



# Replications of fundamental research models in ultra high dilutions 1994 and 2015 – update on a bibliometric study

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**Introduction:** This paper focuses exclusively on experimental models with ultra high dilutions (i.e. beyond  $10^{-23}$ ) that have been submitted to replication scrutiny. It updates previous surveys, considers suggestions made by the research community and compares the state of replication in 1994 with that in 2015.

**Methods:** Following literature research, biochemical, immunological, botanical, cell biological and zoological studies on ultra high dilutions (potencies) were included. Reports were grouped into *initial studies*, *laboratory-internal*, *multicentre* and *external* replications. Repetition could yield either *comparable*, or *zero*, or *opposite* results. The null-hypothesis was that test and control groups would not be distinguishable (zero effect).

**Results:** A total of 126 studies were found. From these, 28 were initial studies. When all 98 replicative studies were considered, 70.4% (i.e. 69) reported a result comparable to that of the initial study, 20.4% (20) zero effect and 9.2% (9) an opposite result. Both for the studies until 1994 and the studies 1995–2015 the null-hypothesis (dominance of zero results) should be rejected. Furthermore, the odds of finding a *comparable* result are generally higher than of finding an *opposite* result. Although this is true for all three types of replication studies, the fraction of *comparable* studies diminishes from laboratory-internal (total 82.9%) to multicentre (total 75%) to external (total 48.3%), while the fraction of *opposite* results was 4.9%, 10.7% and 13.8%. Furthermore, it became obvious that the probability of an external replication producing comparable results is bigger for models that had already been further scrutinized by the initial researchers.

**Conclusions:** We found 28 experimental models which underwent replication. In total, 24 models were replicated with comparable results, 12 models with zero effect, and 6 models with opposite results. Five models were *externally* reproduced with comparable results. We encourage further replications of studies in order to learn more about the model systems used. *Homeopathy* (2015) 104, 234–245.

**Keywords:** Review; Basic research; Homeopathy; Ultra high dilution; Replication

## Introduction

There are several thousand references on fundamental research in homeopathy, including hundreds of references on extreme dilutions. This paper focuses exclusively on experimental models with ultra high dilutions (i.e. beyond  $10^{-23}$ ) that have been submitted to replication scrutiny.<sup>1–101</sup> It follows on from a previous survey of

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2009<sup>102</sup> which gave an overview of fundamental biochemical and biological studies that used high homeopathic potencies and that had been subjected to laboratory-internal, multicentre or external replication trials. Physicochemical or clinical studies were not included, nor studies on dilutions below  $10^{-23}$ , nor studies in relation to which no attempt of replication could be found in literature.

The studies under survey were grouped into broadly defined clusters according to the methodology employed (see below [Methods](#)).

Apart from being a mere update this paper considers suggestions made by the research community in response to the first publication<sup>102</sup> regarding the literature surveyed as well as its clustering, evaluation and discussion. It also compares the state of replication in 1994, when the anthology 'Ultra High Dilution' was published,<sup>99</sup> with that in 2015. Furthermore, with regard to the models presented, we tried to determine whether it makes sense to pursue laboratory-internal and multicentre replication research as a means of mitigating the probability of external replication studies producing zero results.

## Methods

### Literature search

Sources of information were reviews,<sup>99,102–113</sup> personal contact with members of the homeopathic research community, and the MEDLINE ([www.PubMed.gov](http://www.PubMed.gov)) and HOMBREX ([www.carstens-stiftung.de](http://www.carstens-stiftung.de)) databases. Allowed literature sources were publications (in peer-reviewed and not peer-reviewed journals, book sections and books) as well as unpublished academic papers. As a rule, unpublished papers were disregarded wherever published papers on the same study were available. Especially from 2010 to 2015, we focused on PubMed listed publications. Although we have done what seemed possible to identify all relevant studies, the annotated bibliography presented here does not claim to be exhaustive.

### Inclusion criteria

We included biochemical, immunological, botanical, cell biological and zoological studies on ultra high, homeopathically prepared dilutions (potencies), i.e.  $\geq 24x$  ( $=10^{-24}$ ) or  $12c$  ( $=100^{-12}$ ). Studies published after 1940 were required to report evaluation of results by statistical methods (minimum requirement: mean or median, number  $n$  of samples, standard deviation or standard error, OR, number  $N$  of samples, level of significance of a statistical test).

To be included the experiment had to have been repeated. Replications were formally considered as such whenever it was possible to find

- at least two publications by the same initial working group, including a follow-up trial of an initial publication (laboratory-internal replication) or
- at least one publication reporting on a multicentre trial (independent experiments in different locations/labora-

tories, organized by one study coordinator, normally from the initial team), or

- at least one publication by the initial workgroup and one with external authorship, both dealing with the same experimental model.

Furthermore, replication was considered as such when a later study dealt with the same biological system and the same potentized substance as an earlier one. Within such clusters, however, a certain degree of deviation was accepted with regard to the biological system (e.g. the use of *Chlorella vulgaris* or *Chlorella pyrenoidosa*), the potency level (e.g. 25x or 30x) and potency type (decimal (x) or centesimal (c)) and the nature of the control (e.g. prepared step by step or not, succeeded or not, or type not mentioned).

One and the same publication could refer to the results of more than one study. Where numbers of studies are quoted in connection with multicentre trials they refer to the number of trials in different locations/laboratories. Among the initial studies, one of the researchers involved was always considered as the 'initial' researcher. When their name could not be identified from the publication, the first author's name was mentioned. Apart from the main publications, four publications giving additional information were cited.<sup>98–101</sup>

Thus, we extracted all studies from the included publications and grouped them into experimental models.

Studies (i.e. initial and repeated studies) were further grouped according to results achieved:

- Initial studies: as an inclusion criterion to be candidates for replication trials, these had shown a significant difference between test and control group, e.g. enhancing growth
- Repeated studies, the results of which were *consistent* with the initial study, i.e. where a *comparable* result (in the same direction, e.g. enhancing growth) was found
- Repeated studies, where *no* difference between test and control group was found (zero effect)
- Repeated studies, the results of which were *opposite* to the initial study, i.e. when results were *different* in direction (e.g. decreasing instead of increasing).

The null-hypothesis was that test and control groups would not be distinguishable, i.e. there would be no result of treatment with the potency (zero effect). In this survey paper, we focused on a graphical representation of the data rather than statistical calculations. Raw data for further analysis are given in [Table 1](#) (see [Results](#)).

## Results

A total of 126 studies were found. [Figure 1](#) shows the proportion of models and studies.

Numbers of studies performed until 1994<sup>102</sup> and in the period from 1995 to 2015 were: on enzymes 2 + 7, on cultured cells 0 + 2, on plants 4 + 30, on immune cells 12 + 16, on isolated organs 0 + 4, on amphibians/fish 8 + 18 and on rats/mice 9 + 14.

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