medicine only to have it rejected in an early phase increases. This means higher risks for smaller biomedical research companies that may not have the necessary injection of capital, as well as fewer incentives for researchers in academia to engage in projects that are either not well-funded or not high-profile enough. (Light, 2006; Fehr, et al, 2006) According to Leufkens (2007) companies are in the midst of an innovation paradox: progress in molecular and life science is probably more fascinating and challenging than ever before, yet pharmaceutical R&D is not delivering innovative products in line with expectations. More money is being devoted to research, but there is a lack of productivity in the lab. (PWC, 2007) Although questions about drops in productivity are not new, but rather, reflect typical trends in innovation cycles (Leufkens, 2007), there are concerns about emerging research gaps.

Agenda-setting is proposed as a solution to the problems of the pharmaceutical gaps. Understandings of agenda-setting, however, vary in different domains. Selecting diseases of focus and/or active ingredients for potential development into marketable medicines is a diffuse process. With political agenda setting, diseases and medicines (the problems and gaps) are identified first and then necessary research and development to address those problems is considered. In contrast, with industrial agenda-setting, development is often the primary consideration. As a result, those products with indications of good profit potential (large numbers of patients, chronic use of medicines) are selected above those with less market potential. (Trouiller et al, 2001) The industrial process is thus converse to the process that is expected in policy-circles when agenda-setting is discussed. Where there is an apparent notion that striving for better agenda-setting will solve knowledge-gap problems, these different understandings of agenda-setting imply that this is not enough.

### *3.2.2 Research Agenda-Setting Strategies*

Schmid and Smith (2004) break open industrial agenda-setting and align different strategies with different types of companies. Because the pharmaceutical sector is not only slow-moving, but also high risk, high reward we see a stratification of approaches to R&D that vary

---

<sup>2</sup> The work of Prof. Trudy Dehue from the University of Groningen is also interesting in this context. She has conducted research on the rise of CROs and the consequent changes in data-collection, whereby testing and marketing increasingly become intertwined. She presented this work in a presentation entitled, “Merging Trials and Publicity: An STS perspective on commercial clinical trial research,” at the 4S/EASST conference in Rotterdam, the Netherlands, 21 August 2008. Because her work is not yet published, formal reference was not possible at the time of writing. [T.Dehue, personal communication, 1 September 2008]

from calculated strategy to trial and error and betting on luck. In their classification, an example of calculated strategy would be investment in generics, followed by niche originators. Biotech companies are able to lean more toward luck and are therefore frequently regarded as being more innovative than larger companies. However, although this might be true for the combined pool, the individual company is not necessarily going to produce a new medicine because they tend to follow one risky strategy, while a larger firm can follow multiple strategies simultaneously.

The further towards either end of the continuum a company progresses, the more it becomes locked into specific skills bases and capital assets. (Schmid and Smith, 2004) Larger companies have more flexibility to adopt new operating structures that remove barriers to productivity. (Owens, 2007) Companies are currently facing the challenge of ensuring that their strategic R&D decisions support a smooth transition to more targeted portfolios, whereby choices of what products or processes, specifically, to focus the research agenda on also becomes more important. (SustainAbility, 2007) Companies are working further to remove redundancies and develop more productive research management structures and cultures through internal restructuring and the creation of a more “small-company” culture. (SustainAbility, 2007) At the same time larger companies can form more strategic external alliances with one another and with other players in the field (including academic research institutions) (SustainAbility, 2007) and also move into the niche market by conducting a number of small-scale acquisitions of smaller biotech firms. (Owens, 2007) These changes in business approach enable the application of current advances in pharmacogenomics<sup>3</sup>, which, in many cases, means salvaging previously abandoned projects. (SustainAbility, 2007) But, to be successful in these new business models, there is an emphasis on the need to be more networked and collaborative with multiple actors than was the case in the past.

Generally, the pharmaceutical companies and political decision-makers at national and international levels co-determine (public) research agendas. (Mossialos et al, 2004; Fehr, et al, 2006) The public sector (through academia and other institutions) provides the technology and ideas for research on a given medicine, while pharmaceutical companies are mostly expected to translate the expertise provided by the public sector into safe and effective medicines. Although the *private* sector claims to be the largest investor in global pharmaceutical research and development, Light (2006) points out that this is mostly applied research, including clinical trials, rather than in basic biomedical research. Light refers to evidence that governments, companies in *other* sectors, and public funds actually provide the bulk of funding for *basic/upstream* biomedical research,<sup>4</sup> which is necessary for generating knowledge that is later used by industry for *applied/downstream* biomedical research. Pharmaceutical companies have the capacity and knowledge to investigate and develop potential medicines according to the highest standards and quality and therefore, also the task of bridging the translational research gap, that is, the space between basic research and formal drug development. (RGO, 2005; Croft, 2005; Herrling, 2007) This also means that they are dependent on developments in chemistry and biology, and interviewees pointed to how companies profit from a symbiotic relationship with academic laboratories and research centers.

Sismondo (forthcoming) argues that the pharmaceutical industry's links to medical research are the most prominent and largest connections between industry and academia. This is evident in the comments of one interview respondent that we can no longer conceive of research without pharmaceutical funding and that 60-70% of the research conducted in certain academic medical centers is made possible through the pharmaceutical industry. It is also evident in another respondent's comments regarding the comfort of colleagues with

---

<sup>3</sup> For a clear definition of pharmacogenetics and pharmacogenomics, see Mossialos et al (2004).

<sup>4</sup> See, e.g., WHO (2006) and Steenhoek (2008) for explanations of different types and phases of research.

current conditions for collaboration with industry and personally having a minority position in internal institutional discussions on this issue. Sismondo's article contains demonstrable concern about what he calls the "normalization" of these symbiotic relationships. However, it is important to realize that the normalization of such relationships does not necessarily imply the situation than one would expect, namely the *unidirectional* influence of industry on academia. Quite the contrary: as the WHO report (2006) clearly demonstrates, the universities themselves, especially in the United States, are key players in the development of new biotechnologies. Because intellectual property issues also play a large role, increasingly, the universities develop patent portfolios to protect their work. Further, they encourage competition among industries for the results of basic research, meaning that larger companies must expand the scope of where they look for information and resources (PWC, 2007) and universities also increase their roles in downstream research activities that are carried out in partnership with the private sector. This is reflective of what one Dutch respondent referred to as ways of dealing (*omgangsvormen*) with specific rules of engagement (*spelregels*). We are seeing the emergence of an international system, where universities have had an important role in the patenting of compounds, tests, tools and devices that were developed mainly with support from government funds. (WHO, 2006)

Trappenburg and van den Bovenkamp (forthcoming) argue that although there is a research imperative (Callahan, 2003) in the Netherlands, it is different to that of the United States. This is evident in both the scope of financial injections for research and in the opinion of patient organizations with respect to the need for research. As one respondent pointed out, the absence of large-scale subsidized research programs in the US creates a situation where universities are more dependent on industry funds. In the Netherlands, there is considerably less money spent on biomedical research, from both public and private sources of funding. (Ellenbroek et al, 2002) Trappenburg and van den Bovenkamp further argue that the government has considerably less influence in setting research agendas. As interviewees also pointed out, public calls for research from, for example, Zon/Mw are generally broadly formulated meaning that the research community has considerable latitude to determine the actual nature and content of a research project. Further, universities have the lead role in allocating funding for research.

Interest in and reliance upon external funding from companies varies greatly between departments. Where one university department may lend itself completely to industry projects, another will have a mix of funding sources, such that all researchers do *some* industry work, but also have time and resources for non-industry work. Similarly, the interviews reflect that some departments carry out projects primarily with one company, while others strategically work with funds from multiple (competing) companies. One university professor explained that this last strategy enables the research groups to position themselves better in project negotiations, to create a financial buffer for funding research according to their own interests and to ensure the continuity of their research line over time. According to another interviewee, in university research projects where industry financing also plays a role, the parties tend to be in agreement about *basic* research and the three phases of pharmaceutical R&D that precede registration.

The risks of influence from the industry on the research agenda are always present, but research groups have created ways of dealing with conflicting interests in negotiations. Leaders of the research groups have considerable leverage in negotiating the nature of the research to be done and protecting their own topic interests when setting the research agenda. This is not to say that no problems arise; however, examples of problems mentioned in several of the interviews tend to point to problems during the publication phase, rather

than the agenda-setting phase.<sup>5</sup> The situation should not be dismissed though – if the Netherlands continues to follow EU and international trends in, for example, industry sub-sector developments (small biomedical firms, CROs, and DDOs) then this could lead to changes in public knowledge production, especially where intellectual property is concerned.

### *3.2.3 Public-Private Partnerships*

PPPs are public-health-driven, non-profit organizations that combine efforts with industry groups in order to increase the development of medicines for neglected-diseases. (Moran, 2005) These partnerships create new structures of actors, resources and business models, as well as a sense of urgency for addressing specific health conditions or diseases. Most of the PPPs consist of stakeholders from three different areas: 1) the public sector, including governmental agencies or institutions otherwise controlled by governments 2) the for-profit sector, and 3) the civil society sector (Widdus, 2005). Different partner arrangements are possible and can be placed along a spectrum that ranges from partnerships with individual governments on one end to trans-national partnerships on the other. When individual governments form partnerships with the non-profit sector, the relationship is generally simple, with the government influencing the technical strength of the other party. Trans-national partnerships usually involve a larger number of actors (including several different governments) in a complex grouping, generally reflecting a more visible role of the for-profit sector. (Nishtar, 2004) Examples of existing PPPs include the Top Pharma Institute in The Netherlands and the Innovative Medicine Initiative (IMI), which aims to address specific hang-ups in the product development by pooling resources from industry, academia, regulatory authorities and healthcare providers. (Shreidan, 2006) EU money available for the IMI is matched by the industry. (Interview with a Patient Representative) The major difference between these and prior structures is that government actors are involved in the development process from start to finish, including funding early research and administering advance purchasing agreements.

