Draft Guidelines for Natural Health Products Evidence Requirements

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# Introduction

The purpose of the Natural Health Products Bill (the Bill) is to establish a system for the regulation of natural health products (NHPs) in New Zealand.

The Bill is founded on the following principles.

* Permitted NHPs should be fit for human use.
* The regulation of permitted NHPs should correspond with the risks associated with their use.
* Permitted NHPs should be accompanied by information that:
* is accurate
* tells consumers about any risks, side effects and benefits of using the product.
* Health benefit claims made for permitted NHPs should be supported by scientific or traditional evidence.

The Bill establishes a notification system for all NHPs sold in New Zealand or manufactured for the export market. The Bill provides for the Authority to establish a list of permitted substances. Permitted NHPs may only contain permitted substances and must be manufactured in accordance with the Code of Manufacturing Practice. The Bill further establishes the types of claims that can be made about a product, the health conditions that claims can be made about, and the type of evidence that product notifiers must hold to support their claims. The Bill also requires product notifiers to make available to the public a summary of evidence that supports the claim(s) made in respect of the product.

These guidelines provide further information to product notifiers on the types of claims that can be made about a product and the types of evidence that are considered acceptable to support those claims. These guidelines also provide assistance on how to write a summary of evidence.

Homeopathic medicines are exempt from the requirements of the NHP scheme as they contain less than 20 parts per million (ppm) of the active ingredient. Any product containing more than 20 ppm of the active ingredient is not considered a homeopathic medicine for the purposes of the NHP scheme and must comply with the requirements.

Aromatherapy products that are intended to be inhaled are also exempt from the requirements of the NHP scheme as the contents are not ingested by the user. However, these products may be covered by the Psychoactive Substances Act 2013. If you are unsure if your product is covered by the Psychoactive Substances Act, contact the Psychoactive Substances Regulatory Authority at [psychoactives@moh.govt.nz](mailto:psychoactives@moh.govt.nz).

Products that are made by a natural health practitioner for sale to an individual, following a consultation with that individual, are also exempt from the requirements of the NHP scheme.

These guidelines are in draft form as the Authority is currently undertaking public consultation on what information will be included in the Regulations to the Bill and the direction provided in these guidelines. A copy of the consultation document can be found at www.health.govt.nz.

# Health benefit claims

## What is a health benefit claim?

A health benefit is defined in clause 5 (Interpretation) of the Bill as any one of the following:

* maintenance or promotion of health or wellness
* nutritional support
* vitamin or mineral supplementation
* affecting or maintaining the structure or function of the body
* relief of symptoms.

Wording that is consistent with the intent of these health benefits is also acceptable. If you are uncertain whether your claim is consistent with clause 5 of the Bill, we recommend you engage the services of the Association of New Zealand Advertisers’ Therapeutic Advertising Prevetting System (TAPS) or a regulatory affairs consultant. More information on TAPS is available on their website at <http://www.anza.co.nz/Category?Action=View&Category_id=262>. A list of regulatory affairs consultants is available on the Medsafe website at [www.medsafe.govt.nz/regulatory/consultants.asp](http://www.medsafe.govt.nz/regulatory/consultants.asp).

Claims made with respect to NHPs must be accurate and not misleading. Claims must be consistent with clause 5 of the Bill and be supported by either traditional or scientific evidence.

Claims that refer to the terms treatment, prevention or cure are not consistent with clause 5 of the Bill and should not be made in relation to NHPs.

## Named conditions

A named condition is defined in clause 6B of the Bill as any disease, disorder, condition, ailment or defect that is listed or described in the International Statistical Classification of Diseases and Related Health Problems. The current version is the 10th revision. The ICD is a tool to help medical practitioners, researchers, patient organisations and others to classify diseases and health problems. A [copy of the ICD](http://apps.who.int/classifications/icd10/browse/2016/en) can be found at <http://apps.who.int/classifications/icd10>.

## Allowable claims

A claim that the Authority has determined may relate to a named condition is known as an allowable claim. The draft list of conditions that may be used in allowable claims can be found at www.health.govt.nz. Allowable claims must be consistent with the definition of a health benefit claim as stated in clause 5 of the Bill.

