

European Committee for Homeopathy



# A STRATEGY FOR RESEARCH IN HOMEOPATHY

ASSESSING THE VALUE OF HOMEOPATHY

FOR HEALTH CARE IN EUROPE

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## **PREFACE**

Homeopathy is claimed to be effective by millions of patients and thousands of homeopathic doctors all over the world. Despite this, the effectiveness of homeopathy is still not universally recognised and its mechanism of action remains poorly understood.

The main objective of this report is to provide a strategy for assessing the value of homeopathy for health care in Europe.

### **The strategy delineated by this report focuses on increasing:**

- the knowledge of homeopathy
- the understanding of its working mechanism
- the effectiveness of homeopathy

In its introduction to the Sixth Framework Programme, the European Parliament and the European Council stated that this research Programme will be carried out to further the objective set out in Article 163(1) of the Treaty “of strengthening the scientific and technological bases of Community industry and encouraging it to become more competitive at international level”.

This Programme will be structured around the following three headings, under which the four activities as set out in Article 164 of the Treaty will be undertaken:

- Focusing and integrating Community research,
- Structuring the European Research Area
- Strengthening the foundations of the European Research Area

Homeopathic medicine is currently involved in the following areas:

- Studies relating to the treatment of cardiovascular diseases and rare diseases
- Combating resistance to antibiotics and other drugs
- Studies of food quality and safety (including safer and more environmentally friendly production and processing methods)
- Food-related diseases and allergies, particularly in children
- Policy-oriented research, including public health research, consumer protection, and new and more humane production methods to improve animal health and welfare
- Co-ordination of existing nationally funded research on alternative or non-conventional medicine (including comparative studies, the development of European databases and interdisciplinary networks, exchange of clinical practice and co-ordination of clinical trials).

Homeopathic medicine would be involved in new areas answering major health problems:

- Studies relating to aging, life expectancy at birth has risen by five years since 1970 ([www.europe.eu.int](http://www.europe.eu.int)), homeopathy can be used as alternative for health maintenance with age.
- Systematic clinical studies about quality of life and homeopathy.
- Studying homeopathic possibilities for diseases linked to poverty is important for disease control in the future.
- The role of homeopathy in the metabolic disease.

There is no doubt that research in homeopathy is meaningful to European citizens – consumer surveys show increasing popularity of non-conventional medicine, especially homeopathy. Both users and critics agree that serious side effects do not occur and that these medicines are safe to take. Because of this, safety Council Directive 2001/83/EC and 2001/82/EC permits a simplified registration procedure for most homeopathic medicines. In addition, homeopathic care is inexpensive and therefore claims to provide substantial savings to health service and welfare budgets. Homeopathy’s aim to mobilise the self healing

properties of the body in a curative and/or preventive sense is welcomed by European citizens for their personal health care. Furthermore, if homeopathy is introduced into the livestock farming sector, the European citizen could also be better protected from pharmacological residues in animal products.

In general, homeopathy may provide a substantial contribution to improving the quality of life for European citizens and thus seems to qualify for obtaining research funding by the European Union.

This July 2005 report has been drafted and edited by Dr David Spence, Dr Ton Nicolai, Dr Michel Van Wassenhoven and Mr Galen Ives. It is an enhanced and updated version of the original report that was drafted and edited by Dr Fred Wiegant, Dr Dick Koster and Dr Ton Nicolai and published in 1997 and of the 2003 revised version. The European Committee for Homeopathy has asked all individuals that are known to be involved in homeopathic research in the European Union for their additions, comments and suggestions. This final report can therefore be considered to be a consensual view of all homeopathic researchers in the European Union.

Contributions have been made by (in alphabetical order) Prof Dr Madeleine Bastide, Dr Vera Baumans, Dr L. Bonamin, Dr Martin Dicke, Dr E. Eibl, Dr Christian Endler, Dr Peter Fisher, Dr Annie Ginibre, Dr E. Gonzalez-Peirona, Dr Robbert van Haselen, Mr Galen Ives, Dr Gerard Jansen, Dr K. Keller, Dr S. Kivello, Dr Christien Klein, Dr Dick Koster, Dr Klaus Linde, Dr Hans Miltenburg, Dr C. Rezzani, Prof. G. Ruiz-Vega, Dr Lex Rutten, Dr Philippe Servais, Dr Jurgen Schulte, Dr Cyril Smith, Dr J.L. Smout, Dr David Spence, Dr Aslak Steinsbekk, Dr Jeremy Swayne, Dr Harald Walach, Dr Michel van Wassenhoven, Dr Fred Wiegant, Dr Roland van Wijk, Dr Claudia Becker-Witt and Dr Harry van der Zee.

## **TABLE OF CONTENTS**

	<b>Preface</b>	<b>2</b>
	<b>Summary</b>	<b>5</b>
<b>1.0</b>	<b>Introduction</b>	<b>8</b>
1.1	Current position of homeopathy	8
1.2	European Commission Homeopathic Medicine Research Group	8
1.3	Action COST B4 Unconventional Medicines	9
1.4	Objectives of the homeopathic research community	10
1.5	Research infrastructure and methodology	11
1.6	Provings and clinical verification	11
1.7	Aims and contents of this report	12
<b>2.0</b>	<b>Homeopathy as a method</b>	<b>13</b>
2.1	Basic principles	13
2.2	Specific concept of health and disease	13
2.3	Homeopathic medicines	14
2.4	Homeopathy in clinical practice	14
<b>3.0</b>	<b>Clinical and socio-economic research</b>	<b>15</b>
3.1	Introduction	15
3.2	Effectiveness and efficacy of homeopathy	15
3.3	Diagnostic tools in homeopathy	16
3.4	Economic evaluation of homeopathy	16
3.5	Provings	19
3.6	Homeopathy in the livestock farming sector	20
3.7	Auxiliary studies	20
<b>4.0</b>	<b>Fundamental research</b>	<b>21</b>
4.1	Introduction	21
4.2	The similia principle	21
4.3	Preparation, mechanism of action and effect of potentised remedies	22
4.4	Auxiliary studies	24
<b>5.0</b>	<b>Targets and priorities</b>	<b>25</b>
5.1	Clinical and socio-economic research	25
5.2	Fundamental and pre-clinical research	26
	<b>References</b>	<b>27</b>

## SUMMARY

The objective of this report is to provide a strategy for assessing the value and improving the effectiveness of homeopathy for health care in Europe.

Homeopathy is becoming increasingly popular in the European Union – millions of consultations take place each year. Both users and critics agree that serious side effects do not occur and that these medicines are safe to take. Homeopathic care is inexpensive and therefore claims to provide substantial savings to health service and welfare budgets. Homeopathy's aim to mobilise the self-healing mechanisms of the body in a curative and/or preventive way is welcomed by European citizens for their personal health care. The majority of general practitioners in different European countries feel that homeopathy, like some other forms of complementary medicine, deserves a place in mainstream medical practice. Clearly, in the current climate, homeopathy is expected to figure more largely in both primary and secondary health care.

Over the 200 years of its existence, a large amount of documentation has been published on the curative effects of homeopathic medicines. Its longevity and widespread use throughout the world (WHO, 2001 **ref.1**) bears witness to the essential soundness of the homeopathic approach. The fact that homeopathic medicines are effectively used in veterinary medicine for inflammation and hormonal disorders is convincing evidence that homeopathy has more than a placebo effect. Evidence has been accumulating over the last decade derived from animal studies, from isolated organ systems and from cells in vitro.

Although consistent results have been obtained in the performed clinical trials supporting the efficacy of homeopathy, as was shown in several meta-analyses (**ref.2-3-4**), homeopathy is still not universally recognised. In order to be accepted as a valid part of medical practice, both opponents and supporters recognise that more research investment is needed. Research in homeopathy has frequently been hampered by methodological problems as well as by gross under-investment in the academic resources required.

The Homeopathic Medicine Research Group (a joint group of researchers in mainstream medicine and homeopathy formed by the Directorate General XII of the European Commission, **ref.5**) concluded that homeopathy is certainly researchable. They recommended the stimulation of further research in homeopathy and produced guidelines for the review of clinical research protocols in homeopathy, and concluded that the highest priority should be given to clinical research, in which mainly large trials of sound and rigorous methodology should be done. In addition, in fundamental research, previous studies using model systems in which an effect of high potencies have been observed should be repeated.

