Food Supplements Europe Guide to

Good Manufacturing Practice for Manufacturers of Food Supplements

food supplements europe

ACKNOWLEDGEMENTS

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Council for Responsible Nutrition UK, London, United Kingdom

Council for Responsible Nutrition Guidelines for Good Manufacturing Practice for Manufacturers of Food Supplements (1997)

Technical Guide to the Development, Manufacture and Compliance of Quality Food Supplements (1st edition April 2002; 2nd edition March 2007; 3rd edition April 2009)

International Alliance of Dietary / Food Supplement Associations, Brussels, Belgium

IADSA Position Paper on stability requirements for supplements (October 2012)

IADSA Stability Studies on Supplements (June 2013)

Global Guide to Good Manufacturing Practice for Food Supplements (2011)

Berry Ottaway & Associates Ltd, Hereford, United Kingdom

Guidelines for the Product Development of Food Supplements and Health Foods in the United Kingdom (1999)

European Botanical Forum, Brussels, Belgium

Quality Guide for Botanical Food Supplements: Guidance for the manufacture of safe and high quality botanical food supplements across the EU (2011)

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1 Introduction

A Food supplement is defined under European Union (EU) legislation as 'foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders'.

Food supplements that are marketed in a EU Member State have to comply with all relevant aspects of EU food legislation and any specific EU Member State national legislation in terms of their composition, manufacture and control.

As food supplements are designed to supply nutrients, particularly micronutrients, and other nutritional or physiologically active substances in predetermined amounts, specialist skills and equipment are generally used in the manufacture of the majority of such products.

The aim of this document is to produce guidelines which address the specific needs of the food supplement industry in relation to good manufacturing practice, with special attention paid to the requirements of EU food legislation. It covers the complete cycle of production and quality control of a food supplement, from the acquisition of all materials through all stages of subsequent processing, packaging and storage to the distribution or release of the finished product. As such, relevant sections of the document apply also to food supplement companies whose products are contract manufactured and also to those who are solely distributors of products.

All businesses along the food supplement supply chain should ensure that the relevant sections are complied with. For example, distributors should undertake audits on the manufacturers to ensure compliance with good manufacturing practice.

Manufacturers and distributors of food supplements should comply with all relevant EU and specific national legislation in their home country and also that of any EU countries to which they export their products. The EU legal requirements on food hygiene apply also to food supplements that are manufactured in a EU Member State for direct export to countries outside of the EU.

2 Quality Management

Quality is holistic and the interdependence of its component parts must always be recognised. Quality covers all aspects of manufacture, packaging, storage and distribution from the selection of appropriate raw materials to the stability of the product in the market shelf.

In this context, Quality Management can be defined as 'co-ordinated activities to direct and control an organisation with regard to quality'.

To achieve this, there needs to be a comprehensive system so designed, documented, implemented and controlled, and provided with personnel, equipment and other necessary resources to provide assurance that products will be safely and consistently manufactured for their intended use.

The involvement and commitment of all concerned at all stages of the development, manufacture, storage and distribution is essential for the attainment of quality. The quality objective [shall] be achieved by an integrated system which includes Quality by Design, Quality Control, Quality Assurance and Good Manufacturing Practice.

2.1 Quality by Design

An important aspect of quality management is the concept of quality by design. This means that quality is built into a product from the very first stages of product development.

Quality by design should start with the formulation and selection of raw materials and the choice of an appropriate manufacturing process and packaging materials. Each stage in a product's development should be critically evaluated to ensure that the product can consistently meet all specifications.

Guidance on the requirements for product and process development, to enable quality by design, is given in Section 5.

2.3 Good Manufacturing Practice

The basic requirements of good manufacturing practice are that:

a) all manufacturing processes are clearly defined, and known to be capable of achieving the desired ends;

b) all necessary resources and facilities are provided, including:

- appropriately trained personnel;
- adequate premises and space;
- suitable equipment and services;
- correct materials, containers and labels;
- approved procedures (including cleaning procedures);
- suitable storage and transport;

c) operators are trained to carry out the procedures correctly.

2.4 Quality Assurance

The fundamental aim of Quality Assurance is reproducibility, so that the product sold to the consumer is always within the agreed quality measure and as near identical as possible. The objectives of Quality Assurance are achieved when processes have been defined which, when followed, will yield a product that complies with its specification, and when the finished product:

- contains the correct ingredients in the correct proportions;
- has been correctly processed, according to the defined procedures;
- is of the purity required;
- is enclosed in its proper container, which;
- bears the correct label (or is otherwise suitably marked or identified);
- is stored, distributed and recommendations given for its subsequent handling in accordance with the recommended storage conditions, so that its quality is maintained throughout its designated or expected life.

Quality Assurance generally involves the following:

- procedures are written in instructional form, in clear and unambiguous language, and are specifically applicable to the facilities provided;
- the monitoring of the Quality Assurance procedures of suppliers of raw and packaging materials, with regular audits where possible;
- the development of a Supplier Quality Assurance procedure, laying down the criteria for selection, approval, review and ongoing approval, to ensure that the supplied products and services meet the manufacturer's requirements;
- records are made during manufacture (including packaging), which demonstrate that all the steps required by the defined procedures were in fact taken, and that the quantity and quality produced were those expected;
- records of manufacture and distribution, which enable the complete history of a lot (batch) to be traced, are retained in a legible and accessible form;
- a system is available to withdraw or recall from sale or supply any lot or product, should that become necessary;
- rapid feedback of information to manufacturing personnel, e.g. as summaries of quality performance data and related advice, as appropriate, to enable rapid modification or corrective action to be taken when required;
- rapid feedback of information to the purchasing department with regard to any concerns of quality relating to purchased materials, e.g. raw materials, packaging materials etc.;
- the examination of samples relating to customer/consumer complaints, with accompanying investigation of any causes of defects, where feasible, and the necessary steps advised for corrective action to be taken to prevent recurrence (see Chapter 13);
- changes to relevant legislation are noted and applied where applicable, particularly legislative amendments to compositional standards or labelling requirements, which may require adjustments to specifications for raw materials or finished products.

Quality Assurance systems should be constantly reviewed, via self-inspections and/or third party audits, to ensure their continuous effectiveness (see Chapter 14).

2.4 Quality control

Quality Control is the obligation to have in place an effective monitoring system that verifies compliance with specified requirements and parameters, and defines suitable corrective action in the event of non-compliance. As with Quality Assurance, Quality Control must be an ongoing process to ensure that quality of the product is maintained.

To achieve effective control of quality:

- there should be a clear delineation of the relevant authorities and responsibilities of the Production Management and the Quality Control Management functions, to prevent any confusion or misunderstanding;
- ideally, the Quality Control Management and the Production Management should be on separate reporting structures;
- the Quality Control Management should have the authority to make independent decisions on the product quality;
- adequate facilities and staff should be available for sampling, inspecting and testing starting materials, packaging materials, intermediate, bulk and finished products, and where appropriate, for determining environmental quality;
- samples of starting materials, packaging materials, intermediate products, bulk products and finished products should only be taken by authorised personnel and using methods approved by the person responsible for Quality Control;
- results of the inspection and testing of materials, and of intermediate, bulk or finished products, should be formally assessed against specification by the person responsible for Quality Control (or a person designated by him) before products are released for sale or supply;
- product assessment should include a review and evaluation of relevant manufacturing (including packaging) documentation;
- sufficient reference samples of starting materials and finished products should be retained (the latter in the final pack for the finished product) to permit future examination if necessary.