If you wish to make higher level claims than those permitted by the Bill, the product will be considered a medicine and will need to have consent from the Minister of Health before distribution. Refer to <http://www.medsafe.govt.nz/regulatory/regguidance.asp> for further guidance on what is required to register your product as a medicine.

## Traditional claims

Traditional claims are claims that an ingredient or product has been used within a recognised therapeutic model that sits outside modern conventional medicine. Traditional medicine is an integral part of many cultures and includes a diverse range of health practices, approaches, knowledge sets and belief systems relating to medicines.

Examples of traditional medicine models include:

* traditional Chinese medicine
* Ayurvedic (traditional Indian) medicine
* Western herbal medicine
* other indigenous medicines.

Traditional claims must indicate that the health benefit is based on long-term use and experience in a specific traditional model. Feedback on how long is sufficient to indicate traditional use is currently being sought as part of public consultation on the scheme.

Example: ‘Traditionally used in Western herbal medicine to relieve nasal congestion.’

## Claims for multiple ingredients from the same traditional model

For products that have multiple active ingredients from the same traditional model, claims can be linked to individual ingredients or relate to the entire medicine, provided the indications for each ingredient are traditionally used for the same health benefit.

Example: ‘The ingredients in this medicine are traditionally used in Western herbal medicine to maintain a healthy liver function.’

## Claims for multiple ingredients from different traditional models

If all the active ingredients from the different traditional models are traditionally used for the same health benefit, the claims can be applied to the whole product.

Example: ‘Ingredients in this medicine have traditionally been used in Ayurvedic and Chinese medicine to relieve common cold symptoms.’

Alternatively, an indication can be provided for each individual ingredient.

Example: ‘*Trichosanthis kirilowii* (tian hua fen) is traditionally used in Chinese medicine to clear and drain lung heat to help relieve chest congestion.’

**and**

‘*Ocimum tenuiflorum* is traditionally used in Ayurvedic medicine to help remove excess kapha (mucus) from the lungs and nasal passages.’

## Scientific claims

Scientific claims are made in relation to conventional modern medicine and are supported by scientific literature, such as clinical studies or systematic reviews.

Example: ‘Helps relieve common cold symptoms.’

## A combination of traditional and scientific claims

A product with a combination of scientific and traditional claims requires scientific evidence to support the scientific claims and evidence of traditional use to support the traditional claims. For example, a medicine that contains *Panax ginseng, Bacopa monnieri* and folic acid may have the following indications (if supported by appropriate evidence).

Example: ‘This product has been formulated from traditional and non-traditional ingredients to help support a healthy memory. Folic acid helps support cognitive function, while traditionally *Panax ginseng* is used in Chinese medicine to support memory in times of fatigue.’

# Evidence to support claims

## General requirements for evidence

All claims for NHPs must be supported by evidence. The Bill establishes that the product notification process is only complete when the notifier has published a summary of the evidence that they hold to support the health claims for their product.

Evidence can be traditional or scientific in nature or a combination of both, but must match the claim made. Scientific evidence does not take precedence over traditional evidence. If there is conflicting evidence between the traditional use of an ingredient and contemporary scientific evidence, this should be stated on the product label and in the summary of evidence. This is to ensure that your claims are not misleading.

The evidence that you hold to support your claim must be in English, or you must be able to provide a verified English translation if requested by the Authority.

## Relevance and representativeness of evidence

In order to be useful, evidence must be relevant to the claim and representative of the wider body of evidence. As part of the consultation process, feedback is being sought on the criteria of relevance and representativeness.

It is proposed that evidence must:

* relate to the same method of administration,[[1]](#footnote-1) active ingredient, formulation[[2]](#footnote-2) and dose[[3]](#footnote-3)
* be relevant to the target population[[4]](#footnote-4)
* directly measure health benefit
* not conflict with the wider body of evidence.

## Evaluation of evidence by the Authority

The NHP scheme is based on a notification system. This means that the Authority does not:

* approve NHPs
* evaluate NHP notifications before the products are able to be sold.

The Authority **will**, however, proactively audit a proportion of completed product notifications for compliance with the regulatory requirements. If a complaint has been received, the Authority may also audit product notifications.

