Prodis
NATURAL HEALTH PRODUCTS COMPANY

Good Manufacturing Practices (GMP) in Homeopathy

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Faithful to nature, dedicated to health!

Important laws in homeopathic medicines

- **THE LAW OF SIMILARS** means matching the **symptom picture of the illness or injury** to the **symptom picture of the medicine**.
- The central tenet of homeopathy is that "*like cures like*" (in Latin: *similia similibus curentur*), in a holistic approach to the totality of the patient's symptoms.

By choosing a **remedy** for a given natural disease capable of producing a **similar artificial disease** we shall be able to cure the most obstinate diseases"
S. Hahnemann, Hufeland's Journal 2: 381 (1796)

—*Allium cepa* is used principally for "colds." These are symptoms most striking general features of *Allium Cepa*.

Important laws in homeopathic medicines

- **THE LAW OF THE MINIMUM DOSE** means **using as little of a medicine as possible to stimulate the body's own healing mechanism**.
- Homeopathic medicines are based on the principle that **high dilutions of potentially active molecules** retain **a memory of the original substance**.
  1. Give **one dose** and wait to see what relief it brings.
  2. Only repeat the dose if the symptoms **stop improving before a full recovery is reached** or if the **same symptoms return**.
  3. If the **symptoms change** significantly select a new remedy to fit the new picture.

Giving the body more medicine than it needs will not improve or speed up the action of the medicine.

The preparation of homeopathic medicines

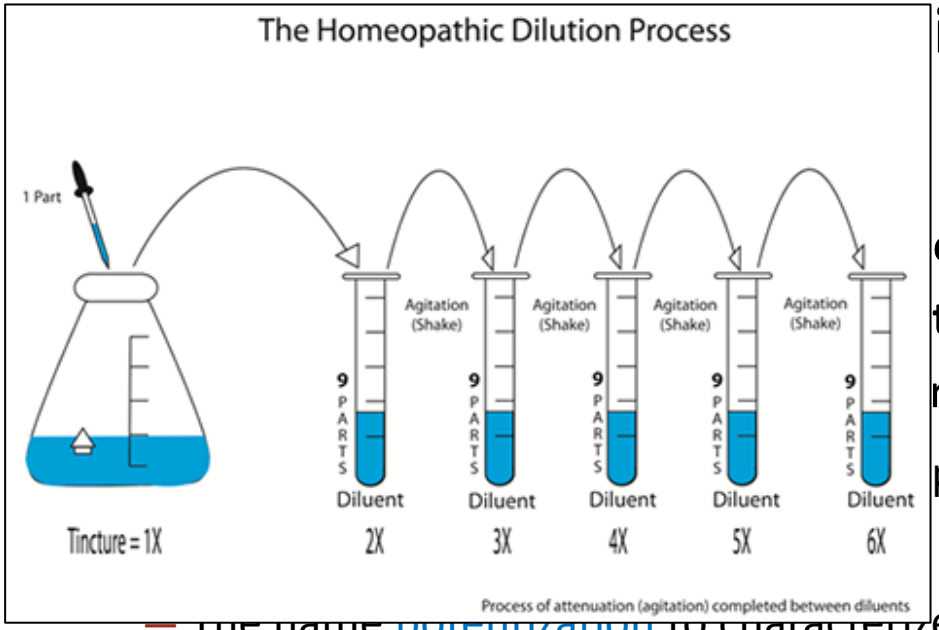
Mother Tincture preparation of plant material

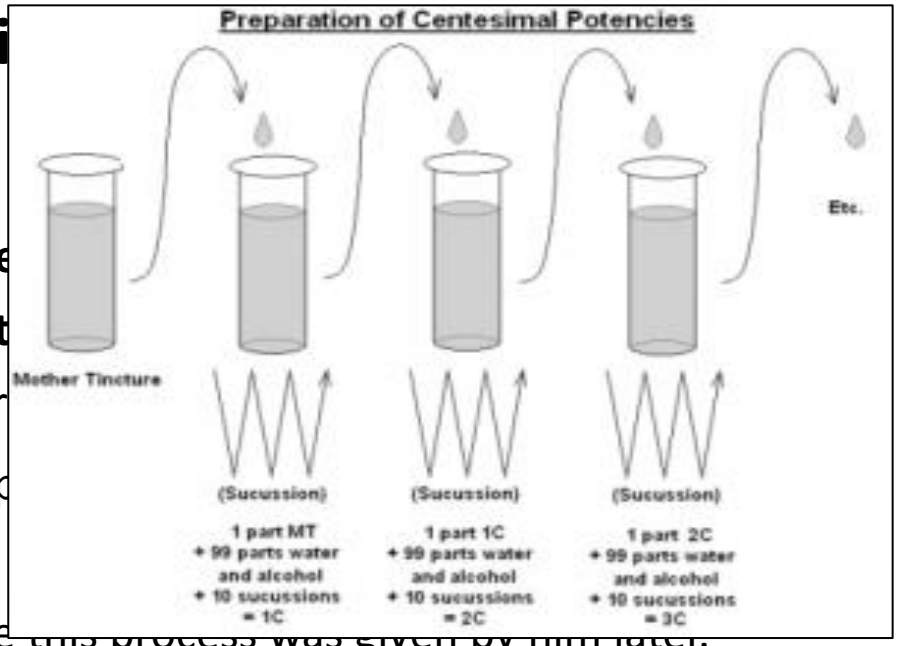
1. OAK mother tincture uses leaves and stems