3 Personnel and training

Compatible with the size and type of business there should be sufficient personnel at all levels with the ability, training experience and, where necessary, the professional and technical qualifications, appropriate to the tasks assigned to them. Their duties and responsibilities should be clearly explained and recorded as job descriptions or by other suitable means. Deputies/delegates should be appointed and appropriately trained to cover the absence of key personnel; these positions should be formally authorised and documented.

3.1 Training

Training for each employee should cover the following:

- particular tasks relevant to the employee's specific role;
- general good manufacturing practice;
- the importance of, and factors involved in, personal hygiene.

Each new employee should receive training upon employment. This training should be repeated, modified or extended as required. Any concerns with language comprehension or reading ability should be considered, as should methods for assessing an employee's understanding of the training received.

It is important that refresher training is given on GMP, and personal hygiene in particular, if poor hygiene practices are identified.

Appropriate training on GMP and personal hygiene should additionally be given to any employees who may come into contact with the manufacturing areas or activities, for example, office, maintenance and cleaning personnel.

Persons* involved in the training of food supplement handlers and in the administration of internal and external GMP audits should be trained to a nationally recognised standard where applicable.

Appropriate training should be planned and recorded for every employee.

*Persons - in this context allows internal personnel or external consultants to be used.

3.2 The training of food supplement handlers

The food hygiene Regulation requires food businesses to ensure that food supplement handlers are supervised and instructed and/or trained in hygiene matters commensurate with their work activity.

Food supplement businesses are responsible for identifying the detailed measures necessary and relevant to their own operation. These measures should ensure that all potential food supplement handlers, including supervisors and managers, have the knowledge necessary for them to play their part in handling the product hygienically so that the health of the consumer is properly safeguarded. What is appropriate in one business may not necessarily be appropriate in another.

For example:

– some businesses have a high turnover of casual workers, making formal training difficult, but making good instruction and supervision very important;
– the nature and type of supervision necessary will depend on the number of food supplement handlers within the unit of the business and the nature of their work.

The supervision, instruction and/or training needs must relate to the work undertaken by food supplement handlers themselves and those in the nearby environment and the risks to product safety presented by their activities. In deciding on the relative risks presented, businesses should consider:

- The nature of the food supplements with which the operators work, e.g. capsule, tablet, liquid or powder forms of food supplements may each present different concerns.
- How operators handle food supplements; i.e. what processing or preparation is being undertaken? Are there risks of which the food supplement handler particularly needs to be aware, e.g. microbiological, chemical or foreign body hazards? This may include, for example:
  - ensuring that operators are aware, when handling food supplements, of the need for high personal hygiene standards.
  - ensuring that all personnel are aware of procedures on a production line to check for and reduce the risk of foreign bodies such as glass or metal in products;
  - where applicable, ensuring that all personnel are aware of procedures to keep toxic substances, such as cleaning materials, separate from raw materials and intermediate, bulk or finished products.

3.3 Personal hygiene

Personal cleanliness and clothing: The Codex General Principles (7.1 and 7.4)1 contain helpful general advice on these requirements.

Infected food supplement handlers: The Codex General Principles contain helpful general advice on these requirements (see Annex V).

3.3.1 Mandatory requirements

i. Personnel must keep as clean as is reasonable all parts of their person, clothing or overclothing liable to come into contact with the product;

ii. Personnel with any open cut or abrasion on any exposed part of their person should not work on open product, but if permitted to continue working in the manufacturing area, must cover the wound with a company-issued blue metal detectable plaster. Company-issued plasters must also be used to replace standard plasters that have been applied to wounds outside of the workplace. All plasters must be formally issued and their application must be checked at the end of production. The loss of any plaster during production must be reported immediately to the relevant manager and the procedures for the control of foreign body contamination must be followed;

iii. Personnel must not spit, smoke, use snuff or chew gum in any manufacturing area, particularly in 'open product' areas. Food and drink must not be taken into or consumed in manufacturing areas;

iv. Personnel must avoid sneezing or coughing over the raw materials, intermediate product or finished product;

v. Personnel must wear sufficient clean and washable or disposable overclothing (including headgear and, where appropriate, neck-covering and/or beard snood);

vi. Persons confirmed as suffering from, or carriers of, certain kinds of infection (typhoid, paratyphoid, any other salmonellae infections, or amoebic or bacillary dysentery or any staphylococcal infection, which could include an infected cut) likely to cause poisoning to the consumer, must not be allowed in any manufacturing areas where they may come into contact with the raw materials, intermediate product or finished product; personnel suffering from any such infection must inform the manufacturer, who must immediately inform the relevant Health Authority.

3.3.2 Best practice requirements

In addition to the mandatory requirements, good manufacturing practice may involve:

i. the provision of safety footwear and suitable protective over-clothing, and the laundering thereof;
ii. the provision of a separate and suitably equipped changing room;
iii. the implementation of pre-employment medical checks or certification, so that no person suffering from, or a carrier of, any of the specified kinds of infection is employed as a food supplement handler;
iv. the implementation of a policy to ensure that, before they enter any manufacturing area, visitors and contractors are asked whether they have suffered or been in contact with any recent illness that may be a potential contamination risk to products;
v. the provision of clear information to all contractors of any hygiene requirements specific to the manufacturing area in which they will be working;
vi. the active encouragement of personnel to report any infections from which they may suffer, and the encouragement of supervisory personnel to look out for signs and symptoms of such conditions, so that any need for medical examination and/or possible exclusion from working in the manufacturing areas can be considered. In particular:
    – jaundice;
    – diarrhoea;
    – vomiting;
    – fever;
    – sore throat with fever;
    – visibly infected skin lesions (boils, cuts, etc.);
    – discharges from the ear, eye or nose;
vii. the implementation of 'return to work' procedures following illness or foreign holidays, particularly in relation to diseases that may have been contracted while away;
viii. the implementation of a personal medication procedure to control personal medicines that could be a potential contamination risk to the product, such as decongestant nasal sprays and those for diabetes or asthma;
ix. the prohibition of the wearing of wrist watches, jewellery and other potentially hazardous objects, except for plain wedding rings or plain sleeper earrings (without studs) for visible piercings in 'open product' areas;
x. the implementation of a clear policy on items that may be allowed for medical, ethnic or religious reasons (e.g. jewellery, head coverings etc.), and the procedures that should be followed to ensure the health and safety of all personnel, while minimising any potential contamination risk to products;
xi. the implementation of a clear policy on the wearing of certain make-up, associated items and perfumed products, to minimise the risk of foreign body or other contamination; in particular:
    – false eyelashes, false fingernails and nail varnish should be prohibited;
    – personnel should be encouraged to keep fingernails clean and short;
    – strongly perfumed products such as eau de toilettes, perfumes or aftershaves should be prohibited in 'open product' areas;
xii. the implementation of a clear policy on the carrying of loose items, such as pens or mobile phones, in the manufacturing areas; outerwear (coats or overalls) should not have external pockets;

xiii. the removal of protective outerwear whenever leaving manufacturing areas, e.g. for refreshment breaks, toilet breaks, end of working shift etc.;

xiv. the implementation of procedures for hand washing, ensuring personnel wash and dry hands immediately:

- prior to commencing work;
- following toilet or rest breaks;
- when returning to manufacturing areas;
- after cleaning or handling waste;
- after sneezing.

xv. the application of antibacterial cream, foam or gel after hand washing when working in areas of high microbiological sensitivity;

xvi. the development of a procedure to control glove issue, to minimise the risk of foreign body contamination; it should be stressed during personnel training that the wearing of gloves does not reduce the need for effective hand washing;

xvii. the use of the correct procedures in the event of breakage of glass or hard plastic lenses in spectacles or the loss of contact lenses in the manufacturing areas.