If your product is selected for an audit, you may be required to provide supporting information to the Authority. If the supporting information is found to be insufficient, the Authority may take regulatory action, including suspension or cancellation of the product notification in accordance with clauses 24 and 26 of the Bill, respectively. The Authority will take this action if it has reasonable grounds:

* to believe that the product has caused, is causing, or is likely to cause any harm to any person
* to believe that the product notifier has provided false, misleading or incomplete information in the product notification
* for concern because of new information about the safety, quality, health benefit claims or manufacturing standards of the product.

As the notifier of a permitted NHP, you must be able to produce evidence to support all the claims you make for your product if asked by the Authority under clause 20(6)(a) of the Bill. The evidence must adequately demonstrate that all claims made for the product are true, valid and not misleading. You must be able to produce evidence for the whole time the product notification remains valid. If your product is discontinued, you must also be able to produce this evidence for a reasonable period following its cancellation while individuals are still likely to be consuming their personal stocks of the product.

## Traditional evidence

Traditional evidence means an extensive history of use of a plant, ingredient or product based on knowledge, beliefs or practices that have been passed down from generation to generation. This means that a traditional claim can still be true even if scientific evidence may exist that disputes the effectiveness of the product.

Traditional claims that have been scientifically proven not to be correct can still be made, but to acknowledge the differences between the two models, claims backed up by traditional evidence must take the form ‘traditionally used for xxx’ or words to that effect. However, we strongly encourage notifiers to include on their product labels and in their summary of evidence ‘this traditional use is not supported by scientific evidence’ or words to that effect. This is to ensure that the information related to your product is not misleading.

The Authority proposes that the time required for something to be considered traditional use is three generations (75 years, 25 years per generation). Feedback on this proposal is being sought as part of the consultation process.

You are required to hold evidence that your medicine or its active ingredient has been used for the required period of time in the context (such as dose form) of the traditional claim. Methods of extraction and manufacture may alter the properties of the active ingredient. It is important, therefore, that your evidence matches the methods of extraction and manufacture used to prepare your product.

## Scientific evidence

Scientific evidence refers to evidence that can be proven or verified in a quantifiable manner by experience or experiment. The general requirements for scientific evidence will be based on the approaches used by the [Oxford Centre for Evidence Based Medicine](http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/) (http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/) and the [Australian Therapeutic Goods Authority](https://www.tga.gov.au/publication/evidence-guidelines) (https://www.tga.gov.au/publication/evidence-guidelines).

For the purposes of the NHP scheme, scientific evidence held to support claims must show effectiveness in humans.

# Summary of evidence

All product notifications must include a reference to a website with a summary of the evidence supporting the health benefit claims for your product. This is so consumers can easily see the basis for the claim and request information from the product notifier. Your summary of evidence should show that you have conducted an objective, comprehensive, transparent and robust review of the literature relating to your claim(s). This is explained further in the sections on assessing your evidence and quality of evidence.

## Summary of traditional evidence

A summary of traditional evidence must:

* support a claim that a particular substance was used within the relevant tradition
* be applicable to the claim.

A summary of traditional evidence must include:

* the claim made in respect of the product
* the source(s) of the evidence (such as approved pharmacopoeia)
* the traditional model that supports the claim (for example, traditional Chinese medicine).

Some claims are more relevant to populations, rather than traditional models. For example, limes and lemons were traditionally used by sailors from many different nations to prevent or treat vitamin C deficiency. In this instance, it may be more appropriate to refer to the context of traditional healing, rather than a particular traditional model.

### Sources of traditional evidence

Schedule 2 of the Bill lists approved pharmacopoeia which can be used as sources of traditional evidence. A pharmacopoeia is a book, usually published under the jurisdiction of the government, that contains a list of products and ingredients, their formulas, methods for making medicinal preparations, requirements and tests for their strength and purity, and other related information. In the context of the Bill, the term ‘approved pharmacopoeia’ is used to describe any pharmacopoeia, monograph, treatise, text or similar that the Authority has approved for use in this way.

The Authority must accept a reference to one of these approved pharmacopoeia as evidence of traditional use; however, these are not the only valid sources of traditional evidence. Other sources include confirmation by an individual recognised within a specific culture as having the authority to speak on such matters, that an ingredient or product has been traditionally used in the manner you are claiming. Published studies detailing traditional use and treatises on traditional medicine could also be considered to be forms of evidence of traditional use. Feedback on what other types of evidence could be considered suitable confirmation of traditional use is being sought as part of the consultation process.

