

**The Regulation of Complementary and Alternative Medicinal
Products in the EU and the U.S. from a Comparative Law and
Economics Perspective**

Master Thesis

Erasmus Programme in Law and Economics

Academic Year 2004/2005

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I hereby declare and confirm that this thesis is entirely the result of my own work except where otherwise indicated.

I have acknowledged on page 1 the supervision and guidance I have received from Professor Wolfgang Weigel

Johan Hulshof

29 July 2005

“The LORD said, If as one people speaking the same language they have begun to do this, then nothing they plan to do will be impossible for them. Come, let us go down and confuse their language so they will not understand each other.”

The Tower of Babel, Gen 11:6-7

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Acknowledgements

This thesis is the product of my passion for health, which I have undeniably inherited from my parents, and for which I am very grateful. The topic under discussion, the regulation of products used by complementary and alternative medicines, attracted my attention for the first time when somebody asked me why it is that cannabis is freely available in The Netherlands and many homeopathic products are not. At that time, before learning about risk regulation and the economic analysis of the law, it became clear to me that risk management is not performed efficiently in many instances. Hence, a healthy dose of naivety and the intention from my side to change the world a little bit may be justified.

Special Thanks

I would like to thank Yana Karserdareva, David Omom, and Pieter Cleppe for being part of the ‘Fantastic Four’ in Vienna, and for giving me inspiration to write on such a ‘dull’ subject. Furthermore, I want express my gratitude to my friends and family who have visited me in Vienna, and who have consequently kept me from doing thesis work. I would also like to thank my supervisor, Professor Wolfgang Weigel, for guaranteeing a marvellous stay in Vienna, giving valuable advice on the thesis, and sharing his passion for Law and Economics. I will always remember his famous quote at meetings: “*There is no such thing as a free lunch!*” Finally, I would like to thank Janske van Santvoort for being there to support me, and for the valuable comments on previous versions of this work.

Johan Hulshof
Asten, The Netherlands
29 July 2005

Introduction

In the past decades the worldwide market for complementary and alternative medicine (hereinafter CAM) has grown considerably.¹ The continuously increasing use of CAM challenges regulators to set standards for quality, safety and efficacy of medicinal products used by CAM in the licensing procedures. Considerations connected to cost containment and reimbursement in health care, the access to medicine, and stimulation of innovation or research may also play an important role in setting appropriate standards.

In general, the licensing of pharmaceuticals can be characterised as complex. Especially for a lay person it is intricate to perceive how decisions in this field of law are made and what they intend to achieve. In addition, scientific uncertainty and a lack of consensus on possible costs and benefits of CAM and the products it uses, complicate ‘things’ even further for these type of products.² To a large extent these problems are the result of a backlog in the research on the possible risks and benefits of CAM relative to the growing use of non-conventional therapies.³ It is therefore not surprising that both the World Health Organisation (hereinafter WHO) and the Select Committee on Science and Technology of the House of Lords (hereinafter the House of Lords) in the UK classify studies in safety, efficacy and cost-effectiveness as one of main priorities in CAM research.⁴

This thesis will investigate what could be the optimal approach to the licensing of medicinal products utilised by CAM in the U.S. and the EU. From a viewpoint of the fundamental goals of licensing, it will try to answer how efficient outcomes in the

¹ Legal Status of Traditional Medicine and Complementary/Alternative Medicine: A Worldwide Review, World Health Organisation, Geneva 2001, p. 3. Available at: <http://www.who.int/medicines/library/trm/who-edm-trm-2001-2/legalstatus.pdf>; WHO Traditional Medicine Strategy 2002-2005, World Health Organisation, Geneva 2002, pp. 1-3. Available at: http://www.who.int/medicines/library/trm/trm_strat_eng.pdf; Fact Sheet of the WHO on Traditional Medicine, available at: <http://www.who.int/mediacentre/factsheets/fs134/en/>.

² WHO Traditional Medicine Strategy 2002-2005, supra note 1. It should be noted that uncertainty is inextricably related to the licensing of medicinal product as there always remains some uncertainty on the effectiveness and the risks that a product may engender (J. Abraham, *The pharmaceutical industry as a political player*, 360 *The Lancet* 2002, p. 1498). See also J. Abraham, *Regulating the Cancer-Inducing Potential of Non-Steroidal Anti-inflammatory Drugs: Some lessons form the 1970s and 1980s*, 46(1) *Social Science & Medicine* 1998, pp. 39-51.

³ C. Choudhury, *Alternative medicine must get scientific validation for rational use*, 82 WHO News story 2004, pp. 635-636; see also T. Hesketh & W. Zhu, *Health in China - Traditional Chinese medicine: one country, two systems*, 315 *BMJ* 1997, pp. 115-117.

⁴ WHO Traditional Medicine Strategy 2002-2005, supra note 1; House of Lords Select Committee on Science and Technology 1999-2000, *Sixth Report on ‘Complementary and Alternative Medicine’*. Available at: <http://www.parliament.the-stationery-office.co.uk/pa/ld199900/ldselect/ldsctech/123/12301.htm>.

regulation of medicinal products used by therapies with a different approach to health and healing than conventional or allopathic medicine can be attained. The hypothesis is that the current regulatory systems for the licensing of medicinal products used by CAM, fall short of reaching an optimal balance between the protection against health risks and the access to beneficial medicines. It is argued that the systems currently in place fail to take sufficient account of the specific characteristics of CAM, as they have been developed to monitor products applied by conventional medicine which adheres to a different approach to healing. Optimal regulation of medicinal products used by CAM will therefore require a fundamental change to the current approach.

The scope of the thesis will be limited to medicinal products used by three types of therapies that are among the most frequently used: homeopathy, phytotherapy or herbal medicine, and anthroposophic medicine.⁵ These medicinal products and their position in comparison to allopathic medicinal products give a representative overview of the issues that play a role in the regulation of complementary and alternative medicinal products on a European and an American level, since they form the bulk of the medicinal products used by CAM.⁶ It will assess current issues related to the licensing of these products and the changes to the European system that will come into force in August and September 2005. As a methodological point of departure it will make use of the ‘classical’ law and economics cost benefit analysis in combination with a comparative law approach. As it is generally accepted that this approach cannot fully align with real life situations,⁷ economic theory and behavioural studies will be used to consider some flaws that stem from pure theoretical reasoning and partial isolation entailed by the use of the cost benefit analysis.

⁵ P. Fischer, *Medicine in Europe: Complementary medicine in Europe*, 309 BMJ 1994, p. 107.

⁶ The attentive reader will note that these groups of products are classified on the basis of their use and not their nomenclature. It may *prima facie* seem more efficient to look at the qualifications these products bear on their label, but the choice for looking at the actual use avoids problems that originate from discrepancies between the legal qualification of the products, their physical characteristics, and their use. A good example of this discrepancy is Echinacea tincture. Because of the pharmacological mechanism this tincture can be qualified as herbal medicine. It would thus belong to phytotherapy. However, the product is also prescribed by homeopathic and anthroposophic practitioners to improve physical resistance, either as a part of or as a complement to the therapy. Moreover, Echinacea tincture often receives a market authorisation under rules applying to homeopathic medicinal products, making it legally speaking a homeopathic medicinal product (See for example: Medicines Data Bank of the Medicine Evaluation Board in The Netherlands, *Product information: A. Vogel Echinaforce*, 2001. Available at: <http://www.cbg-meb.nl/uk/prodinfo/index.htm>). By choosing therapies a complete coverage of the medicinal products and their related problems is therefore guaranteed.

⁷ E.g. the rationality assumption is clearly falsified by the bounded rationality of humans. See for example D. Kahneman, *A Psychological Perspective on Economics*, 93(2) *The American Economic Review* 2003, pp. 162-163; and S. Jasanoff, *The political science of risk perception*, 59 *Reliability Engineering and System Safer* 1998, pp. 91-93.

However, this thesis does not intend to exhaustively discuss all problems or issues of regulating CAM products, nor does it want to draw final conclusions for at least two reasons. Firstly, as the WHO and the House of Lords have already indicated, more empirical research is needed to propose convincing new regulatory approaches.⁸ Secondly, in connection to the first argument, it would go beyond the space and the purpose of this thesis to conduct such research. Instead, it intends to stir the discussion on the optimal regulation of medicinal products used by CAM.

The first Chapter will give an introduction to the regulation of pharmaceuticals and more specifically to the CAM and the regulation of the products CAM therapies use.⁹ In the second Chapter a brief regulatory outline will be given on the licensing of products used by homeopathic, anthroposophic, and herbal medicine in both the U.S. and the EU. Chapter three will discuss the costs and benefits of the two systems using classical law and economics theory. In doing so, it will not only look at the demand and supply side of the market for medicinal products used by CAM, but it will also consider the influence of the systems on the overall wealth. Finally, the fourth Chapter will be used to suggest by what means the regulation can be improved in theory. It will furthermore, without being exhaustive, try to identify which practical problems may occur if the suggestions were to be implemented using insights provided by economic theory and behavioural studies.

⁸ Supra note 4.

⁹ To have a good understanding of the products under discussion, CAM will be generally introduced instead of paying attention only to the products specifically under discussion.

1. Introduction to the regulation of CAM and pharmaceuticals

The market for pharmaceuticals is probably one of the most complex rendez-vous points of commerce and policy making. For barely any other market sector the concept of perfect competition is so remote.¹ Policy making is considerably influenced by the relationship between governments and the pharmaceutical industry.² In addition, governments struggle with the conflicting interests that have to be addressed in the regulation of pharmaceuticals.³ On the one hand they have to implement a good health care policy which protects the public health, and guarantees patients' access to safe and high quality medicines at affordable prices. On the other hand, as part of their social and commercial policy, they intend to stimulate the growth of the pharmaceutical sector, to create and contain jobs, to promote innovation through research and development, and to protect the environment.⁴ The licensing of pharmaceuticals is one of the regulatory instruments governments have to accomplish those goals. Other instruments are, amongst others, intellectual property rules, product liability regimes, and environmental laws.

1.1 Pharmaceutical Regulation: The licensing of medicinal products

Licensing procedures for medicinal products are generally used to monitor the safety, quality, and efficacy of products. As a reaction on a number of scandals with pharmaceuticals,⁵ these pre-market tests were introduced to protect both public health

¹ E. Mossialos *et al.*, 'Regulating pharmaceuticals in Europe: an overview', in E. Mossialos *et al.*, *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, Open University Press 2004, p. 2.

² J. Abraham, *The pharmaceutical industry as a political player*, 360 *The Lancet* 2002, pp. 1498 and 1500-1501; S. Fisher Ellison and C. Wolfram, *Pharmaceutical Prices and Political Activity*, NBER Working Paper Series 2001, No. W8482, p. 3; E. Mossialos *et al.*, 'Regulating pharmaceuticals in Europe: an overview', *supra* note 1, p. 5; G. Permanand and C. Altenstetter, 'The politics of pharmaceuticals in the European Union', in E. Mossialos *et al.*, *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, Open University Press 2004, p. 49.

³ G. Permanand and C. Altenstetter, 'The politics of pharmaceuticals in the European Union', *supra* note 2, p. 40.

⁴ *Supra* note 1.

⁵ *E.g.* in the U.S. about 100 people, mostly children, died after having taken Sulphanilamide prepared from diethylene glycol in 1937. Another example is the Thalidomide disaster at the beginning of the 1960s which caused about 10,000 birth defects worldwide (A. Daemmrich, 'Regulatory Laws and Political Culture in the United States and Germany', in J. Abraham and H. Lawton Smith, *Regulation of the Pharmaceutical Industry*, Palgrave Macmillan 2003, pp. 15 and 21).

and the health of consumers.⁶ To obtain a licence the manufacturer has to provide a dossier containing data on the manufacture of the product, the origin and quality of the ingredients, data on toxicological and pharmacological tests of the medicinal product, and data obtained by clinical trials, to prove the safety, quality and efficacy of the product. This information is used by the competent authorities to make a risk benefit analysis which underlies the licensing procedure.⁷

Since licensing procedures work *ex ante* and represent requirements for the actual access to the market, their outcomes influence consumers' choice of medicine as well. Decisions by governmental institutions to allow or deny market access of a medicinal product therefore rigorously influence the market.⁸ It is therefore of cardinal importance for governments to balance *ex ante* controls against *ex post* controls like for example liability regimes, which do not have a direct influence on consumer choice, but do provide potentially strong incentives for the manufacturers.

Justifications based on a maximisation of overall aggregate wealth should be assessed critically for two vital reasons. Firstly, maximisation of overall aggregate wealth only requires the 'winners' to win more than the 'losers' lose. This does however not necessarily lead to a social optimal outcome, or in terms of health, to an overall improvement of the public health and/or the health of consumers. Secondly, it is virtually impossible to take account of every potential variable that influences individual wealth when assessing overall aggregate wealth. This is even more apparent since there always exists a degree of uncertainty when it comes to the exact effects of medicinal products.⁹ Some even argue that taking away the free choice to use risky products is never beneficial and sometimes even detrimental for consumers.¹⁰

It is essential to note that the requirements set in licensing procedures are in principle similar for every type of medicinal products. Thus, medicinal products used by CAM are fundamentally subject to similar requirements as medicinal products applied in conventional medicine. However, in a number of cases special regimes apply which partially derogate from the normal market authorisation procedures. Illustrative in this respect are the 'special simplified registration procedure' for homeopathic medicinal

⁶ For more information on the historical development, see: A. Daemmrich, 'Regulatory Laws and Political Culture in the United States and Germany', *supra* note 5, pp. 11-41; and S. Gad, *Drug Safety Evaluation*, John Wiley & Sons 2002, pp. 31-43.

