INTERACTIVE LEARNING IN FUNCTIONAL GENOMICS INNOVATIONS

Rens Vandeberg, Wouter Boon and Ellen Moors

Department of Innovation Studies, Copernicus Institute for Sustainable Development and Innovation, Utrecht University, P.O. Box 80115, NL-3508TC, UTRECHT, The Netherlands

r.vandeberg@geo.uu.nl | +31 30 253 7632

Abstract
After the completion of the Human Genome Project we have now entered the functional genomics era in which researchers try to uncover which genes do what when and why. In their slip stream producers are developing now products based on this new knowledge. At the same time this innovation wave brings back images of possible prospects envisioned during the biotech revolution (1990's) and its silent death before the turn of the millennium. Analyses show a mismatch between producer's possibilities and consumer's wishes and expectations about this new technology. The possible benefits of functional genomics should not have the same fate ex ante and therefore the interaction between users and producers of functional genomics products is studied: Interaction between stakeholders in an innovation process can be regarded as a learning process in which wishes and expectations on the one side and possibilities on the other may align the network of involved stakeholders, which can lead to a successful innovation. Accordingly, this paper focuses on the processes of interaction in functional genomics innovations and whether and how interactive learning is taking place? We take an interactive learning approach to user producer interactions in functional genomics in order to get a deeper understanding into the precise mechanisms at work from which do's and don'ts for innovation processes can be derived. We apply our approach to two pilot case studies of pharmaco- and nutrigenomics developments.

Key-words: interaction processes, interactive learning, functional genomics

1. Introduction
Until the 1950s most researchers and policy makers considered innovation to be a linear process: scientists invent, entrepreneurs applies and consumers buy[1]. In this view the innovation primate was with the entrepreneur. The entrepreneur 'knew' which product he could market successfully (nowadays this approach is called *technology push*). However, in the second half of the 20th century more insight resulted in a more realistic view of innovation (Smits, 1994). Several experiences made clear that the paradigm of "scientists invent, entrepreneurs applies and consumers buy" did not always lead to innovation success. Often it became clear that

[1] In this light, it is not surprising that the motto of the 1939 World Fair in Chicago was "Science explores, Technology executes, Man conforms."

users were very reluctant to adopt new developments. One example is the biotech/GM debacle in the late 90s of the last century. This has led to strong opposition and the rejection of GMO-foodstuffs. Now we are at the doorstep of the functional genomics era, not only genomics researchers and industry but also other stakeholders, such as future users should be involved in the research agenda setting process. Lessons should be learned from the debates on biotechnology and genetic engineering, by early anticipating on users' preferences, views and needs and by involving users in the innovation process. Through a more intensified user - producer interaction, the acceptation of functional genomics will improve as well, thereby considering users as actors that possess a potential of ideas that should be exploited far better in the innovation process than till now is the case. After all, the producers of genomics innovations are interested in broad societal acceptance of innovations, in access to tacit knowledge of users and in mobilising the creative potential of users. It addresses the creative capacity of users to shape technological development in all phases of the innovation process (Enzing, 1995; Smits and Kuhlmann, 2002; Oudshoorn and Pinch, 2003).
A problem with intensifying the role of users in the innovation process is that the consumer does not know what she/he wants, especially regarding emerging developments such as genomics that take at least 5 years before the first products come to the market. To overcome this mismatch between producer's possibilities and consumer's wishes and expectations about emerging genomics technology, the interaction between users and producers of functional genomics should be analysed.
In this paper, the interaction between stakeholders in an innovation process is regarded as an interactive learning process in which the wishes and expectations on the one side and the possibilities on the other may align the network of involved stakeholders, possibly leading to a successful innovation or to reduced uncertainty about future genomics developments. Accordingly, the central question of this paper focuses on the processes of interaction in functional genomics innovations and whether and how interactive learning processes in networks of involved stakeholders take place, especially with regard to nutrigenomics and pharmacogenomics innovations?. These insights result in first recommendations for improvement of user-producer interactions and interactive learning processes in the future developments of emerging technologies such as functional genomics.

This paper is inspired by information from various sources. The main source was a literature search, including reports and review articles on functional genomics developments, innovation, interactive learning and user-oriented studies with the aim to develop an analytical framework of interactive learning in user-producer networks in functional genomics innovation processes. Furthermore, key persons in the Dutch food and health care domain were interviewed, specialized in nutrigenomics and pharmacogenomics respectively. In addition, a small international workshop was organized with a group of experts both in the field of genomics developments and innovation studies to validate and discuss the usefulness of the developed analytical framework. The preliminary results of this literature search, orienting interviews and workshop are presented in this paper, both for nutrigenomics and pharmacogenomics innovations.

The structure of the paper is as follows: Section 2 describes the current developments in nutrigenomics and pharmacogenomics. Section 3 discusses various theoretical concepts that may be of use in the analysis of the interactions between users and producers in functional genomics, especially regarding interactive learning processes. This section ends up with a conceptual framework for the analysis of the case studies. Section 4 focuses on interactive learning processes in user-producer interactions in the nutrigenomics domain. Section 5 does the same for pharmacogenomics. Subsequently, section 6 compares the two cases and gives conclusions and suggestions for further research.

2. Nutrigenomics and pharmacogenomics innovations

With the beginning of the new millennium, the Human Genome Project was completed. This meant that the human genome was mapped. Leading from this, the next step will be to investigate the functional manifestation of this genetic information. In short: which genes do what, when and why? This is called functional genomics. Insights in this research topic can be used in several areas such as health and pharmaceuticals, food and nutrients, and industrial applications.

The first area, called nutrigenomics is the study of the genome of human cells and their reaction on diet / ingredients: It is the application of genomics for human health and wellbeing. Possibly new beneficial ingredients can be identified through nutrigenomics studies. The effects of ingredients can be tested through nutrigenomics instead of classical studies with volunteers. Nutrigenomics is a research tool or scientific field: a specialisation within genomics. The genome 'tells' researchers 'which genes do what, when and why' and therefore the interaction between the human body and ingredients can be estimated in advance of epidemiological tests. The following description of nutrigenomics by Kaput (2004), gives a practical insight in the science and possibilities of nutrigenomics:

1. Common dietary chemicals act on the human genome, either directly or indirectly, to alter gene expression or structure;
2. Under certain circumstances and in some individuals, diet can be a serious risk factor for a number of diseases;
3. Some diet-regulated genes (and their normal, common variants) are likely to play a role in the onset, incidence, progression, and/or severity of chronic diseases;
4. The degree to which diet influences the balance between healthy and disease states may depend on an individual's genetic makeup; and

Dietary intervention based on knowledge of nutritional requirement, nutritional status, and genotype (i.e., "individualized nutrition") can be used to prevent, mitigate, or cure chronic disease.

Therefore nutrigenomics is a service for producers looking for new functional foods. Functional foods are products descending from nutrigenomics. A functional food is a food product claiming to have a health-promoting and/or disease-preventing property beyond the basic nutritional function of supplying nutrients. (See also Figure 1).