### Example summary of traditional evidence

Kawakawa has been traditionally used by Māori to relieve upset stomachs. This is stated in *Te Ara: The Encyclopedia of New Zealand* and is available at [www.teara.govt.nz/en/rongoa-medicinal-use-of-plants](http://www.teara.govt.nz/en/rongoa-medicinal-use-of-plants).

## Summary of scientific evidence

A summary of scientific evidence must include:

* the claim made in respect of the product
* the source(s) of the evidence
* the objective and method of the experiment
* key findings and conclusions.

In addition, a summary of scientific evidence must:

* not conflict with a wider body of evidence
* be accurate and not misleading
* be applicable to the claim.

### Types of acceptable scientific evidence

Types of scientific evidence include systematic reviews, peer-reviewed journal articles and unpublished studies (provided the product notifier holds the full details of the studies and the studies are well-designed). Internationally recognised monographs or pharmacopoeias maintained by other international regulatory bodies are also sufficient to support claims made by the monograph or pharmacopoeia and general claims such as nutrient supplementation. Abstracts should not be relied on as evidence because they do not contain sufficient information to determine if a study is well-designed, controlled and analysed.

Unless appropriately justified, extrapolation of studies to different target populations, animal studies, and *in vitro* studies will not meet the standards to be able to provide sufficient scientific evidence for a summary of evidence. The next section has more details on acceptable standards of evidence.

### Objective of experiment

You must describe the objective of the experiment that you are relying upon for the health claim. This is to ensure that the evidence that you have cited is relevant to the claim(s) being made.

### Method of experiment

You should broadly describe the method used in the experiment that you are relying on. This is to make it easy for potential consumers to determine the strength of the evidence to support the claim.

### Key findings

You should provide a summary of the key findings as stated in the study (not what you think the key findings are). Again, this is to ensure that the evidence that you have cited is relevant to the claim being made.

### Conclusions

The conclusions should state exactly what the study has shown and how the effectiveness was shown in the study population. If there are any discrepancies between what the study showed and your summary of evidence conclusions, you must justify your claims with more supporting evidence.

### The relationship between dosage and the claim

The Authority also encourages you to provide the dosage or range of dosages used in the studies so that people can relate the studies to their situation. If the studies are already in the public domain, the Authority encourages you to provide direct links to the studies.

### Example of a summary of scientific evidence

**Claim:** To reduce the duration and severity of the common cold in adults and children.

**Objective:** A systematic review of studies was undertaken to find whether vitamin C (200 mg or more per day) reduces the incidence, duration or severity of the common cold when used either as a continuous regular supplementation every day or as a therapy at the onset of cold symptoms.

**Source:** The systematic review was taken from the Cochrane Database of Systematic Reviews (<http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000980.pub4/abstract>).

**Method:** The authors of the review searched CENTRAL 2012, Issue 11, MEDLINE (1966 to November week 3, 2012), EMBASE (1990 to November 2012), CINAHL (January 2010 to November 2012), LILACS (January 2010 to November 2012) and Web of Science (January 2010 to November 2012). They also searched the U.S. National Institutes of Health trials register and WHO ICTRP on 29 November 2012. Trials which used less than 0.2 g per day of vitamin C and trials without a placebo comparison were excluded from the analysis. The authors assessed ‘incidence’ of colds during regular supplementation as the proportion of participants experiencing one or more colds during the study period.

**Key findings:** The review further found that routine vitamin C supplementation has a modest but consistent effect in reducing the duration of common cold symptoms (by 8% in adults and by 14% in children) based on 31 study comparisons with 9745 common cold episodes. The severity of colds was also reduced by regular vitamin C administration. None of the trials in the review had any reported adverse effects of vitamin C supplementation.

**Conclusions:** The authors concluded that routine vitamin C supplementation may be useful in reducing the risk of contracting the common cold for people exposed to brief periods of severe physical exercise. The authors further concluded that regular supplementation trials have shown that vitamin C reduces the duration of colds.