⁷ J. Abraham, *The pharmaceutical industry as a political player*, *supra* note 2, p. 1498.

⁸ A. Ogus, *Regulation – Legal Form and Economic Theory*, Oxford University Press 1996, p. 190.

⁹ *Supra* note 2, Introduction.

¹⁰ R. Higgs, *Banning a Risky Product Cannot Improve Any Consumer's Welfare (Properly Understood), with Applications to FDA Testing Requirements*, 7(2) *The Review of Austrian Economics* 1994, pp. 5-10, 14.

products, and the ‘traditional use registration’ for herbal medicinal products in the EU.¹¹ In short these procedures do not require proof of efficacy for certain products used by CAM depending on their specific features. Similarly for many CAM medicinal products in the U.S. proof of efficacy is not obligatory for market access if they can be qualified as botanicals.¹² Hence, in the special regimes as described above main focus lies with quality and safety assessment of medicinal products. The main reason for exempting certain products from the requirement of proof of efficacy lies with certain incompatibilities of approaches in CAM and conventional (allopathic) medical science.¹³ These issues will be further analysed in the next paragraphs.

1.2 What is CAM?

The term CAM refers to those therapies that are not regarded mainstream or part of allopathic medicine.¹⁴ In this context, Kaptchuck and Miller define CAM as: “*a heterogeneous assortment of disparate beliefs and healing practices*”.¹⁵ Treatments can differ from rather popular therapies such as acupuncture, homeopathy, phytotherapy, and anthroposophic medicine, to less mainstream ones amongst which are light or colour therapies and spiritual or religious healing.¹⁶ The fact that CAM therapies are so diverse remains the major problem for defining an all inclusive definition of CAM.¹⁷ Moreover, the term CAM may be confusing as it suggests a degree of uniformity and a complete distinction from conventional medicine which is not the case.¹⁸

¹¹ Articles 13-16i of Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use, OJ L311/67 [2001].

¹² A. Bast *et al.*, *Botanical health products, positioning and requirements for effective and safe use*, 12 *Environment Toxicology and Pharmacology* 2002, p. 201.

¹³ H. Fabrega, *Medical Validity in Eastern and Western Traditions*, 45(3) *Perspectives in Biology and Medicine* 2002, pp. 396-397.

¹⁴ J. Kinsel and S. Straus, *Complementary and Alternative Therapeutics: Rigorous Research is Needed to Support Claims*, 43 *Annual Review of Pharmacology and Toxicology* 2003, p. 463.

¹⁵ T. Kaptchuck and F. Miller, *What is the Best and Most Ethical Model for the Relationship Between Mainstream and Alternative Medicine: Opposition, Integration, or Pluralism?*, 80(3) *Academic Medicine* 2005, p. 287.

¹⁶ J. Mann *et al.*, ‘Integrating Complementary & Alternative Therapies with Conventional Care’, in S. Gaylord, S. Norton, P. Curtis (Eds.), *The Convergence of Complementary, Alternative & Conventional Health Care: Educational Resources for Health Professionals*, University of North Carolina at Chapel Hill, Program on Integrative Medicine, 2004. p. 3.

¹⁷ Committee on the Use of Complementary and Alternative Medicine by the American Public, *Complementary and Alternative Medicine in the United States*, The National Academies Press 2005, p. 17.

¹⁸ See for more information: P. Curtis and S. Gaylord, ‘Concepts of Healing & Models of Care’, in S. Gaylord, S. Norton, P. Curtis (Eds.), *The Convergence of Complementary, Alternative & Conventional Health Care: Educational Resources for Health Professionals*, University of North Carolina at Chapel Hill, Program on Integrative Medicine, 2004; and J. Mann *et al.*, ‘Integrating Complementary & Alternative Therapies with Conventional Care’, *supra* note 16.

Notwithstanding the fact that the therapies falling under CAM do not necessarily have much in common, they generally share an individualised or holistic approach, which is one of the key differences with allopathic medicine. In essence, it means that every human being is considered and treated in a manner that takes account of the specific characteristics of the individual, including psychological, sociological and spiritual aspects. A more descriptive term to indicate the idea that a person should be viewed in total, may be 'whole person medicine', as applied by Roy. He uses the following simplification to describe many non-conventional therapies: $P(\text{erson}) = B(\text{ody}) + M(\text{ind}) + S(\text{oul})$, or to be more precise $P = B \leftrightarrow M \leftrightarrow S$.¹⁹ Conversely, $P = B$ lies at the root of conventional medicine and Western medical science.

Since non-conventional therapies suppose that $P \neq B$, their approach to healing is different from regular Western medicine.²⁰ In short, CAM therapies do generally not intend to directly target symptoms in the body as does conventional medicine, but the underlying cause of the disease is its main object of interest.²¹ The following paragraph will further elaborate on the different concepts of healing.

1.3 Different approaches to health and healing

The foregoing paragraph briefly pointed out that there is a fundamental difference in the approaches to healing between CAM and allopathic medicine. For the sake of the argument on the inefficiency of the current licensing systems, it is of cardinal importance that one fully understands these differences. This paragraph will therefore provide a more in-dept exploration of the different approaches to healing, as well as an attempt to provide a terminology to illustrate the fundamental difference in approaches. It should be mentioned though that it remains practically impossible to generalise every therapy that is or can be included in the definition of CAM. Hence, instead of trying to give an exhaustive overview, this paragraph intends to provide a basic understanding on how a large number of CAM therapies approach health and healing in comparison to conventional medicine.

While making use of the $P = B$ assumption, conventional medicine primarily seeks to treat symptoms which it can explain on the basis of measurable biological and biochemical mechanisms. If these mechanisms conform to those normally observed, a

¹⁹ R. Roy *Science and Whole Person Medicine: Enormous Potential in a New Relationship*, 22(5) Bulletin of Science, Technology & Society 2002, p. 380.

²⁰ R. Roy *Science and Whole Person Medicine: Enormous Potential in a New Relationship*, supra note 19, pp. 376 and 380.

²¹ C. Parkman & S. Ullrich, *Keeping Current on Age-Old Practices: A Complementary and Alternative Medicine Guide for Nurses*, Nurse Week Publishing 2000, p. 2.

person is considered healthy. Disease is viewed as one or more symptoms in the body which are the consequence of a failure or improper functioning of the system. In other words, the absence of symptoms indicating a malfunction means that a person is healthy. Consequently, in conformity with the $P = B$ assumption, conventional medicine aims at influencing the body's biological and biochemical mechanisms in order to restore its original state where no symptoms of failure or improper functioning are perceivable or measurable. In the case that it is unable to fully restore the system to its original specifications, it will try neutralise those symptoms that undermine the feeling of well-being in a person. For example, if a patient suffers from an attack of migraine, conventional medicine will treat the pain by using strong painkillers, since it is unable to influence the process that leads to the attack.

CAM therapies generally suppose that there is more to health or certain ailments than the body alone. Health is a complex balance of physical and non-physical factors which interact with each other. Due to this, every dynamic that relates to and/or influences the condition of a person can be the object of scrutiny, depending on the specific therapy. According to most CAM therapies an individual is healthy if there is a state of balance. In such a situation a person will function optimally and there will not be any form of disease, either measurable or immeasurable. Any absence of this balance will therefore catch CAM's attention. In essence, CAM's approach to healing can be described as an attempt to restore and maintain the balance in a person. Contrary to the approach in conventional medicine, it does not try to directly influence the biological and biochemical mechanisms in the body, but it seeks to create the conditions for a state of balance in which the individual is able to correct the problems that have surfaced in the form of symptoms.

E.g. if one assumes that $P = B \leftrightarrow M \leftrightarrow S$, the balance can be restored by influencing one or more of the three variables on the right side of the equation. Moreover, since most CAM therapies consider every individual to be unique with regard to one's constitution,²² the tools for restoring the balance will differ per person. In other words, as no person has exactly the same set of variables the precise form of treatment and medication will differ accordingly. Because of this it may happen that two individuals suffering from angina receive different medication or treatment for symptoms that are at first sight equal in respect of biological or biochemical

²² The term constitution refers to the set of characteristics of an individual (K. Lawson, 'Psychoneuroimmunology', in M. Herring and M. Manning Roberts, *Blackwell Complementary and Alternative Medicine: Fast Facts for Medical Practice*, Blackwell Publishing 2002, p. 20).

mechanisms. With this example one can clearly note the different outcomes in treatment when comparing conventional medicine and CAM. An allopathic doctor will probably prescribe antibiotic therapy for both patients, depending on the severity of the disorder. A classical homeopath on the other hand may prescribe *Belladonna* D6 or D12 for the first of two patients, and *Ferrum Fosforicum* 30K or 200K for the other one.²³

On the basis of the foregoing, the concept of ‘negative’ approach to healing may apply to conventional medicine, since it essentially defines health as an absence of symptoms. The general philosophy of CAM therapies will on the other hand be referred to as ‘positive’ approach to healing, as it describes health as a state of balance – thus laying down positive criteria for the definition of health. In practice, this distinction may seem artificial. However, it provides a means to describe dissimilarities in the fundamental approaches to healing, which have heavily influenced Western scientific medicine,²⁴ and thus also the criteria of the licensing procedures for medicinal products,²⁵ the legal status of healthcare providers and the coverage of healthcare costs.²⁶ For this thesis the distinction is of importance to address questions on the proof of effectiveness as discussed in paragraph 1.4.

1.4 Proof of effectiveness

A considerable part of the pre-marketing tests is directed at gathering data in support of the effectiveness of a medicinal product, which can tilt the balance in favour of a marketing authorisation. The issue of effectiveness is also the most controversial aspect of discussions on the benefits of many CAM therapies. This paragraph will therefore not only discuss how effectiveness is established in the licensing procedure for medicinal products, but it will also treat the problematic impact this procedure has on the majority of products used by CAM.

Preliminary to the discussion of proof of effectiveness in the licensing procedure for medicinal products the concepts of efficacy and effectiveness need to be distinguished. Efficacy refers to results that have been obtained within clearly defined

²³ For more information on homeopathy, see for example: C. Hammond, *Homeopathy, An Illustrated Encyclopedia of Safe and Effective Remedies*, Element Books Limited 1995; D. Ullman, *Discovery of Homeopathy: Medicine for the 21st Century*, North Atlantic Books 1991, pp. 3-32. (available at: http://www.homeopathic.com/articles/intro/modern_understanding.php).

²⁴ R. Roy *Science and Whole Person Medicine: Enormous Potential in a New Relationship*, supra note 19, pp. 377-379. See also H. Fabrega, *Medical Validity in Eastern and Western Traditions*, supra note 13, p. 395-415.

²⁵ A. Daemmrich, ‘Regulatory Laws and Political Culture in the United States and Germany’, supra note 5, pp. 29-30.

²⁶ S. Maddalena, *Alternative medicines: On the way towards integration? A comparative legal analysis in Western countries*, Thèses en droit (Université de Neuchâtel) 2003, pp. 283-284.

boundaries of testing. In conventional medical science the aim is to isolate the physical impact of the substance or product tested from other factors that might influence the process of healing. Only if a product produces the desired effect in isolation, it is considered efficacious.

The tool used for efficacy testing is the RCT (Double Blinded Randomised Controlled Trial).²⁷ This is a form of clinical testing in which there are two groups of randomly selected patients. One group receives a medicament that contains an active substance, also referred to as *verum*. The other group receives a medicament which does not contain the active substance, better known as *placebo*.²⁸ The trial is held in a manner to exclude other potential factors that may be beneficial in the healing process such as the relationship between the physician and the patient, specific patient characteristics, and one's cultural background. This means that neither the patient nor the person providing the medicine knows who receives either the *verum*, or the *placebo*. Thus, it is double blind. At the end of the trial the product or substance is considered efficacious if it shows a significantly better performance than the *placebo*.²⁹

Efficacy in conventional medical science is nowadays equated with the concept of effectiveness.³⁰ A similar conclusion can be adopted for providing proof in licensing procedures.³¹ However, effectiveness has a broader definition in that it incorporates every successful treatment whether it conforms to an RCT or not. Effectiveness can be described as a form of external validity, *i.e.* proof of success in real day life.³² On the opposite side, efficacy can be defined as a form of internal validity which holds within a clearly defined scope.³³ A product may thus be found efficacious without being effective in practice. Conversely, a product or substance may be effective without complying with the efficacy standard. Herein lies one of the problems provoked by clinical trials which conform to the RCT standard, since they cannot give an

²⁷ T. Kaptchuck, *Powerful placebo: the dark side of the randomised controlled trial*, 351 *The Lancet* 1998, p. 1722. See also P. Curtis, 'Assessing the Effectiveness of Complementary & Alternative Medicine', in S. Gaylord, S. Norton, P. Curtis (Eds.), *The Convergence of Complementary, Alternative & Conventional Health Care: Educational Resources for Health Professionals*, University of North Carolina at Chapel Hill, Program on Integrative Medicine, 2004. pp. 1-2.

²⁸ T. Kaptchuck, *Powerful placebo: the dark side of the randomised controlled trial*, *supra* note 27, p. 1724.

²⁹ *Ibid* note 28.