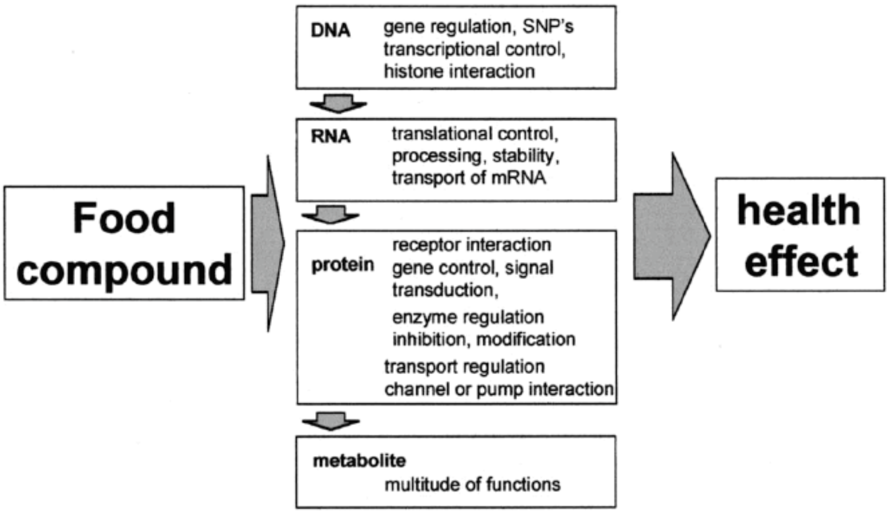

Figure 1 Food-gene-health relation (Taken from Van Ommen, 2005)

The second area, called pharmacogenomics, could help the pharmaceutical industry challenging the improvement of efficiency and effectiveness of drug development. For example, functional genomics tools are stimulating target discovery in the pre-project phase of drug development, as well as assisting the selection of participants in clinical trials (Boulnois, 2000; Dean et al., 2001). Moreover, knowledge of the functional manifestation of genetic information can be used in medical practice, e.g. to determine drug use, dose and choice. This leads to changes in the way medicine deals with drug description (Delden et al., 2004). On a more or less official level the European Agency for the Evaluation of Medicinal Products (EMEA, 2003) tried to define pharmacogenetics and pharmacogenomics as follows: “pharmacogenetics is the study of interindividual variations in DNA sequence related to drug response”, while “pharmacogenomics is the study of the variability of the expression of individual genes relevant to disease susceptibility as well as drug response at cellular, tissue, individual or population level”. This is illustrated in Figure 2.

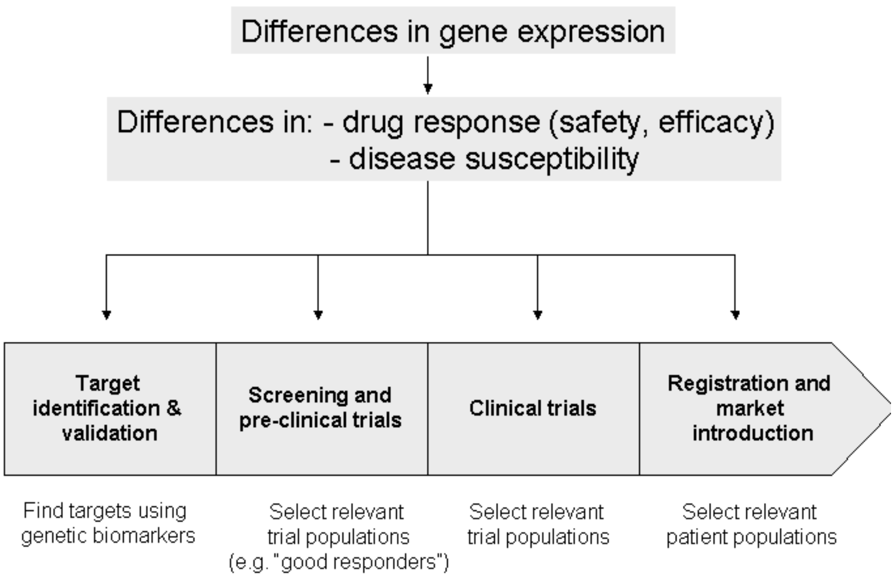

Figure 2 A schematic overview of pharmacogenomics or how gene expression influences differences in drug response and disease susceptibility, and how this has an impact on the drug development pipeline.

Having briefly sketched the nutrigenomics and pharmacogenomics fields, the next section focuses on the conceptualization of interaction and interactive learning processes.

3. Interactive learning in user-producer interaction: conceptualisation

Innovation as iterative process

Within the realms of economic literature by scholars like Rosenberg and Schmookler[2], the problematization of innovation processes was largely centred on the technology push versus market pull debate. The former saw the knowledge generation and technology creation as the driving force behind the processes, while the latter placed a larger emphasis on the influence of the demand of new products, processes and services. Although the discussion has still not been completely resolved, both the approaches have been criticized as being part of a linear model. Nowadays, innovation processes are regarded as iterative in which both demand and supply of knowledge and technology play a role (Mowery and Rosenberg, 1979); Nelson and Winter describe it as a “backing and forthing” between the demand and supply side in the selection environment (Smits and Kuhlmann, 2004; Blume, 1992). In such iterative process, innovation is the result of the combination of a heterogeneous set of actors, the relations between them and the institutional surrounding. These components form the *Innovation System* (IS). This “systems of innovation” approach was introduced by Freeman (1987), Lundvall (1992), Nelson (1993) and Edquist (1997). This approach is used as a heuristic device, being a reaction to the linear model of innovation, in which innovation is conceived as interactions of distinct actors, producing, diffusing, or using technologies which result in the (re-)design of technical systems (Figure 3). It is already widely diffused in innovation science and policy (Edquist & McKelvey, 2000)

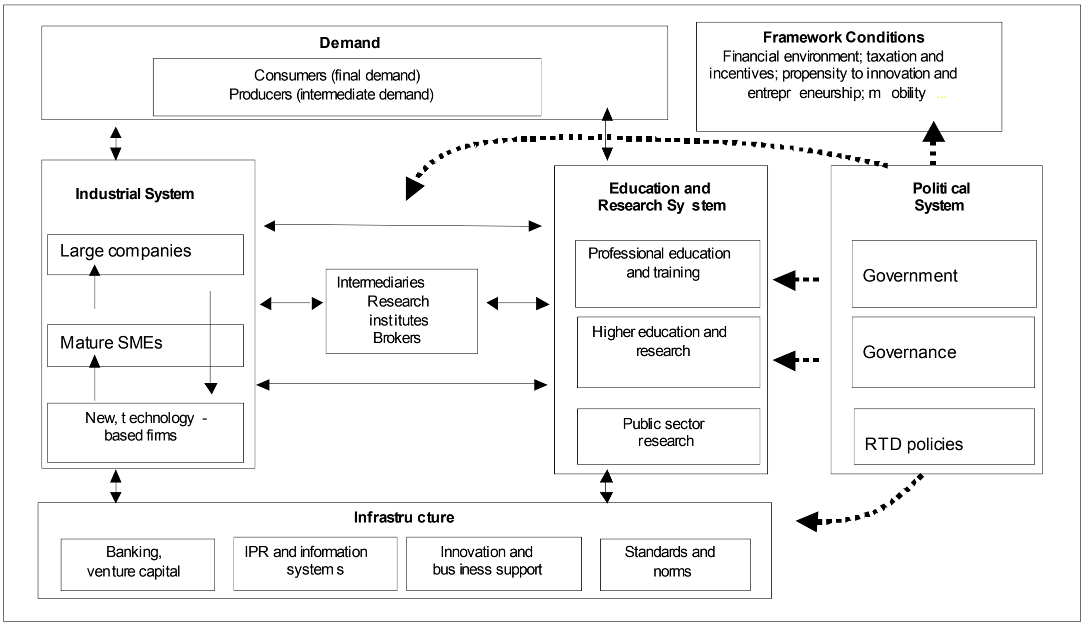

Figure 3 System of innovation (Kuhlmann and Arnold, 2001)

---

[2] Schmookler linked an actor’s innovation activity with its expected economic benefit.