The need for public-private partnerships arose because of the inability on the part of the public sector to provide public goods on their own, owing mostly to a lack of resources. Although there was little trust in PPPs at first, these partnerships have been gaining ground since 2000 and have demonstrated arguable successes in pharmaceutical development internationally. (Moran, 2005) Most PPPs are now relatively institutionalized initiatives in which actors from different sectors engage in collective decision-making (Buse and Harmer, 2006) and facilitate action for addressing public health goals. Further creation and development of PPPs is generally encouraged, because this type of cooperation is expected to lead to an efficient, effective and equitable manner for providing public goods. (Buse and Harmer 2006, Nishtar 2004, Nwaka 2005) PPPs can be expedient in bridging the translational research gap between basic research and clinical development by bringing together knowledge and expertise from the different academic and industry domains. This is accomplished in part through funding and support from governmental, philanthropic and charitable sources. (Croft 2005, Nwaka 2005)

Nishtar (2004) argues that PPPs create a strong mechanism for addressing difficult problems by leveraging on the varied strengths of different partners. The challenge of placing specific health issues onto national and international agendas has been a longer-term challenge. PPPs have been successful in placing the profiles of various diseases on policy agendas. As a result, they have also made it possible to mobilize additional funding for diverse activities related to these profiles. As Moran et al (2005) discuss, comparative measurement of various drug development approaches reflects that both industry and public groups, when working

---

<sup>5</sup> But again, this is contingent on the agreements made at the outset of research. As three respondents from universities or academic medical centers all pointed out, concrete agreements made ahead of time can take care of most of these types of problems.

alone, performed less well in most of the measurement categories than did the public-private collaborations. Thus, the whole of a given PPP is much more than the sum of its parts, which means that all the individual parties have a share of the skills and resources necessary to develop and establish products and services which are needed by the population. However, not everyone is equally positive about the added value of such institutions. According to an interviewee representing patient interests, patient organizations are not always given the room to offer their input in the creation and structuring of top institutes. Participation in such initiatives often still takes place within a very top-down environment.

Another criticism of PPPs relates to the number and nature of pharmaceutical products. The projected number of developments was much higher than what has been achieved until now and in many cases, these are “quick wins.” That is, resources are devoted to retargeting older medications for new markets. (Bradley, 2007) Or, although new medicines are introduced, they are not necessarily innovative because they tend to be developed within existing research structures. A good example is the contrast between the development of new medicines for cancer and the development of new antibiotics. In the former case, active ingredients can be tested within existing lab samples until a potential target is found. This enables simple reproduction of the research process for a new medicine. In the latter case, testing the fit between a medicine and the problem it is intended to treat demands the use of different samples and additional materials, and may even lead to a restructuring of the entire research process. This slows down the development process and is therefore not favored by PPPs. The discrepancy is reflected in statistics that show that most new orphan drugs are new cancer drugs. Between 1990 and 2005, 49 new cancer drugs were given a priority review by the FDA (DiMasi and Grabowski, 2007). By contrast only 2 new antibiotics were reviewed in that same period (Tickell, 2005).

Optimistic perspectives on PPPs also seem to ignore the fact that conflicting interests remain present and must continuously be (re)negotiated long after the initial bridge-building work has been done. Financial injections from the private sector, for example, can come into conflict with policy programs for public health. Moreover, choosing to focus on one critical area for research stimulus still means neglecting another. (Yamey, 2002; Richards, 2008) As the Patient Representative pointed out, focusing on priorities mentioned in an international report, for example, may mean ignoring important domestic priorities or topics that Dutch research centers have a good capacity to address. This leads to the important question of how we can define and determine the public (interest) aspect of PPPs. Governments and intergovernmental organizations are most often pointed to as the parties primarily responsible for protecting the public interest in these collaborations, however, in of specific cases, non-governmental actors and well-organized patient organizations may also play a role. Should the “first p” be interpreted as referring to specific financial aspects, the presence of government representation, citizen participation, or something broader, such as a public goal that is strived for, but not necessarily by government parties? Social considerations, it is argued, should carry more weight when decisions are made about how to allocate funds for the development of medicines. However, current political discourses and courses of action within Europe still emphasize the importance of innovation, production and industry, rather than social considerations (such as lack of treatment for rare and critical illnesses or budget impact). In addition, critics of current assessment procedures for all medicines have further argued that decision-making relies too heavily on the presence of scientific evidence and not enough on other factors, such as burden of illness or medical need.

#### *3.2.4 Reflection on influence of the pharmaceutical industry on biomedical research*

In contrast to what is often asserted or expected, we see a changing system in the relationship between the pharmaceutical industry and public sector biomedical research, by which there is less *overt* commercial influence on research agenda-setting through, for example, a direct funding impetus for basic research in a specific area. Even more subtle forms of steering, such as those highlighted by Sismondo and other authors looking at the

politics of publishing results, are less evident in these early phases. There is a considerable lack of information about how negotiation works in collaborative structures, such as Public-Private Partnerships, and how top-down structures potentially reinforce old problems related to the dominance of industry over public interest, rather than resolving them.

We do see, however, a primary influence that appears to be indirect. Emerging from the system of 20-30 years ago “Big Pharma” actors dominated development, is a new system with a multitude of players, many of whom work under reduced infrastructure costs and an ability to accept lower profit margins. In most Western universities, as well as in the biotech sector, there is increased pressure to commercialize findings, suggesting a transition away from “pure” research and also indicating that commercial interests are no longer confined to the “second p,” but are also increasingly present in the public sector, as well.<sup>6</sup> With research bases in all phases of pharmaceutical research increasingly shifting out of Europe and North America, many small biotech companies are securing more favorable rights, in form of co-promotion arrangements. (PWC, 2007) Protecting intellectual property rights in all phases of the research and development cycle has played such a strong role in this emergent system that smaller companies and university departments, alike, even when they are “collaborating,” are still encouraged to compete in the manner of industry.<sup>7</sup>

In 2005, major international actors proposed a treaty for Medical Research and Development to the WHO. This treaty called for more transparency instead of continued reinforcement of the international patent system, for the establishment of a needs-based research agenda, and the establishment of new funding systems for health research, that would guarantee open access to relevant compounds developed with public research money. (CPTech, 2005, Dentico and Ford, 2005, Fehr et al, 2006) Further, the treaty proposed a system that would encourage international exchange and technology transfer. A recent report indicates that pharmaceutical investors are also interested in novel discovery platforms for sharing solid data on the early stage pipeline. (SustainAbility, 2007) Several authors offer insights into diverse push (for the start of innovation pathways) and pull (for further downstream) mechanisms, and combinations thereof, that might facilitate these processes. (Callan and Gillespie, 2007; Mrazek and Mossialos, 2003; Light, 2006; Danzon, 2007) Light and Leufkens (2007) point to the need for more open grants and contracts, for which universities and public teams are on equal footing when competing for these. They further suggest the need for R&D that is focused on social priorities and more innovation and suggest that having fewer, but better-designed, trials is preferable to the current research system.

### 3.3 Diagnostic R&D

As a growing number of governments shift the focus of public health programs from treatment of disease to prevention, diagnostic and other predictive technologies are increasing in importance and changing the nature of (also pharmaceutical) research. (PWC

---

<sup>6</sup> The work of Rozendaal (2006) provides a different, but striking, example of this point. His work gives examples of patient organizations that actively seek out researchers with similar interests in their research agenda(s) and encourage a system of competition for the rights and resources to conduct the research in question. According to a representative for patients, this is a new trend, seen in the last ten years or so, but that serves as a model for other organizations to follow.

<sup>7</sup> According to one respondent, universities do not only compete *in the manner of* industry, but also *directly with* industry: “Je kunt het probleem alleen oplossen door óf te accepteren dat er geen marktwerking is en dan moet je daar niet verder over zeuren, óf door bewust een marktwerking te creëren. En dat betekent dat er competitie moet zijn. Er moet dus een eigen agenda worden opgesteld en die agenda moet je in competitie met de industrie uitgevoerd zien te krijgen.” This is of special concern if one considers the information from another respondent, which reflects that, more often than not, academic centers lose in this competition. This respondent suggests that this is because pharmaceutical company research protocols for clinical research are of arguably better quality, whereby they have a better chance of approval than do academic research protocols.

2007; SustainAbility, 2007) However, diagnostic and predictive technologies comprise a very large, very diverse field of scans, tests, devices and other products. While doing interviews for this project we noticed that most persons interviewed for purposes of increasing insight into food and pharmaceutical research, upon hearing the overarching question, mentioned “also having experience in the diagnostic field.” Individual understandings of “the diagnostic field,” however, varied greatly and were linked to the particular research or policy activities of the person being interviewed. The fact that the term can be interpreted in multiple ways also points to the diagnostic industry as a large, multi-faceted entity. Similar to the situation in the field of pharmaceutical research, inter-organizational structures are changing. (Hopkins, 2004) Increasing numbers of small and medium-sized companies are emerging as significant players who deliver various health-care technologies. (Hourd and Williams, 2008) We can therefore question if there even is such a thing as “a diagnostic industry.”

As Zuiderent and van der Grinten (forthcoming) rightfully argue, understanding the relationship between technological development and the protection of public interests benefits only from analysis of a specific technology in relation to a specific interest group. Although it is outside of the confines of this research to delve into any such specific technology, we nonetheless find it useful to outline the different understandings of “the diagnostic industry” that we encountered in the interviews. We follow this with an outline of questions raised regarding the different types of diagnostic products. As is noted above, these problems generally fall not so much under the rubric agenda-setting for biomedical research, but rather, under problems related to research of a technology in practice and post-market surveillance.