#### Points to be aware of when writing your scientific summary

A systematic review takes into account the wider body of evidence, therefore the example summary meets the requirement that the evidence must not conflict with a wider body of evidence. The claim was directly investigated in the study, which demonstrates that the evidence is applicable to the claim. The claim is accurate and not misleading because it fairly reflects the findings and conclusions of the study.

The review described above could not be used to support a claim of preventing the common cold unless the claim specifically stated that the product could only do so for people exposed to short periods of extreme physical stress. This is because the review found that routine vitamin C supplementation halved the risk of common cold for people exposed to short periods of extreme physical stress, but did not reduce the incidence of colds within the general population. You cannot ‘cherry pick’ your results because to do so would make your summary of evidence misleading.

The review also found that taking vitamin C in the therapeutic setting (after the onset of symptoms) showed no consistent effect on the duration or severity of common cold symptoms. In order for the claims made about the product to be accurate and not misleading, the claim made in respect of the product would need to be qualified with regard to the prophylactic setting. This could be covered by stating that in order to be effective the product must be taken daily prior to contracting a cold and by giving dosage recommendations stating to consume at least 200 mg daily.

## Multiple claims

If you have made multiple claims you must provide a summary of evidence for each claim.

## Combinations of scientific and traditional evidence

Scientific and traditional evidence may both be used as supporting evidence for an ingredient, provided it is clear what evidence relates to which claim.

## Further detail on acceptable studies

The Authority proposes that scientific evidence must be drawn from studies with a design able to provide evidence to a level equivalent to at least one of the following designs.

### Systematic review

A systematic review critically evaluates and assesses all research studies that have been performed to answer a specific clinical question. A systematic review is a concentrated method of analysing a body of literature on a particular topic using a specific set of criteria, which aims to select only high-quality research evidence.

An [example of a systematic review](http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000980.pub4/abstract) can be found here: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD000980.pub4/abstract.

### Critically appraised topics

Critically appraised topics are similar to systematic reviews in that they acknowledge the highest quality available evidence on a topic, but are shorter and less rigorous.

An [example of a critically appraised topic](http://lgdata.s3-website-us-east-1.amazonaws.com/docs/526/1375418/Critically_Appraised_Topic_full_example.pdf) can be found here: http://lgdata.s3-website-us-east-1.amazonaws.com/docs/526/1375418/Critically\_Appraised\_Topic\_full\_example.pdf.

### Critically appraised articles or papers

In a critically appraised article, the author uses a systematic process to:

* evaluate a published study for the strength of design and statistical analyses
* highlight methodological strengths and weaknesses
* place the study in the context of other research
* discuss the implications of the study.

It should also carefully consider the interpretation of research results, and potential conflict of interests that could arise from the research outcomes. A critically appraised article is not a study that has been published in a peer-reviewed journal. It is a succinct appraisal of a single research study.

You can also find further guidance on how to critically appraise an article here: <http://www.nature.com/nrgastro/journal/v6/n2/full/ncpgasthep1331.html> and here: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2696241/>.

### Randomised controlled trials

Randomised controlled trials randomly allocate those being studied into groups, each receiving different clinical interventions. One of these groups is the control group, who are given a placebo or no intervention at all. These trials provide high-quality scientific data on the effectiveness of a given clinical intervention, as well as identifying potential adverse reactions.

An example of a randomised controlled trial can be found here: http://www.ncbi.nlm.nih.gov/pubmed/17892376?ordinalpos=1&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed\_ResultsPanel.Pubmed\_RVDocSum

### Cohort study

A cohort study is a study that observes a large numbers of individuals over a long period (often years) and compares the incidence rates of the condition of interest in groups that differ in exposure levels. The cohort group is often compared to the general population from which it was drawn. These studies can be undertaken either prospectively or retrospectively.

An example of a cohort study can be found here: http://www.ncbi.nlm.nih.gov/pubmed/15213107?dopt=AbstractPlus

### Case controlled studies

Case controlled studies are observational studies. The subjects are not randomised to exposed or unexposed groups. Instead, they are observed to determine their exposure and subsequent outcome of disease. If a larger proportion of people who develop the disease were exposed in comparison to those that do not develop the disease, it can be hypothesised that what they were exposed to may have caused the disease.