Numerous scholars have described the Innovation System and its components, resulting in as many definitions. Here we present just a few:

> “The network of institutions in the public and private sectors whose activities and interactions initiate, import, modify and diffuse new technologies.” (Freeman, 1987)
>
> “A set of institutions whose interactions determine the innovative performance (...) of national firms.” (Nelson, 1993)
>
> 'A system of innovation is that set of distinct institutions which jointly and individually contributes to the development and diffusion of new technologies and which provides the framework within which governments form and implement policies to influence the innovation process. As such it is a system of interconnected institutions to create, store and transfer the knowledge, skills and artefacts which define new technologies.” (Metcalfe, 1995).
>
> "The various ‘landscapes’ of institutions, corporate actors and processes contributing to industrial and societal innovation." (Kuhlmann, 2001)
>
> “The determinants of innovation processes; all important economic, social, political, organisational, institutional, and other factors that influence the development, diffusion, and use of innovations.” (Edquist, 2004).

Of course these definitions differ from each other; however, they all encompass the same elements:

1. A network of stakeholders;
2. Interactions between the stakeholders in which knowledge and information is transferred;
3. Institutions; and
4. A ‘purpose’ (i.e. innovation success, reduction of uncertainty, economic growth and welfare) of the Innovation System.

The activities in the IS can be described as *learning activities*. *Learning by searching* is another name for R&D activities (fundamental research). The concept of *learning by doing* was introduced by Arrow in 1962, as he was inspired by productivity growth in the production of aeroplane wings. “The unit cost of producing manufactured goods tends to decline significantly as more are produced.” (Von Hippel and Tyre, 1995). This is due to increasing production skills. *Learning by using* as a concept evolved 20 years later when Rosenberg (1982) explained the reduction in costs when “using complex systems and users became more familiar with them” (Lundvall, 2005). One example is the maintenance of jet engines, which showed a reduction of 30% in the cost during a decade (Rosenberg, 1982). Since it is practically impossible to obviate all possible interactions between an invention and every day usage (e.g. the aforementioned production or maintenance in the aeroplane industry), learning by doing and using are key factors in advancing towards a most optimal outcome; innovation is a continuous process with ‘learning’ moments on its way.

The above-mentioned forms of learning are all *internally oriented*, meaning that these learning processes are intra organisational processes. Foray (2000) argues that therefore the knowledge created in these internal learning processes have a limited impact on the whole economy; the learning is local and specific to one user or producer and therefore knowledge stays tacit. *Learning by interacting* enables organisations to ‘draw’ knowledge from external sources.

> “Learning by interacting is fundamental since it transforms the outcomes of learning by doing and learning by using from being local to becoming non-local. Embodying knowledge in new services and products may be seen as an alternative to codification as mechanism of generalizing local knowledge. […] The learning by interacting has the effect of transforming local learning into general knowledge embodied in for instance new machinery, new components, new software-systems or even new business solutions.” (Lundvall, 2005)

Lundvall (2005) here makes the distinction between the Doing, Using and Interactive Learning (DUI)-mode and the Science, Technology and Innovation (STI)-mode: “In the DUI-mode the generalisation of local learning will typically be embodied in new machinery and components while in the STI-mode innovations may reach the user in the form of disembodied codified knowledge.” Consumer’s wishes and expectations are stressed in these STI-learning processes and are subject to change over time. Through mutual, external learning the condition for optimal outcome is set. Learning is not only a mechanism limited to the interaction between users and producers. The same mechanism also occurs in the interaction between stakeholders involved in the institutional framework setting process.

Before the conceptualization of interactive learning takes place, we first focus on the particular role of users and their interactions in the innovation process.

Innovation and users

The iterative model of innovation processes is often substantiated by pointing at the important role of users. Von Hippel (1976) was one of the first authors who showed that in some sectors users dominate the innovation process. He built upon product development literature and empirical work of Utterback and the SAPPHO-project in which the researchers tried to understand the user needs in various industrial sectors. Research in the field of scientific instruments (and later in other sectors such as process machinery in the semiconductor and electronic sector (Von Hippel, 1977)) led to the conclusion that users can initiate, formulate and even develop new products and processes. Thereby they become what he calls the “locus of innovation”. The importance of including users in the analysis of innovation processes is now widely acknowledged and has led to a broad and diverse range of user involvement literature in innovation sciences, organizational studies, and science and technology studies (Moors, 2003; Geels, 2002; Jelsma, 2005; Oudshoorn and Pinch, 2003).

Innovation studies show that intensified user-producer *interaction* increases chances for successful innovations. Von Hippel (1978) and related authors showed the importance of user initiatives[3] in innovation processes (Von Hippel, 2005). In 1978 Eric von Hippel showed in a comparative study that more than half of the innovation

[3] In these cases, users had a need and an idea how to fulfil this need. They even produced a prototype that they introduced to a producer for manufacturing.

was initiated by users (Table 1). Based on his research Von Hippel concludes that the manufacturer active paradigm has partly had it's day and needs to be supplemented with the customer-active paradigm4. Von Hippel's conclusion underpins the modern thinking about innovation in the IS and the role of users within it. Rothwell et al. (1974) showed that the commercial success of an innovative industrial product co-varies with the understanding of user needs by the manufacturer. This was for example shown in their study in which 43 pairs of product innovations consisting of commercially successful and commercially failing products aimed at the same market niche were compared. The question whether user needs "were more accurately understood in one member of the pair than the other?" holds for 33 of the 43 pairs (77%).

Table 1 Frequency with which industrial product and process innovation work has been initiated by a costumer request (Von Hippel 1978)

Study	Type of innovation	n	Data available regarding presence of customer request
Meadows	Chemical Products	29	9 of 17 (53%) commercially successful project ideas were from customers
Peplow	Plant processes, process equipment and techniques	94	30 of 48 (62%) successfully implemented projects were initiated in response to direct customer request
Von Hippel	Innovative process equipment	49	67% of equipment innovations developed by users, not equipment manufacturers. In 20% of these cases, users *needed* an outside supplier to manufacture the innovation in quantity and initiated manufacture via ' customer request'
Berger	Engineering plastics	5	No project initiating request from costumer found
Boyden	Plastic additives	16	No project initiating request from costumer found
Utterback	Scientific instrument innovations	32	75% initiated in response to 'need input'. When need input originated outside product manufacturer (57%) source was 'most often' customer
Robinson	Standard and non-standard industrial products	NA	Customers recognize need, define functional requirements and specific goods and services needed *before contracting potential suppliers*

Whereas Von Hippel mainly focused on new industrial products, more recent studies by Lüthje (2004; 2005) investigated innovating users in consumer goods fields. Lüthje refers to three studies on user involvement in consumer goods, where users were involved in 13%, 32% and 58% of the cases. In his own research on outdoor related products, Lüthje found that more than one third of the customers generated at least one idea for improved or new outdoor related products. 70% were ideas about improvements of existing products and 30% were inventions of new products. More than 9% of the user sample developed at least a prototype (Lühtje, 2004). Next to showing the importance of user initiatives in the innovation process, Von Hippel (1988) explained why users could be highly involved in the innovation process. He found that the functional source of innovation resides in the actors "whose analysis lead them to expect a rent they consider attractive". Regarding users, Von Hippel actually coined a term for users who perceive that their expected benefits are significant, and who face certain needs well before the rest of the market or sector, namely lead users (Von Hippel, 1986). Thirdly, Von Hippel stressed the importance of

[4] Daarnaast onderkend Von Hippel nog het *unfilled known need* paradigma waarbij algemeen aanwezige behoeftes als vanzelfsprekend worden ingevuld door producenten zodra de technologische voortgang dit toelaat.

including users in the innovation processes. Not only do users point to directions of future needs (as is the main target of marketing research), they could also have first-hand information on new research directions, ideas, problems, solutions, etc. This is relevant for new products, processes or services, but also for incremental adjustments to existing ones. The latter is mostly communicated to the producers during the early use of innovations. This trial-and-error process is called learning-by-doing (Von Hippel, 1995). Knowledge on these problems, ideas, adjustments, etc. is not easily transferred to other actors, e.g. because of its situation- and setting-related character. This is called “stickiness” of knowledge (Von Hippel, 2001). Therefore, it is very important for producers to remain in constant interaction with their users.