4 Premises and equipment

Buildings should be located, designed, constructed, adapted and maintained to suit the operations carried out in them and to facilitate the protection of materials and products from contamination or deterioration.

Equipment should be designed, constructed, adapted, located and maintained to suit the processes and products for which it is used and to facilitate protection of the materials handled from contamination or deterioration.

4.1 General requirements for premises

a) Premises must be designed to allow cleaning and maintenance to be carried out to a high level.

b) Layout, design, construction and size should be such as to:
   - permit hygienic cleaning, good hygiene practices, and suitable temperature/humidity conditions where necessary;
   - prevent cross contamination in the premises and contamination from external sources such as pests.

c) Facilities that must be provided:
   - ventilation;
   - lighting;
   - adequate supply of potable water;
   - drainage facilities;
   - washbasins and lavatories;
   - changing facilities for staff.

4.2 General requirements in rooms where food supplements are prepared, treated, or processed

a) Construction and design.

   The following surfaces and fittings must be smooth, free of crevices and easy to clean:
   - floor surfaces;
   - wall surfaces (including any horizontal surfaces);
   - ceilings and overhead fixtures;
   - windows;
   - doors;
   - surfaces in contact with raw materials, intermediate product or finished product.

b) Facilities.

   Adequate facilities must be provided for the cleaning, disinfecting and storage of tools and equipment where necessary. These facilities should be constructed of corrosion-resistant materials, be easy to clean and have an adequate supply of hot and cold water.

4.3 Premises

Premises should:

- provide sufficient space to suit the operations to be carried out, including appropriate storage areas, as applicable;
- allow an efficient flow of work;
- facilitate effective communication and supervision;
- be sited with due regard for the provision of services needed and to avoid contamination from adjacent activities. In existing premises, effective measures should be taken to avoid such contamination;
- be maintained in a good state of repair. The condition of buildings should be reviewed regularly, and repairs effected where necessary. Special care should be exercised to ensure that building materials of construction, repair or maintenance operations are not allowed to affect adversely product quality or integrity;
- be constructed and maintained with the object of protecting against the entrance and harbouring of vermin, birds, insects, other pests and pets;
- be maintained in a clean and tidy condition (including processing areas, laboratories, stores, passageways and external surroundings).

Manufacturing areas should not be used as a general right of way for personnel or materials, or for storage (except of materials in process).

4.3.1 Ventilation and lighting

Buildings should be effectively lit and ventilated, and should:

- be so designed that working conditions (e.g. temperature, humidity, noise levels) are such that there is no adverse effect on the product, either directly or indirectly, via the operator;
- be equipped with suitable air control facilities (including temperature, humidity and filtration where necessary) appropriate both to the operations undertaken within them and to the external environment;
- have suitably designed ventilation systems, to prevent the introduction of contaminants into products (e.g. noxious vapours, gases or solids), whilst giving due regard to the local environment and avoiding external odour, noise or dust emissions;
- have ventilation systems constructed in such a way as to enable filters and other parts requiring cleaning or replacement to be readily accessible;
- ensure that all associated pipework, light fittings, ventilation points and other services in manufacturing areas are sited to avoid creating recesses which are difficult to clean; services should preferably run outside the processing areas and should be sealed into any walls and partitions through which they pass;
- ensure that all lighting appliances are completely covered by shatterproof plastic diffusers or sleeve covers or, if this is not possible, by a metal mesh screen sufficiently fine to contain any pieces of glass in the event of shattering.

Procedures should be put in place detailing the action to be taken in the event of any breakage or damage to glass, ceramic or hard plastic items.

4.3.2 Floors, walls and ceilings

Floors in manufacturing areas should be of adequate construction and material for the wear and tear and conditions of manufacture encountered and should:

- be made of impervious and non-absorbent materials;
- be laid to an even surface;
- be free from cracks and open joints in areas where product is exposed;
- have drains of adequate size with trapped gullies and proper ventilation; any open channels should be shallow to facilitate cleaning.

Walls in manufacturing areas should be constructed from materials that avoid tainting or otherwise contaminating the product and should:

- be intact and free of faults such as cracks, flaking etc.;
- be finished with a smooth impervious and easily cleaned surface;
- have any windows constructed from toughened glass or plastic; these should:
  - o be adequately screened and secured;
  - o have any ledges sloped away from the glass at an angle, to prevent items being left on them;
- have all doors constructed with smooth, non-absorbent surfaces to facilitate easy cleaning and disinfection, when necessary.

Ceilings should be so constructed and finished that they can be maintained in a clean condition. In particular, suspended ceilings and overhead fixtures must be constructed and finished so as to prevent the accumulation of dirt and to reduce condensation, the growth of undesirable mould and the shedding of particles.

The coving of junctions between walls, floors and ceilings in critical areas is recommended.

4.3.3 Cleaning and site hygiene

All operations should be carried out in such a way that the risk of contamination of one product or material by another is minimised.

It is recommended that a Site Hygiene Plan be established appropriate to the manufacturing operation. The Site Hygiene Plan should be regularly reviewed and amended when deemed necessary, in order to maintain a hygienic manufacturing site. The Plan should include written cleaning procedures and schedules for:

- manufacturing and storage areas;
- receiving and despatch areas;
- personnel hygiene facilities;
- vehicles and containers used for transport and distribution (see also Chapter 9);
- external premises.

Vacuum or wet cleaning methods are to be preferred. Compressed air, hoses, pressure cleaners, brooms and brushes should be used with care, so as not to incur the risk of product contamination.

Products used for cleaning and disinfecting purposes should be appropriate for their required function and should be stored in a location which is separate from the processing areas.

4.3.4 Waste

Waste material should not be allowed to accumulate in the manufacturing, storage or other areas. It should be collected in suitable, clearly identifiable, receptacles for removal to specific collection points outside the buildings, and disposed of at regular and frequent intervals. The use of a specific colour, which is immediately recognisable within the company, is recommended for the waste containers.

Particular control must be taken with the disposal of printed packaging materials or raw materials and rejected products.

Disposal of all waste must be in compliance with EU legislative requirements on waste, as implemented by Member States, and must be appropriately documented (see also 6.9).

4.3.5 Receiving and despatch areas

Receiving and despatch areas should:

- provide protection from the weather for materials or product in transit;
- provide a defined deboxing/debagging area for raw materials or packaging materials that arrive in external packaging.

