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Commercialization, Patents and Moral Assessment of Biotechnology Products

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ABSTRACT

The biotechnology patent debates have revealed deep moral concerns about basic genetics research, R&D and specific biotechnological products, concerns that are seldom taken into consideration in Technology Assessment. In this paper important moral concerns are examined which appear at the various stages of development of a specific genetic product: a predictive genetic test. The purpose is to illustrate the need for a more contextual approach in technology assessment, which integrates the various forms of interaction between bio-technology and society or societal segments. Such an approach will generate greater insight in the moral issues at all stages of a product's life-cycle and this will facilitate decision-making on the 'morality'of a specific biotechnological product.

Key words: commercialization, genetic testing, patenting, technology assessment

I. INTRODUCTION

An important purpose of technology assessment (TA) is to assess the impact and consequences of technological developments for man, society and environment in order to facilitate informed policy decisions. This can be undertaken in a (supposedly) morally neutral way through risk-analysis or by studying safety aspects for users. TA can limit itself to this and leave moral evaluation of these data to others.

Another approach is actually to incorporate moral assessment (MA) in TA by exploring moral issues generated by the exploitation and use of a specific

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technological end-product. Such an approach would focus on ethically responsible use of the end-product and it would be in line with two approaches dominant in Anglo-Saxon countries. One is consequentialist: potential benefits for individual and society are weighed against potential harm for individual, community and environment. The other is the 'principle approach': four principles (respect for autonomy, promotion of well-being, avoidance of harm, and justice) are applied to a specific technique or product to determine appropriate use. Both tend to be individual-oriented and are focused on concrete and anticipated effects of a product (Hoedemaekers, 1997). Their rational approach seems to make them eminently suitable to also morally assess a specific technology.

But is this focus on effects sufficient? If the major concern is to provide guidelines for appropriate and morally defensible use, the danger is that these two types of moral assessment take a specific technology or technological development for granted, accept its existence and inherent value-system and do not examine more fundamental questions generated by the technology itself.

A third possibility is therefore also to take a critical stance with regard to the technology itself and explore (and assess) the various sorts of moral issues involved in *all* the stages of the development of a product, including basic research and R&D. Such an approach would involve a much wider range of moral questions. A leading question would be whether the specific technology *as such* is justifiable in the light of fundamental moral, cultural or religious values (ten Have, 1995a; 1995b). This would involve a more contextual and two-way approach, which does not only examine the manner in which a specific technology is embedded in (and is influenced by) specific moral, cultural or religious values (which may be questioned), but also the manner in which technology is transforming important moral and cultural values (which may raise new moral questions).

In order to explore the possibilities of this type of moral assessment in TA, the life-cycle of a specific gen-technological product, a predictive genetic test, will be examined in order to locate the various kinds of moral issues. One of the steps in this life-cycle is the patenting-phase. This phase offers an opportunity to locate wider moral issues related with gene-technology, because in Europe the debate about the EU Directive on the legal protection of biotechnological findings has become a platform to discuss often deeply felt moral concerns about biotechnology. In this paper, major concerns about gene technology voiced in this debate will therefore be incorporated in the moral

exploration of a gene-test's life cycle. The following steps will be distinguished: basic research, R&D, patenting of DNA sequences and genetic tests, manufacturing, testing, marketing and exploitation of the test and finally the test's impact on individual and society. This exploration will be undertaken as a kind of paradigm case illustrating a less traditional role of MA in TA. Before we examine a gene-test's life cycle, a brief survey of the patenting debate may help understand the various sorts of moral concerns.

II. THE GENE PATENTING DEBATE

In Europe's debate on patenting of biotechnology products, many of these concerns could be voiced because in the European Patent Code an appeal can be made to the so-called ''morality provision'' (EPC, art. 53): inventions the publication of which are contrary to ''public order'' and ''morality'' can be excluded from patentability. This ''morality clause'' offered not only competitors an opportunity to fight a patent claim, but also religious groups, interest groups or organizations trying to influence unwished-for developments.