The types of studies described below are less robust than those already described. The Authority is currently proposing NOT to accept the types of studies described below but is seeking feedback as part of the consultation process on whether you think these types of studies should be considered acceptable, and why.

### Case series

Case series studies track subjects who have received a similar treatment over time. Case series have a descriptive study design as opposed to an analytical study design (as for cohort studies, case controlled studies or randomised controlled trials). It is often hard to draw scientifically sound conclusions because of their descriptive nature, their susceptibility to selection bias and the lack of a comparator group.

An example of a case series study can be found here: http://aje.oxfordjournals.org/content/143/11/1165.full.pdf

### Time series

Time series studies analyse data from measurements obtained at specific time points throughout a study. Measurements are taken prior to, during and after the introduction of an intervention or treatment to the subject, to determine what effect an intervention may have. It is often hard to draw scientifically sound conclusions from time series studies, because of their susceptibility to selection bias and the lack of a comparator group.

### Animal studies

Animal studies can provide useful information, but on their own they are insufficient as a basis to claim the effectiveness of drugs in human subjects. Extrapolation of results from animal trials into human populations often shows inconsistencies in the results. A variety of differences between human and animal populations, including anatomy, organ structure and function, toxin metabolism, chemical and drug absorption, and mechanisms of DNA repair lead to these inconsistencies.

An example of an animal study can be found here: http://cancerres.aacrjournals.org/content/60/7/1878.full

# Sources of scientific evidence

We recommend notifiers source their information from comprehensive databases of journal citations and abstracts of internationally reputable biomedical literature such as the following.

### Systematic reviews

* [The Cochrane Library](http://onlinelibrary.wiley.com/cochranelibrary/search/)[[5]](#footnote-5) (<http://onlinelibrary.wiley.com/cochranelibrary/search/>)
* [MEDLINE](https://www.nlm.nih.gov/bsd/pmresources.html) (https://www.nlm.nih.gov/bsd/pmresources.html)
* PUBMED
* Database of Abstracts of Reviews of Effects (DARE)
* [EMBASE](https://www.elsevier.com/solutions/embase-biomedical-research) (https://www.elsevier.com/solutions/embase-biomedical-research)
* [Web of Science](http://login.webofknowledge.com/error/Error?PathInfo=%2F&Alias=WOK5&Domain=.webofknowledge.com&Src=IP&RouterURL=http%3A%2F%2Fwww.webofknowledge.com%2F&Error=IPError) (http://login.webofknowledge.com/error/Error?PathInfo=%2F&Alias=WOK5&Domain=.webofknowledge.com&Src=IP&RouterURL=http%3A%2F%2Fwww.webofknowledge.com%2F&Error=IPError)
* [BIOSIS](http://thomsonreuters.com/en/products-services/scholarly-scientific-research/scholarly-search-and-discovery/biosis-citation-index.html) (<http://thomsonreuters.com/en/products-services/scholarly-scientific-> research/scholarly-search-and-discovery/biosis-citation-index.html)
* [Sciverse Scopus](http://www.elsevier.com/solutions/scopus) (http://www.elsevier.com/solutions/scopus)
* [Cab Health](http://www.cabdirect.org/) (http://www.cabdirect.org/)
* [AGRICOLA](https://www.ebscohost.com/academic/agricola) (https://www.ebscohost.com/academic/agricola)
* [Food Science and Technology Abstracts](http://foodinfo.ifis.org/fsta) (http://foodinfo.ifis.org/fsta)

### Critically appraised topics

* National Guideline
* Clearinghouse

### Critically appraised individual articles

* American College of Physicians Journal Club Evidence Updates
* PUBMED

### Randomised controlled trials

* PUBMED
* Cochrane Central Register of Controlled Trials
* *New England Journal of Medicine*
* *The Lancet*

### Cohort studies

* Pubmed
* Cochrane Central Register of Controlled Trials
* *New England Journal of Medicine*
* *The Lancet*

### Case controlled studies

* Pubmed
* Cochrane Central Register of Controlled Trials
* *New England Journal of Medicine*
* *The Lancet*

Literature searches of electronic databases should be documented to best practice standards. We recommend that your summary of evidence includes a list of search terms, databases used, and number of references retrieved, or at the very least, you must hold this information. You should also document justification for the search approach taken, including the inclusion and omission of studies. This will help demonstrate that you have done your best to ensure your evidence does not conflict with a wider body of evidence.