The Action COST B4 (Action on Unconventional Medicine) was established in 1993 and ended in 1999, **ref.6-7**. The COST initiative encompasses member states of the European Union and enables wider participation from countries within the Council of Europe. The participating countries in COST Action B4 are Belgium, Croatia, Denmark, Finland, Germany, Hungary, Italy, The Netherlands, Norway, Slovenia, Spain, Sweden, Switzerland, United Kingdom. The report concluded: "Without the development of a research infrastructure which reflects the actual prevalence and relevance of complementary therapies in health care, an adequate evaluation of this huge field (complementary therapies) is not possible. However, many complementary interventions *are* already widely used by a large number of physicians and other providers who claim positive experiences. A large number of patients seeks complementary care and perceives such treatment as effective. At least the most relevant topics should be investigated systematically. A sound evaluation of clinical effectiveness will consume relevant resources. However, if such a trial for evaluation is not undertaken the discussion on complementary therapies will remain dominated mainly by prejudices, inadequate generalisations and uncertainty." As far as homeopathy is concerned, the report states that, "although overall the available clinical trial evidence suggests that homeopathy can have an effect greater than placebo, this evidence is not (yet?) compelling". It states also that, "Clinical research on homeopathy has been focussing almost completely on the question "is it placebo?" This general question ignores that homeopathy is used in different ways (of which some, theoretically, might be effective and others not) and for a wide range of conditions. The reason for this "generalising" approach is the fact that homeopathy seems extremely implausible to academic medicine

and the main motive for research so far has been to “justify” homeopathy in front of the scientific establishment. The resulting research is of questionable relevance for actual medical practice as the study models very rarely reflect actual practice. As for acupuncture, we recommend that research on homeopathy should also include investigation of actual practice”. About preclinical research, the Action states that, “Although the existing positive results are very encouraging there is a need for more research, more external replication and more research on the similia principle. The literature review demonstrates at the very least that arguments against research on homeopathy are no longer tenable. Testable scientific hypothesis can be formulated about the working mechanisms of homeopathic dilutions”.

One of the main objectives of this report is not only to promote homeopathy by effectiveness studies, but also to improve it by trying to understand and evaluate its therapeutic success (or failure) in daily practice. Apart from efficacy, important questions concerning safety, mechanism of action, the value of different therapeutic strategies and costs have to be investigated in a systematic way. Improvement is needed because homeopathy is a developing science, many hypotheses have not yet been tested, remedies pictures are incomplete, therapeutic strategies vary considerably, and it is unknown what strategies are more applicable in certain diagnoses. As in conventional medicine diagnostic research is becoming more important. Symptoms are used as diagnostic tools and should be assessed as such.

The House of Lords Committee (**ref.12**) describes a vicious circle: “Several reasons have been put forward to explain why so little high-quality CAM research is being done. The five most common reasons suggested to us are: a lack of research training across the CAM professions; a lack of research funding available for CAM projects; a poor, almost non-existent, research infrastructure within the CAM sector; a lack of interest in this field of research by conventional scientists who are trained in research methodology; and finally methodological issues, with many CAM practitioners believing that conventional research methods are not suitable tools with which to investigate CAM.” Even if research on Homeopathy cannot be compared so easily to research on other CAM, we agree that the following comments are justified.

We must therefore add to the priorities for research in homeopathy:

- Developing proper methodologies for research in homeopathy
- Training researchers in homeopathy, research methodology and epidemiology
- Collaboration with centres of excellence in different countries in Europe in order to establish an infrastructure for research in homeopathy

To increase competitiveness in the pharma/biotech industry, Europe has adopted a wide strategy ([www.cordis.lu/lifescihealth/innovativemedicines.htm](http://www.cordis.lu/lifescihealth/innovativemedicines.htm)), which involves major stakeholders: industry (laboratories), academia, patients’ organizations, clinicians, European Institutions, regulatory agencies, ethical experts, Insurances and health departments constitute the research platform. A similar plan is needed for homeopathy indicating the clear and specific benefits for each participant (patients, laboratories, researchers, authorities...).

## **Clinical and socio-economic research (ref.17)**

To assess the effectiveness and efficacy of homeopathy, the ECH takes the view that a step-by-step approach is necessary, starting from registration and data collection in daily practice and retrospective research aimed at collection of clinical cases, through open outcome studies, to randomised clinical trials. The main advantage of this approach is the systematic way in which knowledge is gathered from the populations under study, allowing prompt feedback which prevents failures based on premature assumptions. A programme for post-marketing surveillance of safety, and the evaluation of cost-effectiveness, patient satisfaction and/or preference and quality of life should be started.

Testing of homeopathic remedies in so-called homeopathic pathogenetic trials or provings needs methodological improvement. One of the main objectives for research in this field is to establish appropriate standards for homeopathy. In addition, new remedies are to be tested and remedies currently used should be retested.

In view of the rules concerning organic livestock farming techniques, the development and introduction of homeopathy where possible into the livestock farming sector is particularly important, with a view to protecting consumers more effectively from pharmacological residues in animal products and promoting

better conditions for livestock.

At all levels of the society, sharing of information and knowledge on homeopathy is part of the promotion of public health.

## **Diagnostic research (ref.19-20)**

In assessing the effectiveness and efficacy, the fact that homeopathy is still a method with many deficiencies is often disregarded. The homeopathic materia medica are partly incorrect and the repertory is outdated. Many homeopathic prescriptions are incorrect because of these shortcomings. This means that many participants in a clinical trial may well receive what is effectively a placebo (because it is not the right medicine) instead of the verum that they should receive. This is analogous to a trial with a conventional medicine which has been produced by a very unreliable production process.

Diagnostic studies remain scarce in homeopathy. This kind of study is based on the Bayesian principle that accumulation of knowledge can be used for prediction and clinical decision making. Homeopathy is largely based on this principle, and use of the method should produce better prescribing, greater patient satisfaction and better performance in clinical trials.

According to William Talbot in the Stanford Encyclopedia of Philosophy “The combination of its precise formal apparatus and its novel pragmatic self-defeat test for justification makes Bayesian epistemology one of the most important developments in epistemology in the 20th century, and one of the most promising avenues for further progress in epistemology in the 21st century”.

## **Fundamental research (ref.17)**

Constraints to the acceptance of homeopathy which are most often cited by opponents are the lack of a scientific basis and the absence of a theoretical model for homeopathy. If one considers the fundamental studies within homeopathy, the large majority (90%) of research is concentrated on demonstrating an effect of potentised agents or remedies. Hardly any research is directed to the similia principle, nor are activities structured in a systematic programme to unravel the underlying mechanism required to explain the effect of high potencies. Research activities should therefore be intensified in the two fundamental aspects of homeopathy, i.e. the similia principle (remedies or conditions that cause symptoms when applied to healthy biological systems, can be used to treat the same symptoms in diseased biological systems) and the specific way in which remedies are produced (by a process of successive dilution and succession, which is called potentisation).

For research on high potencies two main activities are required:

- The repetition of successful experiments in different model systems
- Further elaboration of the theory of homeopathic information and the physical aspects involved in potentisation in order to improve our understanding of how potencies may maintain their information, how this information may interact with the organism and in what way it might be transmitted to exert its curative action.

## 1.0 INTRODUCTION

### 1.1 *Current position of homeopathy*

According to different surveys and comparisons, it is estimated that across Europe the percentage of the various populations that have used complementary or alternative medicine (CAM) at least once in their lifetime is between 20% and 70% (ref.8). The United Kingdom and the Scandinavian Countries appear to have rather low use, while German population seem to be heavy users (COST B4 1999, ref.6-7). Homeopathy is one of the most used CAMs in Europe: 36% of the French, 32% of the Belgian, 31% of the Dutch and 20% of the British public report taking homeopathic medicines in recent public opinion surveys, and its popularity is increasing. In Belgium, CAM treatments are one of the fundamental rights of patients (law passed in 2002 regarding patients' rights). In the United Kingdom, the market for homeopathy is continually growing; growth is more rapid in some southern countries, while in countries with well developed markets (such as France and Germany) the growth rate is slower. The total European market for homeopathic medicines in 2001 was €1,612 million; the largest markets are Germany and France, with 36% and 33% respectively of the total market. The European Union has taken steps to create a single European market for homeopathic medicinal products: EC Council Directives 92/73/ECC and 92/74/ECC applying to homeopathic medicinal products for human and veterinary use came into force in January 1994. Implementation of these directives has been patchy among member states, partly because of scientific problems. The revised versions 2001/83/EC and 2001/82/EC are now implemented in most of the European countries. The European agencies are currently working on a European harmonisation of the registration procedures for homeopathic medicines.