Ethical concerns in the debate on the legal protection of biotechnological inventions can be located in completely different types of arguments (adapted from Svatos, 1997) and take on various forms. The *first* type of argument is related to the moral justification of the patent system itself. Opponents of patents on life-forms have attacked the patent system itself on moral grounds, e.g., by pointing out the danger of a monopolistic control of agriculture or food industries. Others are concerned that costly research will not be undertaken without patents, which will be to the disadvantage of (future) patients.

The *second* type of argument is linked with the extension of the patent system to the domain of life forms. Can the patent system be applied to animate matter? Arguments at this level are often of a rather legal-technical nature and are used to demonstrate whether or not human tissue or DNA sequences satisfy the criteria for patenting such as novelty, utility and non-obviousness. Opponents have voiced their moral concerns (condensed in the slogan 'no patents on life') in various forms. One important concern is that patenting will further transform living things to a commodity which will lead to further disrespect for life forms or nature. There is also concern about more animal suffering in the testing phase of a specific gene product (e.g., by use of animals genetically modified as test-models for human disease).

The *third* sort of argument is connected to extension of the patent system to DNA material. Moral concerns of adversaries here are related, for example, to the belief that patents imply ownership and take away God's sovereignty over nature or the belief that a gene, being a basic building block of nature, is intrinsically valuable, sacred and not to be treated as a commodity. Arguments based on these concerns are not always of a religious nature, however, but can also take on a more legal-technical form. One is based, for example, on the patentability criterion that only inventions are patentable and that genes, being discoveries, are therefore not patentable.

The *fourth* type is related to extension of the patent system to the domain of *human* genetic material (and human gene-based products). Opponents claim that human DNA material is closely related to human identity and that it has a unique status. They are concerned that patenting of human DNA violates human dignity or genetic integrity.

The *fifth* type is concerned with the justifiability of patenting of specific inventions based on gene technology such as genetically modified micro-organisms, plants, animals, tests or pharmaceuticals. Moral concerns at this level are based, for instance, on the assumption that genetically modified organisms are inherently unsafe and hold unknown risks.

The *sixth type* involves moral assessment of the international effects of gene patenting. Critics point out, for example, that the benefits are mainly for countries with strong patent systems, and that research in developing countries is slowed down, because they cannot afford to pay for the patented material.

Each of these six categories comprises many arguments pro or contra patenting of bio-technological inventions – only a few examples have been presented here – and further analysis of arguments (and concepts) used is often needed. But here we take the different types of arguments used in the gene patenting debate as indications that moral issues need not necessarily be associated with appropriate use of a biotech end-product.

In the gene-patenting debate the 'balancing exercise', the weighing of benefits and risks, pros and cons, is often presented as the favored approach to solving morally difficult issues generated by a biotechnological product. However, besides the usual difficulties in developing acceptable criteria to weigh risks and benefits, it should be noted that at the patenting stage of a biotechnological product this balancing exercise need not necessarily be rational. Indeed, in view of many unknown risks it is often hardly possible to assess adequately the risks of a specific technology at this or a later stage of a product's life-cycle, the more so when long-term effects are taken into

consideration. For some scientists this is reason to proceed with experiments, as this may reveal more fully whether a specific biotechnological product is inherently dangerous. For others this is a reason to stop with experiments. In such situations the technology or product can get the benefit of the doubt, especially when there are strong economic or industrial pressures. This kind of situation calls for another role of TA. Instead of a focus on anticipated effects and appropriate use, the biotechnology patent debate illustrates that more weight could be given to the context, through systematic reflection on the specific nature of a technology, its objectives, perceived or stated benefits at various levels, its underlying value-system and the interaction with society at various levels. In the following this will be illustrated more concretely.

