

Regulatory decision making

An analysis of factors influencing the acceptance and implementation of alternative technologies to animal testing by (European) regulatory authorities

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Abstract

Approximately 30% of the animal experiments within the Member States of the European Union is done to meet regulatory requirements. These requirements specify which experiments have to be carried out in order to license and release a compound or product for human, animal or environmental application onto the European market. Over the last decades the heavy reliance on animal testing in this area has encountered serious objections for ethical, scientific and economical reasons. Directive 86/609/EEC, which regulates the protection of animals used for experimental and other scientific purposes at a European level, applies a 'no unless' principle and stipulates that alternatives, if available, should be used. The requirements dealing with the registration and release of products often leave room for regulators to choose the testing method they perceive as most suitable for the job. Regulatory acceptance of alternative methods proves to be a difficult process that meets with a whole range of obstacles. This raises the question how regulators use the discretionary space available and which factors influence the decision-making process preceding regulatory acceptance of new/alternative models. Even though the implementation of EU legislation/regulations has been increasingly discussed, the actual process of regulatory behaviour and decision-making at EU level is still rather underexplored.

With this paper the author wants to contribute to the discussion, by presenting a selective overview of factors determining regulatory decision making, in theory and in practice.

Keywords

Regulatory decision-making, discretion, policy implementation.

I Introduction

Synoniemen voor veel voorkomende termen?

Since the 1980s Europe has gone through an intense regulatory reform (Majone 1996, p 2). Europe has evolved from a society in which public ownership and state monopolies played a leading role into a society which saw a rapid increase of the privatisation of many policy functions and industries. Specialised regulatory agencies were established to control these privatised functions (Majone, 1996, Thatcher, 2002). This change from the interventionist state to the regulatory state has also brought about a shift in the central actors in Europe, from parliaments, ministerial departments and nationalized industries to parliamentary committees, independent regulatory bodies and privatised industries (Thatcher 2002, p 806). One of the actors of regulatory policy is the regulatory authority which functions at arms length from the political system. Regulatory authorities are charged with regulating specific aspects of possibly negative side-effects of an industry (Malyshev, 2006, p 290 & 292) and are supposed to make our lives safer by eliminating or reducing exposure to potentially risky substances or persons (Breyer, 1993). However, the rise of the regulatory state has also given rise to many scientific and societal questions on how legislation is implemented by regulators.

Regulatory animal testing is part of the safety and quality testing done prior to the release of a product or compound onto the market to ensure the safety of humans, animals or the environment and the efficacy of the products. About 30% of the animal experiments within the European Union is conducted to meet safety and quality requirements. As the assessors of new products and compounds, regulators are a key actor in the implementation of the earlier mentioned regulatory requirements.

European legislation for the protection of animals used for experimental and other scientific purposes, stipulates that alternatives to animal testing (3R methods)¹ have to be used if available. But even though the number of 3R methods has risen sharply over the last decades, regulatory acceptance and the implementation of alternative methods has not kept pace with the development of these tests (Balls, 2002). This means that, even though many safety and quality requirements allow the assessors to use these alternative methods instead of the conventional animal model, a preference is often given for the conventional methods. This also begs the question what factors influence this regulatory decision-making.

This paper examines regulatory decision-making by comparing theoretical and empirical factors that influence regulatory decision-making. The aim of this comparison is twofold. On the one hand, the comparison will allow for a better understanding of the mechanisms observed in the field of regulatory animal testing (in short RAT). On the other hand, the comparison is used to formulate hypotheses on factors that influence regulatory decision-making in the field of regulatory animal testing. These hypotheses serve as input for case studies the author will conduct in the near future in the field of regulatory animal testing. These case studies aim at drawing an updated and more detailed picture of the practice of acceptance and implementation of alternative tests for regulatory purposes.

In order to formulate these hypotheses this paper is structured as follows:

¹ Methods that **Replace** animal tests, **Reduce** the number of animals used or **Refine** the method, aiming at minimizing pain and distress or optimizing welfare.

Section II describes regulatory decision-making and a number of theoretical influences, relevant to explain regulatory decision-making in the field of RAT. This section will draw specific attention to the field of risk regulation, since the field of risk regulation offers valuable perspectives for the field of regulatory animal testing.

Section III starts with a description of the field of regulatory animal testing and then presents the empirical factors that influence regulatory behaviour in this field. These factors derive from a general inventory conducted in 2005 on factors stimulating or obstructing the adoption of alternatives to animal testing in the regulatory process (Schiffelers et al, 2005).

Section IV compares the theoretical and empirical factors described in the sections II and III to clarify the mechanisms observed in the field of regulatory animal testing and to formulate hypotheses on factors that influence regulatory decision-making in the field of regulatory animal testing.

II Theoretical factors influencing regulatory behaviour

As mentioned this paper aims at explaining regulatory decisions made in the field of regulatory animal testing. In order to be able do so this section discusses the following aspects:

- Firstly, the mechanisms of regulatory decision-making and discretion are defined.
- Secondly, the theoretical concepts that examine regulatory decision-making and have the potential to explain regulatory decision-making in the field of regulatory animal testing are presented.

Defining regulatory decision-making and discretion

As mentioned in the introduction, regulators are supposed to make our lives safer by eliminating or reducing exposure to potentially risky substances or even persons (Breyer, 1993). The purpose of regulation is to align private behaviour with the public interest.² In order to do so regulation consists of three main processes: information gathering, decision-making and enforcement. This paper mainly focuses on the process of decision making but involves the process of information gathering where necessary.

Regulatory decision-making is defined as the decisions regulatory agencies make to balance trade-offs between the economic and societal costs of government intervention on the one hand and corresponding benefits to public health or environmental quality on the other (Sexton,1995). The process of regulatory decision-making can also be divided into three phases (National Research Council and the Office of Technology Assessment, 1994, OTA, 1993, Sexton, 1995, Breyer, 1993):

- phase 1: research to provide necessary scientific information and understanding of the risk;
- phase 2: the technical estimation of the risks; the risk assessment³;
- phase 3: the more policy-oriented part of risk management to determine unacceptable risks and to take appropriate actions.

In addition a fourth phase is becoming more important, that is the phase of risk communication in which regulatory agencies enter into a dialogue with stakeholders to explain the risk and related actions by regulators (Sexton, 1995).

² http://nrri2.org/index.php?option=com_content&task=view&id=21&Itemid=38 ; consulted, July 16, 2009

³ For a more detailed description of the phase of risk assessment see Breyer, 1993, p9

To demarcate the territory in which regulatory decision-making takes place the simple distinction between policy-making and regulating seems inadequate, since both policy makers and regulators make policy. A distinction Brown makes between macro policy making and micro policy-making seems more suitable. The former is defined as the basic policy parameters and is the domain of government policy makers, while the latter is defined as the actions of regulators to apply, clarify, interpret, and fill in details left unspecified by macro policy-makers (Brown, 2003). Micro policy-making therefore is the playing field in which regulatory decision-making takes place.