4.3.6 Personnel hygiene facilities

Cloakrooms or changing rooms should be provided. These should:

- be separate from, or partitioned from, manufacturing areas;
- provide separate accommodation for clothing and footwear not being worn during working hours.

Adequate sanitary conveniences (flush lavatories) must be provided and these:

- must be kept clean;
- must be connected to an adequate drainage system;
- must not open directly to manufacturing areas.

Notices should be posted reminding users to wash and dry their hands after using the convenience.

Hand-wash basins and accompanying facilities (hot and cold water or temperature controlled hot water, soap or detergent, nail brushes and disposable towels or other suitable drying facilities) must be provided and kept clean, at convenient places accessible to personnel. Battery or electrically powered water taps equipped with touch-free, motion detector photocells are recommended.

Rest and refreshment rooms should be separate from other areas.

First aid materials must be provided in a place readily accessible to authorised First Aiders.

4.3.7 Pest control

There should be either trained personnel to oversee infestation control or a professional infestation control company should be employed for regular inspection, advice and treatment if required. Procedures for pest control should be commensurate with the local habitat and risks.

Useful general information on pest control can be found in the Codex General Principles (see Annex V).

4.4 Equipment

Equipment should be so designed and arranged as to protect the contents from external contamination and should not endanger a product through contamination from leaking joints/glands, lubricant drips and the like, or through inappropriate modifications or adaptations.

Plant and equipment should:

- be designed with sound, secure, quick-release systems for inspection and disassembly;
- be sited in such as manner as to enable appropriate precautions for ventilating fumes from power driven equipment, heaters etc. to be taken;
- be checked for cleanliness and integrity before every use;
- be cleaned and serviced immediately after use and any faults recorded.

Cold storage equipment should:

- be fitted with a temperature-measuring device that indicates the temperature within the storage compartment;
- be fitted with a system that records the temperature automatically at regular intervals, otherwise a system should be in place for manual temperature recording;
- be fitted with an alarm system, (linked to a system that notifies designated persons who are authorised to evaluate the alarm), which gives an alert if there is a significant change in temperature;
- be regularly temperature-calibrated (at least once a year).

Where the lubrication of equipment is necessary, only food-grade quality lubricant should be used.

4.4.1 Surfaces and materials in contact with food supplements

All surfaces and materials in contact with food supplements must comply with the Materials and Articles in Contact with Food Regulation and should:

– be inert to the food supplements under the conditions of use and should not yield substances which might migrate or be absorbed into the food supplements;
– be microbiologically cleanable, smooth and non-porous so that particles are not caught in surface crevices and become difficult to dislodge;
– be visible for inspection or the equipment should be easily dismantled for inspection, or it should be demonstrated that routine cleaning procedures eliminate the possibility of contamination;
– be readily accessible for manual cleaning or, if not readily accessible, then easily dismantled for manual cleaning, or if clean-in-place techniques are used, it should be demonstrated that the results achieved without disassembly are the equivalent of those obtained with disassembly and manual cleaning.

All interior surfaces in contact with food supplements should be so arranged that the equipment is self-emptying or self-draining.

Exterior surfaces of equipment not in contact with food supplements should be so arranged to prevent harbouring of soils, micro-organisms or pests in and on the equipment, floors, walls and supports.

There should be detailed written instructions for cleaning and sanitising. Specified materials, methods, safety precautions and suitable facilities should be provided.

4.4.2 Equipment maintenance and servicing

Preventive maintenance should be considered for all equipment and components. A maintenance procedure should be developed and should:

- be based upon risk assessment;
- cover both preventive and responsive maintenance;
- include the checks to be undertaken before and after the equipment is used.

The maintenance procedure must be brought to the attention of any maintenance and machine-servicing contractors.

Any components (e.g. nuts, springs, clips, etc.) found to be missing during pre- or post-manufacturing checks or routine maintenance must be reported immediately and the procedure for foreign body contamination should be followed. This should include the quarantine of all lots produced since the previous check, until the missing item is found or the lots have been shown to be clear, for example, following metal detection or sieving.

Procedures should be developed outlining the action to be taken in the event of a recognised malfunction of the inspection and testing equipment. These should include the identification, isolation and retesting of all lots produced since the previous acceptable check.

4.4.3 Calibration of equipment

Regular calibration of all measuring equipment (weight, volume, temperature, etc.) should be carried out using appropriate standards.

Detailed records of the calibrations should be maintained. These should be regularly checked to ensure that all calibration is up to date and that the equipment is working to the required level of accuracy.

Calibrated instruments should be protected against accidental or malicious alteration of settings. Any adjustments to calibrated equipment should:

- only be made by authorised personnel;
- follow prescribed procedures;
- be formally recorded.

If an instrument is found to be inaccurate, the potential impact on the lots processed since the previous calibration must be evaluated.

4.5 Water supply

Potable water should be used for all manufacturing purposes and, where applicable, should be periodically analysed according to the requirements of any national legislation. Certain operations may require higher standards of water, e.g. de-ionised water.

In locations where a potable water supply is not standard supply, documentation should be obtained and retained that confirms the water used in production is of at least the minimum standard required.

If recycled water is used for manufacturing purposes it must be of the same standard as potable water.

When manufacturing liquid preparations or other products vulnerable to microbiological contamination, filtering systems or disinfection systems, such as ultraviolet (UV) systems, should be installed on the water supply.

Non-potable water may be used for e.g. fire control, steam production, refrigeration, flushing of toilets and other similar purposes, but it must circulate in a separate and clearly identified system. Non-potable water must not connect with or otherwise enter the potable water systems.

5 Product and process development

A risk assessment should be conducted from the earliest stages of product and process development to eliminate or minimise potential hazards and to aid the incorporation of effective control parameters into the product design.

Since 2006, it has been a mandatory requirement in all EU member states that a Hazard Analysis Critical Control Point (HACCP) system be applied to all stages of manufacture and distribution. The HACCP system is covered in detail in Chapter 10.

Prior to the development of a new food supplement or the modification of the formulation for an existing product, there are essential checks that should be made to verify that the final product will be compliant with all relevant EU and national Member State legislation.

Changes to all relevant legislation must be constantly monitored to make certain that every product remains fully compliant with the law.

The essential points that need to be considered during product development or reformulation are outlined below. These sections include requirements at the product development stage that do not necessarily fall directly under Good Manufacturing Practice (GMP). However, if the product development stage is not carried out correctly, then even the best GMP may not produce a product that can be legally sold in the country of intended market. These checks are therefore extremely important to the quality of the final product.

The documentation that arises as part of the product development stage is an integral part of the GMP that follows as, for example, it can act as the standard for acceptance of raw materials, final product checks etc.

5.1 Legality of ingredients

The following must be checked:

- the formulation complies with any specific compositional legislation;
- all additives are permitted and are within the maximum usage levels laid down for food supplements in the additives Regulation;
- official approval has been obtained for new / novel ingredients, where applicable; i.e. for ingredients that were not in use in foods prior to May 1997, as per the Regulation on novel food and food ingredients;
- all components of compounded ingredients are permitted;
- ingredients that are prohibited in the countries of intended market are not present (this can be of particular relevance to botanical ingredients);
- the levels of active ingredients, particularly micronutrients, are permitted in the countries of intended market;
- the irradiated status of ingredients, particularly botanicals;
- the genetically modified (GM) status of ingredients, in particular that any GM ingredient or GM source of an ingredient is authorised for use in foods in the EU;
- that the composition does not infringe patents.