### 3.3.1 “Diagnostics”

One interview respondent suggested that it was more useful to speak in terms of medical tests, which is a multi-usable and broader term. Because the idea of a test is also multi-interpretable, we did not follow this suggestion, failing to see the added value of shifting between two ambiguous terms.

Respondents differentiated the following diagnostic process/product categories:

1. Pre-diagnostic processes and devices. This would include different screening programs. Lehoux (2006) lists the following examples of screening: prenatal tests, genetic, blood and cytological tests
2. Classical clinical diagnosis in primary and secondary care. This includes any processes and devices used by physicians in the process of completing the anamnesis for a case.
3. Secondary diagnostics. This category is most associated with industrial R&D. It includes imaging, scopes and scanners, as well as laboratory tests (biochemistry pathology, etc). This area also includes function tests, e.g.: lung capacity breath tests, cardio stress tests.
4. Monitoring. Monitoring health in general, but also monitoring that is specific to following the progress of a given treatment or monitoring side effects.
5. New diagnostics. This includes genetic testing on the basis of a mouth swab, and very expensive total body scans, which are currently not available in the Netherlands, although they are easily accessible across the border in Belgium and Germany.
6. The final category that was differentiated was that of diagnostic self-tests for conditions that provide a result, for example, on the basis of blood or urine samples. This category includes testing technologies that were once used to support the work

of the health professional in practice, but that are, for different reasons, increasingly marketed directly to the consumer and available over the counter (OTC).<sup>8</sup>

In each category identified above, there is a multitude of potential tests and uses. For each of these, there is a lack of evidence regarding the relationship between use of the technology or test in question and improvement in the general health condition of the patient. There is no research into what a test/device actually means for specific population groups, let alone the individual patient. The argument from Steenhoek (2008) that shifting playing fields for pharmaceuticals have led to a loss of ground for hospitals holds true in the case of diagnostic testing. Whereas hospitals once had the freedom to decide which technologies they used for what purposes, this is now largely an issue that is made on a national level. (Steenhoek, 2008) Many new technologies are adopted for use in clinical practice with little or no evidence that their use leads to improved patient outcomes and/or lower overall health costs. (Bozic et al, 2004) Currently the burden of testing for all of the aforementioned diagnostic types falls on the commercial producer of the product in question. However, requirements for testing are not very extensive and industry players do not conduct tests beyond what is required. Generally, tests are allowed on the market once safety can be demonstrated, but there is less attention for sensitivity and specificity of the analysis made on the basis of the tests. This is especially important for care institutions. The burden of testing falls to hospitals, which often have neither the time and resources, nor the number of patients necessary, for providing the research evidence that is desired.

Of special concern for the first four categories of diagnostic tests was whether those who offer the tests have been sufficiently triggered to demonstrate how valid the tests are within health care daily practice. Respondents discussed the need for more evidence regarding the efficacy and effectiveness of diagnostic devices in specific patient populations. Similar concerns were voiced about diagnostic self-tests, although these were even more fundamental concerns about the initial results. One reason that was given for the shift from self-tests for use in health care practice to OTC self-tests for use in the home was the increasing skepticism from physicians regarding the reliability of the results produced. There are several important questions about such self-tests, the most frequently mentioned being how to guarantee the quality of results produced. (Health Council of the Netherlands, 2008) Other questions are discussed below.

### *3.3.2 Research questions*

Health technology assessment (HTA) is an established field of applied research in most Western countries. (Perry and Thamer, 1999; Lehoux and Blume, 2000; Bozic et al, 2004) In a growing number of countries, it is a crucial component of political decision-making processes. This is as much the case for pharmaceuticals as it is for (pre-)diagnostic technologies. However, as is mentioned above, most industrial testing rarely goes further than guaranteeing the safety of a product or device, while academic and medical researchers are more interested in questions of efficacy and efficiency. The articles from Perry and Thamer (1999) and Lehoux and Blume (2000) both voice concerns about the current content of most HTA practices. While Perry and Thamer argue that HTA is fragmented, duplicative and variable in quality, Lehoux and Blume argue that the range of evidence centers too narrowly on safety, efficacy and costs, whereby assessments too often neglect the social, ethical and political dimensions of these technologies.

---

<sup>8</sup> Operative and therapeutic aids, as well as medical support devices were also included in answers as falling under diagnostics. Examples mentioned included devices such as wheelchairs and hospital beds, but also anesthesiology. These are important to the provision of care, but ancillary to other aspects of diagnostics and one can question whether they are specifically diagnostic, or rather, more general health technologies, as classified by Lehoux (2006).

Multiple respondents pointed to the need to research whether different tests and devices actually improve health. That is, what is the benefit for the patient? This is tricky because there are multiple understandings of “health” and what benefits a given individual’s health. (Boon, 2008) The question must be operationalized into a series of different points. There is a need, for example, to understand what values and understandings of illnesses are built into such technologies. (Blume, 1999) There is also a need for more user involvement earlier in the design process. (Lehoux and Blume, 2000; Boon, 2008) Boon suggests the practical reason that more user input in the early stages of development would lead to better uptake patterns once a given technology is on the market. Lehoux and Blume make a more ethically-driven point: more attention for end-users earlier in the developmental phase of a single technology would document the different perceptions of different stakeholders, and also make explicit the power relationships between planners, developers, physicians, hospital managers, decision makers, third-party payers and patients. Willems et al (2007) argue that a more ‘fitting’ kind of evidence than that produced in a Randomized Controlled Trial (RCT) is needed for health technologies that are not pharmaceuticals. Breaking away from the dominant RCT structure would provide room for research projects that take into account the practical use of such technologies. (Jansen et al, 2006; Mol, 2006)

Zuiderent and van der Grinten (forthcoming) illustrate, for example, the dependency of industry on physicians, specific care groups and patient organizations for being able to understand the market for a technology such that design and development of technologies can be sustained. The authors argue that the political focus on cost effectiveness leads to frustration in the development process, whereby these evaluative measures can have a positive influence on securing public interests in the end. Both the large distinction between diagnostic types and the nuanced differences between single technologies become important here. For major diagnostic technologies (CT, MRI, EKG, etc.) hospital managers or purchasers and policy makers may be able to counterbalance some industry interests, while this is much less the case when it comes to other categories of tests and devices.

Lehoux and Blume (2000) further argue that research should not ignore the interest (and impact) that commercial players have in shaping the delivery of specific health services. A related point is what kind of health culture is being created through an increasing focus on prevention and, thereby, diagnostics? The Dutch Ministry of Health, for example, is especially concerned with issues of medicalization and angst in relationship to certain types of diagnostic testing. One aspect is the potential of these tests to turn otherwise healthy individuals into chronic patients. That is, the earlier a given health situation (or risk) is diagnosed, the earlier the patient may begin to use a medication or other product. Is a situation emerging where market forces are engaging in “disease promotion”, rather than promoting health?<sup>9</sup> A second aspect is the issue of patient understanding of tests results. Are individuals sufficiently prepared for the results that self tests, but also DNA tests and body scans offer? Do patients understand the basis for the results (in the case of self tests and body scans) or the creation of risk profiles (in the case of DNA tests)?

One question underlying all of these is whether or not the presence of these types of tests actually increase demand for care. Related to the first aspect mentioned in the previous paragraph, earlier use of medicines and products suggests longer dependence on the health system, which would be a direct increase. Related to the second aspect, while there may not be a direct increase in demand for care, GPs are considered to be important counterweights to the information that is provided through such tests and scans. This may imply an indirect increase in the burden placed upon care professionals to vet against health claims coming from these alternative testing sources. This is a familiar line of argumentation, however, that has been used also in respect to, for example, internet-based health information and

---

<sup>9</sup> A similar argument is made by Dehue (2008) in the case of life-style drugs and by Mintzes (2002) in relation to direct to consumer advertising of pharmaceuticals.

services. Until now, however, in the case of the internet, there has been insufficient evidence to back up this concern. (Adams and De Bont, 2007) Also for diagnostic testing, there are many unknowns.

These different authors point to the need for more research in various phases of research and development of products that goes beyond mere safety. They also point to the need for better understandings of *use* and what this means for health care, which implies a need for more investment in post-marketing surveillance. Addressing these types of questions indicates the need not only for more quantitative measures associated with demonstrated efficacy and efficiency, but also qualitative methodologies that take into account not only differences in specific social or patient groups, but also individual experiences. The challenge lies in funding for research.

### *3.3.3 Reflection on influence of the diagnostic industry on biomedical research*

In this case, the answer to the question of how biomedical research is influenced by industry is double. On the one hand, there is a picture of a fragmented industry with multiple markets, where frustrations arising early in development processes lead to products that do not meet patient needs. On the other hand, much of the research being done uses a diagnostic product in one form or the other, with no guarantees regarding the quality of a product or the outcomes that result from its use, implying a very specific influence of the industry.

One of the interview respondents explained it as an issue of timing in three different processes. The first process is innovation and development (such as the development of a Siemens scanner or a Johnson and Johnson test kit), where one can speak of a commercial development and therefore also a demonstrable role of the commercial enterprises in agenda-setting. The second process is the evaluation phase, where public research is less dependent on industry. This research can still run parallel to that of industry or it can already begin to diverge. The third process is that of policy formation related to implementation, which is a joint responsibility of insurance companies at the macro level, hospitals at the meso-level and individual clinics at the micro level. Whereas the industry has the lead in agenda-setting in the first process, this gradually decreases in the other two, where the responsibility to set the research agenda is left to researchers (process two) or hospitals and other decision-makers (process three). In absence of concrete research programs and rules that span the three processes, the developments are disjunctive, further contributing to the fragmented picture as depicted above. Rather than being coupled to one another, research trajectories within each of these processes often develop sporadically, independently of one another. In all three phases, there is little government influence on the agendas, with respect to both policy and funding.