Over the past few decades encouraging results have been obtained in performed clinical trials supporting the efficacy of homeopathy, as was shown in recent meta-analyses (Kleijnen et al. 1991, ref.2, Linde et al. 1997, ref.4, HMRG report 1997, ref.5, COST B4 report 1998, ref.6, Reilly et al. 2000, ref.9). Nevertheless, homeopathy is much disputed by mainstream medicine.

### 1.2 *European Commission Homeopathic Medicine Research Group (ref.5)*

In December 1993 the European Parliament requested the European Commission to conduct a scientific investigation of homeopathy. Directorate-General XII (Science, Research and Development) of the European Commission supported an expert group, the Homeopathic Medicine Research Group (HMRG) to conduct this investigation, with the mandate to discuss methodologies, to undertake a constraint analysis, to develop common standards, and to consider whether homeopathy is a researchable question.

In their report the HMRG concluded that homeopathy is certainly researchable. They recommended the stimulation of further research in homeopathy and produced guidelines for the review of clinical research protocols in homeopathy. An overview of clinical research in homeopathy identified 184 controlled clinical trials of homeopathy. A statistical meta-analysis of pooled results gave highly significant results in favour of homeopathy.

The HMRG also examined the constraints to better acceptance of homeopathy by sending a questionnaire to a sample of 1500 decision makers in Austria, Belgium, France, Germany and Great Britain. Despite wide divergence of attitudes to homeopathy, there was a consensus that more research is required: 77% of supporters and 62% of opponents of homeopathy favoured more scientific investigation.

Two main fields of research in homeopathy can be identified, namely clinical research and fundamental research. Clinical research is given highest priority by the HMRG with an emphasis on the randomised clinical trial and on improving methodology in order to establish the efficacy of homeopathy. Their report provides some useful guidelines on methodology for clinical research in homeopathy "with the objective to allow commonly accepted judgements of clinical efficacy, effectiveness and benefit of homeopathy by future clinical research". With respect to fundamental

research, the HMRG recommends the replication of previously used model systems in which an effect of high potencies has been observed.

### 1.3 Action COST B4 Unconventional Medicines (ref. 6-7)

COST is an initiative of the European Commission which aims to improve pan-European collaboration in science and technology. In June 1993, COST Action B4 in Unconventional Medicine was established. Priorities of this action were to co-ordinate and promote research into the field of Unconventional Medicine and to make information on existing relevant data available to all Signatories. The final report and its supplement were published in 1999. Since the field of Unconventional Medicine is of *medical, social, cultural, psychological, legislative and economic* importance, high quality research in all these areas was integrated into the co-operation. In a publication by Vincent & Furnham (1996, **ref.8**) it was pointed out that Homeopathy patients were most strongly influenced by the ineffectiveness of orthodox medicine for their complaints. As alternative treatment and remedies tend to be less expensive, a reduction in the costs in the outpatient sector could be expected if alternative treatment is used *instead* of classical therapy rather than in addition to it. A prerequisite to ensure this would be the integration of complementary medicine within the official health care system.

Regarding the **clinical effectiveness of Homeopathy**, the Action concluded:

Recent comprehensive systematic reviews have shown that about 190 controlled clinical trials have been performed on homeopathic remedies. About 120 of these trials were randomised. The number of uncontrolled prospective clinical studies on homeopathic treatment strategies is relatively small apart from the area of complex remedies (combinations of several homeopathic). The two recent meta-analysis have shown that overall the available clinical trial evidence suggests that homeopathic remedies can have an effect over placebo. Due to the often insufficient quality of the trials and the lack of independent replications of defined study models this evidence is not (yet?)\*<sup>\*\*</sup> compelling. One set of trials provides some evidence that the use of one remedy (Galphimia) in low potencies has a reproducible effect over placebo in the treatment of pollinosis. The overall quality of the trials is acceptable; however, the analysis of the trials does not meet the actual standard (intent-to-treat-analysis), and despite being multicenter-trials, all have been co-ordinated by the same principal investigator and cannot be interpreted as independent replications. Another meta-analysis of 3 controlled trials has been published which claims reproducible effects over placebo for the treatment of allergic conditions with isopathic nosodes. These studies are performed in different settings, but co-ordinated by the same principal investigator. Further, the treated conditions are not identical (pollinosis and allergic asthma). In conclusion, in both cases confirmation by independent replications would be necessary to make evidence more compelling. Clinical research on homeopathy has been focussing almost completely on the question “is it placebo?” This general question ignores that homeopathy is used in different ways (of which some, theoretically, might be effective and others not) and for a wide range of conditions. The reason for this “generalising” approach is the fact that homeopathy seems extremely implausible to academic medicine and the main motive for research so far has been to “justify” homeopathy in front of the scientific establishment. The resulting research is of questionable relevance for actual medical practice as the study models very rarely reflect actual practice. As for acupuncture, we recommend that research on homeopathy should also include investigation of actual practice.

To our knowledge, systematic research on the safety of homeopathy has not been done. From the point of view of conventional medicine seeing all homeopathic therapy as placebo, direct risks resulting from homeopathic treatment seem unlikely, at least beyond a certain level of potencies (specifically prepared homeopathic dilutions). However, low potencies can contain physiologically relevant concentrations of toxic substances (e.g. heavy metals). Homeopaths rarely discuss the possibility of side effects of homeopathy. So-called “first aggravations” - a deterioration of symptoms in the first phase after applying a treatment and generally thought to precede a significant improvement - are

reported in case reports quite frequently but not interpreted as side effects. It is unclear if relevant risks are associated with such “first aggravations”. Indirect risks (non-application of an effective treatment resulting in harm) are considered more important in regard with homeopathy but little empirical data is available. For example, a case of malaria has been reported in a patient who tried to prevent malaria by homeopathy instead of standard drugs. In conclusion, based on the existing limited knowledge homeopathy seems to be a relatively safe therapy.

An audit of ***fundamental or preclinical research*** papers (Annexe IV - 162 papers, **ref.7**) states that one in three evaluated publications had been published in a peer-reviewed international journal, implying a high scientific quality. To classify the literature with regard to quality, the team used not only conventional quality criteria but also unconventional criteria relevant to homeopathy. The conclusion was that half of the papers were of the best possible quality. Although most papers showed positive results, these results were unfortunately rarely reproduced externally. Internal replication by the investigators themselves was a common phenomenon, confirming the experimental models and replicating the results. For each basic research model, any laboratory wishing to reproduce another’s results must go first through a learning and standardisation process. The few published negative results most commonly result from a first testing of a new model or a first attempt to reproduce an experiment in a new laboratory. Although the existing positive results are very encouraging there is a need for more research, more external replication and more research on the similia principle. This literature review demonstrates at the very least that arguments against research on homeopathy are no longer tenable. Testable scientific hypotheses can be formulated about the working mechanisms of homeopathic dilutions.

## **1.4 Objectives of the homeopathic research community**

By adapting conventional experiments to the complexity of homeopathy, it was possible to detect effects which conventional scientists did not believe could exist.

Successful and extensive efforts have been made in clinical trials. Both conventional methodology and study subjects have been adapted, in particular by selecting diseases and patients that could be expected to respond to a given remedy in order to demonstrate a difference from placebo. Other studies, concerning quality of life for example, do not show so clearly the experience (the effects) that users frequently report. This calls for methodological studies to discover how to adapt conventional research methods to take into account the individualisation of the homeopathic medicine, and the whole person approach (globality) which is characteristic of homeopathy.

Objective studies on the current activities of homeopaths are needed as well, such as the data collection projects on daily practice currently underway. Problems include preserving confidentiality, (patients share much private and personal information with their physicians), and the medical intuition that is also at work. This last aspect is very difficult to observe and record.

Beyond clinical research, there are theoretical questions to be addressed regarding what persists in the remedies when none of the initial active molecules remain\*. Current developments in chemical physics investigating the effects of electromagnetic waves on chemical reactions may give a promising perspective. Single molecule spectroscopy provides tools for observing the environment of active molecules in intermediate dilutions, theoretical calculations give new results showing the complexity of water as a solvent. A logical starting point may be the physical description of dynamised solutions currently used, perhaps those containing non-negligible concentrations of solutes. Official recognition for such broadly based interdisciplinary studies is necessary for progress.