See also Annex II.

5.2 Safety of ingredients

The following must be checked:

- the raw materials and final product meet microbiological criteria, as applicable, to ensure product safety;
- where relevant, the formula has been considered for potential chemical interactions;
- the micronutrient levels (e.g. vitamin A, iron) are within accepted safety levels and are appropriate for the target population;
- the ingredients and final product comply with EU legislation on contaminants;
- any botanical ingredients have been sufficiently characterised (microscopic / chemical identification) and are fully compliant with their specification;
- extraction solvents used for the preparation of botanical extracts and any solvent residue limits are fully compliant with EU legislation on extraction solvents for use in foods;
- where relevant, safety checks have been carried out on individual and combinations of botanicals at the proposed levels of use;
- potential allergen sources have been identified, to ensure correct labelling (see 5.4).

5.3 Stability of formula

The requirements of EU legislation on general food law, on food supplements and on the provision of food information to consumers / food labelling mean that:

- a food supplement must declare on the label the quantity of nutritional or physiologically active ingredients that are present in the product;
- the label must not mislead the consumer as to the quantity of such ingredients contained within the product, i.e. the amount claimed on the label must be the amount present in the product; and
- the claimed date of minimum durability (the Best Before date) must be the date until which the food supplement can still meet the label claim.

The company responsible for placing the food supplement on the market must ensure that the shelf life of the product has been correctly determined, to enable an accurate Best Before date to be placed on the label. If the Best Before date is determined by a contract manufacture, then confirmation should be given to the company whose name is on the label that the dates provided are correct (see also Chapters 11 and 15).

The Best Before date should apply from the date of production for each lot of finished product and it should take into consideration all available information obtained from:

- data from an appropriate stability study on the specific product;
- extrapolation of data from stability studies on similar products (similar products are those with similar matrices and containing the same or very similar combinations of ingredients);
- bibliographical references from scientific literature relating to the stability of the ingredients;
- combinations of the above.

As a minimum, the following properties should be examined under the storage conditions stated on the product label, to check stability of the product:

a) organoleptic properties
   - appearance, particularly colour stability;
   - taste, particularly flavour stability;
   - smell.

b) chemical, physical and microbiological properties, in particular:
   - that the final product does not permit microbiological growth;
   - fat stability (e.g. oxidation/rancidity in fish or vegetable oils);
   - physical changes on storage (appearance, hardness);
   - that no interactions between ingredients have occurred (to verify previous theoretical checks);
   - that the claimed quantities of nutritional or physiologically active ingredients in the product are present to the end of the stated shelf life;
   - the stability in use of the finished product, i.e. the stability of the product after opening the pack and during the expected consumption period.

5.4 Legality of labelling

It must be confirmed that statutory label declarations are in the language(s) required by the countries of intended market and that the information provided complies with all relevant legislation; in particular:

- the quantity of nutritional or physiologically active ingredients that are present per daily intake of the product are stated in the format required by the legislation;
- any GM ingredients or ingredients produced from GM sources are labelled in compliance with EU legislation on GM traceability and labelling;
- any relevant compositional statements (e.g. laxative statement, indication of sweeteners) are in compliance with the provision of food information to consumers / food labelling legislation and are in the appropriate position;
- ingredients that fall within the legally defined list of known substances or products causing allergies or intolerances are highlighted in the ingredients list on the label, in accordance with the requirements of the food information to consumers / food labelling legislation;
- appropriate warnings are made for micronutrient levels (e.g. iron, vitamin A), where required nationally;
- all components of compounded ingredients are listed in compliance with the provision of food information to consumers / food labelling legislation;
- any products that have been legally irradiated or contain legally irradiated ingredients, are labelled in accordance with the legislation on foods and food ingredients treated with ionising radiation;
- any other national legal requirements for product labelling are met for the EU Member State of intended market.

5.5 Legality of claims

The following must be checked:

- claims are not misleading and are fully in compliance with the Regulation on nutrition and health claims;
- although food supplements are exempted from the provision of nutrition information (i.e. energy, fat, protein etc.), where this is voluntarily provided, the energy (calorie) calculations must be in compliance with the provision of food information to consumers / food labelling legislation;
- vitamin and mineral calculations are in compliance with legislation and utilise EU-accepted methods for standardisation;
- active components are correctly calculated, taking into consideration moisture, assay, levels etc.;
- the dose of product in relation to intended nutrition claims is supported by scientific evidence;
- the minimum levels for claims can be met at end of declared shelf life and can be met at the lower end of raw material specification ranges.

5.6 Legality of packaging

- packaging should be appropriate for the product with light/moisture/oxygen barriers;
- product contact surfaces of packaging should be in compliance with EU legislation on materials and articles in contact with foods;
- packaging recoverability (e.g. recycling) should be in compliance with EU legislation on packaging and packaging waste;
- the heavy metal content of all packaging must be compliant with EU legislation on packaging and packaging waste;
- packaging is appropriate for maintaining stability of the product throughout shelf life;
- packaging is not misleading i.e. pack size should not be excessively larger than the contents volume;
- the minimum quantity of packaging is used, while allowing for safety, hygiene and acceptance for the packed product and consumer;
- statutory label information is legible, intelligible and in the appropriate position as required by the provision of food information to consumers / food labelling legislation.

See also section 6.5.

5.7 Confirm by appropriate verification procedures that the product can be made safely and consistently

- take into consideration tolerances on raw material specifications and the ability to meet claims at extremes of specification ranges;
- ensure homogeneity can be achieved by the mixing process;
- if possible, perform trials on production lot sizes to check de-mixing during in-process handling and packing;
- ensure raw materials and product are protected from effects of moisture/oxygen/light during storage and manufacturing processes;
- check tolerances on finished product specifications and the ability to meet claims at extremes of specification ranges;
- check integrity of pack seals/barriers to ensure packaging consistently seals.

6 Manufacture

The operations and processes used in manufacture should, with the premises, equipment, materials, personnel and services provided, be capable of consistently yielding finished products which conform to their specifications and are suitably protected against contamination or deterioration.

Defined and documented manufacturing procedures, including associated activities and precautions, are necessary to ensure that all concerned understand what has to be done, how it is to be done, who is responsible, and to avoid mistakes which could affect product safety and quality. Such procedures should be provided in the Master Manufacturing Instructions for each product.

All personnel responsible for decision-making or authorisation at any stage during the manufacturing process should be formally defined.

6.1 Verification of production processes

Before the introduction of Master Manufacturing Instructions for a product, trials should be carried out to establish whether the formulation, methods and procedures specified therein:

- are suitable for factory production; and
- are capable of consistently yielding products within the Finished Product Specification.

If necessary, amendments and further trials should be made until these conditions are satisfied.

Similar evaluation should be carried out in connection with any significant proposed change of raw material, plant or method.

Similar evaluation should be carried out periodically, to check that:

- the Master Manufacturing Instructions are being followed;
- they still represent an effective and acceptable way of achieving the specified product; and
- they are still capable of consistently doing so.