³⁰ H. Brody, 'The Placebo Effect: Implications for the Study and Practice of Complementary and Alternative Medicine', in D. Callahan, *The Role of Complementary and Alternative Medicine: Accommodating Pluralism*, Georgetown University Press 2004, pp. 77-80.

³¹ This will be assessed in more detail in Chapter 2.

³² K. Carroll and B. Rounsaville, *Bridging the Gap: A Hybrid Model to Link Efficacy and Effectiveness Research in Substance Abuse Treatment*, 54(3) *Psychiatric Services* 2003, p. 355.

³³ *Ibid* note 32. See also P. Curtis, 'Assessing the Effectiveness of Complementary & Alternative Medicine', *supra* note 27, p. 1.

unconditional answer to the question of effectiveness in real day life. Illustrative in this respect is the speech at Duke University of GlaxoSmithKline vice-president Allen Roses in which he admitted that over 90 percent of the drugs only work in 30 or 50 percent of the people³⁴ Thus, the standard of efficacy as a means to proof effectiveness may be inefficient from an economic point of view, as it is both under- and over-inclusive.³⁵ Moreover, there are studies showing that RCTs cannot fully segregate the physical aspects from the mental and spiritual ones.³⁶

With respect to CAM products the efficacy standard is problematic, since it has proven very difficult to apply the concept of double blind randomised clinical trials to CAM products or therapies.³⁷ It has been pointed out in paragraph 1.2 that most therapies adhere to an individualised approach which takes account of more than only the physical aspects of the body. Due to this, persons with similar symptoms from a conventional medicine point of view will not necessarily receive similar treatment or medication under CAM. Choosing people at random and administering the same substance or combination of substances to them, thus takes away a significant part of what actually constitutes the basis of complementary and alternative therapies, namely the provision of proof of efficacy under the conventional RCT standard consequently becomes fairly impossible.³⁸ Thus, even though a CAM product may be effective, it will not receive a market authorisation if it fails to pass the test of efficacy. In Chapter 2 it will be shown that specific mechanisms have been designed to face some of these problems.

1.5 Summary

The authorisation of medicinal products is part of a broader regulatory system for pharmaceuticals. Its main aim is to guarantee consumers access to high quality, safe and effective medicaments. This is based on a cost benefit analysis of the quality, safety and efficacy of the ingredients. Products used by CAM generally differ in their approaches to health and healing from conventional medicine – a ‘positive’ versus a ‘negative’ approach to healing. This mainly poses problems with regard to the presentation of

³⁴ The Independent (London), December 8, 2003.

³⁵ See also subparagraph 4.1. A. (ii).

³⁶ T. Kaptchuck, *The double-blind, randomized, placebo-controlled trial: Gold standard or golden calf?*, 54 *Journal of Clinical Epidemiology* 2001, p. 546.

³⁷ M. Cucherat *et al.*, *Evidence of clinical efficacy of homeopathy, A meta-analysis of clinical trials*, 56 *European Journal of Clinical Pharmacology* 2000, pp. 27-33. See for more information on problems with proof of efficacy: P. Curtis, ‘Assessing the Effectiveness of Complementary & Alternative Medicine’, *supra* note 27, 2004. pp. 8-11.

³⁸ *Supra* note 30.

proof of efficacy, as double blind randomised trials – the standard for conventional medicine – do not allow for individualisation and a ‘positive’ approach to healing. Moreover, as the efficacy standard regularly fails to provide reliable proof of a product's effectiveness in real day life both for conventional and for CAM medicinal products, it can be considered as inefficient in economic terms.

2. The Licensing of Complementary and Alternative Medicinal Products in the EU and the U.S.

The limited knowledge on the fundamental mechanisms underlying most CAM therapies, including the products they use, have complicated fitting in alternative means to present proof of effectiveness in the pre-market procedures. The limited knowledge on the topic stems from a low level of fundamental research in the field,¹ and the reluctance of (medical) scientists to evaluate the existing studies.² Notwithstanding these problems, there have been some proposals introducing alternative models of fact finding which will be further discussed in Chapter 4.³ Furthermore, since 1998 fundamental scientific research on CAM in the U.S. is funded by the NCCAM (National Centre for Complementary and Alternative Medicine), which is part of the NIH (National Institutes of Health).⁴ Surprisingly enough, there is no comparable initiative on an EU level despite a comparable increase in the use of CAM in Europe,⁵ and, as we

¹ Supra note 4, Introduction. See also: G. Feder and T. Katz, *Randomised controlled trials for homeopathy*, 324 *British Medical Journal* 2002, p. 499; and J. Kinsel and S. Straus, *Complementary and Alternative Therapeutics: Rigorous Research is Needed to Support Claims*, supra note 14, Chapter 1, pp. 472-476.

² R. Roy, *Science and Whole Person Medicine: Enormous Potential in a New Relationship*, supra note 19, Chapter 1, pp. 383-384, and 386. For those not familiar with CAM research and related issues, it should be noted that there are quite a number of studies providing outcomes that suggest that certain contemporary models of science might need revision. One of the most interesting issues may well be the mechanisms of homeopathy and the relation between infinitesimal dilutions and what is referred to as the 'memory of water'. Research clearly indicates that the influence of ultra-high dilutions (C. Zausner *et al*, *Die Wirkung van homöopathisch zubereitetem Thyroxin auf die Metamorphose von Hochlandamphibien – Ergebnisse einer multizentrischen Kontrollstudie*, 15 *Perfusion* 2002, pp. 268-276; P. Endler *et al*, *The Effect of Highly Diluted Agitated Thyroxine on the Climbing Activity of Frogs*, 36 *Veterinary and Human Toxicology* 1994, pp. 56-59; L. Rey, *Thermoluminescence of ultra-high dilutions of lithium chloride and sodium chloride*, 323 *Physica A* 2003, pp. 67-74). However, no final answers have been given on the question why that is. In other words, there is still a strong controversy on the theory of the 'memory of water' (A. Andrew, *Modified Water*, 30(1) *Kybernetes*, pp. 80-83; J. Benveniste, *Meta-analysis of homeopathy trials*, 3541 *The Lancet* 1998, p. 367).

³ For example, Maddalena proposes a socio-historical approach to provide proof of efficacy (Alternative medicines: On the way towards integration? A comparative legal analysis in Western countries, supra note 26, Chapter 1, pp. 305-311). Zhang further mentions open clinical trials, and epidemiological and observational studies as options (X. Zhang, *Research and regulation of herbal medicines*, 1(2) *Pharmaceuticals Policy and Law* 1999, p. 12).

⁴ J. Kinsel and S. Straus, *Complementary and Alternative Therapeutics: Rigorous Research is Needed to Support Claims*, supra note 14, Chapter 1, pp. 472-473.

⁵ The research in CAM has clearly no priority for the European Commission. Since 1998 no funding has been granted for CAM, although earlier funded research has shown its potential positive effects (Unconventional medicine, Final report of the management committee 1993-1998 European Commission, Directorate-General Science, Research and Development: COST Action B4, (EUR 18429 EN; Supplement 1999 (EUR 19110 EN). In the proposal for the 7th Framework Program of the European Commission for the period 2007-2013 no changes are foreseen (Proposal for a Decision of the European Parliament and of the Council concerning the Seventh Framework Programme of the European

will see in this Chapter, a regulatory system which looks more ambitious than its American counterpart.

This Chapter will give an overview of the main features of the systems put in place for granting market access to products used by CAM in the EU and the U.S. As mentioned in the Introduction, the focus will be on homeopathic, herbal, and anthroposophic medicinal products, because they give a good overview of the issues that can come up with the regulation of products used by CAM. In the first two paragraphs attention will be given to the evolution of the two systems and their basic legal structure. As a follow up, the third paragraph will analyse the differences between the two systems. It should be noted from the outset that this Chapter only analyses the European harmonising legislation, not its implementations into the national laws of the Member States.

2.1 The regulatory system in the EU

Up to 1965 there were no harmonised laws on the licensing of medicinal products under the umbrella of what then was called the EEC (European Economic Communities). As a consequence of that, the legislation differed considerably among the Member States. Although public health has principally remained a competence of the Member States to this day,⁶ most of the laws on the *licensing* of pharmaceuticals have been harmonised for the attainment of the internal market. However, in principle, to *market* a medicinal product in the EU, one essentially needs to apply for a separate authorisation in every Member State where the product is to be marketed.⁷ The current Directive 2001/83/EC on the Community code relating to medicinal products for human use,⁸ a re-codification of legislation enacted between 1965 and 2000, provides the basis for the authorisation of medicinal products. Articles 6 to 12 of the Directive lay down the general requirements. In short, next to a number of formal requirements, the applicant has to provide data on quality, safety and efficacy.

Community for research, technological development and demonstration activities (2007 to 2013), COM(2005) 119 final).

⁶ See Article 152(4) EC.

⁷ There are also a centralised procedure and a mutual recognition procedure for certain products, but these will not be discussed in full, because of their limited applicability to the products under discussion. For more information on the different systems see: S. Garattini and V. Bertele, 'The role of the EMEA in regulating pharmaceutical products', in E. Mossialos *et al.*, *Regulating pharmaceuticals in Europe: striving for efficiency, equity and quality*, supra note 1, pp. 80-96.

⁸ Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use OJ L 311/67 [2001].

Until the beginning of the 1990s the authorisation system did not include most products used by CAM. This changed with the introduction of Directive 92/73/EEC on homeopathic medicinal products,⁹ which was later incorporated in Directive 2001/83/EC.¹⁰ More changes are coming up in August and September 2005, when in chronological order Directive 2002/46/EC on food supplements,¹¹ and Directive 2004/24/EC on herbal medicinal products,¹² will come into force.

In essence, the Directive on homeopathic medicinal products brought homeopathic medicinal products, and anthroposophic medicinal products which had characteristics similar to those of the homeopathic ones,¹³ under the EU authorisation regime with the exception of products that were registered or authorised before 1 January 1994.¹⁴ Recognising however that homeopathic medicinal products cannot be fully equated with conventional medicinal products because of their specific characteristics,¹⁵ a ‘special simplified registration procedure’ was introduced for those products that are intended for oral or external application, do not have a therapeutic

⁹ Council Directive 92/73/EEC of 22 September 1992 widening the scope of Directives 65/65/EEC and 75/319/EEC on the approximation of provisions laid down by Law, Regulation or Administrative Action relating to medicinal products and laying down additional provisions on homeopathic medicinal products, OJ L 297/8 [1992].

¹⁰ See for more information on the history of EU pharmaceuticals legislation: H. Hanika, *Europäisches Arzneimittelrecht, Die pharmazeutische Industrie in Europa auf dem Weg zur Vollendung des Binnenmarktes für Arzneimittel*, MedR 2000; J. Abraham, *Regulating Medicines in Europe, Competition, expertise and public health*, Routledge London 2000; P. Brunet and C. Alberola, *The new pharmaceutical legislation*, Pharmaceuticals Policy and Law 2005, pp. 33-45; P. Cassia, *L'autorisation de mise sur le marché des médicaments à usage humain dans l'Union européenne*, 403 Revue du Marché commun et de l'Union européenne 1996, p. 749; for homeopathic medicinal products: J. Hulshof, *The Registration and Authorisation of Homeopathic Medicinal Products in the EU and The Netherlands*, Master Thesis European Law School Programme (University of Maastricht) 29 July 2004, pp. 6-13.

¹¹ Directive 2002/46/EC of the European Parliament and of the Council of 10 June 2002 on the approximation of the laws of the Member States relating to food supplements OJ L 183/51 [2002]. Moreover, the validity of the Directive has been opposed to, but the European Court of Justice has ruled the Directive to be valid under Article 95 EC (See for more information joined Cases C-154/04 and C-155/04, *Alliance for Natural Health and National Association of Health Stores v Secretary of State for Health and National Assembly for Wales*, 12 July 2005, not yet reported, paragraph 38).

¹² Directive 2004/24/EC of the European Parliament and of the Council of 31 March 2004 amending, as regards traditional herbal medicinal products, Directive 2001/83/EC on the Community code relating to medicinal products for human use, OJ L 136/85 [2004].

¹³ For products used anthroposophic medicine there is no special regime. Only if the products used comply with the characteristics of homeopathic or herbal medicinal products, or with dietary supplements, they can make use of a special regime. Hence, medicaments used by anthroposophic medicine which do not comply with one of the three groups mentioned, need to be authorised under the procedure for conventional medicines, which has proven to be problematic (See the ‘Position Paper regarding the effects of the current medico-legal framework of the European Community on anthroposophic medicine’ of the International Federation of Anthroposophical Medical Associations (IVAA)).

¹⁴ Article 13(1) of Directive 2001/83/EC.