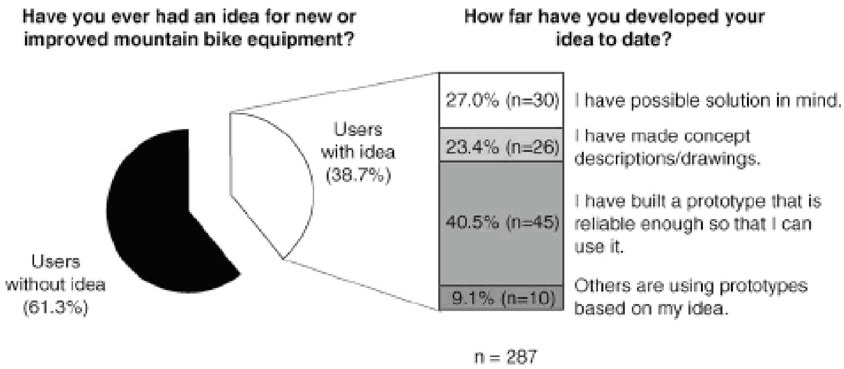

Figure 4 Idea and prototype generation by serious mountain bikers. (taken from Lüthje, 2005)

No matter whether innovations in functional genomics can be classified as new industrial products or as new consumer goods, the above mentioned empirical studies indicate that users matter: users come up with innovative ideas, identify new markets and reduce the danger of wrong interpretation of market information (and hence R&D investments).

> “If manufacturers ignore the innovation potential of their customers, they may miss all promising user innovations [..] They even risk losing their competitive advantage, if the ideas are detected and successfully exploited by competing firms.” (Lüthje, 2004)

The advantages of interacting with users

The empirical studies of Von Hippel (on industrial products, 1978) and Lühtje (on consumer products, 2004 and 2005) show that interaction with users contributes to innovations because 1) expectations of users are incorporated in the innovation process (and resulting outcome) 2) the user’s creative potential is used. This results in less unsuccessful disinvestments and more innovation success. Besides these studies of Von Hippel (1978) and Lüthje (2004; 2005), Van der Poel (2000) and Ebersberger (2005) showed in their studies that 3) most radical innovations are initiated by outsiders because they are *out of the box* thinkers, not restricted by company culture or institutions.

Smits and Den Hertog (2005) identify ‘at least’ five reasons to justify investing in a two-way learning process:

1. More effective articulation of social needs
2. Increased competitive strength of private enterprises
3. Improved acceptance and better social embedding of knowledge and technology

4. Improved learning capacity of society as a whole
5. Enhanced democracy

Especially the day-to-day user of innovation, with his creative ideas, wishes and expectations, plays an important role in the innovation success (Vandeberg, 2005). There is not much hard evidence that directly and causally relates interaction between users and producers with innovation success. At least not in the sense that interactions explain the degree of success. Von Hippel et al. (1978) investigated successful products[5], but did not differentiate between more and less successful ones. Only the SAPPHO-project gives a clue: it was found that differences between successful and unsuccessful innovations are (amongst others) explained by acknowledging user needs (Rothwell et al, 1974).

Summing up, disciplines ranging from economics to psychology have (more or less) a different approach to studying user involvement in innovation processes, and they differ in their emphasis on the producer or user context. Von Hippel and his collaborators empirically enhanced the notion of user involvement in innovation processes: users can be sources of innovation. Furthermore, it is stressed that interaction between users and producers is important to enhance incremental or totally new innovations. All in all, it could be claimed that there is circumstantial evidence that user involvement and user-producer interactions lead to successful innovations.

Interactive learning

We focus on learning by interacting because we are interested in the interaction between users and producers in nutrigenomics and pharmacogenomics innovations. As shown in the previous part user involvement and user-producer interactions have an influence on innovation: success rate increases, creative potential of users is used, public acceptance gains. Furthermore, "in the literature on innovation systems there is a focus on learning and interactivity, which is still underanalyzed" (Meeus, 2005).

When stakeholders interact with each other, they exchange e.g. information, ideas, opinions, wishes, expectations and possibilities. Through the interaction the involved actors might change their attitudes relatively permanent as a result of the interaction: the actors learn from each other. The learning between actors contributes to the alignment of the stakeholders in the network and the formation of a window of opportunity. The interaction itself is the moment of information exchange, whereas the learning mechanism is the resulting effect over time. However, in general this distinction is not always made that clear. Interaction often encompasses learning as well. Therefore, we focus on the learning mechanism of interaction. “The firm’s interaction with its environment determines its access to a diversity of resources, whereas the learning enables firms to transform these resources, […] into innovations”. Various fields of literature tend to examine the outcomes of learning, rather than inquire as to what learning actually is and how these outcomes are achieved (Meeus, 2005). Learning, in the sense it is used here, relates to stakeholders, and comprises both processes and outcomes.

[5] It could be discussed what the definition of successful implies. All the more, because an invention means a new product, process or service, while an innovation comprises the commercial successful implementation of these. A successful innovation would then be a pleonasm.

4. A (preliminary) conceptual framework for interactive learning

In order to construct a conceptual framework to analyze interactive learning we studied the work of various authors, such as (Vand der Sluis, 2004; Lundvall, 2005; Meeus, 2005; Pilotti, 2005; Meeus, 2005b; Von Hippel, 1995; Kamp, 2002; Ruprecht, 2005; Elst, 2005; Leeuwis, 2005; Kerkhof, 2005; Meeus, 2001 and 2001b; Luiten, 2001) – covering education, learning on the job, e-learning and interactive learning between stakeholders as we defined it) From this we could identify the following dimensions for interactive learning, with the firm as focal point (also see Figure 5):

- Knowledge is transferred from one actor to the other. According to Lundvall (1992) interactive learning is restricted when the proximity (or distance) between the actors becomes to great. Proximity can be seen as geographical proximity (regional, national and international) or as cultural proximity: a common background (language, culture, legislation, standardisation). If a gap between two actors exists, caused for example by cultural differences (language, customs, rules, roles), the interplay between them will probably be less efficient.
- According to Smits (2005) and Leeuwis (2005) a network builder is an actor that is capable of ‘creating’ a network in which actors can interact.
- At the same time an *intermediary* can transfer knowledge from one actor to the other in a form suitable to the actor (Van Lente, 2003).
- From an organisational point of view *mutual interest* and trust in the learning process itself is a key factor for learning (Leeuwis, 2005). According to Lundvall (1988) mutual trust is one of the major factors influencing the interaction process between users and producers: an actor’s actions are contingent on another actor’s actions which leads to a fragile adjustment game. Such an interaction has a higher probability of success when the actors involved trust each other, regularly engage in face-to-face contacts, and even maintain friendships.
- From an innovation point of view (the transformation of an invention into an innovation) not only inter-organisational interaction is of importance, but also the *intra-organisational learning* between the R&D department and the marketing/customer relationship department (Smits, 2005). It covers for example the degree of access to communication channels (Lundvall, 1988, Roy et al. 2004), the complexity of innovation activities, and integration of internal innovation activities (Meeus, 2001). Linked to this dimension are the factors centred on the internal resources, competencies, knowledge pool etc. of actors (Meeus, 2001) Complementary to this is the actor’s capability to deal with these flows of resources, in particular knowledge. In this context, the concepts of absorptive capacity, and communication codes (Lundvall, 1988) are used.
- The actual interaction between organisations is mediated through persons. Therefore some personal characteristics of the interactors of and during the interaction process are relevant as well (Leeuwis, 2005).