Tests should be conducted in accordance with previously defined specifications and procedures and a record made of the results. The requirement, extent and degree of the work will depend on the nature and complexity of the product and process as determined by the manufacturer.

6.2 Documentation

Documents should be written in clear, unambiguous, instructional form in the official working language of the manufacturing facility and should form a key part of operator training. Due regard should be given to reading or language difficulties of some personnel. Supervisors should confirm by observing and questioning the production operator, for example, that the instructions, and significance of the instructions, are fully understood.

6.2.1 Product-specific documentation

Each product should have:

- defined and authorised Master Formula.
- defined and authorised Master Method and/or Master Manufacturing Instructions.
- related Standard Operating Procedures.

6.2.2 General manufacturing documentation

The following documents should be developed and brought to the attention of all relevant personnel:

- Plant Operating Instructions for production operators.
- Written instructions detailing the action to be taken in the event of stoppages, breakdowns or other unexpected events that may alter the planned flow of production.
- Formal procedures setting out the action to be taken in the event of foreign body contamination at any stage during the manufacturing process.

6.3 Production

Before any manufacturing operation begins, steps should be taken to ensure that the work area and equipment are clean and free from any starting material, packaging material, products, product-residues or documents not required for the current operation.

Production staff should follow the defined and authorised procedures for each stage of each manufacturing process. Any divergence from defined procedures must only be by prior agreement, and must be recorded and agreed by the person responsible for quality control, or their appointed deputies/delegates.

All personnel should be actively encouraged to immediately report any incident of contamination or potential contamination of the raw material, intermediate or finished product.

The details of all operations should be recorded on the Lot Manufacturing Record or Lot Packaging Record.

At all times during processing, all materials, bulk containers and major items of equipment used should be labelled or otherwise identified with an indication of the product or material being processed, its strength (where applicable) and lot number. Where applicable, this identification should also indicate the stage of manufacture and status.

The status label of the manufacturing area and equipment should also contain information regarding the previous product manufactured and the cleaning status when at rest.

6.4 Raw materials/ingredients

Each raw material/ingredient should have and be in compliance with its specification.

6.4.1 Delivery of raw materials

If necessary, any pallets or deliveries should be cleaned before being brought into the storage area.

Each delivery lot should be given a reference code to identify it in storage and processing. The documentation should be such that, if necessary, any lot of finished product can be correlated with the deliveries of the respective raw materials used in its manufacture and with the corresponding laboratory records. Deliveries should be stored and marked in such a way that their identities do not become lost.

Companies must keep records of the suppliers of every lot of ingredient received, to fulfil the mandatory traceability requirements as laid down in the Regulation on the general principles and requirements of food law (see Annex IV). Records must be kept available for inspection by the competent authorities for the period required by national legislation.

Upon receipt, raw materials should be quarantined until inspected. Temporarily quarantined material should be located and/or identified in such a way as to avoid risk of its being accidentally used. Where there is a validated electronic system in place to manage the quarantine system, the status should be appropriately indicated electronically.

- material found to require pre-treatment before being acceptable for use should be suitably identified and remain quarantined until pre-treatment;
- material found totally unfit for use should be suitably identified and physically segregated pending appropriate disposal.

Quarantined material should not be released until:

– the supplier's Certificates of Analyses have been checked and confirmed; or
– the material has been sampled and tested in accordance with agreed specifications; and
– authority for the release has been given by Quality Control.

Release should not be based upon supplier Certificates of Analyses until confirmation of the reliability of the supplier's test results has been obtained through analytical testing or a process of supplier qualification.

Particular care should be taken where a delivery of containers appears from markings to include more than one lot of the supplier's production, or where the delivery is of containers re-packed by a merchant or broker from a bulk supply. Where appropriate, immediate checks should be carried out for off-flavours, off-odours or taints, and testing should include test of identity, i.e. establishing that the substance is what it is purported to be.

For multi-container deliveries, where it is impracticable to check the identity of the contents of every container on arrival, operators should be trained and encouraged to report immediately anything unusual about the contents when a fresh container is brought into use.

In the case of a bulk delivery by tanker, preliminary quality assessment should be made before discharge into storage is permitted, and systems should be in place so that the material can be traced to a certified source.

6.4.2 Storage and issue of raw materials

Stocks of raw materials in store should be inspected regularly and sampled/tested where appropriate, to ensure that they remain in acceptable condition. All raw materials should be stored:

- under hygienic conditions;
- in specific conditions (e.g. of temperature, relative humidity) appropriate to their respective requirements, as indicated in their specifications;
- with due regard to the requirements of any legislation relating to the control of substances deemed hazardous to health.

Authorised procedures and documentation should be established and followed for the issue of raw materials from store, (for example, Standard Operating Procedures).

In issuing raw materials from store for production use, correct stock rotation should normally be observed, unless otherwise authorised or specified by Quality Control.

When a raw material has been issued but not used as planned (e.g. because of a plant stoppage), Quality Control should advise as to its disposition.

Depending on the product being manufactured, the ingredients involved and the nature of the process and equipment, the dispensing of the required quantities of ingredients could take various forms, including manual dispensing by weight or volume, or continuous metering by volume; the form(s) actually taken should be stated within the Master Manufacturing Instructions. In each case, the weighing and/or measuring equipment should have the capacity, accuracy and precision appropriate to the purpose, and the accuracy must be regularly checked and documented (see also 4.4.3).

Where lot quantities of an ingredient have to be dispensed manually into containers in advance, this should be done in a segregated area. Where manual pre-dispensing of relatively small and accurate quantities (for example, of micronutrients or additives) is required, this should be done by, or under direct supervision of, suitably trained staff. All weighings should be checked by a second operator or by use of a validated computerised weighing control system.

Records should be kept to enable the quantities of materials issued to be checked against the quantity or number of lots of product manufactured.

Where an operator controls the addition of lot quantities of one or more ingredients to a lot, the addition of each ingredient to a lot should be recorded at the time on a Lot Manufacturing Record, to minimise risk of accidental omission or double addition.

The final yield, and any significant intermediate yield, of each production lot should be recorded and checked against the expected yield within defined limits. In the event of a significant variation, steps must be taken to prevent release or further processing of the lot (or of any other lots, or products processed concurrently, with which it may have become admixed) until an adequate explanation can be found which permits release or further processing.

6.5 Packaging and labelling materials

Each packaging material should have and comply with its specification (including any legal requirements), which should be such as to ensure that:

- the packaging complies with the requirements of EU legislation on packaging and packaging waste, which places an obligation on the company to use the minimum packaging while allowing for safety, hygiene and acceptance for the packed product and consumer;
- the packaging provides adequate protection to ensure the chemical and physical stability of the product during the declared shelf life under stated conditions of storage and use;
- in the instance of packaging coming into immediate contact with the product, there is no significant adverse interaction between product and packaging material, and that the packaging material complies with the requirements of the EU legislation on materials and articles in contact with food;
- where the packaged product undergoes subsequent treatment, whether by the manufacturer or consumer, the packaging adequately stands up to the processing conditions and no adverse packaging/product interaction occurs;
- the finished pack has ample space to carry the statutory and other specified information in the required form and location (see also 5.6).