¹⁵ K. Keller, *Homeopathic medicinal products in Germany and Europe: Legal requirements for registration and market authorization*, 32 Drug Information Journal 1998, p. 803.

indication, and do not contain more than a given amount of a mother tincture¹⁶ or substance.¹⁷ Under these (cumulative) conditions, no proof of efficacy has to be provided.¹⁸ For those homeopathic medicinal products which do not fall within the ‘special simplified registration procedure’, the normal rules for conventional medicinal products apply. However, even for these products special rules for pre-clinical tests and clinical trials may be adopted by the Member States. These rules must be in conformity with the principles and characteristics of homeopathy as practiced in that specific Member State.¹⁹

With the introduction of Directive 2004/24/EC on herbal medicinal products, Directive 2001/83/EC will also contain a Chapter 2a for ‘traditional herbal medicinal products’. It provides for a ‘simplified’ or ‘traditional use registration’ for those herbal medicinal products that comply with Article 16a of Directive 2001/83/EC.²⁰

Refusal may only be based on a limited number of grounds.²¹ According to Article 16a(3) of Directive 2001/83/EC, Chapter 2a on ‘traditional herbal medicinal products’ shall not apply if the competent authorities hold that it fulfils the criteria of a normal authorisation procedure, or the ‘special simplified registration procedure’ homeopathic medicinal products. Furthermore, a list of substances will be created by the Committee for Herbal Medicinal Products containing substances and preparations, of which the use in ‘traditional herbal medicinal products’ is accepted. If an application for registration is related to a substance or preparation on the list, no bibliographical data are required, nor data on prior authorisations or denials. The number of grounds for refusal is

¹⁶ A Mother Tincture is a concentrated form of an active substance dissolved in alcohol. The volume percentage of alcohol normally lies between 65 and 85 percent of the tincture.

¹⁷ Article 14(1) of Directive 2001/83/EC indicates that the medicinal product may not contain more than 1/10,000th part of the mother tincture, or 1/100th part of the smallest dose of active principles utilised in allopathy for which a doctor's prescription is needed. It is not exactly clear whether Member States are allowed to impose more stringent standards. In September 2005 there is a possibility to change these requirements via a committee procedure if new scientific evidence proves this appropriate (Article 14(1) after the amendment of Directive 2004/27/EC of the European Parliament and the Council of 31 March 2004 amending Directive 2001/83/EC on the Community code relating to medicinal products for human use OJ L 136/34 [2004]).

¹⁸ Article 14(2) of Directive 2001/83/EC.

¹⁹ Article 16(2) of Directive 2001/83/EC.

²⁰ This essentially means that: (1) Products may only be intended and designed for usage without supervision of a medical practitioner (The more specific criteria for labelling are the composition and the purpose for which they were designed (Article 16a 1(a)); (2) Products may only be administered in a specified strength that is pharmacologically tested (Article 16a 1(b)); (3) The route of administration may only be oral, external or in the form of inhalation (Article 16a 1(c)); (4) The products must have been used for a period of 30 years, and at least 15 years in the EU (Article 16a 1(d) Jo. Article 16c 1(c). Article 16c 4 provides for an exception: If the product is used in the EU for less than 15 years, the Committee on Herbal Medicinal Products, may nonetheless accept it. The Committee on Herbal Medicinal Products forms part of the European Medicines Agency (EMA); (5) The data on safety and efficacy must be sufficient, and plausible on the basis of long-standing use and experience (Article 16a 1(e)).

²¹ Article 16e.

analogously limited further.²² Finally, the product must contain a statement that the indication of use (effectiveness) is only based on long-standing use and that a professional should be consulted if the symptoms do not go away.²³

As an alternative to an authorisation or registration as a medicinal product, Directive 2002/46/EC on food supplements provides the possibility to market certain products as food supplements, if they have nutritional or physiological effects.²⁴ These products may not contain a health claim,²⁵ but it is allowed to make statements that do not claim to prevent, treat or cure diseases. The Directive gives standards for purity and safety.²⁶ Furthermore, since products marketed as food supplements are foodstuffs, they have to comply with quality standards for food. The Directive on food supplements will take full effect in August 2005.

2.2 The regulatory system in the U.S.

In the U.S. the regulation of medicinal products is derived from safety regulation in the food sector.²⁷ From 1906 onwards the intensity of regulation increased on a federal level. In 1938 the Federal Food, Drug and Cosmetics Act (hereinafter the 1938 Act) was introduced as a reaction to the Sulphanilamide Elixir scandal which killed over a hundred people, mainly children.²⁸ Before the introduction of the 1938 Act there was no competence of the FDA (Food and Drug Agency) to remove dangerous pharmaceutical products from the market. Its powers were mainly limited to prosecuting misbranded food and pharmaceuticals.²⁹ With the 1938 Act a pre-marketing notification was introduced in which applicants had to prove drug safety – proof of efficacy was not included yet. If the FDA did not respond to the notification the product was tacitly accepted.³⁰ The 1962 amendment of the 1938 Act laid the basis for the licensing system that is currently applicable by including proof of efficacy, an explicit pre-marketing

²² Article 16f 2.

²³ Article 16g 2 (a) and (b).

²⁴ Articles 1 *Jo.* 2 of Directive 2002/46/EC.

²⁵ Article 6(2) of Directive 2002/46/EC.

²⁶ Articles 4 and 5 of Directive 2002/46/EC.

²⁷ A. Daemrich, 'Regulatory Laws and Political Culture in the United States and Germany', *supra* note 5, Chapter 1, p. 13.

²⁸ *Supra* note 5, Chapter 1.

²⁹ The Massengil Company, responsible for the marketing of the elixir, could therefore only be convicted for misbranding, since the product did not contain alcohol, which was required for elixirs by the U.S. Pharmacopoeia (S. Gad, *Drug Safety Evaluation*, *supra* note 6, Chapter 1, pp. 31 and 35).

³⁰ D. Cullen, 'Quality Assurance, Quality Control and Audit', in A. Fletcher *et al.*, *Principles and Practice of Pharmaceutical Medicine*, John Wiley & Sons 2002, p. 85.

approval of the FDA, and an increased competence of the FDA to monitor clinical testing.³¹

Complementary and alternative medicines can be marketed under three regimes. The first applies to homeopathic medicinal products and is based on the general authorisation procedure in the 1938 Act. Products used by herbal or anthroposophic medicine can alternatively be marketed as food supplements in conformity with the Dietary Supplement Health and Education Act 1994 (Hereinafter the Dietary Supplement Act). Finally, the third regime makes the marketing of those products that do not fit the description of the previous two regimes dependent on the regular authorisation procedure of the 1938 Act including proof of efficacy. The first two procedures will now be discussed in more detail.

Homeopathic medicinal products are considered to be drugs according to the general definition of “drug” in Section 201(g)(1)(A) of the 1938 Act, if they are listed in the official Homeopathic Pharmacopoeia of the United States (hereinafter HPUS), an addendum to it, or in one of its supplements.³² Although homeopathic medicinal products are legally equated with conventional drugs, they are exempted from the provision of data on safety and efficacy in the application for authorisation. Instead, they must comply with the standards for strength, quality, purity and the routes of administrations laid down in the HPUS.³³ These standards are set during the review of a substance for listing in the HPUS.³⁴ Review is done by the Homeopathic Pharmacopoeia Convention of the United States (hereinafter HPCUS), an autonomous body which closely cooperates with the American Institute of Homeopathy, and the American Association of Homeopathic Pharmacists. The FDA distinguishes between homeopathic medicinal products that cannot be dispensed without a prescription of a licensed practitioner, and products that can be bought without a prescription. The latter group of products is regularly referred to as OTC (Over-The-Counter). If a homeopathic medicinal product is marketed for the treatment of “*serious disease conditions*”,³⁵ it falls into the category of prescription drugs and has to bear an additional disclaimer indicating its status.³⁶ In addition, the FDA demands the label to list the ingredients, the

³¹ S. Gad, *Drug Safety Evaluation*, supra note 6, Chapter 1, pp. 37-38.

³² FDA, *Conditions Under Which Homeopathic Drugs May Be Marketed*, Compliance Policy Guides Manual, Sec. 400.400 (1995).

³³ Ibid note 32.

³⁴ S. Strauss and M. Sherman, ‘Homeopathic Drugs – Regulatory Concerns’, in S. Strauss, *Strauss’s Federal Drug Laws and Examination Review*, CRC Press 2000, p. 304.

³⁵ Supra note 32.

³⁶ See Section 503(b)(1) of the 1938 Act.

strength of the product, indications for safe use, and the indications for which the product can be used.³⁷

Due to the Dietary Supplement Act non-homeopathic products are not regularly marketed with a health claim, or as drugs under the 1938 Act, since it allows the marketing of dietary supplements³⁸ under three types of claims: health claims, structure-function claims, and nutrient-content claims.³⁹ Only health claims need a pre-marketing approval based safety and efficacy review by the FDA, which is comparable with a review for conventional drug approval as it involves both data on safety and efficacy.⁴⁰ For efficacy there is the possibility to use observational studies as a complement to or as an alternative for clinical trials, also known as interventional studies.⁴¹ This makes the efficacy criterion better suited for products used by the products under discussion. Manufacturers which make use of structure-function, or nutrient claims do not need an assessment of the FDA.⁴² But if a structure-function claim is made, it has to be submitted to the FDA within 30 days after the product came on the market.⁴³ They must furthermore state that “*the FDA has not evaluated the claim*”.⁴⁴ With regard to quality and safety the rules on foodstuffs apply, which are laid down in Chapter IV “Food” of the 1938 Act. This implies amongst others that the products may not be misbranded and have to give information on the content and the use of the product.⁴⁵

2.3 What are the differences between the two systems?

After having discussed the two regulatory regimes, it is apparent that there are a number of significant differences between the EU and the U.S. systems. The current paragraph

³⁷ NCCAM, *Questions and Answers About Homeopathy*, Pub. No. D183, NCCAM Clearinghouse 2003, p. 5.

³⁸ Section 201(ff) of the 1938 Act defines a dietary supplement as “*a product (other than tobacco) intended to supplement the diet that bears or contains one or more of the following dietary ingredients: (A) a vitamin; (B) a mineral; (C) an herb or other botanical; (D) an amino acid; (E) a dietary substance for use by man to supplement the diet by increasing the total dietary intake; or (F) a concentrate, metabolite, constituent, extract, or combination of any ingredient described in clause (A), (B), (C), (D), or (E);*”

³⁹ Sections 6 of the Dietary Supplement Act. See also A. Bast *et al.*, *Botanical health products, positioning and requirements for effective and safe use*, supra note 12, Chapter 1, p. 201.

⁴⁰ Section 403(r)(3)(b)(i) *Jo.* Section 403 (r)(1)(a) of the 1938 Act.

⁴¹ The FDA states in its Guidance for Industry Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements of 22 December 1999 that: “*In an interventional study, the investigator controls whether the subjects receive an exposure or an intervention whereas in an observational study, the investigator does not have control over the exposure or the intervention. In general, interventional studies provide the strongest evidence for an effect.*” These guidelines are available at: <http://vm.cfsan.fda.gov/~dms/SSAguide.html#scirev>.

⁴² S. Gottlieb, *US relaxes its guidelines on herbal supplements*, 320 *British Medical Journal* 2000, p. 207.

⁴³ A. Bast *et al.*, *Botanical health products, positioning and requirements for effective and safe use*, supra note 12, Chapter 1, p. 201.

⁴⁴ *Ibid* note 43.

⁴⁵ See Sections 401 to 410d of the 1938 Act.

will take a closer look at them. It will give special attention to the structure of the procedures and how they fit into the overall system.

In general both legal systems distinguish between medicinal products and food supplements. With respect to medicinal products, the starting point is the licensing procedure that has been developed for conventional medicinal products. For homeopathic medicinal products special procedures have been created, but the European one is more limited. It only applies to homeopathic drugs for oral or external routes of administration which contain no more than 1:10.000 of the mother tincture or 1:100 of the smallest dose of a substance used in allopathic medicine for which doctor's prescription is required. These safety standards have neither been transparently obtained, nor are they supported by scientific data.⁴⁶ Opposed to the EU, the American system bases the safety standards on the HPUS, which states the dilutions and routes of administration which are allowed to be marketed. The listing of the substances in the HPUS is done in a very transparent manner by specialists in the field of homeopathy in the HPUS Convention who found their decisions on clearly defined studies, also known as 'provings'.⁴⁷ In addition, the initial findings are published and can be opposed by stakeholders.⁴⁸ Moreover, an extra safety criterion has been created for dispensing products which are used for serious diseases. These products may only be marketed as prescription drugs. The EU does not make this distinction for homeopathic medicinal products.⁴⁹

With respect to herbal products the approaches are clearly different. Contrary to the U.S., the EU has a special registration procedure for 'traditional herbal medicinal products' that are administered orally. It will depend on the interpretation by the competent national authorities whether the procedure will prove effective, since the requirements are complexly formulated. Moreover, they may choose to deny the registration, if they consider the product eligible for a conventional authorisation or a registration as a homeopathic medicinal product.⁵⁰ In the U.S. herbal products can only be marketed under the regime for regular medicines or as food supplements. However different from the EU, in the U.S. food supplements can be marketed with a health

⁴⁶ E.g. the fact that empirical data suggests that subcutaneous injections are as safe as the oral route of administration does not seem to matter (See *Safety of Homeopathic Injectables for Subcutaneous Administration as Used in Homeopathic and Anthroposophic Medicine*, Louis Bolk Instituut voor natuurwetenschappelijk onderzoek 2003).

⁴⁷ Supra note 34 see also www.hp.us.com.

⁴⁸ Ibid note 47.

⁴⁹ This issue is further discussed in subparagraph 3.2 A. (ii).

⁵⁰ Article 16a 3 of Directive 2001/83/EC.

claim if conditions for proof of safety and efficacy are met. Notably, this procedure, though *prima facie* as rigorous as the procedure for conventional medicines,⁵¹ does provide more flexibility to prove effectiveness of the product.⁵²

In addition, both systems require the products marketed to comply with safety and quality standards for food, with the exception of the food supplements marketed with a health claim in the U.S. The dividing line between a health claim and a structure-function claim can never be fully clear. Nevertheless, the possibility to market certain products used by homeopathic, anthroposophic and herbal medicine, supports the plurality of medicine by allowing a high number of products on the market that would not be able to stand the rigorous efficacy tests demanded for conventional medicinal products.