2. Which are finely chopped

3. The appropriate amount of ethanol is added (use one part of the oak buds to 10 parts of alcohol)
4. The mixture left for a minimum of 10 days before filtering

Taken in the dose of 20 drops before a meal – helps in **lowering blood pressure**, fighting **impotency** as well as **common physical and mental tiredness**





– The name potentization to characterize this process was given by him later.

– From the **safety point of view**, although homeopathic treatments often utilize **ultramolecular dilutions of the starting material** (above Avogadro's number), there are also homeopathic medicines of **considerably lower dilution** which **do contain molecules** that may be active in the biochemical sense.

– Hence, toxicological aspects should not be neglected especially when using **lower dilutions of unsafe starting material**.

Good Manufacturing Practices (GMP) in Homeopathy

—Good Manufacturing Practice (GMP) is that part of **quality assurance** which ensures that medicinal products are consistently **produced and controlled** to the quality standards appropriate to their intended use and as required by the marketing authorization (MA) or product specification.
—GMP is concerned with **both production** and **quality control**.

It is not enough to build a GMP facility, it is critically important that it **operate at current Good Manufacturing Practice levels.** It must have **standard operating procedures** (SOPs) in place to ensure proper **manufacturing, record keeping** and retention, **environmental cleaning**, and facility and **equipment monitoring**, to mention only a few.

GMP in Homeopathy

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Good manufacturing practice (GMP) guidelines cover the following:

- **manufacturing process**,
- **premises**
- **personnel**
- **packaging and labelling .**

GMP guidelines apply to homeopathic medicines as well as to conventional pharmaceuticals.

Failure to apply GMP may lead to major quality and safety concerns such as:

- **misidentification**
- **impurity of starting material**
- cross-contamination or incidental **contamination.**

GMP in Homeopathy

- **Manufacturers of licensed medicines** are required to prove that **their products meet basic quality standards and adhere to GMP guidelines** → The same goes **for licensed homeopathic medicines**.
- **Most established manufacturers of homeopathic medicines** have already adopted relevant measures for quality assurance procedures and manufacture according to the principles of GMP.
  - This is not always the case in countries where production of homeopathic medicines is **not subject to licensing.**
- Beyond adherence to GMP guidelines, the **distinctive characteristics of homeopathic medicines have implications for quality control.**

GMP in Homeopathy

- **Hygiene:** Pharmaceutical manufacturing facility must **maintain a clean and hygienic manufacturing area.**
- **Controlled environmental conditions** in order to prevent **cross contamination** of drug product from other drug or extraneous particulate matter which may render the drug product unsafe for human consumption.
- **Manufacturing processes** are clearly **defined and controlled**. All critical processes are **validated** to ensure consistency and compliance with specifications.
- **Instructions and procedures** are **written** in clear and unambiguous language.
- **Operators** are trained to carry out and document procedures.
- **Records** are made, manually or by instruments, during manufacture that demonstrate that all the steps required by the defined procedures and instructions were in fact taken and that **the quantity and quality of the drug** was as expected. **Deviations** are investigated and **documented.**

GMP in Homeopathy

- **Records of manufacture (including distribution)** that enable the complete history of a batch to be traced are retained in an accessible form.
- The **distribution of the drugs** minimizes any risk to their quality.
- A system is available for **recalling any batch** of drug from sale or supply.
- **Complaints** about marketed drugs are examined, the **causes of quality defects** are investigated, and appropriate **measures are taken** with respect to the defective drugs and to prevent recurrence.

GMP in Homeopathy

The unique characteristics of the manufacturing of homeopathic medicines demand **specially qualified and experienced personnel** to handle:

- **toxic materials**,
- materials, particularly **fresh ones**, that are prone to degradation processes and microbial contamination; and
- homeopathic medicines derived from **animals or human sources**.