Although regulatory decision-making is partly determined by legislation, regulators almost always have a certain amount of regulatory discretion at their disposal. This discretion is a combination of two dimensions of autonomy, the one granted by the principal and the other conquered by the agent (Delreux 2009, p 721). A legal definition of discretion is:

*The power of a judge, public official or a private party (under authority given by contract, trust or will) to make decisions on various matters based on his/her opinion within general legal guidelines.*⁴

Regulatory discretion is important, since it offers the opportunity to close the gap between general legislation and specific situations. Without this discretionary space, implementation would become far less efficient and effective. This is even more important if legislation is formulated at a central level but has to be implemented at a decentralised level, as is the case with European legislation (Bakker & Van Waarden, 1999, p19-20). Apart from this, flexibility and discretion are important in regulating industries that have to deal with rapid technological changes and in which the introduction of competition requires continuous adaptation (Smith, 1997). So discretion is crucial for the transformation of macro policy into micro policy.

But regulatory discretion also creates a source of uncertainty to policymakers. This uncertainty, referred to as the principal agent problem, addresses the concern of the principle (policymaker) to get the agent to act in the best interests of the principal, even in those cases where the agent has an informational advantage over the principal and/or has different interests from the principal. This concern leads to a situation in which regulatory discretion is on the one hand created and on the other hand restricted by a mix of procedural requirements, a regime of legislative supervision, judicial review and public participation in agency hearings (Majone in Peterson & Shackleton, 2002, p 322). The level of discretion, given to regulators, widely differs between countries and industries. At one extreme, U.S. laws typically delegate broad discretion to regulators. At the other end of the spectrum, some countries implement regulation through tightly specified laws that are designed to eliminate discretion. Most regulatory systems lie somewhere between these extremes.⁵

After having defined what is meant by regulatory decision-making and regulatory discretion, the question remains how do regulators behave within this discretionary space and which factors influence their decision-making. Or as Law puts it:

"We still know little in general about how real world regulators actually behave".....
(Law, 2005 p 459)

⁴ <http://legal-dictionary.thefreedictionary.com/discretion>; consulted June 12, 2009

⁵ <http://scholar.google.com/scholar?hl=en&q=author:%22Smith%22+intitle:%22Utility+regulators:+the+independence+debate%22+&um=1&ie=UTF-8&oi=scholar> ; consulted, 2009-07-16

Theoretical perspectives on regulatory decision making

Before examining how regulators actually behave in the field of regulatory animal testing, this paper presents a number of theoretical concepts that may present us with some explanations as to *why* regulators in this field take certain decisions.

The aim of regulatory animal testing is to minimize the risk of safety and quality problems of products that are introduced onto the market. In this field risk avoidance plays an important role in regulatory decision-making (see section III). The same mechanism is observed in risk regulation in general. Theories regarding risk regulation prove to be particularly interesting to explain this mechanism. Therefore special attention will be drawn to theoretical concepts that look at regulatory behaviour from the angle of risk regulation. For this purpose literature on risk regulation and regulatory decision-making has been consulted.

Over time scientists in the field of policy, economy and law have introduced a broad range of theories on factors influencing regulatory decision-making. These vary from theories in which external stakeholders play a leading role, to theories in which internal organisation factors are dominant. And from theories looking into a broad combination of factors to theories focussing on one specific influence on regulatory behaviour.

The theories in which external stakeholders play a dominant role can be presented as a continuum. At the one end of the continuum the regulatory capture theory can be found. Regulatory capture refers to a situation in which a regulatory agency, predominantly created to act in the public interest, acts in favour of the commercial or special interests of the industry or sector it is supposed to regulate (Stigler, 1971).

At the other end of the continuum are theories in which the public interest prevails. The public interest theory is an economic theory stating that regulation is supplied in response to the demand of the public to correct inefficient or inequitable market practices. Regulation is initially assumed to benefit society as a whole rather than particular interests. The regulatory body is considered to represent the interest of the society in which it operates rather than the private interests of the regulators. (Bonbright, 1961, Posner, 1974)

This continuum focuses on the dichotomy between private and public interests and the balance regulators have to find between these interests. Although some aspects of these theories might provide (parts of) the explanation for the regulatory behaviour in the field of regulatory animal testing, another dichotomy seems to be as relevant, if not more relevant to this field, namely the dichotomy between two conflicting public interests. Regulators, in the field of regulatory animal testing, also have to balance animal welfare (fewer animal tests), on the one hand, and public health and safety (often obtained via animal tests) on the other.

Moreover, both ends of the continuum have been heavily criticized and over the last decades several new theories looking into regulatory behaviour, have been developed. These theories can be divided into three groups:

1. The first group of theories views regulatory decision-making as a function of the influence of external stakeholders. Theories such as the external signals model (Joskow, 1974 and Olson, 1996) can be placed in this group. The external signals model suggests that regulatory agencies can be responsive to a diverse set of external interests. Regulators react to the signals that they receive or expect to receive from various groups outside the agency and the trade-offs they make between these signals may differ from one action to another.

"The key to understanding regulator behaviour is to understand what these trade-offs are." (Olson, 1996, p 405)

2. The second group of theories suggest that regulatory decision-making is a function of internal organisation factors such as the influence of leadership and the organisation culture of the regulatory authority.
3. The third group of theories consists of a combination of the first two groups and adds contextual factors to it. In this group of theoretical concepts regulatory decision-making is a function of the time frame and the context in which the regulator operates. Regulators respond to developments in time and in technical, political and social context. This makes regulatory decision-making a dynamical process.

Within each of these three groups interesting theoretical factors might be found that have the potential to explain regulatory behaviour in the field of regulatory animal testing. The decision to focus on the third group of theories is based on both theoretical and empirical findings. For example Hood et al argue that there is no single factor that is able to explain the varying contents of risk regulation regimes. These authors therefore plead for multi-causal theory in order to explain the observed variations (Hood et al, 2001, p173). This is in line with presumptions that can be made based on the empirical findings.

In the next paragraphs different multi causal theories are described, namely Breyer's theory of the vicious circle of risk regulation, Hood's theory of risk regulation regimes and Sexton's theory of the role of science and communication on regulatory decision-making.

The vicious circle of risk regulation

An interesting theoretical perspective in this third group of theories, that might help to clarify regulatory decision making in the field of regulatory animal testing, comes from Stephen Breyer. In his book: *Breaking the vicious circle; towards effective risk regulation*, Breyer looks into the specific dynamics of risk regulation and explains the complexity of regulating health risks. In the vicious circle of risk regulation three aspects tend to reinforce each other (Breyer, 1993, p33). These three elements are:

1. the public perception of risk problems, which is often far from realistic;
2. the politicians action and reaction to perceived risk and regulatory problems is highly responsive to public opinion;
3. and uncertainties in the technical regulatory process leads to erring on the safe side.