Where funding is concerned, one of the academic medical center interviewees indicated that the amount of money available from diagnostic companies for research is 1/100 of the amount available from pharmaceutical companies. He also indicated that research proposals for financial support from the non-profit sector have much less chance of success if the topic in question is a diagnostic product. What is the responsibility of the product developer, the medical professional, a non-profit organization, or a government institution, such as Zon/Mw, to provide research funding? Industry impetus is absent beyond what regulations require, but what other areas could actually be argued to fall under the responsibility of the industry? In many cases, hospitals take it upon themselves to conduct small research studies, but these are, again, far from systematic. For many hospitals, the necessary resources for research are unavailable. An optimal design would be regional or network partnerships in research studies, but such a structure is difficult to solidify under the current competitive structure. According to another academic medical center interviewee, the MC has made progress in establishing a research program in this area, but there is still a need for larger-scale studies among multiple patient populations. Research could be stimulated from public programs, but these would need to be more specific in their goals. To address many questions mentioned

in this section, a program that openly encouraged qualitative research projects would be an asset. Studying not only effectiveness, but also the effects, of using specific technologies or interventions, would be a beneficial addition to existing research. (Mol, 2006; Willems et al, 2007)

### 3.4 Food R&D

The focus on food is important because, traditionally, research and development on pharmaceutical and diagnostic products and processes are considered to be directly related to medical *practice*, while research on food and nutrition is linked to more generalized areas of health and well-being. However, there are many areas where food and medicine/bio-medical research intersect and the lines between the two industrial sectors are becoming increasingly fuzzy. (Nestlé, 2002; van Delft, 2006; van der Heide in HAI, 2006) Not only is there new interest in research on nutrigenomics and personalized diets (Penders, 2008), but there is also a growing sub-sector within the food industry that specializes in so-called “nutraceuticals” and a growing market presence of functional foods and food supplements. Each of these areas requires the exchange of information and products, within the food industry, between the food and pharmaceutical industries and between the public and private sectors. In this section, we first explain the aforementioned terms in order to illustrate this increasing intertwinement of the food and pharmaceutical sectors. We then look at the food industry and research structure in the Netherlands, followed by an examination of labeling regulations and how these influence R&D activities. We conclude this section with a reflection of influences on research.

#### *3.4.1 Nutraceuticals, Functional Foods and Nutrigenomics*

Nestlé (2002) argues that the terms nutraceuticals and functional foods are inconsistently and interchangeably used and further links them (together with designer foods) in one lump sum under a new term, “techno-foods.” Although Nestlé is correct that there are no universally accepted definitions for these terms, there are actual differences between the two. (AAC, 2008) The term nutraceutical refers to food extracts that are transformed into basic ingredients (e.g.: powders) that are accompanied by a medicinal claim, usually regarding benefit for health. They are rarely a consumer end-product as such, but are used as ingredients in food and medicinal products. The “customers” for such products, thus, are not the general public, but the food and pharmaceutical industries, showing one point where these two industries potentially overlap. Well-known nutraceuticals are beta-carotene, ginseng and garlic oil.

Functional foods are related to nutraceuticals in that they also carry a health claim. They are, however, directly consumable market products that are similar in appearance to, or may be, a conventional food that is consumed as part of a usual diet. They claim a demonstrated physiological benefit, beyond just basic good nutrition. An example of a functional food is Becel ProActiv, for which claims to cholesterol-lowering effects have been clinically proven. For most nutraceuticals and functional foods, however, large-scale credible scientific research is necessary to verify the benefit of any component (IFIC, 2006). Long-term research is also necessary to document the longevity of claims and potential side effects.

Nutrigenomics is an emergent field that links nutrition science with genetic and genomics research. (Penders, 2008) The science of nutrigenomics involves the application of the human genome to nutrition and personal health to provide individual dietary recommendations. (IFIC, 2006) By using an individual’s unique genetic constitution and nutritional requirements, one is able to tailor recommendations and design diets and food products that meet individual needs, such as greater ability to reduce the risk of a given disease. (Nestlé, 2002; IFIC, year) The role of nutraceuticals and functional foods may become increasingly important in this regard.

### 3.4.2 The research structure

Much as in the other two areas, the industrial sector for food is too complex to be referred to as an industry. Nationally, the large players include Unilever, DSM, DMV-Campina, Friesland Foods, and CSM, not to mention influence and competition from large international companies that include, but are not limited to, Danon, Nestlé and Coca-Cola. Additionally, there are smaller (mostly international) niche organizations trying to bring less well known products (e.g.: hoodia, stevia) onto the market. Even within the large companies, departments reflect diverse structures for R&D, whereby their respective relationships with other companies, and with university departments, vary greatly. For example, research devoted to making existing processes more efficient may rely more on a technical university, whereas research devoted to safety testing may be outsourced to TNO, while creating innovative products may rely more on knowledge being produced through basic bio-medical research. The last example mentioned in the previous sentence is comparable to phases in pharmaceutical research where industry enters at the overlap between basic and applied research.

This is evident in statements made by the sole Dutch Public-Private Partnership for food research, the Top Institute for Food and Nutrition (TIFN) in Wageningen. “TI Food and Nutrition plays a major role *in providing its industry partners with leads* for the development of new, healthy foods with regard to major health concerns such as obesity and metabolic syndrome. ...Another focus lies on *generating a knowledge base for use* in developing fermented foods with improved functionality and which may target microbial activity in the gastrointestinal tract.” (TIFN home page a; emphasis added) TIFN is a PPP that grew out of the Wageningen Center for Food Sciences. It has three primary research lines: Nutrition and Health, Sensory and Structure, and Bioingredients and Functionality. TIFN has a Board and Program Council, both including representatives from Campina (and DMV), CSM, DSM, Friesland Foods (and DOMO), NIZO (the Dutch Institute for Dairy Research), Maastricht University, TNO, University Medical Center Groningen (UMCG), Unilever, VION, and the University of Wageningen (WUR). The Program Council is responsible for the general research program and advises the Board on research policies and strategies. There is a secondary group of liaisons between TIFN and its partner organizations. This group comprises appointees from the partner organizations that participate in expert discussions and provide these partner organizations with advice on how they can benefit from TIFN activities. (TIFNb)

There is an overt emphasis on the website on how the research conducted by TIFN eventually contributes to the commercial market. However, TIFN organizes an annual multi-disciplinary scientific workshop, the Food Summit, which is invitation only and closed to industry actors, although the discussions from such workshops are used as input for a science-meets-industry meeting at the end of the annual workshop. (TIFNc) Each year revolves around a given theme, such as genomics, biomarkers, and microbes. Recent themes have also included attention for social issues, such as making sense of food and eating in relationship to stress. The Food Summit seeks to identify issues limiting progress, novel routes to addressing these issues and setting an agenda for future research. On the one hand, this shows the role of researchers in setting research agendas. On the other hand, one can question where industry interests within TIFN play a role in the choice for a topic and the general set-up of each meeting (for example, in determining who is invited). As was mentioned in respect to pharmaceutical PPPs, more information is necessary to understand where the subtle influences in these collaborative structures are found.

TIFN in Wageningen and the Stichting FN Delta are jointly responsible for the Food and Nutrition Delta program to stimulate knowledge exchange for small and medium-sized companies. (MinVWS/LNV, 2008) This works through a voucher system that these industry players can spend at Wageningen-based institutions. It seeks to convert the findings from basic, public sector research into applied research that leads to new products, processes

and services. (MinVWS/LNV, 2008) This is considered to be good for research because it provides a spin-off for smaller companies that are working on new product innovation related to targeting health (eg: genomics, heart, obesity). However, the decisions regarding the research program are largely centered in Wageningen – there is no intervention or influence from the government regarding this type of research program.

This is an important point because it (together with the composition of the board) reflects that this PPP structure is different from those typically seen in the pharmaceutical sector. Namely, it has a reduced government presence in activities. It is self-identified as an alliance between industry and knowledge institutes. In contrast to the pharmaceutical industry and policy attention for priority medicines, there has been less attention from the government in prioritizing foods. Government agencies are largely reactive, rather than proactive, with respect to research agendas, and there is potentially more room for steering in this area. VWS also indicates that although they have contacts within the organization, there is very little structural contact between VWS sub-departments and the Top Institute Food and Nutrition. This is due in part to the fact that food issues do not just fall under VWS, but also, for example, under economic affairs and agriculture.

Despite the structure of TIFN, interview respondents from the industry had the idea that they were well-balanced by the other organizations involved. There have been highly-publicized concerns regarding conflicts of interest that potentially arise when companies (or private sector collaborative groups) sponsor a university professorship<sup>10</sup> or sit on a PhD thesis committee; these concerns, however, were also called into question by interviewees. First of all, they had the idea that the financial stimulus was not significant enough to determine complete research programs. (We can, however, question the correctness of this perception.) Secondly, as was stated above, the respondents also had the idea that university program directors have considerable leverage in determining research programs. However, as was also stated above, it was very difficult to get into how research agendas are set within various branches of the food industry or between industry and the public sector. This meant it was difficult to identify topics that are not addressed. An imbalance in data comes through the fact that we did not have a chance to learn more from researchers at the Top Institute. We largely came to understand agenda-setting for R&D from the perspective of the industry. Industry sees its involvement with public research institutions very differently from the relationship that our research questions seem to assume.