2.4 Summary

The marketing of medicinal products used by CAM is a complex matter. Although the American and European systems are different, the theoretical outcomes as to availability of the products under discussion are generally similar, with the exception of products categorised as homeopathic medicinal products. However, much will depend on the actual implementation. The products under discussion can either be licensed as medicinal products, or marketed as food supplements. Licensing takes as its point of departure the standards developed for conventional medicines. Subsequently products used by CAM are subject to special procedures which vary in scope and intensity. For homeopathic medicinal products the EU system can be considered rigid and dense. Moreover, it lacks scientific legitimacy. The opposite seems the case with the U.S. system, which is highly flexible and utilises a transparent science-based approach. The possibility to market certain products as food supplements guarantees the availability of a high number of products that would not be able to meet the conventional standards of efficacy. However, it will not always be easy to assess whether a label bears a health claim or a structure-function claim.

⁵¹ Supra note 45.

⁵² FDA, Guidance for Industry Significant Scientific Agreement in the Review of Health Claims for Conventional Foods and Dietary Supplements of 22 December 1999.

3. The costs and benefits of the EU and U.S. regimes

With the systems of the EU and U.S. in mind, the costs and benefits that are produced on the demand and supply side of the market, as well as the impact on the overall wealth will now be analysed. More specifically, it will be investigated in how far the systems succeed in creating favourable marketing conditions, supporting free consumer choice, and providing an optimal level of consumer and public health protection for products used by homeopathic, anthroposophic and herbal medicine. Consideration will also be given to the larger framework in which the licensing procedures function.

3.1 Trading Conditions

The marketing of the products used by the therapies under discussion constitutes the first issue to be assessed in this Chapter. The mechanism of pre-market control is a harsh mechanism to monitor product quality and safety.¹ Non-compliance with the procedure simply means no access to the market, regardless of the scope or degree of the irregularity. Furthermore, it may not come as much of a surprise that it is costly for firms to go through a procedure for market access. Hence, the concept of pre-market control can only be justified on economic grounds if alternative less drastic mechanisms fail to produce an optimal degree of protection. Notably the use of systems for information provision and pharmacovigilance,² in combination with liability regimes for health providers and the manufacturers will influence the outcome.³ In addition, manufacturers have to comply with good manufacturing practices, which guarantee a high level of quality.⁴ Since, from an allocative efficiency point of view, the pre-marketing review systems need to reflect an efficient level of safety and quality, it is questionable whether their stringency provides an efficient level of quality and safety at the lowest possible cost.

¹ Supra note 8, Chapter 1.

² Pharmacovigilance regards the monitoring of medicinal products on the market. Not only does it assure a sufficient degree of quality and safety of products which are on the market, but it also provides rules for action in case a safety problem arises.

³ M. Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, George Mason Law Review (Spring 1996), p. 466.

⁴ See for more information for example H. Dumitriu, *Good Drug Regulatory Practices*, Good Drug Regulatory Practices 1997, pp. 15-16.

The object of the paper is however not to fundamentally question the system as a whole, but to analyse its functioning.⁵ This paragraph will inquire whether the EU and U.S. regimes provide an optimal balance between safety and quality considerations on the one hand, and the position of the manufacturers with respect to market access on the other hand. It will do so by making a cost benefit analysis of the regimes from the perspective of the suppliers of homeopathic, anthroposophic and herbal medicinal products.

A. Costs of the procedures for manufacturers

(i) Centralisation or Harmonisation?

In the EU system, a very particular or peculiar cost is created with the provision of harmonisation standards instead of hard and fast rules which impose equal obligations and standards in all Member States. Due to the freedom of interpretation of the applicable Directives by national legislators and the discretion that is left to the competent national authorities for enforcement, the procedures and requirements for marketing of CAM products remain divergent on a national level. Consequently, companies face extra costs if they intend to market a product in more than one Member State.⁶ CTDs (Common Technical Document)⁷ for homeopathic medicinal products and the centralised of substances list for ‘traditional herbal medicinal products’ have been introduced to alleviate this problem,⁸ yet they will not be able to create full uniformity of procedures and requirements. One need not to be a genius to understand that the absence of equal requirements and procedures produces extra costs for companies through added complexity and additional compliance costs. From this point of view, the centralised procedures before the FDA or the HPUS Convention in the U.S. are clearly preferable from a marketing cost point of view. Moreover, in the EU a ‘centralised’ procedure has been introduced as well for certain conventional medicinal products.⁹

⁵ For fundamental critics on the system see M. Krauss, *Loosening the FDA’s Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, supra note 3, pp. 458-473.

⁶ For homeopathic medicinal products this argument has been elaborated on *in extenso* in J. Hulshof, *The Registration and Authorisation of Homeopathic Medicinal Products in the EU and The Netherlands*, supra note 10, Chapter 2, pp. 23-34.

⁷ CTDs are application documents with a harmonised lay out and set-up which are used by the national competent authorities. They have been introduced to simplify applications for the authorisation of products in more than one Member State. See for more information E. van Galen, *Homeopathische geneesmiddelen in 2003 en de innovatie van de homeopathie, resultaten en knelpunten van het registratieproces in Nederland*, 33(2) *Similia Similibus Curentur* 2003, p. 6.

⁸ See paragraph 2.1.

⁹ G. Lewis and J. Abraham, *The creation of neo-liberal corporate bias in transnational medicines control: The industrial shaping and interest dynamics of the European regulatory state*, 39 *European Journal of Political Research* 2001, p. 63.

This procedure is however not available for products used by homeopathic, anthroposophic, and herbal medicine, which fall under special regimes as described above.

(ii) Cost of the technical requirements

Let us now turn to more specific cost analysis of the marketing procedures for the products under discussion. Those products that are marketed as medicinal products are in effect treated rather similarly in both the U.S. and the EU. The most obvious exception to this is the licensing of homeopathic medicinal products in the U.S. which is dealt with under a fully separate regime. Alternatively, the EU exempts certain products classified as homeopathic medicinal products from a number of requirements directed at conventional medicinal products. Thus, as discussed in paragraph 2.1, it is not sufficient to qualify a product as a homeopathic. In addition to the qualification, one needs to fulfil a detailed set of criteria in order to receive an exemption.

At first sight one may contend that the regimes for ‘traditional herbal medicinal products’ also strongly differ. However, if in the U.S. a herbal product is marketed as a food supplement with a health claim, the outcome compared to the EU regime is fairly similar. On the one hand, the EU regime can be considered more efficient, because of the production of list of substances by the Committee for Herbal Medicinal Products.¹⁰ On the other hand, the U.S. system does not make the artificial distinction between traditional herbal medicinal products, and other herbal products with a health claim.

Although it has not been exactly quantified for the products under discussion, the high level of complexity of EU regimes is likely to increase transaction costs for manufacturers in the form of information problems and diminished procedural efficiency. This can be validated with a comparative analysis of the efficiency of the U.S. and the EU systems. Take for example homeopathic medicinal products. Here the differences between the U.S. and EU regimes are probably most striking. Where only a limited number of products fall under the special exemptions for homeopathic medicinal products in the EU, the U.S. has one system that treats all products qualified as homeopathic. For every substance the allowed dosage(s) and route(s) of administration are prescribed on the basis of a scientific evaluation by the HPUS Convention. Additional safety is provided by the distinction between OTC and prescription homeopathic medicinal products. In the EU no distinction is made between products,

¹⁰ See paragraph 2.1.

which have proven to be risky on the basis of their content or route(s) of administration, and products which are safe. Instead general, non-scientific criteria have been given in Article 14(1) of Directive 2001/83/EC to guarantee safety.¹¹ Homeopathic medicinal products with lower dilutions and routes of administration, which are not explicitly mentioned in the Article, in principle, need a conventional authorisation.¹² Hence, since this group of products is considerable, a high number of homeopathic medicinal products in the EU need an authorisation under the conventional regime.

There is a possibility for Member States under Article 16(2) of the Directive to voluntarily deviate from the conventional evaluation with the adoption of rules that make the assessment of pharmacological and toxicological tests and clinical trials in conformity with the general principles and the homeopathic traditions within a Member State. However, not many have made use of this option, and those which did, do not necessarily apply standards different from conventional medicine in practice.¹³ Thus, contrary to U.S. laws, manufacturers of homeopathic medicinal products in the EU frequently have to provide data on pharmacological and toxicological tests and clinical trials in a manner similar to data required for conventional medicinal products.

On paper, the U.S. regime for herbal product is also more flexible than the EU regime as the food supplements with a medical claim cover a larger group of products than the ‘traditional use procedure’ for ‘traditional’ herbal medicinal products.¹⁴ Not only is the coverage of herbal products more limited in the EU, the system is also more complex.

Anthroposophic medicinal products are not covered by a special regime. However, a high number of products fall under the special regimes for either homeopathic and herbal medicinal products, or food supplements. For those products falling outside these regimes, marketing has proven to be extremely costly or

¹¹ Supra note 46, Chapter 2).

¹² With the amendments introduced by Directive 2004/27/EC, the requirements with respect to the degree of dilution will become amendable in a committee procedure on the basis of scientific data. The roots of administration remain fixed. See for more information J. Hulshof, *The Registration and Authorisation of Homeopathic Medicinal Products in the EU and The Netherlands*, supra note 10, Chapter 2, pp. 58-60.

¹³ See for example the regime adopted in The Netherlands, which did not apply a different approach to the tests. Instead the MEB (Medicines Authorisation Board) made no assessment of the data in return for a disclaimer stating that the product has not been evaluated in accordance with scientific criteria. This approach has been held to be contrary to the wording of Directive 2001/83/EC by the highest Dutch administrative court, the Raad van State (See *het College ter beoordeling van geneesmiddelen tegen VSM Geneesmiddelen BV*, Raad van State Afdeling Bestuursrechtspraak, 10 november 2004, 200308614/1, available at: http://www.minvws.nl/images/hoger-beroep_tcm10-64710.pdf; and the letter of Minister Hoogervorst of health affairs to the Dutch Parliament of 11 January 2005, available at: http://www.minvws.nl/images/GMT-2535491B_tcm10-59317.pdf.

¹⁴ As the regime on herbal medicinal products is not in force yet, no final conclusions can be drawn.

impossible.¹⁵ The U.S. system does not have a special regime for herbal or anthroposophic medicinal products. However the possibility to market these products as food supplements with a health claim provides criteria which are more flexible with respect to proof of efficacy. Moreover, as anthroposophic medicine uses a high number of products that can be qualified as homeopathic, the problem is less apparent.

Considering the apparent differences between most CAM products and conventional medicinal products, in comparison with the EU, the centralised ‘tailor made’ system for homeopathic medicinal products, and the flexible approach to food supplements with a health claim in the U.S. make it less costly for manufacturers to market the products under discussion. In the EU for example, for homeopathic substances which are administered in diluted form, but do not meet the requirements set out in Article 14(1) of Directive 2001/83/EC, pharmacological and toxicological data must be provided on the effects of the substance in undiluted form, even though they are not administered as such.

Furthermore, the long standing application of, and the use of natural resources in many homeopathic, anthroposophic and herbal medicinal products pre-empts them from being patentable, clearly lowering profit margins for companies.¹⁶ If one then adds to that the high variety of products produced by most manufacturers in combination with low turnovers per batch,¹⁷ it becomes clear that the registration and authorisation of a considerable number of products is economically not feasible in the EU. In this sense some analogy with orphan medicinal products is present.¹⁸

(iii) Low specialist involvement

In general, it can be observed that the knowledge on homeopathic, anthroposophic and herbal medicine of the legislature and the competent authorities for market access in the

¹⁵ In the Netherlands there is currently a case before the Dutch Court of Appeal, in which a group of manufacturers of anthroposophic medicinal products tries to avoid effective closure of the market for products that fall outside the special regimes (<http://www.antroposofica.nl/nieuws.htm>).

¹⁶ M. Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, supra note 3, pp. 469-473.

¹⁷ ECHAMP Position Paper 2003/02, *Injectables for Subcutaneous Administration as used in Homeopathic and Anthroposophic Medicine*, p. 14. Available at: http://www.echamp.org/upload/Press/group_3/3_Injectables_for_Subcutaneous_Adm_in_Hom_and_Anthr_Medicine.pdf.

¹⁸ The term ‘orphan medicinal products’ refers to products that are to the benefit of only a very small group of patients. As the cost of marketing these products are normally higher than the expected benefits, special regulatory regimes are installed that provide incentives for companies to produce them nonetheless. A regularly applied incentive is the issuance of longer lasting exclusive rights (See for more information: T. Hervey and J. McHale, *Health Law and the European Union*, Cambridge University Press 2004, pp. 244-245).