According to Breyer, public perception influences politicians and politicians help to shape public perception. And both influence the response of regulators to the problems they perceive as important, despite the fact that the public and politicians are unlikely to understand the complexity of the matter which will probably lead them to overemphasize the actual risks.

".....The circularity is reinforced by the fact that the more outside pressures seem to control the agency results, the less confidence the public will have in the agency. The less confidence the public has in the agency, the greater the perceived need for outside action, the greater the pressure upon the agency to prove it has erred on the side of safety, and the greater the tendency to adopt the public's risk agenda of the moment..."

A combination of technical and scientific uncertainties, knowledge gaps, the public's aversion to risks and the difficulties to explain highly technical findings to non-experts, make it difficult for agencies to resist pressure coming from the public and politicians. And since the public and politicians aim for risk-avoidance, risk regulators always tend to be conservative in the decisions they make (Breyer, 1993). This is understandable since regulators have to deal with a great number of uncertainties and are therefore often perceived with scepticism by the public and policy makers. The result, according to Breyer, is an agency that might become hesitant to make rules or to change them once adopted.

"Rules become frozen in place and cannot readily adapt to changing scientific knowledge". (Breyer, 1993 p49)

In short Breyer's vicious circle explains some of the mechanism of regulatory conservatism and the increasing public demand for safety and defines the following factors that influence regulatory decision-making.

- Public perception of risk;
- the politicians reaction to this risk perception;
- technical uncertainties;
- knowledge gaps;
- and the miscommunication between experts and non-experts.

The blame-avoidance imperative

The mechanism of the vicious circle is amplified by recent developments in risk regulation. As Michael Power says; "an age of 'new risk management' has dawned in corporate governance, sparked by high-profile business failures and accidents."⁶ These failures and accidents, especially in the United States, lead to claims made by their victims. Blame-avoidance is therefore an important factor influencing risk regulation (Hood et al, 2001, p176, Hood 2002).

"...The concern for blame prevention seems to be leading to protocolization and risk assessment inflation to establish procedural alibis as a form of bureaucratic insurance" (Hood et al, 2001, p179)

As can be expected this blame/claim culture is yet another factor that leads to a conservative attitude of regulators towards new technologies. At first glance this might not appear to be a problem, since a defensive risk management seems to be in line with what the government and regulators are there for, namely protecting individuals from 'suffering'. But their focus on avoiding blame and liability may well have the opposite effect in many cases. Since politicians and regulators who are mainly concerned with the avoidance of (political) blame over hazard and safety, might end up hardly deciding or running anything (Hood, 2002).

Risk regulation regimes

Hood, Rothstein and Baldwin provide a second interesting theoretical perspective. They look at risk regulation by distinguishing different risk regulation regimes. Risk regulation regimes are the complex of institutional geography, rules, practices and ideas that are connected to the regulation of a particular risk. And regulatory decision-making is a core activity in these regimes. The theory on risk regulation regimes emphasizes the existence of diversity in risk regulation, which is a result of the different pressures that lead to regulating the risk. According to the authors, this means there is no such thing as a risk society or uniformity in the way the state regulates risks (Hood et al, 2001, p171).

The authors define three main shapers of regulatory content: 'type of risk', 'public attitudes', and 'organized interests' but transform and combine these shapers in a later stage of their theory into the market failure pressure, the opinion-responsive pressure and interest-driven pressure. And add to it a fourth pressure of inner life of regulatory organisations (Hood et al, 2001, p144).

The market failure pressure reflects the idea that the government is pressurized to act in order to correct market failures. The type of risk is the main element in this pressure. It implies that the government will not intervene in those cases where the market can operate without failure, or in other words where the activity imposes little or no risk to society.

⁶ M. K. Power, 'The New Risk Management', inaugural lecture of P. D. Leake, Professor of Accounting and Director of CARR, December 1999.

The opinion–responsive pressure is based on the idea that regulation follows public opinion. Hood et al. like Breyer state that there is a relationship between public preferences and the regime content, meaning that the way in which society perceives different risks is reflected in the way these risks are regulated. This might for example explain why some risks are highly and others are hardly regulated.

The market failure pressure and the opinion-responsive pressure partly overlap and show similarities to the public interest theory.

The interest driven pressure is the idea that regulatory activity reflects the interplay and lobbying of organized interests. This is contrary to the idea that regulation generally pursues general welfare through correcting market failures (Hood et al, 2001 p63-65). The interest driven pressure shows similarities to the theory of regulatory capture.

In short the theory of risk regulation regimes defines following four factors that influence regulatory decision-making:

- the type of risk
- public attitudes towards the risk
- organized interests
- internal organization influences

The influence of science and communication on regulation

A third theoretical perspective comes from Sexton, who argues that ideally science is an important factor in regulatory decision-making. Although science is important to regulatory decision-making, many scientific findings will never reach regulators.⁷ This hinders the necessary communication between legislators and regulators on the one hand and scientists on the other. As a consequence scientific knowledge is insufficiently taken into account by policymakers/regulators. In those situations where scientific knowledge and understanding is insufficient this will lead to controversy about the regulators' decisions and the decision making process will become easily subject to political agendas, media pressure, special interests, legal challenges and bureaucratic inertia (Sexton, 1995). The opinions on how important science is to regulatory decision making, differ from science being crucial for better decisions, to science being marginal to regulatory decision making. A third more middle of the road viewpoint that is supported by Sexton, is that science is an important but just one of many factors influencing regulatory decision making (Sexton, 1995).

Regulators respond to the realities imposed on them by a complex and changing environment. Factors that can affect their decisions are:

- public perceptions;
- political pressures;
- statutory mandates;
- institutional constraints;
- scientific and technical issues;
- special interests.

According to Sexton these often conflicting forces foster an informal decision–making process that is, among other things, often uncertain, unstructured, intuitive and chaotic (Sexton, 1995).

⁷ Sauerborn et al distinguish six factors that contribute to knowledge from scientific research remaining unused (Sauerborn et al, 1999):

1. lack of knowledge on the part of the researchers about the policy-making process;
2. lack of 'ownership' of the research agenda on the part of the main stakeholders;
3. unsuitability of research data for the stakeholders;
4. poor communication of the results to the stakeholders;
5. inadequate network between researchers and stakeholders to connect;
6. researchers perceived to play too limited a role

Regulators that have to make the decisions in this "Adhocracy" show the same mechanisms that can be observed in bureaucracies, namely;

- a tendency to make conservative decisions;
- a reluctance to change;
- a tendency to seek/build consensus;
- a reliance on codified rules/published procedures;
- a tendency to delay decisions;
- and a dislike of surprises.