From our discussions with industry, we noticed the following points: 1) the prevalence of the assumption, even within departments that work closely with researchers from Wageningen and Groningen, that companies have enough in-house knowledge to meet their own research needs.<sup>11</sup> This implies that they rarely have to turn to universities for supplemental research. 2) Following this, the idea that where companies *do* employ university researchers, this is a strategic move for (generally) short-term projects. This move is made when the industry believes that there is something specific to be gained from working with the university. One industry concern is that the options for commissioning outside research are

---

<sup>10</sup> The case of the Corporate Director of Research for Campina also being an Extraordinary Professor (bijzonder hoogleraar) in Wageningen has been highlighted in the news and was also mentioned in various interviews. His position is not funded by his company, but rather, by the professional collaborative NZO, the Dutch Dairy Organization, in which competitor companies also participate. One can argue that competing interests of individual companies within NZO would balance one another out such that research agendas are not affected. However, one can also argue that the NZO as a whole represents industry influence on the position, given that the collective has a vested interest in promoting milk as a healthy product. Whether we approach a given industry (sector) as homogeneous or as fragmented is thus also relevant here.

<sup>11</sup> The increasing concentration of in-house industry R&D processes is also mentioned in the policy memo from Prof. dr. J.A. Knottnerus to the KEMO beraadsgroep Gezondheidsethiek en Gezondheidsrecht dated 23 November 1998.

limited and the competitor enterprises make use of the same options.<sup>12</sup> Thus, to protect company interests, companies do not divulge too much information about their developments, which means that they must also limit the scope of external research projects. Where they do commission research, there are formal agreements made ahead of time about how results may be used (e.g.: for publication). Usually, a general call whereby universities must tender for projects leads to one-on-one research. This means that the industry owns the data and results are usually not publishable. Projects developed in partnership with TIFN, however, are given as an example of research projects where the *university* controls the research set-up and use of data. 3) The strategy of which potential university contracting is a part is increasingly governed by market forces and accompanying regulations. That means that the agenda for investing in one project over another is generally determined by the anticipated resulting product and the claim that can be made about that product. We address this point further in the following section.

### 3.4.3 Making healthy claims

An important distinction to be made is the distinction between products that make a health claim and those that make a medical claim. This is, of course, not always a clear distinction, but it is significant because it influences the nature of research being done. Products that make a medical claim fall under pharmaceuticals, for which there are stricter regulations prior to market release. This means that the products must undergo four phases of research, including clinical trials. Products that make a health claim fall under food regulations, which, until recently at least, have been less stringent than pharmaceutical regulations and focus primarily on product safety. An implication of this is that many companies bringing quasi-pharmaceutical products to the market have been able to get around issues of pharmaceutical regulation by labeling the products as food supplements.

Since 1997, there have been regulations at the EU level regarding the nature of claims being made about new foods brought to the market<sup>13</sup> and the European Regulation on nutrition and health claims for food products (1924/2006) took effect on July 1, 2007. This EU Regulation harmonizes the national regulations of Member States regarding nutrition and health consumer product claims. It supplements Guideline 2000/13/EG, which carries a general ban on information that is misleading or that makes medical claims about foodstuffs, by distinguishing (comparative) nutritional claims, health claims, and risk- or non-risk-reducing claims and by providing more specific rules regarding nutritional and health claims for consumer food products. In the Netherlands, this falls under the Warenwetbesluit voedingswaarde-informatie levensmiddelen, which delineates the conditions for nutritional labelling.

Companies search for ways to differentiate their products and have learned to formulate their claims carefully. Much in contrast to what is desired, regulations can provide a structure wherein the legal departments of companies engage in a semantic game of formulating a non-binding claim that will still interest customers. As in the case of diagnostic self-tests, products that have not undergone any extensive testing (e.g.: clinical trials) are brought to the market with suggestive health claims. Because there is some EU regulation, the current structure allows the major players to dominate the market above smaller, niche companies, because they have more resources to devote to the legalities of claim-making and to creating the dossiers that are required at the EU level.

---

<sup>12</sup> This is the converse to the point made by one interviewee (see section 3.2.2) that academic research groups can strategically position themselves by dealing with multiple companies, rather than being dependent on one.

<sup>13</sup> For more information on the release of new products and regulations regarding novel foods, see: Health Council of the Netherlands (2007) and the website of the Dutch Medicines Evaluation Board (CBG): [http://www.cbg-meb.nl/CBG/nl/nieuwe\\_voedingsmiddelen/definitie-nieuwe-voedingsmiddelen/default.htm](http://www.cbg-meb.nl/CBG/nl/nieuwe_voedingsmiddelen/definitie-nieuwe-voedingsmiddelen/default.htm).

As a result, there has been a clear need to establish the scientific basis to support and further validate claims regarding functional components and foods. (IFIC, 2006) There is a need for increased consumer confidence in the validity of claims being made, which also means confidence in the criteria used to judge a product. The European Commission is working on a "positive list" of permitted 'functional' health claims in the EU (such as "calcium is good for your bones") by January 2010. In July 2008 the European Commission asked the European Food and Safety Authority (EFSA) to prepare a scientific opinion on the Community list of permitted health claims. The Commission also sent EFSA a draft list of health claims that contained 2,870 entries. Some of these claims referred to multiple health relationships and, therefore, multiple claims.

EFSA will support EU decision-makers in implementing the Regulation on the use of nutrition and health claims for foods, and provide scientific advice to support this list-creation process. EFSA's scientists have worked to set up nutrient profiles (to be completed by 2009) and have agreed upon six criteria that ensure thorough and consistent pre-screening of the 2,870 entries. Conducting pre-screening has allowed them to differentiate between the claims which could already be assessed and those for which more information was needed. EFSA's NDA Panel has started evaluating those health claims that passed the pre-screening stage.<sup>14</sup>

Nonetheless, it is not just an issue of rules regarding claims made. Knowing if even the most carefully formulated claim holds up from a scientific perspective means good control and good trials. Regulations, thus, must provide a structure that leads to grounded research. However, as Sismondo (forthcoming) also points out in relationship to the pharmaceutical industry, conflicts of interest are not easily resolved by formal rules that enforce scientific standards. Researchers in food already illustrate what Sismondo shows with the pharmaceutical industry: a certain "interpretive flexibility" with respect to rule-following.<sup>15</sup>

Where research is done, the case in the food industry is also similar to that of diagnostic devices: an additional dilemma lies in deciding who is responsible for funding such research. In the diagnostic and food sectors, respondents indicated the need for research based on a clinical trials model. However, the clinical trials research model is an expensive and time-consuming research model, in which industries, especially, are reluctant to invest. Should this type of research indeed be funded through companies with a good return on investment or is it in the public's interest to support this type of research through public funding? We further address this point in the following section.

#### *3.4.4 Reflection on influence of the food industry on biomedical research*

How the market, and the rules that govern product release, affect industrial research are clear. Similar to the diagnostic industry, the food industry does the minimum research that is required by law, which is currently mostly focused on product safety. Although there are clear links between the industry and biomedical researchers in the Netherlands, there is lack of detail regarding the informal influences on research in programs for basic research. With respect to the health and medicine claims of specific food products, companies abandon detailed (clinical) research in favor of rewording the claims being made. This implies that commercial interests govern research decisions, whereby the research not being done

---

<sup>14</sup> Information in this section is derived from the EFSA website. See: [http://www.efsa.europa.eu/EFSA/efsa\\_locale-1178620753812\\_article13.htm](http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_article13.htm); [http://www.efsa.europa.eu/cs/BlobServer/General/claims\\_art13\\_request.pdf?ssbinary=true](http://www.efsa.europa.eu/cs/BlobServer/General/claims_art13_request.pdf?ssbinary=true); [http://www.efsa.europa.eu/EFSA/KeyTopics/efsa\\_locale-1178620753812\\_NutritionAndHealthClaims.htm](http://www.efsa.europa.eu/EFSA/KeyTopics/efsa_locale-1178620753812_NutritionAndHealthClaims.htm).

<sup>15</sup> In light of this insight, it will be important to observe how research behaviour develops with respect to the new criteria for review (and review processes) and once the final list is published.

mostly falls at the level of applied research within the industry, extensive product testing through clinical trials and post-market surveillance.

This is of course attributable to industry influence, but also to current (supra-)national regulations and current Dutch and EU research programs. One of the interviewees indicated that if we compare the food industry with the pharmaceutical industry, the situation in the food industry is actually worse. This is because of the nature of pharmaceutical regulation, as well as the availability of additional structures that support supplementary pharmaceutical research that is independent of industry funding. This is much less the case with funding for food-related issues. Another interviewee indicated that there is still room for more *structural* government attention for and steering of the research being done.

One respondent likened the food industry to the diagnostic industry in that the resources available for commissioning funding are significantly reduced in comparison to resources coming from pharmaceutical companies. Other respondents pointed out that the amount of current public research funding that is available is also minimal. EU research programs, such as those that fall under the Brainwork program, tend to address research gaps, but they also require collaboration between different actors, including the industry – so they support PPP structures, rather than solitary public-sector research. This is also the case with FES reserves that are used to stimulate research. Obvious sources of public funding within the Netherlands are Zon/Mw programs and VWS-funded research. However, according to one university professor, in food research, especially, the clinical trial is not fundamental enough for the Zon/MW programs and too fundamental for the VWS programs, which already look toward public education and other forms of information distribution at the citizen level. The relevant questions that are not being addressed by industry are thus also not addressed in the public sector because projects do not quite fit within existing programs.

#### 4. Answers to the Research Questions

##### 4.1 What are the most important groups in the Netherlands involved in pharmaceutical, diagnostic and food research?