\*Homeopathy is not restricted to very high dilutions. The homeopath uses also dilutions where active molecules still remain.

\*\*Looking at the literature in 2005: there is evidence that highly diluted homeopathic preparations have biological activity; the presence of a “footprint” of the original substance can be detected in the high diluted homeopathic preparations; human studies reveal clinically significant improvement in 70% of patients

(more in children), these effects cannot be attributed to placebo effect only, for some indications the efficacy of homeopathy reaches a high level of statistical significance (**ref.21**).

## **1.5 Research infrastructure and methodology**

If we are to broaden the horizon of homeopathic research we have to take into account the fact that different approaches require different research methodologies.

Recent reports from various countries and institutions (WHO 2002, **ref.10**, WHCCAMP USA, 2002, **ref.11**, House of Lords 2000, **ref.12**, BMC 2001, **ref.18**) point out that the average quality of research in complementary and alternative medicine (CAM), including homeopathy, is poor.

The House of Lords Committee describes a vicious circle: "Several reasons have been put forward to explain why so little high-quality CAM research is being done. The five most common reasons suggested to us are: a lack of research training across the CAM professions; a lack of research funding available for CAM projects; a poor, almost non-existent, research infrastructure within the CAM sector; a lack of interest in this field of research by conventional scientists who are trained in research methodology; and finally methodological issues, with many CAM practitioners believing that conventional research methods are not suitable tools with which to investigate CAM."

We must therefore add to the priorities for research in homeopathy:

- Developing proper methodologies for research in homeopathy
- Training researchers in homeopathy, research methodology and epidemiology
- Collaboration with centres of excellence in different countries in Europe in order to establish an infrastructure for research in homeopathy

## **1.6 Provings & Clinical verification**

There is a qualitative difference between a proving (test the action of a substance on healthy volunteers) and the clinical verification (test the efficacy of the proved substance). This aspect of the experimental development of a homeopathic remedy is essential. Without numerous provings homeopathy would not even exist. To be accepted as homeopathic, a remedy must be tested following a step by step procedure. This procedure has been fully described by Constantin Hering.

Following Hering's book on "Guiding Symptoms", clinical verification of homeopathic symptoms is the last of the various steps needed in order to understand a characteristic symptom, described by healthy volunteers testing the remedy, before it can be used for homeopathic treatment:

- **Possibility:** a substance provokes certain symptoms, or is perhaps even toxic
- **Probability:** this substance, diluted and dynamised, provokes various symptoms in volunteers in good health (first proving).
- **Confirmation:** the same substance, diluted and dynamised and given to volunteers in good health, confirms some of the symptoms previously found and provokes probable new symptoms
- **Corroboration:** noting how and where the probable symptom occurs and its confirmation by its relation to known physiology and pathology.
- **Clinical verification:** the correspondence of the probable symptom to the remedy is confirmed and verified by positive clinical results in actual patients.

Such research activities are of the greatest importance to prove and improve the success of homeopathy. This should be part of the scientific evaluation of homeopathy because it comprises the foundations on which homeopathy has been built. There is however bias in the clinical verification procedure originally proposed by Hering. In the first place, this confirmation is based on a retrospective procedure, which leads to confirmation bias. In the second place, remedies that are

frequently used show confirmation of certain symptoms even if these symptoms do not frequently occur in those remedies. Remedies that are seldom used are disadvantaged in this respect (ref.19).

Therefore, the ideal procedure from a clinical perspective would be a prospective assessment of well-defined symptoms. The prevalence of a symptom in the population cured by a remedy relative to the prevalence of the symptom in the rest of the population (likelihood ratio) indicates the importance of the symptom for the remedy.

## ***1.7 Aims and contents of this report***

The aim of this report is to encourage homeopathic researchers to adopt a common strategy or structured framework, and to follow a step-by-step procedure to evaluate homeopathy. This type of approach to research will provide a structure or strategic “backbone”, connecting different fields of research and identifying the successive steps which are required to further our understanding of various aspects of homeopathy. The advantage of such an approach is to identify blind spots at an early stage and to improve communication and collaboration between research groups and research activities.

The aim of this ECH report is therefore to identify different research activities in clinical and fundamental research, and to promote a systematic strategy among researchers for evaluating different aspects of homeopathy.

This report begins with a brief description of homeopathy as a method and its specific concept of health and disease. This is necessary to understand its conceptual depth and therapeutic possibilities (chapter 2).

The two main fields of research in homeopathy are then described:

- Clinical research (on human beings and animals) is dealt with in chapter 3;
- Fundamental research (in laboratories) is described in chapter 4.

Finally, several targets for homeopathic research are defined in chapter 5.

## 2.0 HOMEOPATHY AS A METHOD

### 2.1 *Basic principles*

Homeopathy is a system of medical practice based on three pillars: the similia principle, the use of potentised medicines or remedies, and the homeopathic methodology.

#### The similia principle

This principle states that substances or remedies that cause symptoms when applied to healthy biological systems can be used to treat the same symptoms in diseased biological systems. The similia principle, which forms the fundamental basis of homeopathy, is specific to homeopathy in the sense that it has not been fully recognised, accepted or studied by mainstream medicine. In pharmacology, paradoxical reactions are known (Eskinazi,1999), i.e. opposite biological effects observed for different doses of a given agent or opposite reactions observed in different individuals. Till now, these paradoxical reactions are not enough studied. This phenomenon could be a bridge between sciences.

#### The use of potentised medicines

Homeopathic medicines, some of which in their crude state are potentially toxic, are prepared according to a specific process of successive dilution and succussion (for liquid preparations) and successive trituration (for solid preparations) – this process is called potentisation – in such a way as to nullify their toxic properties. A number of variations exist on both the dilution steps and the way in which succussion is performed.

#### The homeopathic methodology: individualisation

The key to successful homeopathic treatment is identifying the similarity between the effects of the original substance in healthy people and the pattern of the illness in the individual who is ill (Swayne, **ref.13**). Homeopathic treatment is highly individualised – the patient's personal physical and psychological characteristics, his/her clinical picture, diagnosis, aetiology, constitution, and present, past and family illnesses are all relevant and significant.

Two centuries of homeopathic practice have not altered these three basic principles.

### 2.2 *Specific concept of health and disease*

The basis of homeopathic thought is that health is not a static condition but a dynamic process that tends to maintain a state of optimum equilibrium. This concept presupposes a built-in self-regulation mechanism, which protects against a loss of balance. Disease reflects an intensified attempt to restore an out-of-balance state, resulting from disturbing physical, chemical, biological and emotional factors. Disease is conditioned by susceptibility and it manifests itself through symptoms in the mental/intellectual, emotional and physical plane. The self-regulation mechanism is regarded as responsible for protection against the loss of balance as well as for its restoration. All that a doctor can do is to assist the process of restoration, to stimulate this self-regulation or self-recovery mechanism.

Homeopathic medicines are supposed to induce a process of reorganisation of vital functions by stimulating this self-regulation mechanism. This reorganisation can result in complete cure in cases where only functional derangement had caused the symptoms. Of course, the therapeutic possibilities depend on the extent to which the organism is able to recover. The more structural the changes that have been caused by the deregulation, the more partial a recovery will be. Limitations are specific surgical indications, deficiency diseases and very serious diseases in which gross anatomical changes have evolved. If a disease process has come to an end and the tissue damage has become irreversible, homeopathy may only have a palliative or relieving effect.

Homeopathy is used to treat a wide range of disorders; a review in 1991 of the research literature (**ref.2**) found the following main areas had been scientifically investigated: trauma and pain, respiratory infections, mental and psychological disorders, pollinosis and rheumatology. Homeopathy can even offer therapeutic options where other treatments have failed or plateaued, where conventional treatments do not exist for the problem, or where they are contraindicated or not tolerated.

### **2.3 Homeopathic medicines**

Homeopathic medicines, mostly called remedies, are of botanical, chemical, mineral, zoological or microbiological origin. They are prepared from products, substances or compositions, called homeopathic stocks, in accordance with a homeopathic manufacturing procedure described by the pharmacopoeias currently used, officially, in the Member States. They are obtained from stocks by the process of potentisation, i.e. successive dilutions and succussions for liquid preparations and successive triturations for solid preparations.