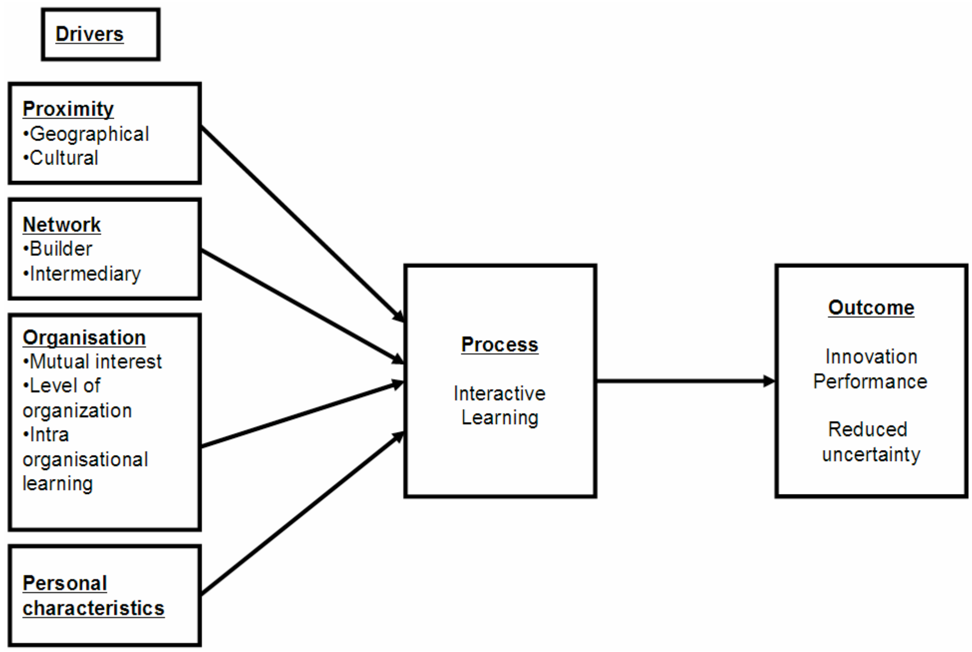

Figure 5 Preliminary conceptual framework: Drivers for interactive learning and influence on innovation outcome.

To test our (preliminary) conceptual framework for studying interactive learning in functional genomics, we did two explorative case studies based on interviews with stakeholders and experts: Nutrigenomics and Pharmacogenomics.

5. Interactive learning in nutrigenomics innovations

The GM and biotech debacle at the end of the 1990s showed that inventions in the food (related) industry are not automatically met with open arms by the general public. One of the major reasons for this debacle was the misfit between scientific inventions and producers possibilities on the one side and user preferences and expectations on the other. Interaction between these stakeholders in an early stage of development can facilitate the alignment between the expectations of the stakeholders. From a technical point of view nutrigenomics is not directly affiliated with genetic modification. In nutrigenomics the interaction between ingredients and the human genome is studied with the ultimate goal of promoting health. Genetic modification is the alteration of genetic material (of plants and animals that could be used in food production). However, for most people nutrigenomics is not different to modern biotechnology and genetic modification (Moors, 2003). Because people equal nutrigenomics to genetic modification, the expectation is that nutrigenomics will encounter the same hurdles.

> “Researchers have not been carefully enough in communicating the clear difference between genomics an genetic modification.” (T. Verrips, UU, 13 June 2005)

The GM-food discussion has shown that the majority of consumers is apposed to technologies that fiddles with the essence of life itself. Generally, most precarious[6] emerging technologies that are imposed on the market through technology push

[6] The outcome is very insecure.

encounter problematic market or social introduction. Interaction with users and other stakeholders in an early stage of technology development might forestall these hurdles. When we take a look at the Innovations System for Nutrigenomics in the Netherlands, we identify several stakeholders in the Nutrigenomics network (Table 2).

Table 2 Stakeholders in Nutrigenomics in The Netherlands (not extensive)

Stakeholder ‘group’	Examples in The Netherlands
Industrial System Nutrigenomics / Functional Food companies	▪ Campina – Healthy dairy ▪ Coberco – Healthy dairy ▪ DSM Food Specialties – specialty food and feed ingredients (semi manufactures) ▪ Numico – Target Groups Nutrition ▪ Sensus - food ingredients ▪ Unilever – Functional Foods
Demand Side Organised Users	▪ Consumentenbond (on EU-level: BEUC, the European Consumers' Organisation) ▪ Nederlands Patiënten Consumenten Federatie (on EU-level: EPPOSI, European Platform for Patients' Organisations) ▪ Stichting Consument, Biotechnologie en Life Sciences (CB&LS) ▪ Vereniging Samenwerkende Ouder- en Patiëntenorganisaties (VSOP)
Demand Side Intermediairy users	▪ Nederlandse Biotechnologie Associatie (Niaba)
Education & Research System	▪ Centre for BioSystems Genomics (CBSG) ▪ Genomics Centre Utrecht (GCU) ▪ Kluyver Centre for Genomics of Industrial Fermentation ▪ Nizo Food Research ▪ TNO Voeding ▪ Wageningen Centre for Food Sciences (WCFS) ▪ Wageningen University & Research Centre ▪
Intermediairies	▪ Netherlands Genomics Innitiative ▪ Voedingscentrum
Institutions	▪ Ministry of Agriculture ▪ Ministry of Health ▪ Reclame Code Commissie ▪ Voedsel en Waren Autoriteit (VWA)

Whether or not interactive learning between these stakeholders in nutrigenomics occurs is the question. In the functional food innovation process 4 phases can be identified. In different phases, different forms of interaction can be distinguished. Table 3 gives an overview of the different phases in Nutrigenomics / Functional Food product development and the kind of interaction that is found in the different phases.

Table 3 Phases in Nutrigenomics product development and Interactions

Phase	Interaction
Pre competitive	Precompetitive basic research Cooperation between researchers
Idea phase	Consumer Science; identification of trends in consumer behaviour
Concept phase	Clinical trails Consumer preferences
Market phase	Interviews Consumer desks

Figure 6 illustrates an example[7] of the interactions between several stakeholders in Nutrigenomics. For this example we used the interviews in which the relation between the interviewed stakeholders were discussed. The yellow column represents the development stages as discussed in Table 3. Especially in the concept phase the interaction between user and producer is evident, manifesting itself in consumer trails and preference testing. At the same time the VSOP has a partnership with Unilever for a 'mutual understanding'. After market introduction the relation between producer and consumer is prolonged through interviews and consumer help desks.

> "In general consumers are the driving force. It is almost never the case that a technology is implemented because it reduces production costs."[8] (S. Brul, Unilver / UvA, 18 May 2005)

The formation of the institutional landscape occurs simultaneously in a parallel process. The interaction between stakeholders in the institutional landscape (in The Netherlands) is coordinated by the Voedingscentrum.

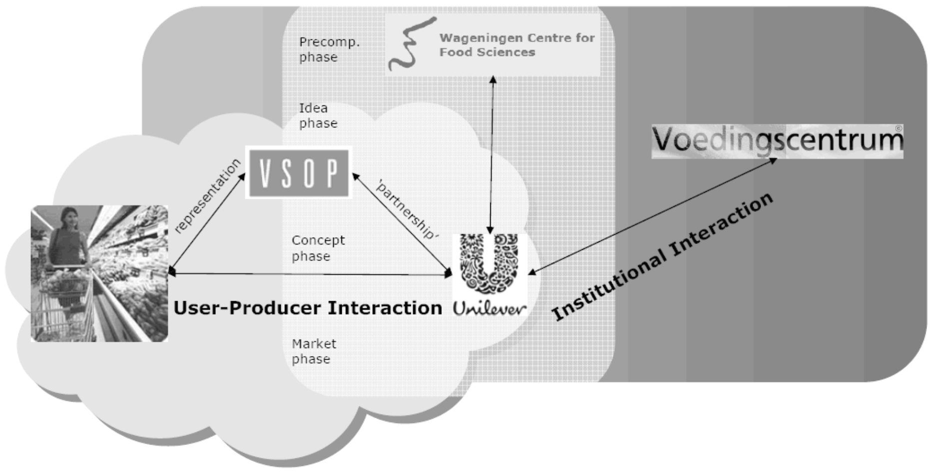

Figure 6 Real life example of user-producer interactions and stakeholder interaction in The Netherlands, based on interviews (May-June 2005)

[7] For clarity not all relations are depicted.