In retrospect, this research question is somewhat self-evident. All Dutch university medical centers (UMCs) have departments that focus on biomedical research. Given that the distinction between basic and applied research as pointed to above indicates that different departments at different times can contribute to industry research in one of the three areas addressed in this report, it is not the intention to suggest that one UMC or department is more important than the other. Several groups have specializations and try to make themselves more prominent in one area or the other. The AMC, for example, has worked to establish a center that focuses on research related to diagnostic instruments that are introduced into care practices. We do, however, want to highlight universities that have a more overt, formal link to an industrial group, and answer this question by identifying those that are listed as formal collaborators in a Public-Private Partnership.

Top Institute Pharma lists, in addition to the major Dutch UMCs, the following partners and participants on its website:

CHDR (Centre for Human Drug Research)	University of Leiden
Erasmus University Rotterdam	University of Utrecht
Radboud University Nijmegen	TNO Quality of Life
Hubrecht Laboratory	University of Amsterdam
NIN (Nederlands Instituut voor Neurowetenschappen)	Academic Medical Center Amsterdam

In the area of food research, the most obvious center of research is in Wageningen, where the Top Institute Food and Nutrition is also located. TIFN is linked to different research groups at the Wageningen University and Research Center. However, it is also formally linked to the University of Maastricht and the University of Groningen.

The links between industry and the public sector for diagnostics are most clear in the technical universities, notably, in Delft and Eindhoven.

#### 4.2 How are research agendas developed within these groups?

As we indicated at the beginning of the results section it is difficult to describe on the basis of interviews how research agendas are created. On the basis of the interviews, we saw some specific strategies, but these are department specific and not necessarily generalizable. One of the first themes that we saw was that universities have their own priority areas where they want to profile themselves. They seek to align strategically with funds or programs that give them the room to carry out this research. Because many public research programs are broadly defined, there is plenty of room for researchers to fill in the specificities of the project and include their own agendas. However, because there is a competition for funding, they also must put together a methodologically sound study that will be approved. In filling in the specificities, thus, researchers tend to focus on specific patient groups, such as those that make the most use of a medication or product, or those most in need of a new medication or product. They tend to shy away from complex groups, such as senior citizens, because they present with multiple complications that are difficult to control for. They also tend not to look at the general population, which is too large and too complicated to research.

A second theme was the more opportunistic use of other external funding. One can distinguish two types of industry-related research that take place within a research group: investigator-initiated, where a scientist has an idea for a specific topic but needs some industry funding to carry out that research and industry-initiated, where the industry brings a research topic to the table and a group of doctors (often with their own enterprise) participate in the research, for example by providing patient participants.<sup>16</sup> One university professor describes how departments or research groups can collaborate with industry in an intelligent and transparent manner in order to complete research that otherwise would be precluded by a lack of funding. His department is efficient in dealing with the funding flows; for example, by having a PhD student work on an industry-funded project one day in the week and other projects on the other days. As is stated above, this allows a research group to build a financial buffer for funding their own research, while ensuring continuity in the research line over a longer period of time.

We can extend the second category from above (industry-initiated) to include other outside sources that bring research ideas and funding to the table, such as patient organizations (third-party initiated). As the representative for patient interests indicated, specific organizations often bring an offer to both industry and academic players, looking for research interest from one or both. In such cases, the patient organization comes to the table as an equal negotiating partner with academics and industry representatives and carries out (in)formal negotiations for research. This is also evident in the cases presented by Abma et al (2006) regarding increased patient organization participation and voice in setting research agendas and carrying out research projects. Abma et al demonstrate how the phased

---

<sup>16</sup> Taken from one of the interviews.

approach (stappenplan) created in partnership with the Dutch Paralysis Organization (Dwarslaesie Organisatie Nederland) can be successfully transferred to other contexts (where necessary or desired), such as for use with kidney patients or persons with a cognitive handicap/disability. In these cases, a social infrastructure is created where “client researchers” from the organization work on equal footing with academic researchers in all phases of the research process, including the agenda-setting phase. For patient organizations to have this type of influence on biomedical research agendas, however, it is important that there are public funds available, which returns to the first point made in this section – one agenda-setting strategy used by research groups is attempting to align their priorities with opportunities created by public research programs.

In these examples we see that there is a mix of a structured program with defined research priorities and opportunistic moments of doing research funded by an outside party. This mix is present in varying degrees in different departments and research groups. Delving further into the specific politics of agenda-setting and negotiation between different actors in scientific cooperation with one another requires longer-term, ethnographic research, which provides an in-depth and situated study of multiple sites. (Penders, 2008) Public research in the Netherlands is governed by a combination of actors and policies, and the resultant inter-organizational structures continue to shift and change. These different factors can influence agenda-setting in various phases of the research projects, and there is always a risk of industrial influence. The question then becomes an issue of which phases (such as phase four pharmaceutical research or phase one diagnostic product development) are most prone to industry influence and how much influence a company has over a given research group. However, what research is chosen and what is not is difficult to capture in an interview. As one interview respondent said, what is not being done is by definition invisible.

For the other three phases of knowledge production (development, dissemination and practical application) distinguished for attention at the outset of this project, there is much more (published) evidence. Bringing issues related to agenda-setting to the fore requires extended presence within research groups, where observations specifically focus on decision-making and negotiation processes. Ideally, this would take place within a representative sample of groups, to allow for more generalizability of the findings.

#### 4.3 Where is the influence of different industrial sectors evident in the agenda-setting processes of these groups?

Biomedical research dependence on industry varies greatly from departments that have incidental, opportunistic contacts with a company for short-term projects to those that are structurally funded through links to one or more companies. There are even those departments that have an enterprise component and there has been an increasing trend during the last 10-20 years of small biomedical spin-off companies that break away from public institutions, continuing research as a business enterprise. Where industry funding is present, one can follow the work of van der Weijden (2007) and break down where and how this flow of research funding structures the project being done. However, much influence is potentially more subtle and is also contingent on types or phases of research and development (see section 3.2.2 and footnote 4).

An important aspect is that is not just the presence or absence of corporate funding that influences agenda-setting. It is also the (supra-)national, local and professional structure in which a research group or groups works. In the pharmaceutical industry for example, concerns about intellectual property have fostered a more competitive environment. Even where public funds are at stake, universities are encouraged to compete with other and with companies for lucrative research (see section 3.2.3 and footnote 6). In one of the duo interviews, it was suggested that there are also professional prestige issues: specific molecules and receptors hold more prestige than others. We can question what the role is of industry in shaping this prestige, and more importantly, how this influences government

attention for high profile receptors or specific issues, whereby it also trickles into funding programs. The food industry has mostly seen criticism regarding professorship sponsoring that can lead to conflicts of interest. The degree to which this is problematic is contingent upon one's view of "industry" as a homogenous entity that exerts influence and needs to be balanced against by governments and special interest groups or as a fragmented landscape of competitors that often serve as a countervailing presence for each other.

Another respondent also suggests that it is not so much an issue of funding, but of control over project content. He argues that researchers lose control at the level of hospital policy, which seeks to align with national political statements. He further points to the structure that governs research programs, which includes regulations at the national and EU level. The sections on diagnostics and food point to the creativity of developers in dealing with regulations, whereby research is only done if it can lead to a specific marketing claim, and research to test that claim is more often than not avoided, in favor of deferring to a creative legal (or marketing) department.

Multiple interviewees indicate the need for a better structure, offering different suggestions for programs to provide such a structure. Although some looked at content (such as the need to focus on quality when it comes to diagnostic products and processes) and some pointed to regulatory structures, most suggestions encountered in the interviews nonetheless focus on alternative financial structures to those currently in place to support biomedical research. Suggestions included more attention from insurers, following the SP's proposal to create a fund to which both government and industry contribute, but which is further free of industry influence, and reviving old stimulus programs to encourage research in certain areas. As the RGO has also argued, (temporary) supplementary funding can effectively stimulate the desired research in areas that currently receive too little attention. However, whether there are other means to guarantee the longer-term responsiveness of researchers to these areas remains unknown. (RGO, 2007)

## **5. General Discussion**

Public-Private Partnerships have emerged as a dominant (exemplary) form of trying to secure public interests in technology development by bringing together public and private sector stakeholders and identifying research priorities through discussion and active agenda-setting. However, some interview respondents suggested that we should be wary about mixing public and private funding (and interests) too intricately. There are many questions left unanswered about the exact nature of the effects of PPPs – where they are successful and where they are not, what role parties such as patient organizations actually play in negotiations, and what unexpected influences these structures may have on the nature and organization of research and development. Existing evidence suggests that this is ambiguous at best, e.g. transferring existing knowledge on medication to third world countries (which has been moderately successful) versus creation of new knowledge on medications and diseases within Europe (which has raised more doubts), or the case of quick wins and the development of cancer drugs versus the difficult process of developing new antibiotics, as mentioned above. These collaborative structures also raise worries that following too many international trends may lead to neglecting important domestic issues. We can question to what degree it is important to have a national approach to biomedical R&D and serving the public interest, as well as to what degree this can be fulfilled at an EU level.

When looking at the role that EU structures already play in governing this research and comparing across the three different sectors under study here, we can identify various conflicts. Regulation and practices that have been developed over the years for the pharmaceutical sector are much less developed in other sectors. This means that industries seek the 'easiest' route to conducting research; for example, in the case of diagnostic and

food companies, who rarely go beyond the minimum research requirements and favor utilizing legal avenues to protect their interests when bringing a new product to the market. Much research that is lacking from the agenda is thus not in the development of knowledge at the level of basic biomedical research, but at the level of application and post-marketing surveillance. There is an insufficient formal structure in place to provide checks and balances to these types of practices; yet, even in a more highly regulated environment, interpretative flexibility leads to creative evasion of certain rules. It is unrealistic to believe that companies will self-discipline and conduct clinical trials, even though they may understand the importance of such research.