### **2.4 Homeopathy in clinical practice**

Homeopathic treatment is aimed at methodically improving the level of health of an organism by the administration of proven potentised medicines, which are individually selected in accordance with the similia principle. The symptoms of a diseased organism, the so-called disease picture, are classified and interrelated in such a way as to trace patterns that match with the “remedy picture”, i.e. the symptoms provoked by a remedy in a healthy organism. The more detailed, peculiar and individual the pictures are, the more chance that they fully match for a specific remedy, which implies that a deep and prolonged curing response is likely to follow. In case of incomplete similarity only partial or temporary effects are noticeable. Homeopathic treatment is compatible with other medication, but a homeopathic doctor seeks to reduce medication to a minimum.

Practical experience has shown that a hierarchy of functions plays a role in the application of the similia principle. Symptoms and signs that arise from higher functions (like emotional symptoms or individual patterns of responding to environmental factors) appear to be more indicative within the frame of reference of the similia principle. Even if the patient seeks help for somatic complaints (like headache or gastritis), all hierarchical levels of the patient – mental, emotional and physical – are methodically screened and the highest level of disturbance – from a hierarchical point of view – is detected. Both human beings and animals may successfully respond to a homeopathic treatment. However, since mental, emotional and individual symptoms are more difficult to elicit in animals, in veterinary practice symptoms lower in hierarchy often lead to the most appropriate remedy.

## 3.0 CLINICAL and SOCIO-ECONOMIC RESEARCH

### 3.1 Introduction

In general, “clinical research” is an umbrella term for a hierarchy of research methods ranging from uncontrolled, clinical observations to controlled, experimental studies (Figure 1). In order to assess the value of homeopathic therapy and increase our knowledge in this area, European researchers seek to employ a broad range of methods, including epidemiological studies and randomised clinical trials. This approach emphasises research into both *effectiveness* (the extent to which a specific intervention procedure, regimen, or service does what it is intended to do for a specified population when deployed in the field under normal circumstances) and *efficacy* (the extent to which a specific intervention, procedure, regimen, or service produces a beneficial result under controlled conditions). In homeopathy the prescription is not only based on the conventional diagnosis, but also on the ‘homeopathic diagnosis’. The tools for this homeopathic diagnosis are outdated and should be assessed using up-to-date instruments.

The following comprise important steps in the development of research:

- Data collection in homeopathic daily practice for quality assurance
- Socio-economic studies to evaluate the spectrum of diagnoses, treatment and costs of therapy
- Clinical studies to investigate efficacy

In addition, research on other aspects of homeopathy should be encouraged and supported:

- Proving to describe and validate homeopathic remedy pictures
- Process analysis of routinely collected information to improve the quality of treatment, including safety (quality assurance) and to increase our knowledge about symptom aggravation, syndrome shift, etc.
- Data collection in homeopathic practice for diagnostic research
- Prospective and retrospective assessment of daily practice; retrospective analysis of cases to indicate items for prospective research

### 3.2 Effectiveness and efficacy research in homeopathy

Due to the relative lack of epidemiological information, most studies are undertaken without full knowledge of basic information such as the optimum length and frequency of treatment, the dynamics of disease manifestations in patients under treatment, or the success of various treatments in specific types of disease. This emphasises the importance of data collection, on the basis of which it will be possible to design prospective observational studies to obtain more systematic information about the effects of homeopathic treatment under normal clinical conditions. This can be done either with or without a comparison with conventional treatment. As a next step, it would be possible to select specific diseases for which efficacy studies (clinical trials) could then be conducted. The power of efficacy studies should be increased by assessment of diagnostic procedures.

In a clinical study concerning homeopathic therapy, it is absolutely necessary to classify the patients into levels of health. In clinical protocols, different parameters of therapeutic process, have to be clearly written, according to patients’ level of health, such as time limits, conventional therapy as an obstacle to homeopathic cure, evaluation and treatment of reappearance of previous diseases, treating acute diseases during homeopathic therapy for a chronic one, evaluation of initial aggravation, prescription of one remedy or sequence of remedies during a clinical study, single or repeated doses, higher or lower potencies. All these are parameters that have to be differentiated according to patients’ level of health, in order false negative results to be minimized. Preferably, patients of group A (see figure 2), would be the best choice to enter a clinical study. Common mistakes in clinical protocols concerning comparison of homeopathic with conventional treatment are: suppressing of homeopathic initial aggravation with conventional treatment, suppressing of reappearing of old diseases with conventional treatment, mistimed change of homeopathic remedy, misinterpreting the palliation of a homeopathic similar (not simillimum) remedy as positive result (false positive).

### **3.3 *Diagnostic tools in homeopathy***

Diagnosis in homeopathy is based not only on conventional diagnosis, but also on specific personal characteristics (symptoms) of each individual patient. These characteristics are treated as diagnostic instruments. Each homeopathic medicine has a limited number of more specific characteristics (keynotes) and a larger number of more general traits.

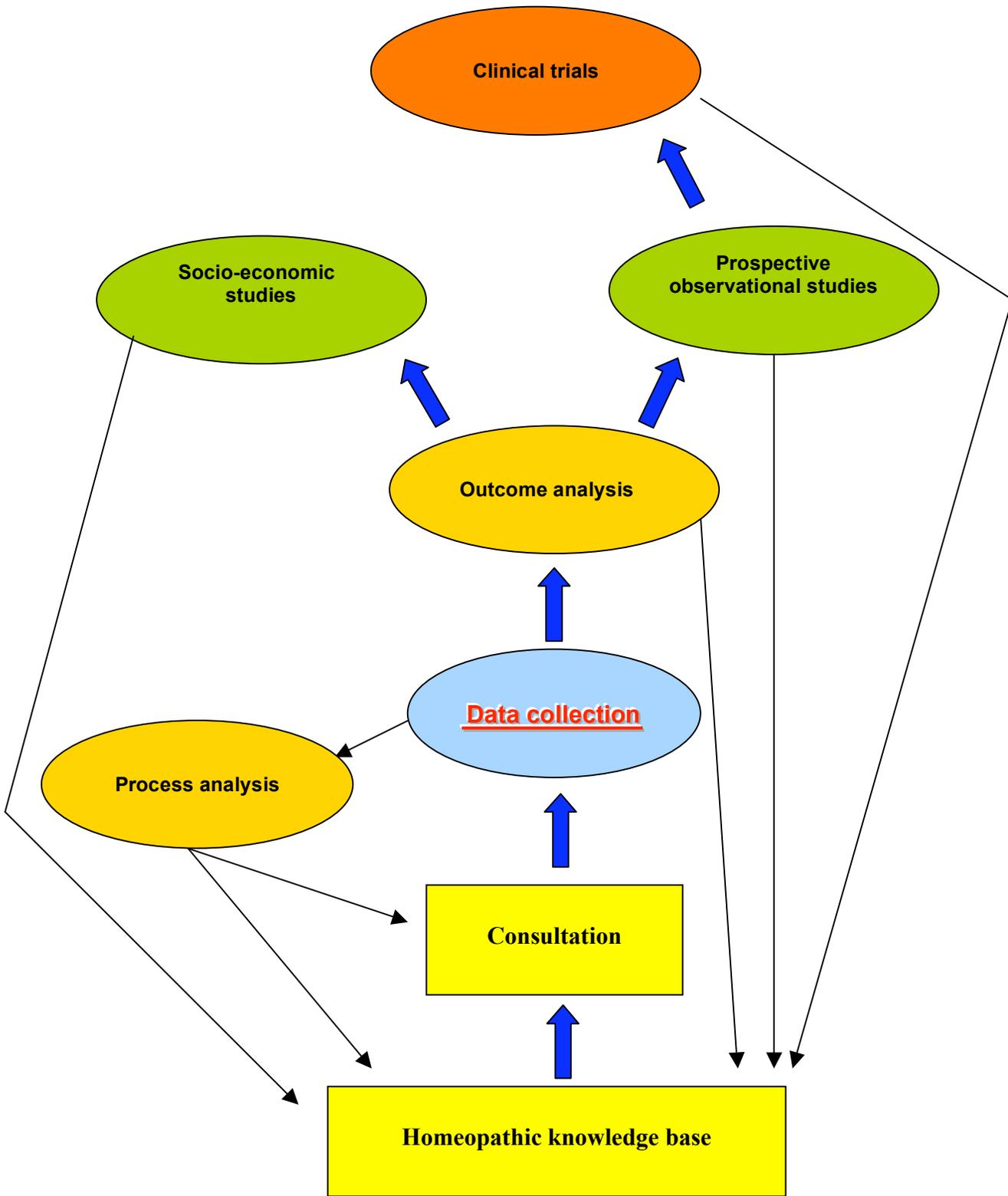
Homeopathic symptoms are handled in a Bayesian way, whereby prior experience informs current estimates of the chance of a curative effect taking place. Homeopathic doctors have implicit knowledge about the occurrence of characteristics in patients cured by a certain medicine relative to the occurrence in the rest of the population. This relation can be expressed as an implicit likelihood ratio (LR), a 3 or 4 step grading in the repertory of homeopathic symptoms. At the moment this information is based on retrospective expert opinion from various, sometimes unknown, sources.