The properties of homeopathic medicines can be compromised by:

- accidental or intentional contamination of **source materials**,
- contamination of **excipients or diluents**,
- or by the **vessel or bottle** in which the dilution is made.

Quality control of homeopathic medicines

The specific nature of homeopathic medicines have as consequences:

- Some methods for quality control and some test systems (mandatory in pharmaceutical regulation) may be **inapplicable or irrelevant**.
- These **include identification and quantification of active substance** and toxicological testing of the **final homeopathic product**.
  - Identification and assay of source materials may not be feasible **at high potencies**.

In such cases the quality should be demonstrated by **complete validation of the manufacturing and dilution process**.

- **How do we know that the pills given to patients really are the pills they wanted to give?** → All homeopathic pills have been **diluted to such an extent** that all pills are **physically and chemically identical**, **there is no test** you can do that would reveal which homeopathic remedy you have should the labels ever be removed.
- To register homoeopathic medicine → supporting data on the **production and control of the homoeopathic stock**.
- The **quality and control of stocks** is therefore of considerable importance.
- Homoeopathic stocks must be prepared in accordance with a manufacturing method set out in **a homoeopathic pharmacopoeia**.
  - The British Homoeopathic Pharmacopoeia, the German Homoeopathic Pharmacopoeia, the Homoeopathic Pharmacopoeia of the United States and homoeopathic monographs cited in the French Pharmacopoeia may be used.

Since the **Homoeopathic Directive** (92/73/EEC) applies the provisions of the Pharmaceutical Directives, (65/65/EEC and 75/319/EEC et seq), the quality standards applied to homoeopathic medicines **are similar to those applied to all other medicinal products.**

Formulation Master Files

The formulation master file should contain the following information:

- **Formulation details**
- **Development pharmaceutics**
- **Container** to be used for marketing
- **Method of manufacture, in-process controls,** including application of the diluted stock
- **Specification** of inert or un-medicated dosage form
- **Batch data** of inert or un-medicated dosage forms
- **Stability** of inert or un-medicated dosage forms.

FORMULATION

- **Complete composition**
  - Full details of the formulations including the **theoretical composition of excipients** in the final formulation.
- **Development pharmaceutica**
  - Details of any development work which is relevant to the formulation such as **preservative efficacy** data for topical creams, oral liquids and eye drops.
  - The **role of the excipients** should be described.
- **Container**
  - A description of the **container and closure** should be provided, including specifications.

MANUFACTURE

- Applicants will be expected to comply with GMP requirements and take account of any special requirements for the production of homoeopathic products as set out in the **Annex to the Orange Guide to GMP**.
- **Batch size and manufacturing formula**
  - Details of a typical batch size should be provided.
  - The **quantity of stock** to be added to the dosage form and the degree of dilution
- **The manufacturing process**
  - The key elements of the manufacturing process and any SOPs used should be summarized.
  - Details should be provided of all **measures taken to avoid cross contamination**.
  - Any **sterilization procedures** should be described.
- **In-process controls**
- **Process validation**

Process validation

GMP guidelines - general guidance for homeopathic medicines.

GMP guidelines – do not necessarily address the special requirements on, e.g., process validation or quality assessment of the starting material.

Validation of the manufacturing process is crucial:

- compliance with the **master formula** - information on the **system of potentization** (e.g., **decimal, Hahnemannian**) and the relevant pharmacopoeial method;
- **processing of raw materials** (e.g. **maceration or percolation**);
- number of **succussions** during each potentization step;
- duration of **trituration**;
- method of impregnation;
- in-process controls;
- procedures to be followed for handling of the final product.

Finished product

FINISHED PRODUCT SPECIFICATION

- The specification should control **organoleptic and physical characteristics** of the product.
- An **identity test** should be included for the stock **at low dilutions**.
  - Any special characteristics of the dosage form.
    - For example, creams should include a control for **preservatives**, eye drops should be **sterile**.
- **Analytical controls**
  - All methods used should be **pharmacopoeial** (BP or PhEur). Where a method is not appropriate, a suitable, **validated alternative** should be used.
- **Batch data**
  - Batch data should be made available for **at least three batches** which should preferably be production batches.

Finished product

Homeopathic dosage forms should comply with pharmacopoeial requirements and should be tested to determine the following:

- **identity and content** (if applicable); normally the test for uniformity of content is not appropriate either to determine the potency or to demonstrate that the source material or its characteristic constituents cannot be detected;
- **quality of dosage form** **uniformity of mass, hardness and friability for tablets – test for disintegration** can only be omitted when justified); test for **viscosity or rheology** (for ointments);
- **residual solvents, reagents or incidental contamination** as a result of the manufacturing process
  - e.g. European Pharmacopoeia 6.0, “Residual solvents; limiting residual solvent levels in active substances, excipient, and medicinal products”;
- **stability**; the stability tests for the dosage form should be the minimum requirement.