EU and its Member States is very low, as most specialists employed are trained in conventional medicine.¹⁹ This statement is even more apparent with regard to the manufacture of products used by these therapies. Hence, the risk of (bureaucratic) paternalism²⁰ and information problems which increase costs is evidently present as most alternative forms of medicine are perceived to be ineffective by conventional medicine based on a lack of knowledge.²¹ Illustrative is the high number of practical problems that have surfaced with the introduction of the first harmonisation effort in the field of medicinal products used by CAM, Directive 92/73/EEC on homeopathic medicinal products. One very striking example is the status of nosodes – a homeopathic product that has been prepared from human or animal tissue. Although most of these products comply with the criteria for a ‘special simplified registration procedure’, they were nevertheless denied access because viral safety could not be guaranteed according to the national competent authorities. It should be emphasized here that this regards mainly products with a degree of dilution which is so high that no molecular derivatives of the starting material can be found in the end product.

As mentioned briefly in previous subparagraph, the EU does not currently require specialist involvement, and this may change only marginally for homeopathic medicinal products with the possibility to create a committee procedure for the assessment of safety standards with respect to the degree of dilution. However, it does not state how and what type of specialists should be involved in the evaluation process. Theoretically, homeopathic specialist can still be left out of the process. Here again the American model seems more transparent, scientific and flexible. For herbal medicinal products in the EU this seems more promising with the Committee for Herbal Medicinal Products. Although the American model seems less equipped with the conventional FDA review for food supplements with a health claim, the approach of the FDA is a more flexible for these products than for conventional drugs.²² On the basis of the

¹⁹ To the extent that it is testable, the Dutch MEB for example only has one qualified staff member (J. Hulshof, *The Registration and Authorisation of Homeopathic Medicinal Products in the EU and The Netherlands*, supra note 10, Chapter 2, p. 50).

²⁰ A. Ogus, *Regulation – Legal Form and Economic Theory*, Oxford University Press 1996, pp. 53, 190, and 218-219. See also M. Cohen, *Beyond Complementary Medicine: Legal and Ethical Perspectives on Health Care and Human Evolution*, University of Michigan Press 2000, pp. 111-113; E. Vedung and F. van der Doelen, ‘The Sermon: Information Programs in the Public Policy Process – Choice, Effects, and Evaluation’, in M. Bemelmans-Videc *et al.*, *Carrots, Sticks, and Sermons*, Transaction Publishers 2003, pp. 109-111; and C. Sunstein, *Behavioral Law and Economics*, Cambridge University Press 2000, pp. 46-49.

²¹ O. Caspi *et al.*, *The Tower of Babel: Communication and Medicine, An Essay on Medical Education and Complementary-Alternative Medicine*, 160 *Archives of Internal Medicine* 2000, pp. 3193-3195.

²² As pointed out in paragraph 2.2, the FDA allows for more types of evidence than randomised controlled studies (See also note 41, Chapter 2).

foregoing, the comparative cost imposed by the U.S. system suggests to be lower than the EU system.

(iv) The efficacy debacle

The cost of proving effectiveness can generally be considered higher in the EU than in the U.S. on the basis of the argumentation presented in subparagraph 3.1 A. (ii), that the procedures are more complex and smaller in scope. It should moreover be noted that the imposition in the EU of the efficacy requirement more frequently produces prohibitive costs in comparison with the U.S. because RCTs fail to evaluate effectiveness in a non-discriminatory manner. Examples may once again be found with subcutaneous injections used by homeopathic and anthroposophic medicine.²³ To cut a long story short, injections are not covered by the ‘special simplified registration procedure’. Therefore, proof of efficacy on the basis of RCTs must be provided. However, this type of injections is used in very specific situations and the choice for a particular substance is highly dependent on the characteristics of the individual. At random application is thus highly problematic. In addition, the high batch differentiation and the low turnover per batch make it economically unfeasible to obtain the requested data.²⁴

B. Benefits of the procedures for the manufacturers

(i) High product quality guaranteed which avoids a ‘market for lemons’

When it comes to the benefits of the EU and U.S. regimes for manufacturers, the most apparent one is probably the guarantee of a high level of quality. As medicinal products are mostly credence goods of which use may not entail direct information on the quality,²⁵ the procedure assures manufacturers that they will not be driven out of the market by inferior goods. In other words, a ‘market for lemons’ is avoided.²⁶ However, a high level of quality may already be safeguarded by the guidelines for good manufacturing practices with which manufacturers must comply.²⁷ Moreover, other

²³ Supra note 46, Chapter 2.

²⁴ Supra note 17.

²⁵ R. Van den Bergh, ‘Competition Law and Consumer Protection Legislation’, forthcoming in A. Hatzis (ed), *Law and Economics. A European Perspective*, Edward Elgar 2006. See also A. Vining and D. Weimer, *Information asymmetry favoring sellers: a policy framework*, 21 Policy Sciences 1988, pp. 281-303; and P. Nelson, *Information and Consumer Behavior*, 78(2) The Journal of Political Economy 1970, pp. 311-329

²⁶ G. Akerlof, *The Market for “Lemons”: Quality Uncertainty and the Market Mechanism*, 84 Quarterly Journal of Economics 1970, pp. 488-500.

²⁷ Supra note 4.

forms for signalling product quality such as certification may reach similar outcomes at lower costs.²⁸

(ii) Lower probability of liability

A less apparent and indirect benefit may be that the chances to be held liable for issues related to the medicinal product may be lower for manufacturers if their products comply with the high quality criteria for market access. However, manufacturers will still be held strictly liable for failures in design, and defective products.²⁹ Moreover, even if the expected liability is lower due to a system of pre-marketed review, it can be questioned whether the system leads to an optimal level of protection, as the quality and safety requirements have been imposed top down and do not frequently excel in flexibility. Therefore, from a liability law point of view, chances are considerable that the incentive to take care is either above or below the optimal amount of care.³⁰ It goes beyond the scope of this paper to assess this issue more thoroughly. Nevertheless, it shows that *prima facie* benefits may be outweighed by the actual cost of the system.

3.2 Free Consumer Choice

To inquire whether free consumer choice is supported by the regimes under discussion, the issues of access to medicinal products, and the provision or communication of information regarding the quality, safety, and effectiveness have to be considered. Accordingly, this paragraph will consider the costs and benefits the EU and U.S. regimes create for consumers with respect to access to products and information on their characteristics.

A. Costs for Consumers

(i) The cost of access to products

The cost of access to products used by homeopathic, anthroposophic and herbal medicine under the two regimes can be divided in two main categories. The first one regards the price consumers have to pay for the desired products. The second category regards the cost that consumers bear for products which are not supplied on the market

²⁸ D. Klein, *Quality-and-Safety Assurance, How Voluntary Social Processes Remedy Their Own Shortcomings*, II(4) *The Independent Review* 1998, pp. 539-549. See also M. Krauss, *Loosening the FDA's Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, supra note 3, pp. 462-469.

²⁹ Ibid note 28. See also W. Oi, *The Economics of Products Safety*, 4(1) *The Bell Journal of Economics and Management Science* 1973, pp. 3-28.

³⁰ See for more information G. Dari Mattiacci, 'Tort Law and Economics', forthcoming in A. Hatzis (ed), *Law and Economics. A European Perspective*, Edward Elgar 2006., p. 9.

due to the regimes in place. In the first category, the price of the products supplied will reflect the additional costs a manufacturer has to make to comply with the requirements imposed by the regimes. Therefore, the more costly the procedure is for the manufacturer, the more consumers will have to pay for the product. As a consequence, access to medicine comes at a higher cost because of the procedures.

The second category reveals the cost of restraint, while it deals with costs that are created by the absence of a particular choice for consumers. This absence is either created by the impossibility of compliance with the requirements by the manufacturers, or a too high cost of compliance triggered by the fact that the product in question is only beneficial for a relatively small group of people – a characteristic that is rather typical for many CAM products and orphan medicinal products.³¹ On the basis of the comparative costs of the U.S. and the EU systems, the American model once more suggests to be the winner, because it imposes less costs for the absence of products.³²

(ii) The cost of information

Compliance with the requirements laid down in the licensing procedures for the products under discussion, reveals information on the quality and the safety of the products. In those occasions where proof of efficacy is required some information on effectiveness may be revealed as well. The price consumers have to pay for the information that is disclosed as a result of the licensing procedures will, just as the cost for access to medicine, be reflected by an increase of the price caused by the additional costs a manufacturer has to make for compliance.

With respect to the provision of information to consumers, the distinction between prescription and OTC drugs for homeopathic medicinal products in the U.S. guarantees that consumers will be better informed by healthcare providers when a product is used to treat “*serious disease conditions*”.³³ Moreover, these products can only be obtained via prescription of a healthcare provider. Failure of the healthcare provider to give this information to the patient can be sanctioned under a liability

³¹ Supra note 18.

³² The variety of products on the U.S. market is higher than in the EU. For example, the number of homeopathic starting materials regulated in the U.S. is approximately 1300 (J. Riedlinger, *An Introduction to Homeopathy*, 25(3) U.S. Pharmacist 2000, available at: http://www.uspharmacist.com/oldformat.asp?url=newlook/files/Alte/homeopathy.cfm&pub_id=8&article_id=484) compared to 500 in Germany (K. Keller, *The Regulatory Framework for Homoeopathic Medicinal Products in Germany and in the European Union*, available at: http://www.who.int/medicines/library/qsm/icdra02/ppt/26_Keller_ICDRA_Homeopathy.ppt), one of Europe’s largest consumers of CAM.

³³ See paragraph 2.2.

regime (informed consent) and may even lead to professional punishment as well.³⁴ Here the cost for providing understandable information is shifted from the manufacturer to the healthcare provider and monitored by a regime of liability and professional punishment. The distinction between prescription and OTC may thus indirectly lower the cost of information for consumers, since a more stringent evaluation of risks and benefits that would increase the cost of compliance for manufacturers is not necessary for homeopathic medicinal products that are used to treat “*serious disease conditions*”. Although an increased expected liability of the healthcare provider may neutralise these gains, a strong correlation between the OTC/prescription-distinction, and an increased probability under the theory of informed consent is not apparent, as a product forms part of the therapy for which the duty to inform already existed.³⁵

B. Benefits for Consumers

(i) High level of quality and safety protection

The primary benefit of the licensing systems for consumers is the high level of quality and safety of the products on the market. However, the question whether the levels of quality and safety are also optimal arises here again.³⁶ Notwithstanding the questionability of the overall system, if one considers that there is no perceivable difference between the number of incidents that occurred in the U.S. and the EU with respect to products used by CAM, the comparatively lower cost of the U.S. system seems to indicate a higher efficiency in the evaluation of the quality and safety of individual products. The openness of the evaluation of new homeopathic substances in the U.S. comes, furthermore, closer to a democratised procedure that may enhance consumer trust in the overall system.³⁷

³⁴ M. Cohen, *Complementary and Alternative Medicine, Legal Boundaries and Regulatory Perspectives*, The Johns Hopkins University Press 1998, pp. 60-64, and 87-88.

³⁵ *Ibid* note 34. Moreover, even if this is the case, there is a reasonable chance that parties can easily contract around this problem. Patients can for example sign a statement in which they declare to be aware of the risks the product or therapy poses, and that they have been informed about alternative treatments, but that they nonetheless choose that specific product or therapy. It would go beyond the scope of this thesis to fully discuss this issue, but the healthcare provider seems to be the cheapest cost avoider.

³⁶ *Supra* note 3.

³⁷ J. Abraham and T. Reed, *Trading risks for markets: the international harmonisation of pharmaceuticals regulation*, 3(1) *Health, Risk & Society*, pp. 122-125. See also S. Jasanoff, *The Fifth Branch, Science Advisors as Policymakers*, Harvard University Press 1990, pp. 9-14, 229-234, 241-242, and 249-250; and R. Baldwin and M. Cave, *Understanding Regulation, Theory, Strategy, and Practice*, Oxford University Press 1999, pp. 142-145.

(ii) Increase in available information?

As mentioned in subparagraph 3.2 A.(ii), the information provided by the licensing systems engenders costs for consumers which is reflected by an increase of the price of the products on the market. The benefits of the licensing systems will therefore depend on the availability and appreciation of information compared to other systems that reveal information. As information is closely related to the ability of consumers to make informed choices with respect to quality and safety, the systems may give more protection as well if they provide incentives to reveal more and better (understandable) information than other systems. Consequently the benefits are not directly apparent.

3.3 Overall Efficiency of the Systems

Having considered the costs and benefits on the demand and supply side of the market for products used by homeopathic, anthroposophic, and herbal medicine, this paragraph will have a look at the efficiency of the systems as a whole. It will assess whether the licensing systems in the EU and U.S. are efficient in satisfying safety, quality, and in revealing product information at the lowest possible cost for society.

A. Overall Costs of the procedures

The overall cost of the procedure does not only include the cost for the players on the demand and supply side of the market, it also refers to the cost of enacting the rules and enforcing them. A system of pre-market authorisation is likely to impose higher costs on governments compared to *ex post* control, since every product has to be screened instead of analysing products at random or those under suspicion of being dangerous.³⁸ Furthermore, a more efficient system of pre-market authorisation is likely to entail fewer costs, if it is directed at ‘actual risks’.³⁹

³⁸ Moreover, in line with the observation by Klein that unapproved drugs can have both positive and negative influences on physical health (D. Klein, *Quality-and-Safety Assurance, How Voluntary Social Processes Remedy Their Own Shortcomings*, supra note 28, p. 544), it should be noted that the denial of access is likely to take a lot of lives as well as it saves. Both costs should be emphasized, but the safe side for competent authorities is to choose the ‘easy way’ by focussing on the prevention of adverse drug reactions at the lowest possible risk, at the expense of approving potentially beneficial but more risky products (D. Weimer, ‘Safe – and Available – Drugs’, in R. Poole (ed), *Instead of Regulation: Alternatives to Federal Regulatory Agencies*, Lexington Mass. 1982, pp. 263-276. See also M. Krauss, *Loosening the FDA’s Drug Certification Monopoly: Implications for Tort Law and Consumer Welfare*, supra note 3, pp. 466-469).