The implicit LR of homeopathic symptoms should be made explicit by prospective research. There are several methodological problems that should be addressed, such as vagueness of clinical symptoms, imperfect gold standards and confirmation bias. Normal clinical conditions should be approximated as far as possible.

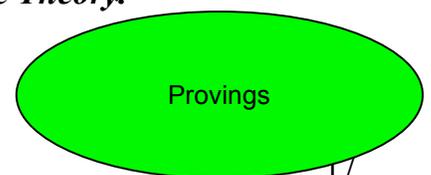
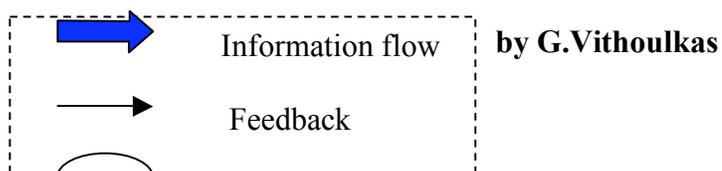
### **3.4 *Economic evaluation of homeopathy***

Cost-effectiveness is an integral part of health care policy, and in some European countries is a prerequisite for the approval of new drugs and therapeutic methods. Because homeopathic drugs are generally inexpensive and homeopathic treatment strategies do not usually include the use of costly diagnostic procedures, it can be hypothesised that homeopathy may be effective in cutting health care costs. In order to test this hypothesis, it will be necessary to develop a programme for the health economic evaluation of homeopathic treatments. Due to differences in health care systems across Europe, we suggest conducting the research programme across a range of European countries.

*Figure 1: A Strategy for clinical and socio-economic research*



*Figure 2: Levels of Health according to Classical Homeopathic Theory.*



<p><b>Group A</b> <b>Levels 1-3</b></p>	<p><b>HOMEOPATHIC POTENCY</b> UP TO 50M</p>	<ul style="list-style-type: none"> <li>• ALL DISEASES BUT MOSTLY FUNCTIONAL DISTURBANCES</li> <li>• MORE CURABLE BY HOMEOPATHY, SYMPTOMS LEAD TO CLEAR HOMEOPATHIC REMEDIES</li> <li>• NOT FREQUENT INFECTIONS, MOSTLY TYPICAL BACTERIAL CHILDHOOD DISEASES</li> <li>• IN UPPER LEVEL THERAPEUTIC HOMEOPATHIC AGGRAVATION MAY NOT APPEAR</li> <li>• IN LOWER LEVEL MILD THERAPEUTIC HOMEOPATHIC AGGRAVATION MAY APPEAR</li> <li>• IN UPPER LEVEL STRONG HEALTH, USUALLY NO REPETITION OF THE HOMEOPATHIC REMEDY OR OTHER REMEDY WILL BE NEEDED</li> <li>• IN LOWER LEVEL, 2-3 HOMEOPATHIC REMEDIES WITH THE APPROPRIATE ORDER WILL BE NEEDED</li> <li>• IN LOWER LEVEL, ACUTE DISEASES APPEAR MORE FREQUENTLY</li> </ul>
<p><b>Group B</b> <b>Levels 4-6</b></p>	<p><b>HOMEOPATHIC POTENCY</b> 10M-1M</p>	<ul style="list-style-type: none"> <li>• AS WE GO DOWN THE LEVELS, WE HAVE THE APPEARANCE OF MORE FREQUENT AND SEVERE ACUTE CONDITIONS (e.g. pneumonia)</li> <li>• BACTERIAL INFECTIONS MORE RESISTANT TO ANTIBIOTICS</li> <li>• MORE SEVERE AGGRAVATION</li> <li>• MORE HOMEOPATHIC REMEDIES, ONE AFTER ONE, WILL BE NEEDED</li> <li>• IN LOWER LEVEL, ACUTE DISEASE FOLLOW ONE THE OTHER. AFTER USING MORE CHEMICAL REMEDIES, THE LEVEL OF HEALTH WILL GO DOWN</li> <li>• IN LOWER LEVEL, THERAPEUTIC HOMEOPATHIC AGGRAVATION CAN LAST A LONG TIME</li> </ul>
<p><b>Group C</b> <b>Levels 7-9</b></p>	<p><b>HOMEOPATHIC POTENCY</b> 200 CH</p>	<ul style="list-style-type: none"> <li>• MORE SEVERE CHRONIC DEGENERATIVE DISEASES (e.g. Crohn disease, Ulcerative Colitis)</li> <li>• IN UPPER LEVEL, LESS ACUTE DISEASES, LESS SEVERE, THEY GO AWAY EASILY</li> <li>• IN LOWER LEVEL, NO APPEARANCE OF ACUTE CONDITIONS</li> <li>• IN UPPER LEVEL, VERY SEVERE INITIAL THERAPEUTIC HOMEOPATHIC AGGRAVATION</li> <li>• IN UPPER LEVEL, HOMEOPATHIC THERAPEUTIC AGGRAVATION CAN BE DANGEROUS, EVEN CHEMICAL INTERVENTION MAY BE NECESSARY.</li> <li>• 4-5 HOMEOPATHIC REMEDIES, IN THE APPROPRIATE ORDER WILL BE NEEDED.</li> <li>• A WRONG HOMEOPATHIC REMEDY CAN BE DETRIMENTAL</li> <li>• IN LOWER LEVEL, HOMEOPATHIC AGGRAVATION MAY MEAN THAT THE REMEDY WAS WRONG</li> </ul>
<p><b>Group D</b> <b>Levels 10-12</b></p>	<p><b>HOMEOPATHIC POTENCY</b> 30CH-12CH REPEATEDLY</p>	<ul style="list-style-type: none"> <li>• SEVEREST CHRONIC DISEASES, EFFECTING IMMUNE AND CNS</li> <li>• STARTING WITH A HOMEOPATHIC REMEDY, 3-4 OTHER WILL BE NEEDED BEFORE AN ACUTE DISEASE APPEARS</li> <li>• NO ACUTE INFECTIONS AT ALL</li> <li>• NO INITIAL AGGRAVATION. IF HOMEOPATHIC AGGRAVATION APPEARS, THEN THE REMEDY WAS DEFINITELY WRONG.</li> <li>• IN LOWER LEVEL, INCURABLE CASES BY HOMEOPATHY, ONLY PALLIATION IS POSSIBLE</li> </ul>

### 3.5 Proving

Homeopathic pathogenetic trials or “provings” are a type of research in which compounds are tested on healthy human volunteers in order to observe as many effects as possible, at a non-toxic level. Such careful experimentation is a prerequisite for identifying the true pathogenetic picture of a homeopathic medicine, i.e. its capacity to alter the state of health. Homeopathic pathogenetic trials can in fact be considered as a type of pilot study.

Testing potential remedies on selected volunteers and describing the induced symptoms in order to establish the “remedy picture” has been carried out since homeopathy’s inception. Hahnemann performed the first systematic study of drug action in the history of medicine, and this method, essential for evaluating the indications for homeopathic remedies, has continued ever since, although over time the procedures have changed. New protocols are currently under development which are in accordance with modern pharmaceutical and Good Medical Practice (GMP) procedures for testing new substances or re-testing incompletely tested old substances.

It is essential that homeopathic medicines are tested on human beings rather than animals. The reason for this is that disease has two distinct forms of expression, namely tissue changes or objective signs, and subjective symptoms which include types of pain, emotions and other sensations. These subjective symptoms are of particular importance because they help to characterise the patient’s individual illness and allow the selection of a homeopathic remedy that matches this personalised state of illness.