GMP in Homeopathy

Two decisive issues for the quality of homeopathic preparations:

- determining **the authenticity and the origin of the starting materials** and
- defining the **manufacturing procedure**.

- **Identity and purity testing** is performed with the starting material and with **the least diluted source employed for potentization** (e.g. mother tincture).

Consistency of product quality is assured by

- defining **appropriate specifications** especially for **starting materials**, and
- by defining the **manufacturing procedures** standardized according to official homeopathic pharmacopoeias and other officially recognized documents, and validated according to GMP.

GMP in Homeopathy

- Quality control should perform **identification and quantification of materials before processing**; using validated techniques and relevant analytical tests on source identity, possible contaminants and toxic constituents → These tests should be of pharmacopoeial or equivalent status.

Raw material used for homeopathic preparations should be characterized to determine, **the origin, the history and the nature of the starting material**:

- if of **botanical origin**, the scientific name – **genus, species, subspecies** /variety, authority and name of family (cross-reference to general name); **ecotype, chemotype, and phenotype**; part employed; the state of material; possible pharmacologically active or toxic constituents; **macroscopic and microscopic description;**
- if of **biological origin**, by the **physical, anatomical and histological state**; and
- if of **mineral or chemical origin**, by the **physical form, structural formula** and **relative molecular mass.**

Quality control of homeopathic medicines

There are two major groups of potential hazards: **source materials** and **procedures for manufacture** of the finished product.

The quality of source materials and of the excipients used in the manufacture of homeopathic medicines is important.

Homeopathic medicines may employ material from **problematic sources**:

- **nosodes** comprise **dilutions of pathogenic organs or tissues**;
- **causative agents** (**bacteria, fungi**, ova, **parasites, virus particles, and yeast**);
- **disease products**;
- **excretions or secretions**.

All materials of **animal or human origin** are at risk of containing **pathogenic agents**.

- Homeopathic medicines may be based **on toxic source materials from animals or plants,** while others, particularly in their fresh form are **prone to degradation processes or microbiological contamination.**

Plant materials may be contaminated with **pesticides and heavy metals.**

Impurities and contaminants

- Quality and safety of homeopathic medicines can be affected by **impurities and incidental constituents** ⟶ a byproduct of manufacturing and storage, contamination or low-quality raw materials, or may be formed during the production process.
  - Such constituents include **microbial toxins**, microorganisms, **metals, pesticide** residues or **degradation products**.
- Hence, the manufacturer should validate and manage the production, processing and storage practices.
- The following questions should be considered :
  - what specific **impurities and contaminants** need to be considered?
  - **what tests** (validated and reproducible limit tests which comply with a pharmacopoeia in official use or other officially recognized documents should be applied?
  - **what limits** should be specified? (If possible, pharmacopoeial references should be used – others have to be justified.)
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About PRODIS

- **PRODIS – international pharmaceutical producer** of a wide range of homeopathic remedies, organic and conventional products and vitamins.
- PRODIS products are designed for people who follow **healthy diet** and make the right choice in terms of guaranteed quality of our beneficial products, have a healthy lifestyle and care about **their future and the health of their family.**
- The factory of **PRODIS** is build up in accordance with **GMP, HACCP** and **ISO standards**.

Prodis-Helios

The range of homeopathic products HELIOS* offer **mono-component** and **poly-component products**.

The company create its **own capacities** for production of homeopathic remedies.

* *Production by the English company HELIOS license*

About HELIOS

Twenty seven years of experience; sixty dedicated homeopathic professional staff, at Tunbridge Wells and Covent Garden locations ; use of HAHNEMANN technique and a bank of over 3,500 remedies, serving customers in 140 countries

About PRODIS

Prodis planned **second phase** will completely cover homeopathic needs of the population with a wide range of homeopathic offer.

Our mission

Prodis produces **high-quality and healthy products**, and establish standards for proper nutrition and care about the health of the people. We provide our customers with **environmentally clean products**, preserving and protecting nature.

DankaD BIO / DankaD Wellance cereals and bars

Organic products **DankaD BIO:**

- **Organic oat flakes for a quick meal**
- **Cereal muesli**
- **Cornflakes**
- **BIO bars**

Dietary meals **DankaD Wellance:**

- **Classic cornflakes**
- **Cornflakes with red fruits**
- **Fruit bars**

МакSan

Range of МакSan teas:

- 9 types of herbal teas
- 8 types of organic herbal teas
- 3 types of organic classic teas

Thank you for your attention and be healthy!

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