³⁹ S. Jasanoff, *The political science of risk perception*, 59 *Reliability Engineering and System Safety* 1998, p. 92. See also C. Sunstein, *Risk and Reason, Safety, Law, and the Environment*, Cambridge University Press 2003, p. 216; and E. Vos, *Antibiotics, the Precautionary Principle and the Court of First Instance*, 11(2) *Maastricht Journal of European and Comparative Law* 2004, pp. 187-200.

In the previous paragraphs it has become clear that generalising risks posed by various products used by a certain therapy is not efficient.⁴⁰ A similar reasoning applies to the evaluation of effectiveness on the basis of the efficacy criterion.⁴¹ Furthermore, information problems and paternalism resulting from insufficient knowledge through education,⁴² can lead to higher costs not only for manufacturers and consumers, but also for governments due to procedures that are not solely directed at ‘actual risks’. Moreover, the high complexity of a system increases these costs even more. As a result of these findings, the costs of the EU system are in principle very high for society, even if certain products are partially exempted from the requirements for conventional medicinal products.

The U.S. system though far from perfect, seems to have a comparative advantage over the EU as it is less complex, more flexible, and it has a higher level of transparency and specialist involvement. In other words, it is better equipped to protect against ‘actual risks’ at a minimum cost.

B. Overall benefits of the procedures

Probably the most apparent benefit of the licensing systems in the U.S. and the EU is the guarantee of high quality and safety standards which are not only to the benefit of consumers and manufacturers as discussed in paragraphs 3.1 and 3.2, but they also reduce the probability of scandals which can endanger public health. Yet licensing systems are not even close to being ‘waterproof’, because, as Kaufer puts it: “*There is no such thing as a ‘safe’ drug!*”⁴³ The benefits of guaranteeing efficacious products on the market are significantly less apparent, since the criteria for proof are in most cases either over- or under-inclusive.⁴⁴ Exceptions to the rule may be found in the list of substances of the EU procedure for traditional herbal medicinal products,⁴⁵ and the U.S.

⁴⁰ See for example subparagraph 3.1 A. (ii). See also K. Claxton, *Bayesian Approaches to the Value of Information: Implications for the Regulation of New Pharmaceuticals*, 8 Health Economics 1999, pp. 269-274, on arbitrary amounts of information required for the licensing of medicinal products.

⁴¹ Supra note 34, Chapter 1.

⁴² Supra note 21.

⁴³ E. Kaufer, ‘The Regulation of New Product Development in the Drug Industry’, in G. Majone (ed), *Deregulation or Re-regulation, Regulatory Reform in Europe and The United States*, Pinter Publishers 1992, p. 171. Weil alternatively points out that: “(...) *the only difference between a drug and a poison is dose.*” (A. Weil, *Health and Healing*, Houghton Mifflin Company New York 1998, p. 96).

⁴⁴ See paragraph 1.4.

⁴⁵ An equal conclusion may apply for the licensing of homeopathic medicinal products in certain Member States such as Austria under the exception of Article 16(2) of Directive 2001/83/EC (Homeopathic Medicinal Products, Commission report on the application of Directives 92/73/EEC and 92/74/EEC regarding Homeopathic Pharmaceutical Products, COM(1997)362 final, p. 2).

procedures for homeopathic medicinal products and food supplements with a health claim.

3.4 Summary

The regimes for the licensing of products used by homeopathic, anthroposophic, and herbal medicine generally come at a high cost for manufacturers, consumers and society as a whole. The additional benefits that the regimes yield compared to other means of quality and safety control are indeterminate. In the assumption that licensing with pre-market testing is necessary, the systems have to be directed at providing an optimal level of quality and safety at the lowest possible cost. Therefore, the procedures should only focus on 'actual risks'. Furthermore, generalisation of risks, complexity of the rules, information asymmetries, and paternalism should be avoided or kept at a minimum. By providing more flexibility, transparency and specialist involvement than the EU procedures, the U.S. regime is comparatively more efficient. However, the only procedure that really seems to minimise costs by taking full account of the specific characteristics of the products involved in the course of risk management, is the licensing procedure for homeopathic medicinal products in the U.S.

4. Improvements on the basis of efficiency considerations

The analysis of the costs and benefits in Chapter 3 has led to the general conclusion that the licensing of products used by homeopathic, anthroposophic and herbal medicine can be done more efficiently. The first part of Chapter 4 will provide five suggestions to improve the efficiency of the regimes under discussion. These suggestions may be divided over three main issues: A. an efficient level of protection; B. less complexity; and C. better information. As the licensing system for homeopathic medicinal products in the U.S. provides a good example of a comparatively efficient system, it can serve as a role model throughout the first part of the Chapter. The second part of the Chapter will subsequently assess whether these proposals can be attained in practice. Without being fully comprehensive, a number of practical problems that might occur during the implementation effort will be discussed. In doing so, insights provided by economic theory and behavioural studies will be used.

4.1 What would make the systems more efficient?

A. Efficient level of protection

(i) Differentiation of risk

As mentioned in paragraph 1.1, the licensing of medicinal products is a form of risk regulation that intends to protect consumers and public health on the basis of safety, quality and efficacy considerations. It should be recalled that the pre-market authorisation systems have been developed to avoid toxic disasters as the Sulphanilamide and the Thalidomide scandals.¹ Although it is not regularly brought in for consideration, comparable scandals have not surfaced with the long established use of the complementary and alternative therapies, and thus the products under discussion. This does not mean however that products used by homeopathic, anthroposophic and herbal medicine do not pose any health risks at all.² It can be questioned however whether these risks are similar in nature and extent as those generated by conventional medicine.

¹ Supra note 5, Chapter 1.

² E. Ernst, *Risks of herbal medicinal products*, 13 *Pharmacoepidemiology and Drug Safety* 2004, pp. 767-771. See also K. Keller, *Homeopathic medicinal products in Germany and Europe: Legal requirements for registration and market authorization*, supra 15, Chapter 2, p. 803.

According to Weil, for example, natural or non-synthetic medicinal products can frequently be distinguished from synthetic ones, because many of them have built in safety mechanisms which withhold the user from taking a too high dosage.³ This clearly lowers the risk of use. Moreover, in homeopathy and many related therapies, the dosages of the active substances are sufficiently low not to pose severe health risks, even if the starting material (the active substance in undiluted form) may have highly toxic or other health contravening qualities. Conventional pharmaceuticals are almost by definition synthetic in nature,⁴ because the synthetic qualities lead to high efficiency gains in the production process.⁵ Many conventional medicinal products are however copies of substances that can be found in natural resources. Aspirin for example is based on a synthetic version of acetylsalicylic acid which can be found in the bark of the white willow tree. It is known that many ancient cultures already used it as a medicine.⁶ The isolation and imitation of the active substances available in natural resources, the development of new synthetic molecular structures, and the high concentration in which synthetic substances are applied, does however not come without cost, since these factors increase risks.⁷

A system that is developed to manage risks on the basis of insights, traditions, and characteristics of a particular form of medicine does not necessarily gain equal outcomes where it is applied to other approaches to health and healing. In connection to this, an optimal level of protection can only be attained if a licensing system takes the ‘actual risks’ of a specific medicinal product into account. In other words, differentiation of the risks posed by various products connected to diverse therapies is

³ The argument made is that many natural substances start producing symptoms indicating overuse in gradual stages due to specific characteristics of the plant material. Products containing pure isolations of the active principles of plant material and/or the synthetic copies made thereof, principally fail to produce similar characteristics. Where for example the natural product digitalis is taken, it will first produce nausea or vomiting, then mild cardiac arrhythmia, and finally arrhythmia in the main or lower chambers of the heart which can be fatal within minutes. So if one stops taking the product in either the first or second stage of overuse, no severe risks are produced. Alternatively, the synthetic copy of the natural substance, mostly digoxin or a relative, will directly produce the third stage problems due to the failing natural ‘safety device’, and the higher concentrations of the active principles (A. Weil, *Health and Healing*, supra note 43, Chapter 3, p. 103).

⁴ J. McKenna, *Natural Alternatives to Antibiotics*, Avery 1998, p. 67.

⁵ This is mainly due to the fact that their properties are more easily controllable than those of natural ingredients (B. Goldberg, *Alternative Medicine: The Definitive Guide*, Celestial Arts 2002, p. 252). Hence meeting standards of quality and purity are less costly, and the production of drugs containing highly concentrated dosages becomes less problematic. Moreover, the natural substances cannot be patented decreasing the expected commercial value of natural pharmaceuticals (J. Stone, *An Ethical Framework for Complementary and Alternative Therapists*, Routledge 2003, p. 228).

⁶ W. Pierpoint, *Edward Stone (1702-1768) and Edmund Stone (1700-1768): Confused Identities Resolved*, 51(2) Notes and Records of the Royal Society of London 1997, p. 211.

⁷ A. Weil, *Health and Healing*, supra note 43, Chapter 3, pp. 97 and 99.

indispensable for not becoming under- or over-inclusive, and thus inefficient. It follows that a licensing procedure for medicinal products should be tailored to the risks at hand.

To minimise costs, however, not every obscure therapy should be regulated separately. It is very well possible to find groups of products used by more than one therapy that can be regulated under one system, as their characteristics and risks are more or less similar. The use of products which share the same properties by anthroposophic and herbal medicine are a nice illustration of this. Another group could consist of products used by therapies that can be classified as Homeotherapy.⁸ Classical Homeopathy is probably the best-known therapy within this group which also covers Isotherapy for example.⁹ However, due diligence is needed for the determination of these groups to avoid the situation of ‘exclusion’ where certain products applied by anthroposophic medicine in the EU are currently in. Because some of the products used by *e.g.* anthroposophic medicine do not fall within the scope of any special regime, they have to comply with the rules for conventional medicine, which have occasionally proven to be prohibitive.¹⁰ On the basis of the foregoing, the first suggestion for the regimes under discussion is to separate the licensing procedures for products used by conventional and non-conventional medicines, since the characteristics, risks, and the therapeutic application of the products are highly different. The separation of procedures has the additional advantage that it may make the applicable rules more easily accessible.

An additional means to differentiate risks posed by products used by homeopathic, anthroposophic, and herbal medicine is related to the therapeutic indication. The use of a distinction between products which are indicated to treat ‘minor’ health problems, and those provided for treatment of serious conditions, can provide consumers with additional guidance where the ‘stakes’ are higher. If one allows the former group to be distributed as OTC products and the latter only as prescription drugs, consumers will be explicitly informed by the healthcare provider on the risks and benefits of the products used.¹¹ The restricted dispense of these products under supervision of a healthcare provider then justifies less stringent requirements for market access with respect to effectiveness, since consumer protection is also provided by other mechanisms – *i.e.* the rules applicable to the healthcare provider. Moreover, a large part

⁸ ECHAMP, *Homeotherapy, Definitions and Therapeutic Schools*, Brussels 2004, p.4.

⁹ *Ibid* note 8.

¹⁰ *Supra* note 15, Chapter 3.

¹¹ See subparagraph 3.2 A. (ii).

of these products are already used solely under supervision of a therapist, which makes implementation relatively easy.¹²

(ii) More flexible models to prove effectiveness

The rationale behind the pre-market evaluation for the licensing of medicinal products is to make a cost benefit analysis of the positive and negative characteristics of the product on the basis of safety, quality and effectiveness. In theory, if the positive aspects outweigh the negative ones a licence will be granted. At the moment efficacy is predominantly put on a par with effectiveness in the licensing systems.¹³ Considering that the efficacy requirement, as designed by conventional medical science, has proven to be inefficient in many cases, it is fairly surprising that in general no other means to provide proof of effectiveness are allowed, except for food supplements in the U.S and ‘traditional herbal medicinal products’ in the EU. This observation is even more apparent for the products used by homeopathic, anthroposophic, and herbal medicine, since they do not have characteristics and approaches to health and healing that are similar to those of conventional medicine. Moreover, there is little disagreement on the fact that there are other means for proving effectiveness are available.¹⁴ For these reasons, the second suggestion favours the introduction of more types of studies to provide proof of effectiveness in order to make an ‘all-inclusive’ efficient cost benefit analysis possible.

B. Less complexity

(i) Straightforward rules

Rules that are straightforward and clearly defined lead to a decrease in costs because of fewer information problems. Both for the competent authorities and the manufacturers involved, the cost of applying and complying with the rules will be lower, as the impact of the rules can be relatively easily anticipated. Therefore, the separation of licensing

¹² Subcutaneous injections for example are not likely to be used without a qualified practitioner, because the effectiveness of these therapies are highly dependent on the accurate administration of the injection (*Safety of Homeopathic Injectables for Subcutaneous Administration as Used in Homeopathic and Anthroposophic Medicine*, supra note 46, Chapter 2). On top of this, the use of injections by consumers is very limited.

¹³ See note 30, Chapter 1.