A review of homeopathic pathogenetic trials has revealed that nearly 150 such trials (**ref.14**), of a wide range of substances, have been conducted in Europe since 1945. The methods used, however, have varied considerably, and developments in methodology are therefore needed to refine and standardise homeopathic pathogenetic trials. A main objective of the ECH was to establish a standard for these.

Apart from improving the methodology of homeopathic pathogenetic trials, several additional activities should be encouraged, such as:

- Establishing priorities for re-testing currently used remedies. Some information in old standard homeopathic texts and databases is probably not completely reliable and needs to be verified.
- Establishing priorities regarding which new remedies are to be evaluated. There is no doubt that testing the large numbers of plant and animal species, as well as minerals, which have yet to be used as remedies could increase the therapeutic possibilities of homeopathy even further.
- Obtaining valuable information from an evaluation of toxicological data (evidence-based clinical toxicology), or side-effects of remedies, etc. In various studies accidental exposures to toxic compounds such as insecticides, heavy metals, etc. have been carefully recorded. This information can be of relevance either to validate or to extend remedy pictures of compounds used in homeopathy.
- Developing a policy on what kind of symptoms should be inventoried or studied in homeopathic pathogenetic trials (biochemical changes in the body, physiological and emotional alterations, types of dreams, etc), as well as establishing their relevance in relation to self-recovery processes.
- Establishing the hierarchical order of symptoms. In this respect it is important to differentiate between the quantitative and qualitative characters of symptoms. A symptom which a substance induces in a majority of healthy volunteers may offer less information than a specific symptom induced in a minority of individuals, but which may refer to the essence of the tested substance. This is the corroboration of a symptom.
- Clinical verification of these symptoms in the patient is the final but absolutely necessary step of this type of research. The probable symptom observed in proving is verified by actual clinical results.
- Establishing a database and a network for exchange and evaluation of data from observational studies, etc.

### **3.6 Homeopathy in the livestock farming sector**

In the livestock farming sector, homeopathic medicines may replace antibiotics, hormones and other drugs in some cases of infection, inflammatory disease or reproductive disorders, or may shorten the duration of antibiotic treatment. Homeopathic dilutions from  $10^{-6}$  M onwards will cause either no residue at all, or in the worst case residues which are negligible, in the low ppb range.

The development of homeopathy in the livestock farming sector and its introduction where possible would therefore be particularly important, protecting consumers more effectively from pharmacological residues in animal products. It would also help to create better conditions for livestock, and this is relevant in view of new rules soon to be introduced concerning organic livestock farming techniques. Research in this field is necessary and ongoing (**ref.15**).

### **3.7 Auxiliary studies**

This research field relates to phenomena which are frequently observed in the course of homeopathic practice. Examples are:

- Self-recovery
- Placebo effect
- Symptom aggravation
- Adverse effects
- Syndrome shift

All these research fields may in the long run be required to obtain an improved understanding of all aspects of homeopathy, as well as its relation to mainstream biomedical knowledge. It should be noted that these phenomena are probably not exclusive to homeopathy, but may also be observed in mainstream medicine as well as in other forms of complementary medicine. (**ref.16**)

## 4.0 FUNDAMENTAL RESEARCH

### 4.1 Introduction

Constraints to the acceptance of homeopathy which are most often cited by opponents are the lack of a scientific basis and the absence of a theoretical model for homeopathy. In order to improve our knowledge of the fundamental basis of homeopathy (the similia principle and specific preparation of remedies) and to increase the understanding of the working mechanism of its remedies, fundamental research is a prerequisite.

The HMRG (**ref.5**) recommends the replication of previously used model systems in which an effect of high potencies has been observed. Whilst multi-centre trials are of great importance, where different experimenters repeat previous experiments in simple model systems under well controlled conditions, the ECH also favours increasing the number and widening the scope of fundamental studies.

The majority (more than 90%) of fundamental studies within homeopathy (**ref.7**) have concentrated on demonstrating an effect of potentised agents or remedies. Hardly any research has been directed towards the similia principle, nor is there any structured programme to unravel the underlying mechanism of action of high potencies, or to discover ways of optimising their effect. From a strategic point of view, this imbalance between research aimed at demonstrating effects and explanatory research is far from optimal, especially when such effects cannot be explained in a satisfactory way.

Fundamental research into homeopathy can be divided into two main fields:

The similia principle

The preparation, mechanism of action and effect of potentised remedies.

### 4.2 The similia principle

*Curative approach:*

The similia principle states that remedies or conditions that cause symptoms when applied to healthy biological systems can be used to treat the same symptoms in diseased biological systems. Any biological system (cell, organ, plant, animal, human being) in a diseased or disordered state can be investigated, and the stimulation of recovery by any compound applied according to the similia principle can be studied. The essential question is whether the degree of stimulation of self-recovery by low doses is related to the degree of similarity of the remedy. For research purposes, the similia principle can be investigated by two main routes, homologous and heterologous studies. Homologous studies use a compound to disturb a biological system and subsequently to cure it with a low dose of the same substance. This is also called *isopathy*. In heterologous studies, the substances or drugs used to disturb and subsequently cure a biological system are different.

The similia principle cannot be readily studied in one single type of experiment, since multiple aspects have to be analysed and demonstrated either in a parallel or in a sequential manner. A research programme is therefore required using a biological model that allows the systematic unravelling of the various aspects involved. A full analysis of the similia principle will require a number of steps. The example below describes these steps at the cellular level, but they can also be applied to more complex systems, e.g. organs and organisms.

Step 1. Selection of parameters for self-defence and self-recovery to be evaluated.

The effect of various compounds or toxins on normal undamaged cells is studied. This is analogous to the description of the symptoms induced by different compounds at higher system levels, known within homeopathy as "*provings*", "*remedy pictures*" or "*homeopathic pathogenetic trial*".

Step 2. The homologous aspect of the similia principle.

The question is asked whether self-defence and self-recovery, induced by disturbing e.g. a cell culture with a sub-lethal application of a damaging agent, can be further stimulated with a low dose of the identical damaging substance or condition.

Step 3. The heterologous aspect of the similia principle (specificity of low dose stimulation)

Studies investigating the specificity of substances require the results of steps 1 and 2 and include:

- provings of different compounds at the system level under study;
- development of methods to determine the degree of similarity between the symptom pattern of the disordered or diseased system and the remedy picture of the proven compounds. Based on the degree of similarity measured, the effectiveness of a certain compound to stimulate self-recovery may then be predicted and tested;
- demonstration of stimulation of self-recovery by low doses of heterologous compounds (ranging from similar (analogous) to non-similar). This step serves to verify the above prediction and the question can be answered whether the degree of stimulation correlates with the degree of similarity.

#### *Preventive (i.e. protective or prophylactic) approach*

Although the similia principle is mainly used as a therapeutic tool, it is also used for prophylaxis. Essentially the same steps as above are required:

- definition of the parameters of tolerance
- stimulation of tolerance or desensitisation to a compound applied in high dose by a previous incubation with a low dose of the identical compound,
- specificity of the stimulation of tolerance by low doses of analogous compounds.

In this field of research the relation with so-called hormesis and the adaptive response should be further established, especially in relation to the aspect of specificity.

#### *Potencies vs. dilutions in the study of the similia principle*

In essence, the similia principle can be studied without the use of (high) potencies (the founder of homeopathy, Hahnemann only introduced potencies ten years after he first described the similia principle). Thus, for the above mentioned research strategy to verify the similia principle, both normal dilutions of various compounds as well as low and high potency preparations, preferably in a potency range, should be investigated.

### **4.3 Preparation, mechanism of action and effect of potentised substances in various biological systems**

#### **4.3.1 Preparation of potentised substances**

An important aspect of homeopathy is the specific way in which remedies are prepared (potentised). Potentisation includes a number of different protocols, and there is as yet little consensus about which types of potency should be used in different conditions, how to store potencies, etc. There is also little agreement about which chemical, physical or informational model is most appropriate to explain their mechanism of action. Needless to say, increasing knowledge of these aspects is crucial to improve the quality and the stability of the potencies used.