Summary theoretical factors

After having taken notice of these three different theoretical perspectives on regulatory decision-making in the area of risk regulation, it will have become clear that regulators respond to the complex reality and the constantly changing environment they have to work in. However there is consistency in the factors that are mentioned. The following factors appear to play a role in two or three of the examined perspectives and can therefore be pointed out as important factors affecting regulatory decisions in the area of risk regulation:

- the type of risk;
- the public attitude towards the regulated risks;
- the political pressure;
- the discretion regulators dispose off;
- the institutional constraints they face;
- the existing scientific and technical possibilities and limitations
- the difficult communication between stakeholders
- and the special interests that need to be balanced.

In this section regulatory decision-making is presented as a function of a combination of these factors. In the figure below the different groups of theoretical factors influencing regulatory behaviour are visualised. The external stakeholders influences are those influences that derive from the public, politicians, industry and interest groups. The internal organisation factors refer to influences like the organisations budget, leadership, the institutional geography of the regulatory authority and the discretionary space they dispose off. The contextual influences refer to factors like the scientific possibilities and limitations, the type of risk that needs to be regulated, the economical situation and the communication between stakeholders. All these categories of factors have the potential to influence regulatory decisions. Regulatory decision-making is therefore presented as an area within the grey box. The exact location of this area depends on the trade-offs regulators make between the different factors. It is assumed that the actual trade-offs differ per sector/ per product and maybe even per industry. The question is which groups of factors predominantly influence regulatory behaviour in the area of regulatory animal testing? This question will be partly answered in the next section.

To identify the relative force of these different shaping factors on regulatory decision-making in the field of RAT, the examination of case-studies is needed.

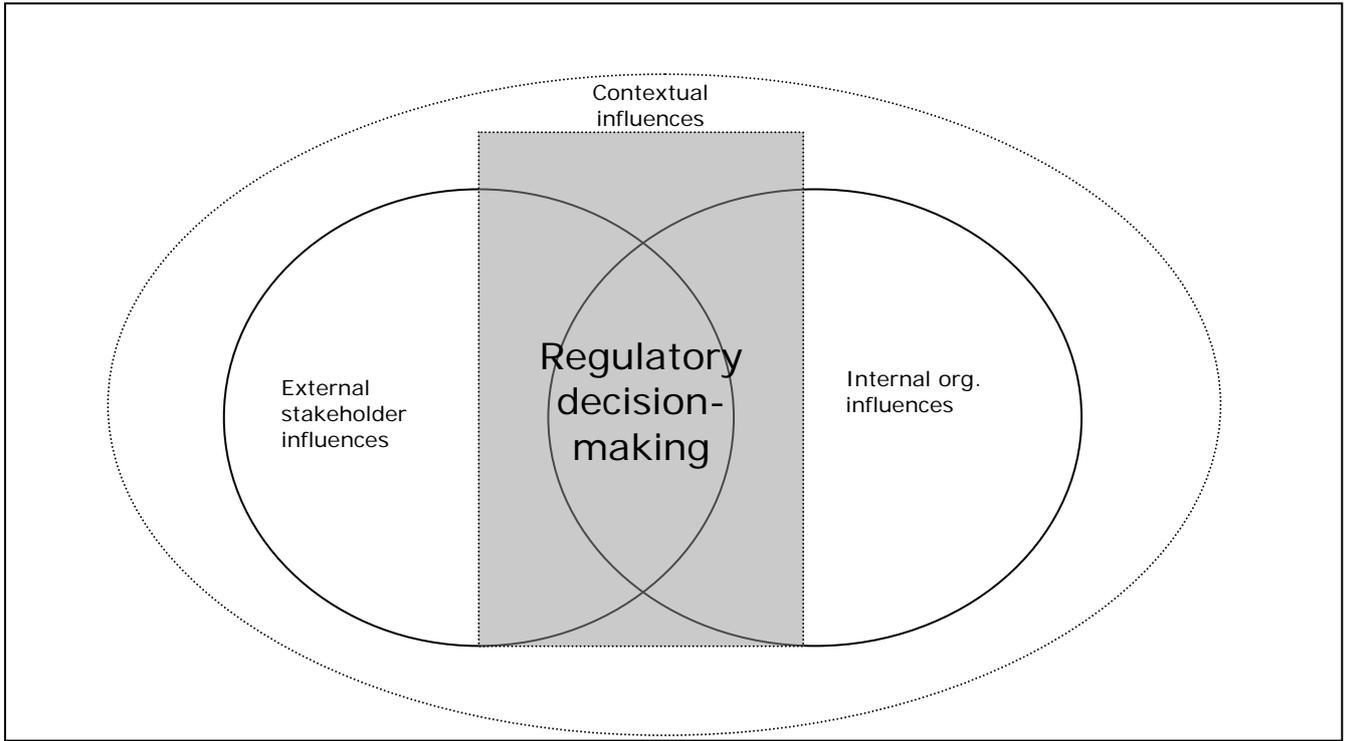


Figure 1: Categories of factors potentially influencing regulatory decision-making

Section III Factors influencing regulatory decisions in the field of regulatory animal testing

In the previous section a selection was made of theoretical concepts that might be useful in explaining regulatory decisions in the field of regulatory animal testing. In this section a description is given of the field from which these empirical findings derive and the research that has been conducted to collect these findings. This section then presents the main empirical findings, coming from the field of regulatory animal testing.

The field of regulatory animal testing

Regulatory animal testing is a persistent element in assessment procedures before releasing a product onto the market. It is often repetitive in nature and more likely to cause severe suffering than other types of animal testing, due to the procedures used and the predefined experimental endpoints. The tests therefore meet many objections varying from ethical, to economical and scientific objections. Approximately 30% of the animal experiments within the European Union is done to meet a whole range of safety and quality requirements. For example in the EU alone, there are more than 800 laws, regulations, directives and other documents regulating the aspects that products must be tested on (like the toxicity, carcinogenicity etc) before they are released for commercial purposes (de Leeuw, 2004). Member States and more specifically their regulators are given discretion to interpret these requirements within the limits of national law and to choose the testing method best suitable for a particular job. This might result in differences in the interpretation of requirements between different EU Member States and between different regulatory authorities.

Depending on the product and the market, national, European and/or international Regulatory Agencies are responsible for the quality/safety assessment and the release of these products onto the market. This paper mainly focuses on regulatory behaviour at European and Member State level.

Because of the earlier mentioned characteristics, regulatory animal testing is an important area to evaluate in terms of the so called 3R approach (i.e. possibilities to replace, reduce or refine these animal tests).

Directive 86/609 on the protection of laboratory animals⁸ states that:

*"An experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available."*⁹

So the 3R principle serves as a starting point of EU policy for the protection of laboratory animals.^{10 11} But despite this principle and the fact that the number of 3R test methods keeps increasing (Balls, 2002), these new methods are neither easily adopted into the regulatory requirements nor are they, in those cases where test guidelines leave discretionary space to the regulator, easily accepted as full fledged alternatives to the conventional methods. This means that the availability of 3R test methods is no guarantee at all for the actual use of it for regulatory testing purposes. In practice regulatory authorities, and in their slipstream industry, often prefer to stick to the conventional testing methods, despite the availability of alternative methods (Schiffelers et al, 2005).