For a detailed overview of how to record a search see: Systematic Reviews: CRDs guidance for undertaking systematic reviews in health care. Appendix 3, Documenting the search process. (https://www.york.ac.uk/media/crd/Systematic\_Reviews.pdf)

You may also wish to conduct clinical trials on your product. Conducting your own clinical trials will be of particular benefit if evidence to support the claims you wish to make about your product has not previously been published. Since notifiers must hold full details of studies used to support a scientific claim, other notifiers would not be able to make the same claim because they would not hold the full information required. For more information on how to conduct your own clinical trials, refer to guidance provided by the [European Medicines Agency](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000085.jsp&mid=WC0b01ac0580027549) (<http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000085.jsp&mid=WC0b01ac0580027549>). You may also find the [Medsafe website](http://www.medsafe.govt.nz/medicines/clinical-trials.asp) helpful (<http://www.medsafe.govt.nz/medicines/clinical-trials.asp>).

# Assessing your evidence for relevance

Various types of evidence from a range of sources will be found in the literature when searching the existing body of scientific evidence. An assessment of all relevant evidence found from the literature is required to form a robust summary of evidence. Relevant evidence includes any study using comparable active ingredient(s) and health benefits. Dose form, populations and context of use may also be relevant, for example. This is discussed further below.

## Health benefit

Your research should be relevant to the specific indication that you are making a claim for. Regardless of the quality of the study, if the health benefit that is linked to the ingredient does not match the study, your health benefit claims will not be supported. For example, a study that shows that vitamin C supplementation may reduce the duration and severity of the common cold cannot be used to support a claim that vitamin C prevents the common cold. You should not exaggerate the extent of the effects achieved in a study or imply greater scientific certainty than what is claimed or shown in the study.

## Ingredient and usage information

The active ingredient(s), dosage, and route, duration and frequency of administration of the product must be consistent with the summary of evidence and what has been demonstrated in the scientific evidence.

For the evidence to be applicable to your product, the active ingredient(s) should be prepared in a comparable manner. If the preparation, dosage, or route, duration or frequency of administration is different to the scientific evidence, there must be sufficient justification to show that these differences will not alter the effectiveness of the product.

## Study populations

Unless your NHP is targeted to a specific population subset, a study population should:

* include both male and female participants
* have overall good health
* be aged 18 to 65
* be representative of the New Zealand population.

If your NHP is targeted to a specific population subset, the health and cultural background of the study used for evidence must reflect this. If these factors are not taken into account, the evidence that is gathered will not be acceptable to support a robust summary of evidence.

If there are no relevant studies available on the particular population subset your NHP is aimed at, an evidence-based justification may be used to explain why the evidence documented may be extrapolated to your particular population subset. When deciding whether the results of a study may be extrapolated to your target population, you should consider biological, environmental and behavioural factors.

Care must be taken, however, when applying evidence shown in a diseased population group to a healthy population group. This is because the active ingredient(s) that are effective in a diseased population group may not be appropriate to support the same indications in a healthy population group.

Other factors such as pregnancy, gender and ethnic background may also have an impact on the effectiveness of a product. For example, some ethnicities may metabolise certain substances in a different manner (or not at all).

Non-clinical data such as *in vitro* studies and animal studies may also be used as further evidence to support evidence shown in different population groups.

# Assessing your evidence for quality

As well as the relevance of the evidence, the quality of evidence needs to be taken into account.

## Balanced view of scientific evidence

Your evidence must not be subjective and must not be in conflict with the wider body of evidence.

As mentioned in the sources of evidence section, your evidence must take into account all of the available evidence, not just the data which supports your health benefit claim. Poorly designed studies can be rejected to ensure you are only considering good quality evidence. The criteria for excluding studies should be predetermined to prevent cherry picking or skewing of the data to suit your intended claim. For example, if your product is intended to deliver 200 mg of vitamin C a day, you could exclude all studies that investigated the effects of less than 200 mg a day. You could also choose to exclude all studies that don’t have a control group or that aren’t blinded or randomised. Your research must conclude that the weight of good-quality evidence is in favour of the stated health benefit claim associated with your NHP, rather than against it.