[8] Translated from Dutch: "De drijvende kracht is toch doorgaans de consument. Het is bijna nooit zo dat er een nieuwe technologie is die op zichzelf alleen maar de kosten verlaagt voor een product en daardoor al voldoende interessant is om in te investeren."

In the case of nutrigenomics we can observe interactive learning. Below we describe the interactive learning in nutrigenomics according to the preliminary conceptual framework:

- The *geographical proximity* in the Dutch Nutrigenomics network is evident, since all stakeholders are rooted in The Netherlands.
- The stakeholders/partners in the WCFS have the same *cultural* background. Although Unilever (knowledge intensive producer) and the VSOP (patient representation) have a different *culture*, their professionals are able to communicate in a constructive manner. This probably also holds for the relation between Unilever and the Voedingscentrum (specialised in institutions). However, this was not discussed explicitly in the interviews.
- Unilever does have direct contact with consumers (for example through 0800 numbers). In this contact there is a knowledge difference between the two actors. Therefore the relation between Unilever and the VSOP is highly appreciated because the VSOP can represent the consumer in a constructive way.
- In the discussion about the future of the functional food market in The Netherlands (i.e. the position of soft versus hard claimed functional foods) the Voedingscentrum is a *network builder*.
- At the same time the Voedingscentrum is an *intermediary* transferring scientific knowledge to information for consumers (lay men). However, this is merely an information service instead of an two-way interaction process.
- Both Unilever and the VSOP are *interested* in the interaction because Unilever can learn about consumer's wishes, whereas the VSOP is able to see what developments are going on at Unilever and has a change of steering these towards their whished possibilities.
- In the emerging knowledge field of nutrigenomics most learning processes are *internally* oriented because product development is the idea or concept phase, in which no interaction between users and producers is visible (see Table 2).

6. Interactive learning in pharmacogenomics innovations

It is widely acknowledged that the pharmaceutical industry will be challenged in the near future, because of a declining amount of marketable products in the face of increasing R&D investments, the so-called 'pharmaceutical paradox' (Gassmann et al., 2004). Technologically, much is expected from the recent pharmacogenomics developments: functional information of the human genome is linked with disease susceptibility and drug response. As is illustrated in Figure 7, several steps in the drug development pipeline are influenced by these developments.

Besides these technological improvements, the innovation processes themselves can be enhanced. One of the major parts of these processes is interactive learning, as has been introduced above. The first question that can be asked is whether in the fields of pharmacy and medicine interactive learning does occur at all. To answer this we need to show which actors do play a part in these fields. This illustrated in Figure 7 below.

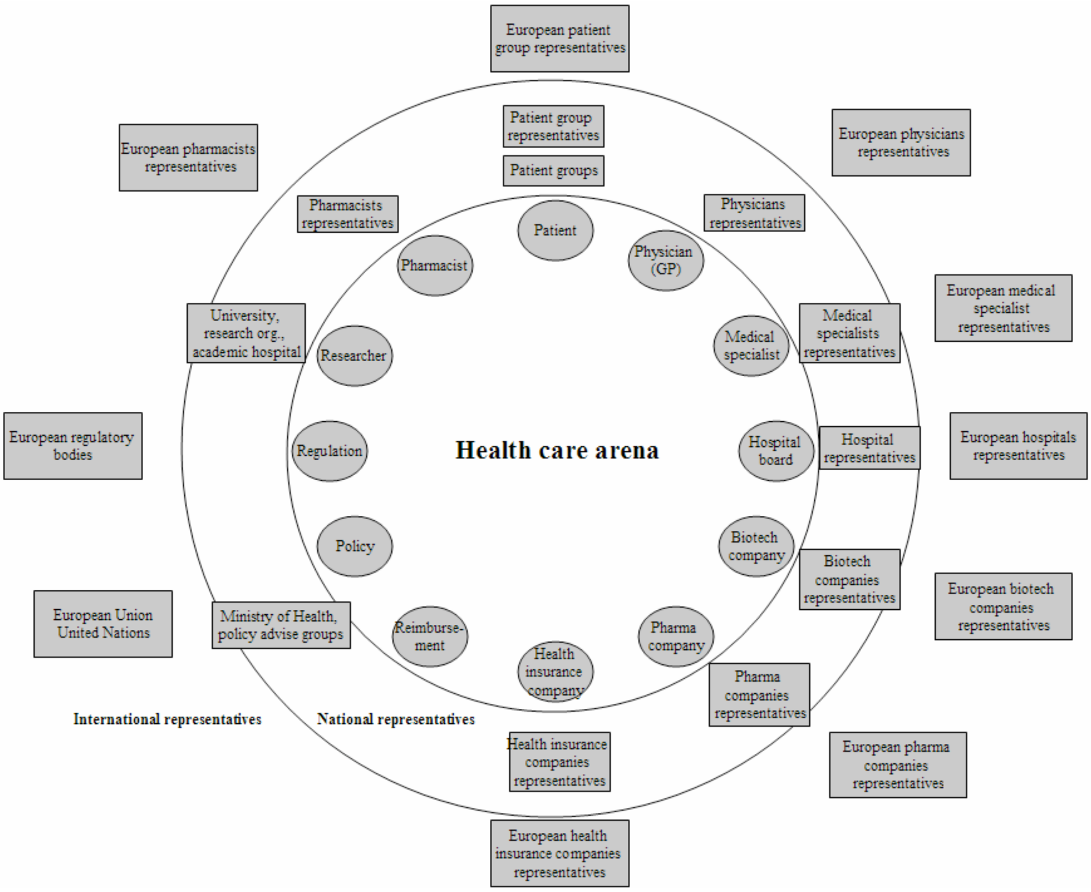

Figure 7 Social map of relevant actors in the field of medical applications of prevention, diagnosis and therapy in the Netherlands, embedded in the European context (based on interview results).

In the pharmaceutical industry few actors are involved in the development of a new drug, and probably still fewer actors are actually influential. The pharmaceutical (and biotechnology) companies spring in mind in this respect: “Pharmaceutical innovations are technology push” and “The pharmaceutical companies expect that once a product is approved, it *should* be used” (interview results, umbrella organization of health care insurance companies). They develop their products largely in-house, but in recent decades also engage more and more in strategic alliances with for example biotechnology companies and university spin-offs (Hagedoorn, 2002). It is thought that learning automatically occurs between these cooperating partners.

Another influential actor in this field is the regulatory body, such as the FDA or EMEA, which grants permits for pharmaceutical products to enter the market. Between pharmaceutical companies and these bodies learning also occurs. For example, the EMEA has several working committees in which representatives of companies also take part that discuss upcoming trends and their repercussions on current regulatory practice.

The other actors also do play a role but opinions on their influence of the pharmaceutical innovation process through learning are more ambiguous. Hara (2003) states that a prerequisite for the adoption of a new drug in Japan is the approval of a few highly regarded medical specialists. Also the influence of patients’ organizations could be substantial: “They are crucial, steering and the engines that fuel new developments” (interview result, medical specialist). For example, in some cases they co-decide on future biomedical research topics (Caron-Flinterman and Broerse, 2005).

All in all, interactive learning does occur in the case of pharmaceutical innovations, but it is not clear whether the relevant participating parties come from outside the business and regulatory sector. Still, it is interesting to investigate to what extent the important dimensions of interactive learning, as they are introduced in Section 3, are relevant in this case. They are discussed below.