III. THE SEARCH FOR MOTIVES, INTERESTS AND VALUES

A. Basic Research

When in the 1980s the plan was taken up to map the human genome, basic research was mainly carried out in academic and other state-subsidized institutes. Major motives driving researchers included the wish to reduce or alleviate suffering, to advance basic knowledge (about man and disease causes), scientific status, and employment. In the 1990s the profit motive found its way into basic science, at first through intensifying cooperation between academia and private industry, and after that basic research was increasingly also undertaken by private industries, which sought to patent their scientific findings to protect their investments. At present also academic institutions file patents in an attempt to find money for their costly research.

This ongoing process of commercialization of basic research calls for a careful analysis of motives. It could well conflict with other important values, such as fairness, for example. If only commercial drives direct and determine what kind of basic research is to be undertaken, development of genetic tests for rare genetic conditions could come to a halt. Commercialization of basic research has also resulted in feelings of injustice among researchers, because not all who have contributed to the detection of a specific gene-sequence are rewarded. Besides, patents are often also based on publicly funded research, and a patent on a specific gene usually benefits only a few of those involved. Another problem is that patents may bring changes in the allocation of research funds according to what is deemed profitable.

The commercialization of basic research also challenges important scientific values. Attempts to get patents on DNA sequences threaten such traditional values as scientific openness and access to research results, since attempts to get patents usually impede immediate publication of scientific findings. Also, if a broad patent is filed and granted, specific gene-sequences are not available for further research for quite some time. This would go against the Human Genome Project's stated objectives. Easy access to scientific findings was one of the main objectives underlying the human genome project.

B. Research and Development

After detection of a specific DNA alteration associated with a serious disease, a marketable product (such as a specific genetic test) can be developed. Here the private sector can accelerate a process of transfer of basic knowledge into R&D. But financial interests can conflict with other values at this level as well. Commercial interests may drive the private industry to create genetic tests for which they estimate there will be a great demand. Therefore they may focus on predispositions for common diseases, such as cardiovascular diseases (Andrews, Fullarton, Hotzman, & Motulsky, 1994). But the question arises whether it is (medically) useful to develop genetic tests devised to detect genetic risk-factors when there are so many other well-known risk-factors. Will the test really bring a substantial health benefit? And patient organizations fear that there will be no incentive to develop tests for rare genetic conditions.

C. Patent Protection

Patent protection of new genetic tests is thought to be of the utmost importance to preserve competitiveness in biotechnology (''It's an understanding in the United States that if you can't patent it, don't invest in it'' (Marcus, 1996)). It is also thought to be of the utmost importance for progress in science. Yet, patenting of these tests is not morally unambiguous. Delays in patenting can cause substantial delays in the development of a genetic test (cf. the patent fight over the BRCA 2 gene between the British CRC and American Myriad Genetics). Also, in the case of prolonged legal fights, the costs of the genetic tests can rise considerably. Patents can lead to huge legal and administrative costs, which is to the disadvantage of individuals and health care as prices will be considerably higher.

D. Manufacturing Phase

In Europe, an E.U. directive (European Parliament, 1998b) on *in vitro* diagnostics is concerned with the quality of these devices manufactured in order to protect the health and safety of those handling or using these devices. Protection of health and safety is only part of the problem, however. Effectiveness is another important aspect. What degree of reliability and effectiveness is required? Which level of false-positives and/or false-negatives is acceptable, for example for tests designed to detect the BRCA1/2 genes? Detection of these genes will usually lead to agonizing decisions as to what should be done. Is it morally acceptable to offer a genetic test with inadequate reliability? Also, should a test be offered if there is a wide range of severity of the clinical manifestations associated with the disease? Should a test be developed for untreatable genetic conditions? And what are the consequences of unreliable tests or tests designed for conditions with a wide range of severity for health care? These questions have not been adequately answered by Directive 98/79/EC. And leaving market forces to determine which tests are to be developed might not be the best approach to solve these kind of moral questions.