If there are inconsistencies in the scientific data, you should be able to provide justifications as to why your intervention will have the intended health benefit claims. These inconsistencies could be attributable to such things as the dose form, duration and administration route, and differing population groups. It is also important to critically evaluate the weaknesses of studies; not all studies you find will be scientifically robust, or high enough quality to be used to support your summary of evidence. Having a thoroughly researched and well-balanced summary of scientific evidence will allow you to confidently ensure the claims that you are making are true and not misleading, and will be valid and consistent with the contemporary scientific view for your product.

## Methodology

Although there is no specific protocol for undertaking scientific research, there are some basic principles that are generally accepted as best practice. Scientific studies should be critically appraised in terms of methodological quality, and the possibility of bias produced by study design and potential confounding factors.

The appropriate duration of a study is a key aspect of correct methodological design. A study should be long enough to clearly be able to show the health benefit. This will mean differing study durations dependent on the health benefit being observed. The minimum study duration must be justified with regard to the specific health benefit claim; any study that is not long enough for the proposed benefit to be observed is not considered high-quality evidence.

The number of participants in the study will also greatly affect the strength of the study’s findings. More participants in a study will produce conclusions with much greater statistical significance. A higher number of participants will also negate the effects of participant dropout through the duration of the study.

Blinding of subjects and researchers is likely to increase the robustness of results, as is randomisation of subjects into treatment versus control groups. The randomisation method should be described in the study. Studies that appear in a well-respected, peer-reviewed journal article may be more likely to be robust because the study has been scrutinised by suitably qualified third parties with no conflicting interests.

## Analysis

For the health benefit of an ingredient to be considered effective, the evidence should be able to show both clinical and statistical significance.

Statistical significance means that a study must show that there is a less than 5% chance that the benefit observed with the intervention appeared by chance. This is where the number of study participants (the power of the study) is crucial. A higher number of participants will show a much stronger profile of statistical significance. A study with two participants showing that they both received the health benefits of the intervention isn’t as conclusive as a study with 100 participants showing that 98 of the participants received the health benefits associated with the intervention.

High rates of individuals dropping out of a study can introduce large bias into a study because the reasons for non-completion may vary across treatment and control groups that were initially randomised. It is also possible that individuals will drop out because they don’t think a treatment is working. A good-quality study will perform an intent to treat analysis which accounts for the effects of dropouts. If it is not possible to obtain outcome measurements from dropouts at the end of the study, baseline measurements of the study parameters should be used as the outcome measurements. This potentially makes it harder to show a difference, but any difference that is able to be shown is far more robust than when dropouts are not accounted for.

Statistical significance alone, however, is not enough to justify the effectiveness of the NHP – clinical significance is also a key factor in this determination. Clinical significance is somewhat subjective, but is considered to represent a benefit that is significant enough to justify the intervention taken. In other words, the benefits of the intervention far outweigh the associated risks, such as side effects, costs and inconvenience to the user.

When looking at statistical and clinical significance, control groups are crucial. Control groups provide a comparative look at what would occur in a similar population without intervention, and therefore add more power to any findings shown in the trial group.

1. Such as topical or oral. [↑](#footnote-ref-1)
2. Formulation refers to species (eg, *Citrus aurantium* vs *Citrus bergamia*) or part of the plant (eg leaf vs root) rather than formulation aids. Formulation aids are defined in clause 5 of the Bill as anything that is added to a product to provide a carrier for the product’s active ingredients; modify the pH, viscosity, or handling properties of the product during its manufacture; or provide a vehicle for its administration. [↑](#footnote-ref-2)
3. Oral dosage forms are likely to be similar enough to be considered ‘the same’ whereas a topical cream and a tablet are clearly not. [↑](#footnote-ref-3)
4. Such as age, sex and ethnicity if relevant. For example, ethnicity could be important if genetic factors are known to cause differences in metabolism. [↑](#footnote-ref-4)
5. The Ministry of Health provides free access to the Cochrane database for all New Zealanders. [↑](#footnote-ref-5)