### 4.3.2 Mechanism of action of potentised substances

It has been suggested that potentisation changes the characteristics of the substance in such a way that the information content of the remedy is more relevant than its material content, especially in high potencies. For research purposes a rough division into low and high potencies can be made, related to the way in which an effect might be explained:

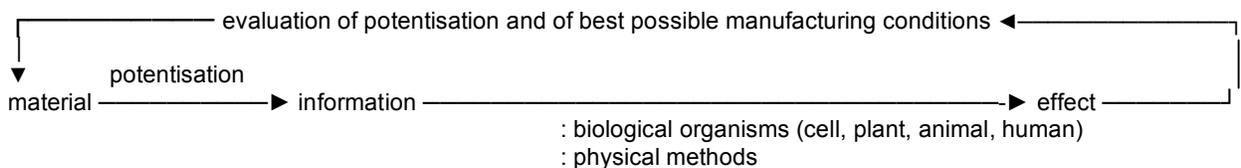
- Low potencies are substances which have been diluted and potentised only a small number of times (for instance D12 or C6 and below). Since these remedies contain material concentrations of molecules of the original substance in the millimolar to picomolar range, any effect of low potencies might be explained in terms of biochemistry and current biomedical terminology
- High potencies are substances which have been diluted and succussed beyond Avogadro's limit (for instance D24 or C12 and above), and are unlikely to contain any molecules of the original substance. Any effect of high potencies must invoke areas of knowledge other than biochemistry, such as physics or information theory, in order to explain their action.
- There will be a transitional range (between D12/C6 and D24/C12) where the informational aspect becomes more important than the molecular aspect.

The claims made for very high, so-called ultra-molecular dilutions, (i.e. dilutions which, according to Avogadro's Law, are very unlikely to contain even a single molecule of the starting substance) which are commonly used in homeopathy are very challenging, and raise fundamental scientific questions. Until quite recently it was possible to argue that these extreme dilutions had no real effects, and that all the apparent clinical effects of homeopathy were due to placebo or non-specific effects. However, the growing evidence of their effects from rigorous, randomised controlled trials is making such a position increasingly untenable.

A possible explanatory hypothesis for the mode of action of extremely high dilutions is the Information Medicine Hypothesis, which proposes that the actions of homeopathic medicines should be understood in terms of physically stored information rather than in chemical terms. The Information Medicine Hypothesis states: "Under certain circumstances, water (and perhaps other polar solvents) are capable of receiving and storing information about substances with which they have previously been in contact and of transmitting this information to pre-sensitised biosystems". If verified, this hypothesis would represent an important scientific advance, with implications extending far beyond homeopathy.

### 4.3.3 Effect of potentised substances

Specific model systems and parameters in the field of chemistry as well as physics are required to study the claims that remedies which have been prepared in a specific way indeed show specific characteristics. This field of research mainly concerns the demonstration of an informational content of high potencies by evaluation of: a) biological effects, and b) structural aspects of potencies.



#### a. informational aspects of high potencies as measured in biological systems

This research aims to determine any effect in any biological organism (ranging from bacteria to man) on the application of high potencies.

#### b. informational or structural aspects of (high) potencies as measured by physical methods

This research aims to determine any change in structure of the solute in potentised remedies. Since changes in the structure of water and the importance of electromagnetic fields or frequencies are topics of speculation, physical methods which are able to analyse these aspects

should be used or developed to further our knowledge in this field of research.

#### **4.3.4 Priorities in systematic research on high potencies:**

- First, research should be focussed on the validation of model systems with which a demonstration of an informational content of the potency is possible using biological and/or physical methods; reproducibility by other laboratories is essential. A number of model systems may be selected for these studies.
- Second, when a model system has been clearly defined in which an effect can be repeatedly demonstrated, the following questions can be tackled:
  - Is there a variability in effect due to the different steps in preparation (material and the type of potentiation procedure)?
  - Is the stability of the potency influenced by electromagnetic fields, temperature, duration of storage, etc.?
  - Can the information in the potency be copied?
  - What cellular or biological systems function as an information receiver?
  - How can the storage and transmission of information be explained (memory of water, chaos theory, turbulence, quantum physics, etc)?

#### **4.4 Auxiliary studies**

As well as the phenomena mentioned above in section 3.6 there are two further matters which may yield promising areas for research:

*Hormesis* is the paradoxical phenomenon that a toxic substance becomes a stimulating agent at concentrations well below the toxic level. This non-specific stimulation by low doses of any toxic compound or stressful condition of a large number of physiological processes, including growth and longevity, has attracted the attention of homeopathic practitioners as a possible contribution to explaining homeopathy.

*Physical phenomena* such as turbulence and chaotic processes in the preparation of homeopathic remedies, the structure and “memory” of water and/or electromagnetic fields may be of relevance to an explanation of the high potency effect.

All these research fields may in the long run be required to obtain an improved understanding of all aspects of homeopathy as well as its relation to mainstream biomedical knowledge. In order to develop more complete explanatory schemata, a system theoretical point of view may be of relevance as well as specific studies of complex biological systems.

## 5.0 TARGETS AND PRIORITIES

Homeopathy cannot be satisfactorily investigated by any one single type of experiment. Multiple aspects have to be analysed and demonstrated, either in a parallel or in a sequential manner. The ECH therefore stresses the need to develop research programmes that allow the systematic unravelling of the various aspects involved in clinical as well as in fundamental research. In addition, appropriate methodologies have to be developed and researchers, that have the knowledge of homeopathy, have to be trained in research methodology and epidemiology. Collaboration with research expert centres in different European countries is essential for the establishment of a research infrastructure in homeopathy.

Research agenda containing explicit objectives to achieve in a clear defined schedule of activities (deadlines) would be assessed by a board and a peer review committee. A common database is needed to generate a Booklet of Procedures with a detailed explanation of each trial to facilitate the sharing of this experience and to make those data and indicators comparable across the countries. Regular meetings between collaborators are needed to strengthen links between clinical and basic scientists. Research training for each medical homeopath is needed to ensure the interface between complex systems studies and theories (biophysics, thermodynamics, information theory) and clinical studies and practice.

### 5.1 *Clinical and socio-economic research*

A variety of research fields present possibilities, ranging from effectiveness and efficacy research, cost-effectiveness and safety studies to homeopathic pathogenetic trials.

Effectiveness and efficacy research requires a number of sequential steps. Effectiveness research should range from simple data collection in daily practice via observational studies to outcome and cost-effectiveness studies which adhere to strict protocols. Efficacy research focuses on specific questions using randomised controlled research designs.

The ECH considers the following steps to be essential:

- surveys of daily practice
- post-marketing surveillance
- observational studies
- assessment of likelihood ratio of homeopathic symptoms
- randomised but non-blind comparison studies
- randomised clinical trials, including both the development of new trials and the replication of previous successful trials.

Research on different aspects of homeopathic clinical practice should be further stimulated, such as the various steps in the diagnostic process, the steps leading to the selection of a remedy and the development of treatment protocols in different diseases.

From a socio-economic perspective the following studies are necessary:

- demographic studies (who goes to see a homeopathic doctor and why)
- satisfaction and quality of life studies
- economic evaluation of homeopathic health care (cost-effectiveness)

Homeopathic pathogenetic trials (provings) are necessary to further improve our knowledge of existing homeopathic remedies and the quality of homeopathic treatment, and also to widen the range of remedies used.

- some standards for this kind of trial have been developed
- different compounds need testing and re-testing
- toxicology studies are to be carried out and a database is to be developed

The development and introduction where possible of homeopathy into the livestock farming sector is particularly important, promising more effective protection of consumers from pharmacological residues in animal products and better conditions for livestock currently being reared.

Various phenomena described within homeopathy such as initial aggravation, syndrome shift, disease substitution, and placebo effects all need further research.

## **5.2 *Fundamental and preclinical research***

To improve knowledge of the scientific basis of homeopathy, a number of actions are required:

- A shift in emphasis is required in fundamental research activities towards a more balanced distribution of research activities between the two fundamental aspects of homeopathy, i.e. the similia principle and the use of potentised remedies.
- A theoretical model for homeopathy, expressed in terms of mainstream biomedical knowledge, is required which takes account of the regulatory processes underlying the stimulation of recovery by application of the similia principle.
- The relation between the similia principle and hormesis, the paradoxical stimulatory effect of low doses of toxic substances, should be further investigated.
- Experiments on a limited number of promising model systems in which an effect of high potencies has been observed should be reproduced. It would be useful to identify two or three conceptually sound test systems for further development.
- The conditions under which the optimum effect of potencies occurs in biological model systems should be further investigated.
- The importance of physical phenomena such as turbulence and chaotic processes in the preparation of homeopathic remedies should be further investigated. Furthermore, it should be determined whether the structure and “memory” of water and/or electromagnetic fields are of any relevance in the establishment of an effect of potencies.

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