- Proximity: geographical or cultural distance between different actors only plays a role when looking at it from a national vs. international perspective. That is, the research and development of pharmaceutical products takes place on an international level and distances seem to be of no importance. One of the reasons for this is the relative international codes of science and technology on which these products are based. On the other hand, when a potential product moves more towards the market introduction phase in the drug development pipeline, the national context begins to grow in importance. For example, the registration is now also internationally organised (through the FDA and EMEA), but the decision whether a product will be reimbursed is still made on a national level.
- Network builder: pharmaceutical companies strategic ally themselves with biotechnology firms, (university) spin-offs, or platform technology firms, but also with other parties in the field of medicine. Therefore, they can be seen as core actors in the field and network builders at the same time.
- Intermediary organization: intermediary organizations are important within the field of medicine. In Figure 7, a lot of representative organisations are depicted which can be seen as instances of intermediaries. These kinds of organisations try to influence the direction of innovation outcome or policy.
- Mutual interest in learning: when pharmaceutical companies interact with each other they can do this in several ways, such as licensing, take-over, or strategic alliances. In the latter case the companies engage in a long-term exchange based on mutual trust and close interactions, because the exchange not only covers codified but also tacit knowledge, two important aspects of the internal knowledge base of these firms on which they base their competitive advantage. These strategic alliances can therefore be seen as a higher form of mutual interest in learning (Jungmittag et al., 2000). As is explained above, also pharmaceutical companies and regulatory bodies are mutually interested to learn. For all the other interactions this is less clear (interview results, regulatory body).
- Intra-organizational learning: up to the 1980s pharmaceutical companies tried to do their research and development completely in-house. There existed a division between fundamental and applied research and therefore, intra-organizational learning was difficult but necessary. From this period on, besides the dominant strategy of in-house R&D, cooperation with other companies, universities, or research institutes increased in importance (Jungmittag et al., 2000).
- Personal interaction: “Patients’ representative organisations are often founded by a small group of people” and in discussion groups often “the same people are raising their voices” (interview results, governmental steering committee). This means that personal interaction is important. Nevertheless, it should be stressed that although personal interaction is important, the unimportance of

distance and the central role of pharmaceutical companies makes interaction through other ways, e.g. contracts, just as important.

We can conclude that interactive learning takes place, especially amongst companies themselves and with regulatory bodies. The theoretic dimensions that were seen as important for interactive learning were compared to the case of the pharmaceutical industry and the field of medicine. All the dimensions seemed highly relevant, at least when focussing on the current situation. Whether these filling out of these dimensions will change in the future as a result of pharmacogenomics innovations is far less clear to see.

7. Conclusions and discussion

In the nutrigenomics field different stakeholders interact and interactively learn from each other in four phases (used as a conceptual framework): The pre competitive, the idea, the concept and the market phase.

It could be concluded from the first exploratory case study in the field of nutrigenomics that in the emerging knowledge field of nutrigenomics most learning processes are internally oriented because product development is the idea or concept phase, in which no interaction between users and producers is visible (see Table 2 Phases in Nutrigenomics product development and Interactions). This situation calls for transfer to external learning.

Based on the exploratory case study on pharmacogenomics, it can also be concluded that the locus of interactive learning takes place within a pharmaceutical companies. In recent years this is complemented, or in some cases even replaced, by interaction with other, smaller companies to bring in new technological knowledge or to smoothen the organization of, for example, the clinical trials. With new technological developments like pharmacogenomics, pharmaceutical companies are interested to let their needs be in tune with the requirements of the regulatory bodies. Therefore, interactive learning takes place between those two agents. Other instances of interactive learning are less evident.

It seems that geographical and cultural proximity (distance), the presence of a network builder, intermediary organizations, mutual interest in learning, intra-organizational learning processes and personal interactions are important interactive learning dimensions in nutri- and pharmacogenomics innovations.

As the results of this paper are based on exploratory case studies in the field of nutri- and pharmacogenomics, the following discussion points need to be further elaborated:
In the case of the pharmaceutical industry, the dimensions were filled in according to the current situation. However, The pharmacogenomics future is far less clear to envisage and therefore valuing these dimensions for such a future is more difficult.
In the case of the pharmaceutical industry, the focus lies on interactive learning with (or in) the pharmaceutical company, because it has a central role within this industry. More research is needed on interactive learning with and between other kinds of organizations. Especially the intermediary organizations would be, because of their

large presence in the network and their specific (and particular) tasks within the field of medicine, interesting to study.
In the nutrigenomics field, the interaction with users is crucial. However, the question remains who the essential negotiation partner for the food producers are: ingredient suppliers, regulatory bodies or is the costumer king? It seems that food-producing companies try numerous new combinations and play wait and see to determine the success factor of the innovation.
The developed conceptual framework still needs further elaboration, especially with regard the operationalization of the dimensions of interactive learning. The focus thereby will be on interactive learning in networks of stakeholders.
This paper presented the first results of two ongoing PhD studies on mechanisms of user-producer interactions and interactive learning in nutri- and pharmacogenomics innovations. Future work will elaborate further on the specific conditions determining interactive learning processes in user-producer interaction. The focus will be on interactive learning processes in networks of emerging nutrigenomics technologies and on processes of demand articulation and the role of intermediaries in pharmacogenomics developments.

Although the evidence of the two case studies is certainly not decisive, it appears that interactive learning is an important interaction process in genomics developments. The approach followed in this paper could give starting points for change and could be helpful in analysing user-producer interaction in other emerging technology fields.

References

Arrow, K.J. (1962), "The Economic Implications of Learning by Doing", Review of Economic Studies, Vol. XXIX, No. 80.

Blume, S. S. (1992). Insight and industry: on the dynamics of technological change in medicine. Cambridge, Mass, The MIT Press.

Boulnois, G. J. (2000). "Drug discovery in the new millennium: the pivotal role of biotechnology." Trends in biotechnology **18**: 31-33.

Caron-Flinterman, J. F., J. E. W. Broerse, et al. (2005). "The experiential knowledge of patients: a new resource for biomedical research?" Social science and medicine **60**: 2575-2584.

Dean, P. M., E. D. Zanders, et al.(2001). "Industrial-scale, genomics-based drug design and discovery."Trends in biotechnology**19**(8): 288-292.

Delden, J. v., I. Bolt, et al. (2004). "Tailor-made pharmacotherapy: future developments and ethical challenges in the field of pharmacogenomics." Bioethics **18**(4): 303-321.

Ebersberger, B., K. Laursen, et al. (2005). "The Origins of Radicalness and Complexity in Product Innovation - An Analysis of the Finnish Innovation Database." Paper to be presented at the 4th European Meeting on Applied Evolutionary Economics (EMAEE): Geography, Networks and Innovation, Marinus Ruppert Building, Utrecht University, De Uithof, Utrecht, The Netherlands, 19-21 May 2005.

Edquist, C. (2004). Systems of Innovation: Perspectives and Challenges. The Oxford handbook of innovation. J. Fagerberg, D. C. Mowery and R. R. Nelson. Oxford, Oxford University Press: 181-208.

Edquist, C. and M. McKelvey (2000). Introduction. Systems of Innovation: Growth, Competitiveness and Employment. Cheltenham, UK, Edward Elgar Publising Limited.

Edquist, 1997: *Systems of Innovation. Technologies, Institutions and Organisations,* London/Washington: Pinter.

Elst, J. v. d., R. Tol, et al. (2005). "Innovation in practice - Philips Digital Systems Laboratories." IJTM.

EMEA (2003). Position paper on terminology in pharmacogenetics. London, European Agency for the Evaluation of Medicinal Products.

Enzing, C.M. (1995) *Overzicht van wetgeving, maatregelen en activiteiten betreffende biotechnologie activiteiten van bedrijven,* Achtergrondstudie in opdracht van het Rathenau Instituut, TNO-STB, Apeldoorn.