Similarly, evaluation frameworks that exist for the pharmaceutical industry are also not comparable to those in the diagnostic and food industries. Although attempts have been made to transfer some practices and research structures from one area of science to another, these do not always fit. RCTs, for example, do not provide the data necessary to understanding the intricacies of using a diagnostic product in daily practice. Both the diagnostic and food industries reveal that different technological developments, serving different markets and governed by different regulatory structures, require diverse forms of data and evidence, which has significant implications for the nature of research being done. Focusing on the market and the release of *new* products, for example, diverts attention away from older products and processes that have become “normalized” within medical practice. Similarly, unproblematically accepting or focusing on the effects of using a medicine or diagnostic device shifts attention away from reasons and conditions of *nonuse*. Finally, short-term research on safety or effectiveness means that the questions left open are generally about the longer-term influence of a (public) health intervention. Examples that cut across these include lack of attention for the effects of using longer-standing medicines to treat a chronic illness and the potential need to wean an individual OFF of a medication, or the overall effects of long-term use of certain food ingredients on weight and general health (with the sugar versus artificial sweetener debate being among the best-known).

There is a need for new research structures (not only funding programs, but policy regulations and independent reviews) that address issues related to (public) health interventions in the three sectors, as well as the societal impact of these. Research on interventions, however, is tricky, as it often looks to changes in behaviour among certain groups of actors, e.g. patients/consumers or health care professionals. As interview respondents also indicated, it is not always easy to draw lines around an intervention. In this type of research it is difficult to control against spill-over effects, where the knowledge of participating in research on a given topic may affect behaviour, even when the details of the intervention are unknown to the control group. (Lindsay et al, 2008) Proposals for research are generally judged against the dominant, classical (RCT, statistical) research model, which, as is indicated above, only works for addressing specific research questions. Rejection of such proposals on grounds of the research set-up leads to a situation where easily testable subjects are repeatedly addressed through research trials, while important ethical, legal, political and social aspects of interventions, over the longer term, remain unaddressed. (Lehoux and Blume, 2000) Multiple articles point to the need for alternative methodologies and trial designs that will provide the different kinds of evidence necessary to answering questions related to the effects of using medical technologies in daily practice or promoting healthy behaviors, such as those related to food and pharmaceutical consumption. (Jansen et al, 2006; Mol, 2006; Willems et al, 2007; Zuiderent and van der Grinten, forthcoming)

Research programs with adequate funding established to address these goals are important, but they, alone, are not enough. As is stated above, research is situated within a complex environment with multiple stakeholders. Therefore, to make a program work, the environment in which it is situated must be conducive to long-term sustainability. (Smid, 2007) Especially in the areas of diagnostic and food-related biomedical research, there is a need to move away from incidental and toward structured contact between government agencies,

researchers and industry. The RGO (2007) also pointed to this with their suggestion that a structured dialogue between UMCs and various stakeholders about social interests in health research, and feedback on the social impact of projects and programs, should take place at a national level, preferably with the RGO involved. According to the RGO, such insights would identify focal points for future responsiveness, whereby public interests are protected in research over the longer term.

## 6. Conclusions

We conclude with a reflection that we find to be important for the purposes of this study. In this research we discovered primarily the embeddedness of different actors in complex networks of knowledge production. At all levels there is heterogeneity: the heterogeneity of the industry in each of the three sectors, the heterogeneity of products and their markets, and the heterogeneity of biomedical research being conducted in university settings. This makes it difficult to draw any overarching, simple conclusions about how industry interests influence agenda-setting in public-sector biomedical research. Furthermore, in relation to all three industrial fields, it is clear that this absolute distinction between the public sector and the private sector is actually incorrect. It is not always possible to indicate where one stops and the other begins. Universities are increasingly becoming interested in the commercialization of research, mainly evident in the life sciences (e.g.: genomics). Even when they attempt to remain independent, they are encouraged by the policies in place and the practices of other actors to compete in the manner of industry.

This leads to questions regarding the plausibility of suggestions made in several interviews about combining public and private funds into one overarching fund for public (or independent) research that is free of private interest. Given that the lines between public and private cannot always be distinguished, it is unrealistic to believe that such a governance structure can guarantee an absence of industry influence. Protecting the public interest in research in these fields rests on the more fundamental issue of how one determines what is public and/or independent.

It has become clear that many problems related to lack of research are due to a combination of factors in the current research structure. This includes the rules and regulations that govern required research, as well as the presence or absence of funding programs to stimulate other research. Most specifically, the following *areas* are in need of research attention:

- Knowledge losses in the transfer of basic research results to applied research (often between the public and private sectors), which may affect (pre-)clinical trials.
- Continued stimulation for the development of medications for orphan and neglected diseases and the development of new antibiotics.
  - The question of where PPPs are successful for leading to new developments, and where they are not, in the development of new medications, remains an important secondary research topic.
  - How public interests are protected in PPP research collaborations must also be further researched.
- Encouraging pharmaceutical research that is initiated to solve/address a specific patient group, illness, or social problem (rather than on the basis of a potentially profitable product).

- Research on social issues related to pharmaceuticals and specific foodstuffs is often missing.
  - This includes:
    - comparative research on the therapeutic value of (new) medications
    - research on longer-term effects of using medications (e.g.: for chronic illnesses), dietary substitutions, and/or specific food ingredients
    - research on trends in use of “normalized” over-the counter medications
    - research on reasons for or conditions of non-use of medications and products
    - research on weaning patients off of medications or other products
- The relationship between the use of diagnostic instruments or tests and improvements in patient health.
  - This includes:
    - evaluation of implementation and use in practice
    - sensitivity and specificity of the analysis made on the basis of test results and validity of results when used in daily practice
    - how diagnostic tests work for specific *target groups* and *individual* patients (including efficacy and efficiency of use)
    - whether patients are prepared for and understand the results of diagnostic tests
      - this includes not only diagnostics in institutions, but also commercial diagnostics, such as OTC self-tests or genetic risk profiling and the full-body scan
- Knowledge on the quality of results of OTC self-tests is insufficient.
- Research on the ethical and political dimensions of diagnostic instruments and tests is also lacking.
  - Including members of the target group in development and design can also be improved.
- The social effects of diagnostic practice and the use of self tests.
  - This includes:
    - attention for the potential creation of a medicalized culture
    - guarding against “disease promotion”
    - analysis of the relationship between testing and angst, which may lead to more demands on the health care system
- Research on the long-term effects of public health interventions must be expanded.
- Post-marketing surveillance of products in *all three areas* should be increased.
  - For pharmaceuticals, the suggestion is that fewer, but longer-running and better-designed, trials would be an asset.
  - For food products, more clinical trials on actual benefits (and the longevity of these results) and on potential negative side effects, is recommended.

There is a role for government-led research programs in mitigating certain problems in the current research structure. To define this role more completely requires more, longer-term research, within a representative sample, on the agenda-setting practices in university-based biomedical research groups. The establishment of public research programs that stimulate forms of research other than the RCT would be an asset, as would be more interest in and experimentation with including other parties (such as patient organizations, hospitals and

insurers) in research agenda-setting and in earlier phases of the development of products and devices.

## References

Abma, T.A., C. Nierse, E. Adriaanse en G.A.M. Widdershoven (2006) Onderzoekssturing door patiëntenverenigingen. Over de waarde van een stappenplan voor onderzoekssturing door cliëntenorganisaties. *Medische Antropologie* 18(1), 213-232.

Adams, S. and A. De Bont (2007). "Information Rx: Prescribing good consumerism and responsible citizenship." *Health Care Analysis* 15, 273-290.

Agriculture and Agri-food Canada (AAC). 2008. What are functional foods and nutraceuticals? Available online: <http://www4.agr.gc.ca/AAFC-AAC/display-afficher.do?id=1170856376710>. Updated on: 31 July. Last Accessed: 14 September 2008.

Blume, S. 1999. Histories of cochlear implantation. *Social Science and Medicine* 49, 1257-1268.

Boon, W. 2008. Demand articulation of intermediary organizations in emerging pharmaceutical innovations. Utrecht: Universiteit Utrecht.

Bradley, D. 2007. Finding new formulas for pharma success. *Nature reviews drug discovery* 6 (June), 423.

Callahan, D. 2003. What price better health?: hazards of the research imperative. Berkeley: University of California Press.

Callan, B. and I. Gillespie. 2007. The path to new medicines. *Nature* 449 (7149), 164-165.

Callon, M. (1998). Introduction: The embeddedness of economic markets in economics. The Law of the Markets. Oxford, Blackwell. Pages 1-57.

Croft, S.L. 2005. Public-Private Partnership: from there to here. *Transactions of the Royal Society of Tropical Medicine and Hygiene* 99 (s1), S9-14.

van Delft, D. 2006. Veel claims, weinig kennis. An interview with Martijn Katan. *NRC*. 25 maart, 47.

Dehue, T. 2008. De depressie epidemie. Amsterdam: Uitgeverij Augustus.

DiMasi, J. and H. Grabowski. 2007. Economics of new oncology drug development. *Journal for Clinical Oncology* 25 (2), 209-16.

Ellenbroek, SPH, G van Ark, EC Klasen, 2002. Vergelijking van de uitgaven aan gezondheidsonderzoek in 7 Westerse landen in 1997: Nederland op de laatste plaats. *NTvG* 146 (29), 1369-1374.

Fehr, A., P. Thümann and O. Razum, 2006. Drug development for neglected diseases: a public health challenge. *Tropical Medicine and International Health* 11 (9), 1335-1338.

Frantz, S. 2006. The trouble with making combination drugs. *Nature reviews drug discovery* 5 (November), 881-882.

Gezondheidsraad. 2008. Performance and Perspective. No.A08/03. The Hague: Gezondheidsraad, March.

Herrling, P. 2007. Patent sense. *Nature* 449 (13 September), 174-175.