⁸ article 7.2 of Directive 86/609 on the protection of animals used for experimental and other scientific purposes
⁹ <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:31986L0609:EN:HTML>; consulted 26th May 2009

¹⁰ Replacement: the substitution of insentient material for conscious living higher animals.

Reduction: reduction in the numbers of animals used to obtain information of a given amount and precision.

Refinement: any decrease in the incidence or severity of inhumane procedures

¹¹ This principle was first introduced in 1959 by William Russell en Rex Burch in their book '*Principles of Humane Experimental Technique*'.

This is due to a combination of factors. The empirical factors presented in this paper derive from a study conducted in this field in 2005 (Schiffelers et al, 2005). The 2005 study was an inventory of obstacles and opportunities influencing the implementation of 3R test models for the purpose of regulatory animal testing and was initiated by the project group "Regulatory Animal Testing". This project group consisted of Dutch advocates of alternatives to animal testing, which came from a variety of organisations in the field.¹² They felt the need to identify possible solutions to implement the objectives of the three R's in testing for regulatory purposes without the loss of scrutiny in safety and/or efficacy evaluation. The study resulted in a general overview of factors leading to the persistent character of regulatory animal testing and functioned as a starting point for further discussion on how to reduce these tests and increase the acceptance of 3R methods.

The 2005 study was exploratory and descriptive in nature. The empirical data were collected through triangulation. First and most importantly 33 semi-structured interviews with representatives from different stakeholder groups (legislators, regulators, industry, academia and animal welfare organisations) were conducted (see appendix A). The main question to be answered was which factors they perceived to stimulate or obstruct the acceptance and implementation of alternatives to animals testing for regulatory purposes. The respondents gave their views on these factors. The results are therefore mainly based on the respondents' ideas and perceptions of the factors they see as influential. The findings presented in this paper are the ones the majority of the respondents throughout the different stakeholder groups, agreed upon. However it must be emphasised that respondents were very much aware of the fact that the actual situation might differ very much between different countries, product groups, industries and agencies. The findings therefore represent a general picture the respondents have of the field of regulatory animal testing. Second the existing literature on regulatory animal testing was studied. And third a group of experts was established whose members were specialized either in the development or the implementation of policy and guidelines requiring animal experimentation. Each of this group's members provided input by giving an interview. In addition, the study concluded with a half-day meeting with members of the expert group and the project group. The purpose of the workshop was to check and discuss the preliminary findings that derived from the interviews and the literature.

In short the 2005 study gives a general picture of factors influencing regulatory animal testing and is mainly based on perceptions from the different involved stakeholder groups. Although the factors that are described are widely agreed upon, the results are mainly guesstimations¹³ of the actual influences on regulatory decision-making. And since the regulatory field differs per sector (chemicals, food and feed, cosmetics etc) and may even differ within a sector these general factors have to be treated with care.

What follows below is an overview of empirical factors influencing regulatory decisions towards the use of the 3R test methods for the release of a product to the European Market.

¹² *Bas Blaauboer* Utrecht University, Institute for Risk Assessment Sciences (IRAS), *Coenraad Hendriksen* Netherlands Vaccine Institute (NVI), Bilthoven; Netherlands Centre Alternatives to Animal Use (NCA), Utrecht University, Utrecht, *Marije Fentener van Vlissingen* Erasmus University Medical Center, Erasmus Laboratory Animal Science Centre (EDC), Rotterdam, *Janne Kuil* Dutch Society for the Protection of Animals (DSPA), The Hague, *René Remie* Solvay Pharmaceuticals, Weesp, *Joop Thuring* Notox B.V., 's Hertogenbosch, *Manon Vaal* Utrecht University, Science Shop for Biology, Utrecht.

¹³ An estimation made without a clear methodological justification

Empirical factors influencing regulatory behaviour

The behaviour of regulators in the field of regulatory animal testing is often characterised as conservative towards new (alternative) testing models. Alternative methods, once developed and validated, are subject to a very time consuming period of negotiations before they can/will be accepted for regulatory purposes.

According to respondents, regulators at the national, European and global levels are usually reluctant to include alternative methods in registration procedures. The reluctance of regulators to incorporate alternatives seems to result from a combination of factors such as the level of risk acceptance and the knowledge of the new techniques. These factors are discussed in this section.

Risk averse society

A first and very important factor influencing regulatory behaviour in this field is the tendency within Western society towards a so-called "zero risk concept". This refers to a mechanism in which society, legislators, regulators and industry all focus on risk minimization. The ongoing call for extra research based on the precautionary principle is a manifestation of this. According to the respondents, the advocates of the "zero risk" concept are insufficiently aware of the consequences this has in terms of the increased use of animals for testing purposes. Various respondents for example expressed their concern in this respect about environmental groups that have put the potential dangers of chemicals high on the REACH agenda.¹⁴ Applying the precautionary principle, they demand research to determine whether substances are harmful to humans and the environment. However the focus on risk minimization leads to an increase in the number of animal used for testing purposes. This is due to the fact that such research is still largely performed on laboratory animals (for many tests there are no alternative methods available yet). But the focus on risk avoidance does not only increase the number of animals used, it is also detrimental to the acceptance of alternative test models. In response to the risk aversion of society the alternative methods that do exist are often not accepted by regulators (see paragraph on conservative attitude regulators). In this respect, respondents state that much could be gained if a more realistic degree of risk would be accepted and if society would be more aware of the consequences of their demands in terms of the number of animal tests required.

Political Agenda

The EU concerns itself first and foremost with the internal market. Other issues near the top of the agenda are safety and risk limitation. Animal welfare has a lower priority. This also leads to limited budgets for academia and industry to develop alternatives. Respondents stated that ethics comes into play if safety is guaranteed and there is no negative economic side effect. In the struggle for scarce resources such as time and money, animal welfare usually loses. In addition it was stated that European politicians and national governments are sometimes inconsistent in their views. They want maximum safety and at the same time as little animal tests as possible. According to some respondents, politicians are mainly drawn to issues on which they can score politically. This can have both positive and negative effects on implementation of the 3Rs. When animal testing is in the public eye, politicians usually sit up and take notice too. But when product safety is a hot topic,

¹⁴ New European Community Regulation on chemicals and their safe use. It deals with the **Registration, Evaluation, Authorisation and Restriction of Chemical substances**. The new law entered into force on 1 June 2007.

animal welfare tends to get snowed under. Although there is public resistance to animal testing in general, the growing focus on consumer safety has so far outweighed the concern for animal interests.

Respondents said it would be ideal if the need for animal testing was determined mainly by experts (regulators and scientists) in the field. However in reality the need to test is primarily a political decision based only to a limited extent on scientific grounds.