Where packaging material carries information required by law (e.g. labels, printed packages, lithographed cans), Quality Control should ensure that the specification is updated as required to comply with new legal provisions, and that stocks of packaging materials that no longer comply are quarantined for modification (if possible and desired) or destruction.

Each time a new pack or label design is introduced for a product, the superseded packaging or labels should be removed from the manufacturing area and destroyed. This disposal should be recorded.

Each label should contain a code or similar means of identification that will cross-reference it to the formulation to ensure that changes in formulation are reflected in the label copy.

6.5.1 Delivery and storage of packaging materials

Each delivery or lot of packaging should be given a reference code to identify it in storage and processing, and the documentation should be such that, if necessary, any lot of finished product can be correlated with the deliveries of the respective packaging materials used in its manufacture and with the corresponding quality inspection records. Deliveries should be stored and marked in such a way that their identities do not become lost.

Deliveries of packaging material should be quarantined upon receipt and released for use only once it has been assessed and its release authorised. Operators should be trained and encouraged to report immediately anything unusual about the appearance, odour or behaviour of packaging materials issued.

Temporarily quarantined packaging material should be located and/or marked in such a way as to avoid risk of its being accidentally used before release. Material found totally unfit for use in packaging operations should be suitably marked and physically segregated pending appropriate disposal.

All packaging materials should be stored in hygienic conditions, and as indicated in their respective specifications.

Packaging materials should be assigned a shelf life where appropriate.

Stocks of packaging materials in store should be inspected regularly to ensure that they remain in acceptable condition. Packaging materials should also be inspected immediately before use.

6.5.2 Issue of packaging materials

A secure area should be used for the issue and return of all printed packaging components. This area should be accessed only by authorised personnel.

In issuing packaging material from store for production use, stock rotation should normally be observed, unless otherwise authorised or specified by Quality Control.

Formal procedures should be in place for the following:

- the issue of packaging materials from store;
- the return of part-used lots of packaging to store;
- the re-sealing of part used boxes of packaging, to prevent foreign body contamination;
- the reconciliation of all printed packaging component stock from quantity issued, quantity used, wastage and that returned to store.

6.6 Processing and packaging

Where a company manufactures more than one product or more than one version of a product, and there is more than one production line, production layout should be such that confusion is avoided.

Particular care should be taken, in terms of production layout and practices, to avoid cross-contamination of one product by another. Multiple packaging lines should be adequately segregated to avoid the risk of cross-contamination.

Before production begins, checks should be carried out to ensure that:

- the name and appropriate reference to the product being processed/packaged is clearly displayed on each production line;
- the production area is clean and free from any products, product residues, waste material, raw materials, packaging materials or documents not relevant to the production to be undertaken;
- the correct materials and documents have been issued;
- the correct machine settings have been made;
- all plant and equipment is clean and ready for use.

Where a company manufactures more than one product, or more than one version of a single product, the greatest care must be taken to ensure that:

- the correct packaging is issued for the product to be manufactured;
- no incorrect packaging materials, left over from a previous production run of a different product or a different version, are left in the production area where they might accidentally be used.

Primary product packaging must only be used for its intended purpose.

Where packaging is reference-coded and date-marked for use, care must be taken to ensure that only material carrying the correct reference and date codes are used. Surplus material left from earlier production and bearing an invalid reference or date should not be left in the production area. Where the reference and/or date is applied during the manufacturing operation, care should be taken to check and ensure that the marking machine is set for the correct reference and date.

Processing should be strictly in accordance with the Master Manufacturing Instructions subject to any variations approved, and by detailed procedures set out for operators in the Plant Operating Instructions.

Process conditions should be monitored and process control carried out by suitable means including, as appropriate, sensory, instrumental and laboratory testing, and on-line checking of correct packaging and date-marking. Where continuous recorders or recorder/controllers are in use, the charts should subsequently be checked by Quality Control and retained as process records.

There should be regular and recorded checks on the accuracy of all instruments used for monitoring processes (e.g. thermometers, temperature gauges, pressure gauges, flowmeters, checkweighers).

Effective cleaning of production premises and equipment must be carried out.

All persons working in or visiting the production area must comply with the requirements of personal hygiene. Adequate facilities must be provided, including appropriate over-clothing for personnel (see also 3.3 and 4.3.6).

General ‘good housekeeping’ should be practised, including prompt removal of waste material, precautions to minimise spillage or breakage, prompt removal and clean-up of any spillage or broken packaging occurring, and the removal of any articles that might enter the product as foreign matter.

6.7 Intermediate products

After its preparation, an intermediate product should be quarantined until checked and approved by Quality Control for compliance with its specification.

If required to be stored before further processing, it should be stored as designated in that specification, and suitably reference-marked and documented so that it can be correlated with the lots of raw materials from which it was made and the lot(s) of finished product in which it is subsequently incorporated.

A lot of intermediate product found to be defective should remain quarantined pending re-working or recovery of material or outright rejection as the case may be (see Chapter 7).

6.8 Finished products

Packed finished products should be quarantined until checked and approved by Quality Control for compliance with the appropriate Finished Product Specification. Finished product must be reconciled, approved and signed-off by the authorised person before it can be released for sale.

At least two samples of approved lot of finished product should be suitably marked to identify it, and stored under the appropriate conditions (e.g. of temperature or relative humidity) stated in the Finished Product Specification. The samples of each lot of finished product should be retained for at least the shelf life of the product.

Each lot of finished product must bear an identification mark that will provide a means of tracing product to any retailer to whom part of that lot is sold, as required under EU traceability requirements (see Annex IV).

Where a lot of finished product fails to meet the Specification, the reasons for failure should be thoroughly investigated.

Defective finished product should remain quarantined pending re-working or recovery of materials or disposal as the case may be.

6.9 Disposal of waste and effluent

When disposing of surplus raw materials, waste or reject product, process chemicals and laboratory reagents it is essential that attention is paid to all EU legislative requirements on waste, as implemented by Member States.

The European Union's approach to waste management includes the following principles, which should be taken into consideration:

- the prevention or minimisation of waste;
- the reuse of material wherever feasible;
- waste recycling where possible;
- controlled waste disposal that ensures the protection of health and the environment.

The disposal of printed packaging materials, raw materials or rejected products should be carefully controlled and a reconciliation should be carried out on quantities used and/or produced against those being destroyed.

All waste materials and effluent should be disposed of in accordance with current local regulations by a route appropriate to the class of material.

All disposal must be appropriately documented.

7 Recovery or re-working of materials

Material may be recovered, re-worked or re-processed by an appropriate and authorised method, provided that the material is suitable for such treatment, that the resulting product complies with the relevant specification and that the related documentation accurately records what has occurred.

Recovered material must be identified and quarantined until the material review is conducted and a disposition decision is made.

Procedures should be developed for the acceptance, tests, treatments, sampling, authorising or rejection of recovered materials. These should be carried out according to the Standard Operating Procedures.

EU legislation on food contaminants specifically prohibits the mixing of material that is not compliant with the maximum levels of contaminants laid down in the law with materials that are compliant in order to dilute the contaminant levels. Thus, contaminated product cannot be recovered, re-worked or re-processed and should be destroyed.