E. Clinical Testing

Concerns related to clinical trials of biotechnology products in humans or animals, whether patented or not, have been subject of ethical debate for quite some time now. Moral concerns about the ultimate beneficial effects of a product, conflicting interests and concerns about autonomous decision-making of individuals involved in medical clinical trials have led to various sorts of regulation. As for the testing of genetic tests, there are specific moral problems. During this phase the safety and effectiveness of a specific test can be determined, and although IRBs will usually assess the moral acceptability of clinical testing of a medical device, genetic tests offer specific problems not so easily solved by IRBs. For example, in the case of genetic tests it can take a very long time to establish the effectiveness and safety, as only the appearance of clinical manifestations can confirm many genetic tests and for some tests this can take a long time (Holtzman & Watson, 1997). One solution is to tell the test-subject about the investigational nature of the genetic test and leave the decision to the test-subject. Another is the statistical approach: to investigate to what extent a test whose medical value is uncertain will be acceptable for certain groups. The presupposition is that if a sufficient percentage of people are interested, the test is acceptable. Such examinations

have been undertaken for carrier screening for CF, and for various kinds of prenatal tests. This may lead to a kind of statistical ethics where numbers determine moral acceptability. But should opinion polls decide controversial moral issues?

F. Promotion and Marketing

Concern about individual autonomy also underlies this phase. New medical devices and products must be generally accepted before a private company can make a profit. Much will depend on how the general public and health professionals are ''educated'' about the new possibilities. There is some reason to consider a genetic test as a potentially harmful product, because of its inherent potential for psychological, psycho-social and social harm (Hoedemaekers, 1998). For marketing reasons, however, educational and informational material about specific tests can be inadequate (it can be one-sided or omit information about possible harms). The moral paradox presented by the promotion of a genetic test (emphasis put on the burden of a disease and hence the need for a test may raise disproportionate anxiety; adequate information about potential harms may make people reluctant to buy the test, which will reduce profit) needs to be resolved adequately. And in a medical practice where non-directiveness is an important requirement, information about specific genetic tests must not be deceptive, biased, manipulative or persuasive (Hoedemaekers and ten Have, 1999a).

It should be noted that moral assessment need not stop here. The question could also be posed whether a specific technology does not create needs that did not exist before. Will predisposition genetic tests in all cases be of real medical benefit? Will manufacturers not play on feelings of fear and anxiety of risk-avoiding persons? Demand might be created, even for tests which have no clear medical benefit, but these tests will also create greater use of medical services. Profit for private companies will consequently lead to greater public expenses.

G. Appropriate Use

TA of predictive genetic tests could lead to regulation ensuring adequate genetic test quality, adequate laboratory quality, adequate informational material and adequately trained personnel to protect the test-subject from harm (Holtzman and Watson, 1997). But predictive genetic tests can generate harmful consequences even if the quality of tests and testing services are adequate. Regulation is devised for the various types of predictive genetic tests

to limit or eliminate the harmful effects for the end-user (the test-subject) as much as possible. For various types of predictive genetic tests this includes a balancing exercise of (potential) benefits and harms.

But which effects are chosen for moral examination, and on the basis of which arguments? And why should the focus of such an exercise be only on the final user? There are disadvantages for other interested parties, such as health care institutions, health care professionals and health insurers. For health care institutions, for example, there are the financial and personnel consequences, for health insurers there is the problem of which tests (and counseling) should be reimbursed, and for medical professionals a considerable number of predictive genetic tests (which might often include counseling as well) could mean an extra work load they are not willing to take on. And why focus on effects only? It is also possible to consider the objectives of genetic testing. In principle there are three important objectives: genetic tests are offered for medical benefit, to enhance well-being (by offering ''certainty'' or ''reassurance'') and to enhance autonomy (genetic testing can help make important life-choices). Which objectives deserve priority? For which objectives is reimbursement reasonable, in view of limited health care resources?