Technical limitations and scientific uncertainties of 3R methods

Most alternative test models developed so far are intended to replace relatively simple test methods e.g. for local toxicity / one target organ. However, most animal experiments are complex tests for which it is difficult to find alternatives. For example, many animals are needed for tests in reproductive toxicology (embryo toxicity) and systemic toxicology, which are much more complicated to replace. Science is now facing the task of developing such complex alternative test methods, either by refinement, reduction of the number of animals needed per test, or replacement. Opinions on the feasibility of this task are divided.

For those alternatives that are developed it is stated that alternative methods must be proven three times over before they are perceived just as safe, sensitive and specific as conventional methods. A number of respondents believe that politicians and regulators are waiting for a scientific consensus before they dare incorporate alternatives into regulation. But this consensus is very long in the making, and consequently so are the changes in regulatory decisions towards alternative tests.

Knowledge deficiency regulators

Technical expertise is a crucial factor in the decision-making process whether or not to implement the 3Rs in safety and efficacy testing for regulatory requirements. Since the field is very complex, only a select number of experts are able to contribute to discussions on the matter. Regulators are often relatively unfamiliar with the properties and scientific qualities of these new test methods. Up till now, 3R methods are often insufficiently or too narrowly publicized and are therefore known to a limited audience and used to a limited extent. Regulators quite often have limited knowledge of alternative methods since they do not have detailed and updated scientific information at their disposal or lack to knowledge to interpret the different scientific endpoints. An example of this is the use of statistics. According to one expert specialized in alternatives to animal experiments, statistics offer great opportunities for developing such alternatives. Mathematical analyses can provide a scientifically sound underpinning for in vitro methods because the tests are easily reproducible. However, regulators lack the ability to interpret these mathematical analyses, according to this respondent. This means they are insufficiently capable of judging alternative methods on their merits and therefore tend to adhere to classic (animal) models.

As a consequence regulators are therefore strongly influenced by the extent of scientific consensus concerning animal experiments and alternatives. Without this type of scientific backing, politicians are reluctant to take a political stand and regulators are reluctant to take the risk of incorporating the alternative into their product assessment procedures. This process of reaching scientific consensus, by the very nature of scientific methodologies, is difficult to achieve and takes a long time. And so are the changes in regulatory behaviour towards these methods.

Apart from these possible explanations respondents gave another reason why regulators are reluctant towards these new methods: they hold power based on their knowledge of the old frame of reference (animal testing models). If regulators have to assume a new frame of reference, they run the risk of losing (part of) this power.

The respondents make several nuances to the factor of knowledge deficiency of regulators. For example it is stated that there is a big difference between the 'old school' and the 'new school' regulators. The present generation of regulators was mainly educated some 20 to 30 years ago when the credo still was "in vivo veritas" referring to the animal test being the central point of reference. The new generation of regulators has had more exposure to alternatives in the course of their education. Some respondents predict that the next generation will therefore see it as self-evident to work towards the introduction of alternatives and will most likely incline towards in vitro methods that make no use of live animals. There is, however, a risk that each "school" will exclude the other methods to a certain extent. The new generation of scientists/regulators may run a risk by making the transition too quickly, thus missing the opportunity to convince others by demonstrating valid evidence, while the older generation may be too dismissive of novel in vitro methods. This would impede the acceptance of alternatives. Respondents therefore emphasize that a "stand-alone" position, of either in vivo or in vitro methods, is neither feasible nor desirable. This makes it very important for the two schools to interact where possible.

Knowledge deficiency scientists

On the other hand, the scientists who do have expertise on alternative test models often lack the knowledge of, and access to, the policymaking process, and therefore cannot effectively inform legislators and regulators about the possibilities of the tests (see also Sauerborn et al., 1999). This hinders the necessary communication between legislators and regulators on the one hand and scientists in the field of the 3Rs on the other. Much of the knowledge with regard to the 3Rs therefore remains unused, according to the experts consulted. A few respondents noted that scientific developments implementing the 3Rs are inadequately publicized and explained to the public. The articles that are published tend to end up in third-rate journals, while in fact the results should be widely publicized to encourage implementation of the 3Rs.

Industry's conservatism

Along with the reluctance of regulators, industry is identified as a conservative force, preferring to play safe by anticipating the most strict registration requirements, regulators in the USA, Japan and elsewhere will set. This leads to a very cautious attitude from the regulatory affairs departments of industry towards alternative test methods for regulatory purposes. Regulatory affairs departments sometimes even go so far as to have their companies conduct extra tests in order to satisfy the authorities in the most conservative countries (such as Japan). In their fear that the authorities might reject certain results, they take these kinds of pre-emptive action. Next to this, industry, especially in a US context, is confronted with claims coming from consumers that experiences negative effects of a product. This claim culture adds up to the conservative attitude of industry towards alternative test methods.

In the R&D stage, the industry has much more freedom than in the registration and release stages. Alternative test methods are commonly used in this stage. Ultimately, this may also positively affect the development and acceptance of alternatives for use in registration and safety evaluations. But when it comes to testing for the release of a product onto the market the industry prefers to stick to the old, animal based models, even when alternative models are available. Regulators legally have authority over the industry regarding application and release of their compounds and products. But industry, in turn, exerts influence on regulators through lobby and expertise. Some respondents feel that duty of care requires industry to take more initiative to bring alternatives that are being

used in the R&D stage more actively to the attention of regulators. Currently, this occurs only to a limited extent.

The economic argument probably is, according to the respondents, another important argument for the industry whether or not to choose for an available alternative testing model even if Directive 86/609 states they should choose the alternative if available. The industry is basically driven by economic factors. In case industry foresees any economic or regulatory hurdle they prefer to stick to the old method (Schiffelers et al, 2005, 2007.) In the best scenario, cost efficiency and reducing animal testing converge. In this respect the large-scale industrial lobby to influence REACH is frequently referred to.¹⁵ In this case the industry's lobby gave counterweight to the call for more testing since it has no interest in regulations that increases the number of required tests any further.

The influence of the animal welfare lobby

In the past, animal welfare organisations have proven very capable of mobilizing politicians and the public, for example resulting in the new Cosmetics directive in which the use of animal tests for cosmetics is phased out. However, respondents did point out that they are most successful in areas where the ethical debate is relatively unambiguous. The animal welfare lobbyists seem to focus on the agenda-setting stage and the beginning of the policy-making stage. They target their message primarily at politicians and policy-makers and mostly only indirectly at regulators. These NGOs often have the advantage of understanding the legal procedures and they know the ropes in Brussels. To directly exert influence on regulators other expertise is required. In the area of testing techniques it is very difficult to keep up with the rapid pace of science and industry. Respondents indicate that animal welfare NGOs lack the knowledge, funds and an internationally coherent approach to exert real influence and as a consequence have little impact on regulators. Therefore their ability to raise the alarm in the implementation stage, when national authorities are interpreting regulatory requirements, has so far been limited.