- Health Action International (HAI), 2006. Pills, politics and practice. 25 years of promoting people-centred medicines policy. Amsterdam: Health Action International Europe.
- Health Council of the Netherlands. 2007. The safety assessment of novel foods. The Hague: Health Council of the Netherlands, publication no. 2007/23
- Health Council of the Netherlands. 2008. Screening: between hope and hype. The Hague: Health Council of the Netherlands, publication no. 2008/05E.
- Hopkins, M.M. 2004. Technique-led technological change in the "hidden research system": genetic testing in the NHS. Brighton: University of Sussex.
- Hourd P.C. and D.J. Williams. 2008. Results from an exploratory study to identify the factors that contribute to success for UK medical device small- and medium-sized enterprises. *Proceedings of the Institution of Mechanical Engineers* 222 (5), 717-35.
- International Food Information Council (IFIC). 2006. Backgrounder on Functional Foods. November. Available online: <http://www.ific.org/nutrition/functional/index.cfm>. Last Accessed: 14 September 2008.
- Jansen, Y.J.F.M., R. Bal, M. Bruijnzeels, M. Foets, R. Frenken and A. de Bont. 2006. Coping with methodological dilemmas; about establishing the effectiveness of interventions in routine medical practice. *BMC Health Services Research* 6(160). Available online: <http://www.biomedcentral.com/1472-6963/6/160>. Last Accessed: 14 September 2008.
- Kaplan, W. and R. Laing. 2004. Priority Medicines for Europe and the World. Geneva: World Health Organization.
- Kleinman, D.L. 2003. Impure Cultures: University Biology and the World of Commerce. Madison, WI: University of Wisconsin Press.
- Lehoux, P. 2006. The Problem of Health Technology; Policy implications for modern health care systems. New York: Routledge.
- Lehoux, P. and S. Blume. 2000. Technology assessment and the sociopolitics of health technologies. *Journal of Health Politics, Policy and Law* 25 (6), 1083-1120.
- Leufkens, H.G. 2007. Introduction in Pharmaceutical Policy Analysis. Lecture given at the summer course on Pharmaceutical Policy Analysis, held by the Division of Pharmacoepidemiology and Pharmacotherapy, Utrecht Institute for Pharmaceutical Sciences, 2-6 July.
- Light, D.W. 2006. Basic research funds to discover important new drugs: who contributes how much? In: Burke, M.A. and A. de Francisco, eds. Monitoring Financial Flows for Health Research 2005. Geneva: Global Forum for Health Research.
- Lindsay, S., P. Bellaby S. Smith and R. Baker. Enabling healthy choices: is ICT the highway to health improvement? *Health: an interdisciplinary journal for the social study of health, illness and medicine* 12 (3), 313-331.
- Metlay, G. 2006 Reconsidering Renormalization: Stability and Change in 20th-Century Views on University Patents. *Social Studies of Science* 36(4), 565-598.

Ministerie van Volksgezondheid, Welzijn en Sport (Min VWS) en Ministerie van Landbouw, Natuur en Voedselkwaliteit (Min LNV). 2008. Gezonde voeding, van begin tot eind. Nota voeding en gezondheid. Den Haag. Juli.

Mintzes, B. 2002. Direct to consumer advertising is medicalising normal human experience. *BMJ* 324, 908-909.

Mol, A. 2006. Proving or improving: on healthcare research as a form of self-reflection. *Qualitative Health Research* 16 (3), 405-414.

Moran, M. 2005. A breakthrough in R&D for Neglected Diseases: New ways to get the drugs we need. *PLoS Medicine* 2 (9), 828-832.

Moran, M., Ropars, A.L., Guzman, J. Diaz, J. and C. Garrison. 2005. The new landscape of neglected diseases drug development. London: The London school of economics and political science.

Mossialos, E., T. Walley, M. Mrazek. 2004. Regulating pharmaceuticals in Europe: an overview. In: Mossialos, E., T. Walley, M. Mrazek, eds. 2004. Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality. Maidenhead: Open University Press. Chapter 1, pp 1-37.

Mrazek, M. and E. Mossialos. 2003. Stimulating pharmaceutical research and development for neglected diseases. *Health Policy* 64, 75-88.

Nestlé, M. 2002. Food Politics. Berkeley: University of California Press.

Nisthar, S. 2004. Public-private 'partnerships' in health – a global call to action. *Health res policy syst* 2004 (1), 5.

Nwaka S. 2005. Drug discovery and beyond: the role of public-private partnerships in improving access to new malaria medicines. *Transactions of the Royal Society of Tropical Medicine and Hygiene* (99S), S20-S29.

Out, H.J. and A. Broekmans 2007. Kritiek op geneesmiddelenonderzoek is ongegrond. *Medisch Contact* 62(24), 1024-1027.

Owens, J. 2007. 2006 drug approvals: finding the niche. *Nature reviews drug discovery* 6 (February), 99-101.

Pécoul, B. 2004 New drugs for neglected diseases: from pipeline to patients. *PLoS Medicine* 1, e6.

Penders, B. 2008. From seeking health to finding healths: the politics of large-scale cooperation in nutrition science. Maastricht: Universitaire Pers Maastricht.

Permanand, G. and C Altenstetter 2004. The politics of pharmaceuticals in the European Union. In: Mossialos, E., et al, eds. 2004. Regulating Pharmaceuticals in Europe: striving for efficiency, equity and quality. Maidenhead: Open University Press Chapter 2, pp. 38-54.

Perry, S. and M. Thamer. 1999. Medical Innovation and the role of health technology assessment. *JAMA* 282 (19), 1869-1872.

Pricewaterhouse Coopers (PWC), 2007. Pharma 2020: The vision. Which path will you take?

Raad voor Gezondheidsonderzoek (RGO), 2005. Advies Kennisinfrastructuur Farmaceutische Zorg. Publication no. 51. The Hague, November.

Raad voor Gezondheidsonderzoek (RGO), 2007. Research that matters. Responsiveness of university medical centers to issues in population health and health care. Publication no. 57. The Hague, December.

Richards, T. 2008. Orphan Diseases: Which ones do we adopt? *BMJ* 337, 1225.

Rozendaal, S. 2006. Het is mijn lijf. Soesterberg, the Netherlands: Aspekt.

Schmid, E.F. and D.A. Smith, 2004. Is pharmaceutical R&D just a game of chance or can strategy make a difference? *DDT* 9(1), 18-26

Sheridan, C. 2006. Budget cuts curb Europe's enthusiasm to revive innovation. *Nature Reviews Drug Discovery* 5 (August), 621.

Sismondo, S., Forthcoming. Ghosts in the machine: publication planning in the medical sciences. Submitted to SSS.

Smid, H.J. 2007. Lessen uit onderzoeksprogrammering. *TSG* 85(5), 245-246.

Steenhoek, A. 2008. De rol van de farmaceutische industrie. Rotterdam: instituut Beleid en Management Gezondheidszorg, Erasmus MC. 23 July.

SustainAbility, 2007. PharmaFutures: Prescription for Long-term value. <http://www.sustainability.com>.

Tickell, S. 2005. *The antibiotic innovation study: Expert voices on a critical need*. Available online: <http://soapimg.icecube.snowfall.se/stopresistance/Innovation%20study%20april%20low%20res.pdf> Last Accessed: May, 2007.

Top Institute Food and Nutrition (TIFN)a. Top Institute Food and Nutrition: unique public/private partnership. Available online: <http://www.tifn.nl/webdb/AP/Organisation>. Last Accessed: 12 September 2008.

Top Institute Food and Nutrition (TIFN)b. Organizational Structure. Available online: [http://www.tifn.nl/webdb/AP/Organisational\\_structure](http://www.tifn.nl/webdb/AP/Organisational_structure). Last Accessed: 12 September 2008.

Top Institute Food and Nutrition (TIFN)c. Food Summit. Available online: <http://www.tifn.nl/webdb/ap/Foodsummit>. Last Accessed: 25 August 2008.

Trappenburg, M. And H. van den Bovenkamp. Forthcoming. Democracy and Medical Research.

Trouiller, P., Torreele, E., Olliaro, P. , White, N. , Foster, S. , Wirth, D. and B.Pécoul. 2001. "Drugs for neglected diseases: a failure of the market and a public health failure?" *Tropical Medicine & international Health* (6), 945-951.

van Weely S, Leufkens HGM. 2004. Background paper: orphan diseases. In: Kaplan W, Laing R, eds. 2004. Priority medicines for Europe and the World - a public health approach to innovation. Geneva: World Health Organization. Available online: <http://mednet3.who.int/prioritymeds/report/index.htm>.

van der Weijden, I.C.M. 2007. In search of performance: research management within the Dutch public medical and health sector. Amsterdam: Vrije Universiteit.

Widdus, R. 2005. "Public-private partnerships: an overview. *Transactions of the royal society of tropical medicines and hygiene*. 99 (s1), s1-8.

Willems, D. L., R. Vos, et al. 2007. Passend bewijs. Ethische vragen bij het gebruik van evidence in het zorgbeleid. Den Haag: Centrum voor Ethiek en Gezondheid.

World Health Organization (WHO), 2006. Public health, innovation and intellectual property rights. Report of the commission on intellectual property rights, innovation and public health.

Yamey, G. The world's most neglected diseases: ignored by the pharmaceutical industry and by public private partnerships. *BMJ* 325(7357), 176-177.

Zuiderent, T. and T. van der Grinten. Forthcoming. Zorg voor medische technologie: over het ontwikkelen van zorgtechnologie, vormgeven van technologiebeleid en behartigen van publieke belangen. Verkenning voor het programma van het Rathenau Instituut: Wie draagt zorg voor medische technologie? Rotterdam: iBMG.