¹⁴ On the basis of paragraphs 1.4 and 2.2, a number of observational studies can be identified for that may provide proof of effectiveness. Without trying to be exhaustive, among these studies are: cohort (longitudinal) studies, case-control studies, cross-sectional studies, uncontrolled case series or cohort studies, time-series studies, ecological or cross-population studies, descriptive epidemiology, and case reports (See The FDA Guidance for the Review of Health Claims for Conventional Foods and Dietary Supplements, supra note 41, Chapter 2). See also Zhang and Maddalena; supra note 3, Chapter 2.

procedures for conventional and non-conventional medicinal products is again of cardinal importance, since it avoids the creation of a system that uses highly complicated exemptions.

(ii) Unification of standards

The harmonisation effort for homeopathic medicinal products in the EU has proven to be rather ineffective. The high level of differentiation that remained after the adoption of harmonising measures for homeopathic medicinal products in the EU suggests that more uniformity is needed to successfully attain the Directive's objective.¹⁵ Although, no final conclusions can be drawn for products used by anthroposophic and herbal medicine in the EU, the chance that similar problems will occur is not merely theoretical. The uniform U.S. regime clearly shows a comparative advantage in this respect. One precise set of rules and equal enforcement of these rules in all states by the FDA make the licensing procedures less differentiated and thus less costly.¹⁶ The creation of uniformity in rules and enforcement consequently represents the third suggestion.

C. Better information

(i) Specialist involvement

The role of science, and especially specialist involvement, is of significant importance for the efficient functioning of the licensing procedures for the products under discussion. As pointed out in subparagraphs 3.1 A. *(iii)* and 3.3 A., a lack of knowledge is likely to lead to information problems and unjustifiable paternalism which impose unnecessary costs on consumers, producers, and society as a whole. In addition, a lack of transparency and accountability of specialists increases the danger of capture and thus decreases objectivity.¹⁷ Hence, the fourth suggestion stresses the involvement of more qualified specialists for the assessment of the risks related to the products under discussion. Moreover, a high level of accountability and transparency analogous to the system for homeopathic medicinal products in the U.S. is vital.¹⁸

¹⁵ J. Hulshof, *The Registration and Authorisation of Homeopathic Medicinal Products in the EU and The Netherlands*, supra note 10, Chapter 2, pp. 69-70.

¹⁶ This may also be an argument in favour of a centralised review procedure for products used by homeopathic, anthroposophic, and herbal medicine in the EU which is currently not present.

¹⁷ J. Abraham, *The pharmaceutical industry as a political player*, supra note 2, Chapter 1, pp. 1499-1500.

¹⁸ Ibid note 17.

(ii) Differentiation between prescription and OTC drugs

The fifth and final suggestion, regards the introduction of a distinction between prescription and OTC drugs in the EU and extension in the U.S. to herbal and anthroposophic medicinal products. This is not only preferable from the point of view of efficient protection through risk differentiation, it is also an important mechanism to improve the provision of information to consumers at no or very low additional cost.¹⁹

4.2 Can these changes be attained?

Now that the five suggestions for improvement of the systems have been discussed, this paragraph will briefly try to provide some insights on the feasibility of these proposals. Three issues that may be problematic for the effective attainment of the suggestions from an economic and behavioural point of view have been chosen for further discussion: political distortions, path dependence, and bounded rationality. It should be emphasized once more that this list is however not meant to be exhaustive, and many other issues may be vital for the attainment of regulatory change as well.

A. Political distortions

Setting up a new separate system for medicinal products with a different approach to health and healing may be politically too costly. In the EU this was already apparent with the introduction of Directive 92/73/EEC on homeopathic medicinal products. Here the imposition of a unified regime for products which do not fall within the ‘special simplified registration procedure’, has proven politically unattainable.²⁰ Analogous to the political inability within the EU to adopt special rules for certain homeopathic medicinal products, it is likely that the adoption of the suggestions in this thesis is at least equally, if not more, problematic. In addition, the strong role of the conventional industry in the political process may be of considerable importance for the conservation of the current systems. As this topic is also related to theories on path dependence, it will be discussed in more detail in the next subparagraph.

¹⁹ See paragraph 3.2 A. (ii).

²⁰ The fact that Directive 92/73/EEC tries to create an ‘equal level playing field’ for homeopathic medicinal products, discloses the ambition to capture every type of product. However, uniformity, at least on paper, has only been provided for a small group of products. The ‘residual’ groups are only subject to facultative regimes. Although the (censored) internal documents do not reveal it, there was a political compromise since unified standards could not be attained.

B. Path dependence and Lock-in effects

The problem of path dependence and lock-in effects is maybe one of the most apparent problems in the discussion on change of licensing systems for products used by homeopathic, anthroposophic, and herbal medicine. One does not need to have much knowledge on the subject to see that the whole system has mainly evolved around the licensing systems for conventional medicine. New specialised authorities or agencies in the spirit of the HPUS Convention may well be needed. Because other agencies would lose prerogatives, something no administrative institution likes, changes will not be without costs.

Another issue is related to policy choices. Much of the legislation currently in place in the EU and the U.S. has been developed in cooperation or under the influence of the conventional pharmaceutical industry.²¹ Moreover, most competent authorities for the licensing of medicinal products are not fully disentangled from the influence of the industry.²² Regulatory agencies such as EMEA and the FDA have shown to be sensitive to regulatory capture.²³ Interest groups related to the CAM products under discussion have not (yet) evolved into equally strong players that can exert the influence necessary for a shift to a new system of governance.²⁴ Hence, it may therefore be rather difficult to change the current regulatory system.

C. Bounded rationality

Finally, some words on problems related to change and bounded rationality. Sunstein points out that error on the reality of risks caused by human intuition undermines the creation of good public policies.²⁵ Such intuitive failure is amongst others based on availability heuristics,²⁶ intuitive toxicology,²⁷ and social cascades.²⁸ Even with a

²¹ Supra note 2, Chapter 1. See also G. Permanand and E. Mossialos, *Theorising the Development of the European Union Framework for Pharmaceutical Regulation*, LSE Health & Social Care Discussion Paper Number 13, LSE Health & Social Care 2004, pp. 22-28; and G. Lewis and J. Abraham, *The creation of neo-liberal corporate bias in transnational medicines control: The industrial shaping and interest dynamics of the European regulatory state*, supra note 9, Chapter 3, pp. 56-58.

²² J. Abraham, *The pharmaceutical industry as a political player*, supra note 2, Chapter 1, p. 1498.

²³ Ibid note 22.

²⁴ For more information on path dependence and lock-ins, see G. Unruh, Understanding carbon lock-in, 28 *Energy and Policy* 2000, 817-830; B. Sandén and C. Azar, Near-term technology policies for long-term climate targets – economic wide versus technology specific approaches, 33 *Energy Policy* 2005, 1557-1576; and P. David, *Clio and the Economics of QWERTY*, *Papers and Proceedings of the Ninety-Seventh Annual Meeting of the American Economic Association*, 75(2) *The American Economic Review* 1985, 332-337.

²⁵ C. Sunstein, *Risk and Reason, Safety, Law, and the Environment*, supra note 39, Chapter 3, p. 29.

²⁶ According to Kuran and Sunstein an availability cascade is: “a pervasive mental shortcut whereby the perceived likelihood of any given event is tied to the ease with which its occurrence can be brought to mind” (T. Kuran and C. Sunstein, *Availability Cascades and Risk Regulation*, 51 *Stanford Law Review*

thorough cost benefit analysis on the ‘actual risks’ of the products under discussion there may be a considerable chance that no optimal form of licensing is attainable, as politicians are generally no medical or chemical specialists and medicinal products are considered risky. Moreover, social norms through public pressure can blur their distinction between ‘actual’ and perceived risks,²⁹ as the Love Canal case illustrates.³⁰

Based on for example a combination of availability heuristics and social cascades, a majority in parliament may believe that the risk connected to the use of homeopathic medicinal products derived from, but not containing starting material obtained from animal tissue (nosodes), is equally great as the risk of eating meat containing high amounts of dioxin. This will be even more apparent if the homeopathic product is applied in the form of an injection, since injections are intuitively more dangerous. If however, the homeopathic medicinal product were to be replaced by an injection containing water, fewer parliamentarians would consider it as dangerous. The plain water may nevertheless pose higher risks by means of residual metals, pesticides, or antibiotics³¹ than the initial homeopathic medicinal product, which contains pure, high quality water as its main constituent, because of compulsory guidelines on good manufacturing practices.

This small exposé shows the importance of avoiding political choices based on erroneous perceptions or ‘shortcuts’ of the mind. This remark does not however try to trivialize the different types of risk perception between lay people and specialists.³² It

1999, p. 685). Hence, the risk of being shot by a sniper during in autumn 2002 in Washington D.C. was perceived to be higher than the risk of dieing as a consequence of smoking, although statistical data clearly suggests the opposite (See Sunstein, *Risk and Reason, Safety, Law, and the Environment*, supra note 39, Chapter 3, pp. ix-xii). Because the images of the deaths and injuries caused by the sniper were shown on television, people could more easily identify the impact of being shot compared to suffering from smoking cigarettes.

²⁷ It refers to the human failure to ‘correctly’ react to toxic risks. Many individuals for example believe that risk is black and white: it is there or it is not. Another example can be found in the higher confidence of humans in natural processes. Natural products are normally preferred over manmade ones with respect to risk. Clearly things are more complicated in both instances. See for more information: N. Kraus, T. Malmfors, and P. Slovic, ‘Intuitive Toxicology: Expert and Lay Judgements of Chemical Risks’, in P. Slovic (ed), *The perception of Risk*, Earthscan Publications 2000, pp. 285-315.

²⁸ The term defines the perception of risks through social interaction. People often assess risks with reference to the position others in society take towards a specific risk (C. Sunstein, *Risk and Reason, Safety, Law, and the Environment*, supra note 39, Chapter 3, pp. 37-39).

²⁹ E. Posner, *Law and Social Norms: The Case of Tax Compliance*, 86 Virginia Law Review 2000, pp. 1781-1819. See also R. Ellickson, *The Market for Social Norms*, 3(1) American Law and Economics Review 2001, pp. 1-49.

³⁰ T. Kuran and C. Sunstein, *Availability Cascades and Risk Regulation*, supra note 26, pp. 691-698.

³¹ P. Blackwell *et al*, *Evaluation of a Lower Tier Exposure Assessment Model for Veterinary Medicines*, 53 Journal of Agricultural and Food Chemistry 2005, pp. 2192-2201; and Boxall *et al*, *Are Veterinary Medicines Causing Environmental Risks?*, Environmental Science and Technology 2003, pp. 286-294.

³² P. Slovic, ‘Perceived Risk, Trust and Democracy’, in P. Slovic (ed), *The Perception of Risk*, supra note 27, pp. 316-326.

merely attempts to indicate that information problems can once again negatively influence regulatory choices and the functioning of governmental institutions, as long as politicians have not been properly informed about the ‘actual risks’ and benefits of the products under discussion and their own mental shortcuts. Risk communication by stakeholders can be a valuable tool to minimize the inconsistencies or failures that are a product of bounded rationality.³³ An in-dept assessment of this topic goes however beyond the scope of this thesis.

4.3 Summary

The systems under discussion can be improved using the model provided by the licensing procedure for homeopathic medicinal products in the U.S. In this context five suggestions were provided, namely: the separation of the licensing procedures for products used by conventional and non-conventional medicines to address ‘actual risks’; the increase of flexibility through the acceptance of more types of studies to provide proof of effectiveness; more uniformity with respect to the requirements for licensing; the involvement of more qualified specialists who can be held accountable in highly transparent procedures; and the introduction or extension of a distinction between prescription and OTC drugs. Admitting that the changes suggested may be influenced by certain factors identified by economic theory and behavioural studies, it is subsequently shown that implementation may be hampered in practice by political distortions, path dependence and lock-in effects, as well as bounded rationality. More factors may be of influence.

³³ D. Ropeik and P. Slovic, *Risk Communication: A Neglected Tool in Protecting Public Health*, 11(2) Risk in Perspective 2003, pp. 1-4. See also F. Mebane, *The importance of news media in pharmaceutical risk communication: proceedings of a workshop*, 14 Pharmacoeconomics and Drug Safety 2005, pp. 297-306.

Conclusion

The licensing of products used by CAM is a complex and costly business for both manufacturers, consumers, and society as a whole. Most procedures available are not cost efficient, as they are designed for conventional or allopathic medicinal products which have different characteristics and approaches to health and healing. Consequently, the procedures fail to limit attention to ‘actual risks’.

In conformity with the hypothesis of this thesis that the products under discussion would be more efficiently regulated, if the applicable licensing procedures were fully separated from the ones for conventional medicinal products, the U.S. system for homeopathic medicinal products shows a comparative cost advantage over the other procedures under examination. Furthermore, its requirements for obtaining a licence are relatively easily understandable and accessible. Moreover, the system is well tailored to the specific (individual) characteristics of homeopathic products, their mode of application, and the risks their use may engender. Therefore, costs that yield from a lack of flexibility, information asymmetries, and paternalism are either avoided or minimised.

In order to make the other procedures under discussion more efficient it is proposed to differentiate more between risks by separating the licensing of allopathic medicinal products and products used by CAM. In addition, the thesis suggests to make the systems more flexible with regard to proof of effectiveness. Furthermore diminishment of complexity, the further harmonisation of rules, and the increase of ‘good’ information through more specialist involvement are supported. Although these changes are feasible in theory, political distortions, path dependence in combination with lock-in effects, and bounded rationality, may amongst others hamper the attainment of the proposed changes.

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