A number of respondents state that animal welfare organizations are however professionalizing. One example cited is that observers from animal welfare organizations have been attending OECD meetings, bringing them close to the actual process of regulatory decision-making. Finally several respondents indicated that the animal rights movement does not do the image of the animal welfare organizations any good. As one respondent put it:

"You should not underestimate the resistance politicians and regulators feel towards animal lobbyists. They tend to lump all these organizations together."

Since these organisations are often viewed upon with scepticism, this also has a negative impact on the influence these NGO's can exert on regulators.

Conservative attitude regulators

All in all regulatory authorities in the field of RAT face increasing demands for consumer safety and risk minimization and are expected to take the increasing demand for safety into account when implementing policies. Regulators bear a heavy responsibility which leads them to adhere to the old frame of reference. They are particularly susceptible to a negative sense of responsibility ("If anything goes wrong, we will be held accountable"). They therefore have cause to be conservative. This is especially true when it comes to the registration of substances and products that pose potential health or environmental risks. As one respondent from industry did put it:

¹⁵ New European Community Regulation on chemicals and their safe use. It deals with the **Registration, Evaluation, Authorisation and Restriction of Chemical substances**. The new law entered into force on 1 June 2007.

*"The aim is to protect the consumer. That is what these authorities are there for. I understand very well why they work this way and do not take our documentation at face value."*¹⁶

Due to this striving for risk minimisation, the test guidelines are often interpreted in quite a rigid manner, the so-called "tick box approach". This refers to a situation in which assessors simply request every test described in the protocol (often animal models) to be executed, without having a critical look at the necessity of conducting all these tests or the possibility to use an alternative testing model. It will therefore not come as a surprise that new methods often meet resistance from those who bear the responsibility. After all, new ideas are to some extent risky, and no one can guarantee that they can be successfully implemented (Bosch van den, 2000) (Leeuw, de, 2004). Hence, any cost/benefit assessment usually favours an existing policy rather than a new one. A change in regulation is often seen as a potential liability. This point is illustrated by a civil servant's comment:

"It's better not to change ten times, than to make nine changes for the better and one for the worse."

It should however be noted here that the various regulatory agencies however widely differ in their willingness to consider alternative methods. Japanese agencies, for instance, are seen as very conservative authorities, while British, Dutch and German agencies are said to have a relatively open attitude towards alternative methods. Respondents indicated that these differences are due to a combination of factors, in which cultural differences, the degree of risk acceptance and public opinion appear to play an important role. But also within a country differences can be observed between the attitudes of regulators towards alternative test methods. These differences may for example be observed between different sectors or with regards to different product groups.

Summary empirical factors

In the 2005 study the following main factors have been observed to influence regulatory decision-making in the field of RAT whether or not to adopt alternative testing methods:

1. the public demand for risk minimization;
2. the political agenda following this public demand;
3. technical limitations and scientific uncertainties of alternative methods
4. limited knowledge of regulators of these methods
5. limited knowledge of scientist of the decision making process of regulators
6. insufficient pro-active attitude of industry
7. relatively low influence of animal welfare lobby

¹⁶ Presentation B. Garthoff, Ecopa workshop, November 27, 2004.

IV Reflection on regulatory decision-making in the field of RAT

In the previous sections theoretical and empirical factors influencing regulatory decision-making have been presented. In this final section the theoretical and empirical factors will be compared to clarify some of the mechanisms observed in the field of RAT. This comparison will result in several hypotheses regarding the factors that influence regulatory decision-making in the field of RAT. These hypotheses serve as input for case studies the author will conduct in the near future in the field of regulatory animal testing. The aim of these case studies is to draw an updated and more detailed picture of the practice of acceptance and implementation of 3 R test models for regulatory purposes.

The vicious circle in the field of RAT

The mechanism of the vicious circle as described by Breyer shows many similarities with what can be observed in the field of RAT. Most of the aspects described by Breyer, like the public perception of risk, the existing technical and scientific uncertainties, the knowledge gaps and the difficulties to bridge between disciplines, can actually be observed in the field of regulatory animal testing (see section III).

Regulatory decision-making in the field of RAT is to a great extent driven by the public interest of risk minimization. Politicians react to this demand by putting public health issues high on the political agenda and thereby pushing the regulatory agenda and attitude towards risk minimization. This risk aversion leads to an increase in animal tests on the one hand and an overly conservative attitude towards new techniques, like alternative testing methods, on the other. The conservative attitude towards the alternative methods is reinforced by the fact that regulators have to work with considerable knowledge deficiencies. Alternative methods are often highly specialized science and difficult to comprehend for somebody with a somewhat different scientific background.

An additional observation that was not found in Breyer's theory, is the reflection of the regulators' attitude in the way industry behaves. This mechanism of anticipation on the regulators' requirements might provide an additional aspect to Breyer's theory.

When comparing Breyer's theory to the empirical factors observed in the field of RAT, it becomes clear that many of the factors observed in this field are typical to risk regulation in general. Breyer's theory helps to understand that the empirical factors do not operate independently from each other but are intertwined in various ways. This is important to keep in the back of the mind when trying to clarify the mechanisms influencing regulatory decision-making in the field of RAT.

Risk regime shapers and the field of RAT

As mentioned in section II the original theories of regulatory capture and public interest focus on the dichotomy between private and public interests and the balance regulators have to find between these interests. However in the field of RAT another dichotomy was identified that seems to be even more relevant, namely the dichotomy between the two conflicting public interests public health and animal welfare. This means that regulators in the field of regulatory animal testing do not only have to balance public and private interests. They also have to make a balance between the public interest of animal welfare (less animal tests) on the one hand and public health and safety (often obtained via animal tests) on the other.

The theory of risk regimes offers the opportunity to take both dichotomies into consideration when examining regulatory decision making.

Regulators in the field of regulatory animal testing first of all seem to respond to a combination of the market pressure (to regulate the risk of a product) and the opinion-responsive pressure (the demand for risk minimization). The interest driven pressure, although present, has been observed to a lesser extend. When looking into the balance between the two public interests (animal welfare and public health) regulators in the field of RAT are said to primarily act in the interest of public health. Animal welfare will only get a serious chance to be accepted if the public health is safeguarded and/or if the benefits of adopting the alternative method outweigh the (perceived) costs. The higher the risk of a product, the higher the cost of accepting an alternative method, the more conservative the attitude of towards this new method. So the level of the potential risk of a product or compound has a negative correlation with the chance of a 3R testing method being accepted and implemented.

The influence of science and communication on RAT

Sexton states that ideally regulatory decisions should predominantly be influenced by science. Respondents in the field of RAT agree this would be the ideal situation. However the actual decisions whether or not to adopt a 3R methods are only partly influenced by scientific arguments. In line with what Sexton states, science is important but only one of the factors influencing the regulatory decisions in the field of RAT. Factors like risk perception and the political reaction on this perception even seem to outweigh the factor of science. However science is a very important tool when trying to change old decision mechanisms and to break Breyers vicious circle since knowledge of, and familiarity with alternative methods make it possible for regulators to judge these models on their merits. This process can be stimulated by improving the communication network between scientists and regulators.