Foray, D. (2000), The economics of knowledge, Cambridge Massachussets, The MIT-press.

Freeman, 1987: *Technology Policy and Economic Performance: Lessons from Japan*, London: Pinter.

Gassmann, O., G. Reepmeyer, et al. (2004). Leading pharmaceutical innovation. Berlin, Springer.

Geels, F. (2002). Understanding the dynamics of technological transitions. Enschede, Universiteit Twente.

Hagedoorn, J., 2002. Inter-firm R&D partnerships: an overview of major trends and patterns since 1960. Research Policy 31: 477-492.

Hara, T. (2003). Innovation in the pharmaceutical industry. Cheltenham, UK, Edward Elgar.

Jelsma, J. (2005). Bridging gapsbetween technology and behaviour: a heuristic exercise in the field of energyefficiency in households.User involvement in innovation processes -strategies and limitations from a scio-technical perspective. H. Rohracher.Munchen, Profil.

Jungmittag, A., G. Reger, et al. (2000). Changing innovation in the pharmaceutical industry. Berlijn, Springer.

Kamp, L. (2002). Learning in wind turbine development - A comparison between the Netherlands and Denmark. Utrecht, Utrecht University.

Kaput, J. (2004). "Diet-disease gene interactions." Nutrition **20**(1): 26-31.

Kerkhof, M. v. d. and A. Wieczorek (2005). "Learning and stakeholder participation in transition processes towards sustainability: Methodological considerations." Technological Forecasting & Social Change **72**(2005).

Kuhlmann, S. & Arnold E., 2001: RCN in the Norwegian Research and Innovation System, *Report* for Research Council of Norway, Oslo, 47pps.

Leeuwis, C., B. v. Mierlo, et al. (2005). "Innovation systems and social learning: linking the meso and the micro level."

Luiten, E. (2001). Beyond Energy Efficiency. Utrecht, Utrecht University**:** 300.

Lundvall, B. (2005). Interactive learning, social capital and economic performance. Advancing knowledge and the knowledge economy, Washington.

Lundvall, 1992: *National Systems of Innovation: Towards a Theory of Innovation and Interactive Learning,* London: Pinter.

Lundvall, B. A. (1988). Innovation as an interactive process: from user-producer interaction to the national system of innovation. Technical change and economic theory. G. Dosi, C. Freeman, R. Nelson, G. Silverberg and L. Soete. London, Pinter**:** 349-369.

Lüthje, C., C. Herstatt, et al. (2005). "User-innovators and “local” information: The case of mountain biking." Research Policy **34**: 951–965.

Lüthje, C. (2004). "Characteristics of innovating users in a consumer goods field - An empirical study of sport-related product consumers." Technovation **24**: 683–695.

Moors, E., C. Enzing, et al.(2003)."User-producer interactions in functional genomics innovations."Innovation:management, policy&practice**5**(2-3): 120-143.

Mowery, D. C. and N. Rosenberg (1979). "The influence of market demand upon innovation: a critical review of some recent empirical studies." Research Policy **8**(2): 102-153.

Metcalfe, J.S. (1995). The Economic Foundations of Technology Policy: Equilibrium and Evolutionary Perspectives. In Handbook of Economics of Innovation and Technology Change, edited by P. Stoneman. Oxford: Blackwell.

Meeus, M. and L. Oerlemans (2005). Innovation Strategies, Interactive Learning and Innovation Networks. Chektenham (UK), Edgard Elgar Publishing.

Meeus, M. and L. Oerlemans (2005b). Innovation Strategies, Interactive Learning and Innovation Networks. Chektenham (UK), Edgard Elgar Publishing.

Meeus, M. T. H., L. A. G. Oerlemans, et al. (2001). "“Sectoral Patterns of Interactive Learning” An empirical exploration of a case in a Dutch Region." Technology Analysis & Strategic Management **13**(3): 407-431.

Meeus, M., L. Oerlemans, et al. (2001b). "Patterns of Interactive Learning in a High-tech Region." Organisation Studies **22**(1): 145-172.

Nelson, 1993: *National Innovation Systems: A Comparative Analysis*, Oxford/New York: Oxford University Press.

Oudshoorn, N and T.J. Pinch (eds) (2003) *How Users Matter. The co-construction of users and technologies*, NewYork: MIT Press.

Pilotti, L. and S. R. Sedita (2005). "Human capital development in a complex learning system: the virtuous interaction between individuals, organizations and communities." Working Paper Università degli Studi di Milano Dipartimento di Scienze Economiche, Aziendali e Statistiche.

Rothwell, R., C. Freeman, et al. (1974). "SAPPHO updated - project SAPPHO phase II." Research Policy **3**(3): 258-291.

Rosenberg, N. (1982), Inside the black box: Technology and economics, Cambridge, Cambridge University Press.

Roy, S., K. Sivakumar, et al. (2004). "Innovation generation in supply chain relationships: a conceptual model and research propositions." Journal of the Academy of marekting studies **32**(1): 61-79.

Ruprecht, W. (2005). "The historical development of the consumption of sweeteners – a learning approach." J Evol Econ **2005**(15): 247–272.

Smits, R. and P. d. Hertog (2005). "TA and the management of innovation in economy and society." IJFIP

Smits, R. and S. Kuhlmann (2004). "The rise of systemic instruments in innovation policy." International Journal of Foresight and Innovation Policy **1**(1/2): 4-32.

Smits, R. and S. Kuhlmann (2002) *Strengthening Interfaces in Innovation Systems: rationale, concepts and (new) instruments*, report prepared for EC STRATA Workshop, Brussels, 22-23 April 2002.

Smits, R. (1994). "Elk land krijgt de technologie die het verdient - maar lang niet altijd die technologie die het nodig heeft." Inaugurele rede 7 oktober 1994 Katholiek Universiteit Brabant.

Vandeberg, R. (2005). Open innovatie: de innoverende gebruiker. Open stellingen - Essays over Open innovatie. A. v. W.-e. Technologiebeleid. Den Haag, Adviesraad voor Wetenschaps- en Technologiebeleid**:** 41-64.

van Ommen, B. (2004). "Nutrigenomics: exploiting systems biology in the nutrition and health arenas." Nutrition **20**(1): 4-8.

Van der Poel, I. (2000). "On the Role of Outsiders in Technical Development." Technology Analysis & Strategic Management **12**(3): 383-397.

Van der Sluis, L. E. C. (2004). "DESIGNING FOR LEARNING AND INNOVATION AT WORK." Free University Amsterdam Faculty of Economics and Business Administration Department of Management and Organisation: 20.

Van Lente, H., M. Hekkert, R. Smits and B. van Waveren (2003). "Roles of systemic intermediaries in transition processes." International journal of Innovation management **7**(3): 1-33.

Von Hippel, E. (2005). Democratizing innovation: the evolving phenomenon of user innovation. Advancing knowledge and the knowledge economy, Washington.

Von Hippel, E. (2001). "Perspective: user toolkits for innovation." Journal of product innovation management **18**: 247-257.

Von Hippel, E., and M. Tyre (1995). "How "Learning by Doing" is Done: Problem Identification in Novel Process Equipment." Research Policy: **24**: 1-12.

Von Hippel, E. (1988). The sources of innovation. Oxford, Oxford University Press.

Von Hippel, E. (1986). "Lead users: a source of novel product concepts." Management science **32**(7): 791-805.

Von Hippel, E. (1978). "Acustomer-active paradigm for industrial product idea generation." Research Policy **7**: 240-266.

Von Hippel, E. (1977). "The dominant role of users in semiconductor and electronic subassembly process innovation." IEEE Trans. Engineering Management **24**(2): 60-71.

Von Hippel, E. (1976). "The dominant role of users in the scientific instrument innovation process." Research Policy **5**: 212-239.