H. Societal Implications

In the domain of clinical genetics, there is a tendency to leave the often agonizing decisions about genetic testing and follow-up to the individual, a tendency facilitated by the present dominance of the principle of autonomy in western health care and the emphasis on non-directiveness. Adequate information and informed consent have become the most important guiding principles. One consequence of this is that policy decisions regarding the introduction of predictive genetic tests tend to focus on *individual* harms, and assessment of large-scale and long-term societal consequences can thus be evaded. But is this approach adequate? Consider the following tendencies.

Many individual decisions to be tested for genetic conditions can have the effect of generating greater social pressure on others also to use these tests and this, in its turn, may lead to a further increase of demand (and pressure), which may well threaten autonomous decision-making and free choice (Hoedemaekers & ten Have, 1998).

Many individual decisions can also lead to changing societal norms. The possibility of prenatal genetic screening and the option of selective abortion, for example, can have the effect that an increasing number of parents begin thinking about their future children in terms of quality of life. This can lead to

gradually changing societal standards of what is considered normal and abnormal and to different attitudes towards suffering, for suffering becomes less acceptable in the light of the new screening possibilities and the subsequent options it offers to eliminate or reduce suffering. It is debatable whether this will be beneficial for society in the long run.

Predictive genetic testing also has the potential to reorient medical practice, for example towards greater emphasis on prevention of disease, which is believed to lead to savings in health care costs. But this would imply that more and more people are to be informed about any genetic alterations leading to disease, and its time of onset and severity. It is doubtful whether everyone will see this as an advantage, and the moral question arises where the limits of a right not to know should be.

Reorientation of medical practice can be further reinforced by a change in use of concepts. One example is that many ''healthy'' persons after testing will become ''potentially ill'' persons. And potentially ill persons, having been alerted to specific health risks, could consult physicians more frequently, which could well lead to greater use of health care and health care resources.

Regulation devised for appropriate use of predictive genetic tests can also change under the influence of changing societal attitudes. Criteria like genetic testing only in the case of a serious disease, or in the case of sufficient certainty that a particular disease develops, can easily change under the influence of a spreading ''let's play it safe'' attitude, the use of worst-case scenarios by counselors, or decision-making on the basis of perceived risks rather than calculated risks, especially in a climate that emphasizes patient autonomy.

In addition, individual experience can change under the impact of the new screening and testing possibilities. Pregnancy, for example, tends to be experienced differently. Until the results of prenatal tests are available, a pregnancy is now perceived as ''tentative'' – there is always the possibility to terminate in the case of an unborn child with a defect.

IV. CONCLUSION

This brief overview reveals that moral assessment of new biotechnological devices should not be limited only to the immediate impact of a specific device on an individual. The European patent debate has demonstrated the need for a more coherent and integral form of moral assessment of biotechnological

products and processes. At *all* stages of development there may be moral implications. The role of moral assessment in technology assessment should therefore not be interpretated in too narrow a sense. More concretely it would imply:

1. Analysis of the various forms of interaction of a specific technology with society or societal segments at all stages of development.
2. Exploration of (new) moral issues resulting from this interaction at various levels. This involves mapping and analysis of interests, objectives, claims, arguments and concepts used in the various (moral) debates generated by a specific technology.
3. Exploration of value systems generated by a specific technology and its products and its interaction with important societal values.
4. Examination of the transformational and conditioning powers of a specific technology. This includes assessment of the promotional and marketing phase.

These pointers for a more important role for moral assessment in TA will take technology assessment to a more fundamental level, with different sorts of questions. Its first task is not problem-solving. This need not necessarily be a disadvantage, however, especially if TA's task is understood as facilitating decision-making of policy-makers and/or government authorities. Policy-makers might be even more interested in a better understanding of the interaction between a new technology, society and the individual and the moral issues generated. Clear insight into the various moral questions can be the beginning of adequate regulation at all stages of development, or the beginning of a more general public debate leading to adequate regulation. It could also help the European Patent Office to decide whether the 'morality clause' should be applied, a task this office does not feel adequately equipped for (Schatz, 1997).

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