Hypotheses

When comparing theoretical and empirical factors influencing regulatory decision-making, the overlap is striking and some factors seem to play a bigger role in regulatory decision-making than others. The following factors play an important role both in the theory and in the practice of RAT and therefore serve as input to formulate hypotheses (H1 till 5) with regard to regulatory decision making in the field of RAT

- the risk of a product (H1);
- the public attitude towards the regulated risks (H2);
- the political reaction on this public attitude (H2);
- the difficulty to bridge between stakeholders (scientists and regulators) (H3)
- the existing scientific knowledge and technical possibilities and limitations (H4)

And finally in the field of RAT the balance that has to be made between the two conflicting public interests of animal welfare and public health. This dichotomy served as the basis for hypotheses 5.

These hypotheses will be tested in several case studies in the near future.

	Hypotheses	Dependent variable	Independent variables
H1	<i>The acceptance of a 3R model is lower if the risk of the product it is used for, is higher</i>	<i>Regulatory decision-making: acceptance of 3R model</i>	<i>Products' risk</i>
H2	<i>The acceptance of a 3R model is lower if the public demand for risk minimization is higher</i>	<i>Regulatory decision-making: acceptance of 3R model</i>	<i>Publics demand risk minimization</i>
H3	<i>The acceptance of a 3R model is lower if the communication between 3R scientists and the regulator decreases</i>	<i>Regulatory decision-making: acceptance of 3R model</i>	<i>Communication between 3R scientists and regulators</i>
H4	<i>The acceptance of a 3R model is lower if the level of the regulators knowledge of the model is lower</i>	<i>Regulatory decision-making: acceptance of 3R model</i>	<i>Knowledge of 3R model</i>
H5	<i>The public demand for risk minimization has more influence on regulatory decision-making than the demand to increase animal welfare</i>	<i>Regulatory decision-making</i>	<i>Publics demand for risk minimization versus the demand to increase animal welfare</i>

Table 1: Hypotheses on regulatory decision making in the field of RAT

Future research

The empirical study conducted in 2005 resulted in general factors that were perceived by the respondents to influence regulatory decisions in the field of RAT. This however provides us with a very general and therefore limited picture. In reality the field of RAT consists of different sectors, different regulatory authorities and many products with different risks.

This paper shows that only a theory that combines different factors is likely to provide a useful frame to explain the mechanisms that can be observed in the field of RAT. But even such a theory will have its limitations since regulatory decision-making is a dynamical process which adapts to changes in time and context. Actual regulatory behaviour depends on the level of knowledge regulators dispose of; the cultural differences between countries; the differences in risk acceptance of these different cultures; the differences in risk perception regarding different products etc, etc. As Hood et al and Olson already stated: To identify the relative force of these different factors influencing regulatory decision-making, the examination of cases is needed.

Olson argues that there is a necessity.... *"to focus more on the micro-level decisions made by regulators and the information and trade-offs regulators face (at this level: ed.)"*... (Olson, 1997, p400) Only this can provide us with real understanding of the mechanisms that influence regulatory behaviour.

To create this picture at a micro-level in the field of RAT several case studies will be conducted in the near future in different sectors (e.g. pesticides and vaccines). These case studies will zoom into the actual process and outcome of regulatory decision-making with regard to 3R models. As part of these case studies the hypotheses presented in this paper will be tested.

The aim of this future research is to get a better understanding of regulatory decision-making in the field of RAT in order to cut the Gordian knot and in the end to speed up the process of regulatory acceptance of 3R models.

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Appendix A: List of respondents

- Drs. I. Arendzen (Dutch Ministry of Health, Welfare and Sport / Inspectorate of the Food and Consumer Product Safety Authority (VWA))
- Dr. B.J.M. Arts (Faculty of Policy Sciences, University of Nijmegen)
- Dr. B.J. Blaauboer (Interfaculty Institute for Risk Assessment Sciences (IRAS; Utrecht University))
- Mr. E.C. de Bordes (Faculty of Veterinary Medicine, Utrecht University)
- Drs. B.R.A. van den Bos (PRAD/ former MEP for the D'66 party)
- Dr. J. H. Fentem (Unilever- Safety and Environmental Assurance Centre)
- Dr. J. M. Fentener van Vlissingen (Erasmus Animal Experimentation Centre (EDC; Erasmus University Rotterdam))
- Drs. B.J. Fernhout (Intervet)
- Dr. B. Garthoff (Bayer CropScience; European Consensus Platform for Alternatives (ecopa); the European Federation of Pharmaceutical Industries (EFPIA))
- Ms. A.Gautrais (Enterprise DG, European Commission) DVM
- Dr. E.R.M. Geuns (Solvay) Msc Pharm D.
- Dr. M. van der Graaff (Nefarma)
- Dr. Ir. B.C. Hakkert (national coordinator of the OECD/EU directives programme at the National Institute for Public Health and the Environment (RIVM))
- Prof. Dr. T. Hartung (European Centre for the Validation of Alternative Methods (ECVAM); Joint Research Centre of the European Commission)
- Mr. M. Heinen (Eurogroup for Animal Welfare)
- Prof. Dr. C. F. M. Hendriksen, Netherlands Centre for Alternatives to Animal Use (NCA); Netherlands Vaccine Institute (NVI))
- Drs. E. Honig (Intervet)
- Drs. H.B.W.M. Koëter : former scientific director of the European Food Safety Agency (EFSA), Brussels
- Prof. Dr. R. Kroes †: former scientific director of the Interfaculty Institute for Risk Assessment Sciences (IRAS;Utrecht University) and president of EUROTOX and the International Life Sciences Institute (ILSI) Europe
- Drs. J. Kuil: Dutch Society for the Protection of Animals
- Dr. J.W. van der Laan (Medicines Evaluation Board (CBG); European Agency for the Evaluation of Medicinal Products (EMA))
- Drs. W.A. de Leeuw (Inspectorate of the Food and Consumer Product Safety Authority; VWA)
- S. Louhimies (Environment DG, European Commission)
- Prof. Dr. G.J. Mulder (Leiden/Amsterdam Center for Drug Research (LADCR))
- Prof. Dr. I.F.H. Purchase (ICI/Zeneca, University of Manchester)
- Prof Dr. R. Remie (Solvay Pharmaceuticals)
- Dr. T. Rijnders (Vice President Research, Organon)
- Drs. S.C. Schutte (Organon)
- Dr. R. Stolp (Intervet) DVM
- Dr. P.W. van Vliet (Dutch Health Council)
- Dr. J.M.G. Vorstenbosch (Ethics Institute, Utrecht University)
- Dr. D. Wagner (Organisation for Economic Co-operation and Development (OECD))