Residues and re-worked or recovered material which might adversely affect product quality, efficacy or safety should not be used in subsequent lots.

The treatment of product residues and re-worked or recovered material, and the means of their inclusion in a subsequent lot, should be specifically authorised and documented.

Limits, approved by Quality Control, should be established for the amount of any such material which may be added to a subsequent lot.

Lots incorporating residues should not be released until the lots from which the residues originated have been tested and found suitable for use.

Methods of re-processing should be specifically authorised and fully validated and documented once any potential risks have been evaluated and found negligible.

The need for additional testing of any finished product that has been reprocessed (or to which residues have been added) should be considered.

A finished product returned from the manufacturer's own stores or warehouse (because, for example, of soiled or damaged labels or outer packaging) may be relabelled, or bulked for inclusion in subsequent lots, provided that there is no risk to product quality and the operation is specifically authorised and documented. If such products are re-labelled, extra care is necessary to avoid mix-up or mislabelling. Care should be taken to ensure that any re-labelled product is marked with the appropriate date of minimum durability (Best Before date) and lot number, to permit product traceability as required under the Regulation for general food law (see Annex IV).

Finished products returned from the market and which have left the control of the manufacturer should be considered for re-sale, re-labelling or bulking with a subsequent lot only after they have been critically assessed by Quality Control. The nature of the product, any special storage conditions it requires, its condition and history, and the time elapsed since it was issued should all be taken into account in this assessment. Where any doubt arises over the quality of the product, it should not be considered suitable for re-issue or re-use, although basic chemical re-processing to recover active ingredients may be possible.

All records relating to recovery, re-working or re-processing must be kept for a previously decided period, with consideration given to any legal requirements.

8 Storage

Effective storage operations should be designed to ensure the following:

- that all products are easily accessible for load assembly as required;
- that aisles and assembly areas are planned so that unimpeded movement is possible to and from all parts of the storage area;
- to facilitate proper stock rotation such as first in first out, particularly important in relation to short-life and date-marked products;
- to obtain maximum utilisation of available space, consistent with the above requirements.

Storage and transportation of finished products should be under conditions that will:

- prevent contamination, including development of pathogenic or toxigenic micro-organisms;
- protect against undesirable deterioration of the product and the container;
- assure the delivery of safe, clean and wholesome products to consumers.

Deterioration includes, but is not limited to, contamination from insects, rodents and other vermin, toxic chemicals, pesticides and sources of flavour and odour taint.

The buildings, grounds, fixtures and equipment of product storage areas and vehicles should be designed, constructed, adapted and maintained to facilitate the operations carried out in them and to prevent damage.

8.1 Access to storage areas

Access to material and product storage areas should be restricted to those working in those areas and to other authorised persons.

A suitable curtain should be provided at all entrances and exits in order to maintain the internal conditions of the storage area at an appropriate level for the product therein.

When the storage area is connected directly to the manufacturing area, a buffer area/pass box should be provided between the storage area and the manufacturing area.

8.2 Temperature and lighting

Storage area temperatures should be kept at an appropriate level to maintain the wholesomeness of the particular products received and held in such areas. Prior to storing materials or products, the temperature should be mapped and recorded, to ensure that there are no wide variations in different parts of the storage area. The mapping and recording should take into account the variations of temperature that may occur during different seasons of the year and should be repeated as frequently as is considered necessary.

The lighting should be as high as possible above the product, as the lower the lights are positioned on the wall, the greater the shadows created by the pallets/shelves.

Where applicable, lighting appliances should have a shatterproof protective covering (see also 4.3.1).

8.3 Materials and product storage

In order to provide effective protection from contamination, materials and products should be stored under conditions stated in their respective specifications. Particular attention should be paid to the avoidance of microbiological cross-contamination and tainting. Where special conditions are required, they should be regularly checked for compliance.

Materials and products should be stored in such a way that cleaning, the use of pest control materials without risk of contamination, inspection and sampling, retention of delivery identity or lot identity, and effective stock rotation can be easily carried out.

Consideration should be given to the following:

- materials and product should be suitably stacked, with due regard given to safety;
- aisles should be kept clear and not used for temporary storage of materials.
- pallets should be sited according to an organised and agreed system;
- adequate spacing should be maintained between pallets to ensure sufficient ventilation;
- periodic visual checks should be made of all pallets, to ensure structural integrity;
- the use of corner boards on the corner of each stack should be considered, where appropriate, in order to increase the visibility of the corner and to provide protection against accidental impact damage by high lift and powered pallet trucks;
- all materials and product should be clearly marked with their relevant identification/lot number, to ensure that traceability is maintained, as required under the Regulation on general food law (see Annex IV). The identification marking should be easily accessible even when the material or product is stacked.

Products which have been recalled or returned, and lots which have been rejected for re-working or recovery of materials or disposal, should be so marked and physically segregated, preferably in an entirely separate storage facility.

Material deliveries and product lots temporarily quarantined pending the results of testing, should be so identified, suitably segregated, and effective organisational measures implemented to safeguard against unauthorised or accidental use of those materials or despatch of those products. A suitably consistent control system should be used. Where there is a validated electronic system in place to manage the quarantine system, the status should be appropriately indicated electronically.

If a lot of finished product is temporarily stored unlabelled, to be labelled at a later date, the greatest possible care should be taken to maintain its exact identity; it is essential that the containers holding the product are clearly labelled with their contents and lot number. This information will help ensure that the correct final product label is applied and that the label is marked with the correct date of minimum durability (Best Before date), as required under the food information to consumers (food labelling) legislation.

Storage areas should be checked on a regular basis to identify lots of materials that have exceeded their shelf life or, in the case of date-marked finished products, that leave insufficient time for retail display. All checks, and any subsequent actions taken, should be clearly documented.

8.4 Damaged goods

Damaged goods should be placed in a designated place as they are discovered. Care must be taken not to expose stored product to contamination or infestation. The same may also apply to returns from customers. Damaged goods which cannot be re-packed must be dealt with prior to disposal so as to prevent their accidental re-entry into the distribution chain.

Only products which have been properly inspected to ensure that the product and packaging are fully acceptable may be re-packed into outer packaging in a suitable area. If it is necessary to re-pack goods of different production codes into the same outer-packaging, the package should be marked with a date of minimum durability (Best Before date) that relates to the oldest packet in the case.

8.5 Cleaning of storage areas

Effective cleaning of storage premises and equipment must be carried out at the frequency and using the methods and materials specified in well designed cleaning schedules and instructions. Cleaning materials should be stored in a separate location to the raw materials/product in order to avoid contamination or tainting.

Storage areas should be regularly inspected for cleanliness and good housekeeping. All such inspections should be formally documented, alongside a record of any corrective action taken, if necessary (see also 4.3.3).

9 Transport and distribution

All vehicles, containers etc. should:

- be appropriate for the materials or product that is to be transported in them;
- be free from rodents, birds and insects or contamination from them;
- be free from odours, nails, splinters, oil and grease, accumulations of dirt and debris;
- be in good repair, without holes, cracks or crevices that could provide entrances or harbourage for pests.

Contaminated vehicles, containers etc should be kept in a separate area away from those that are clean.

Prior to loading, the vehicle interior (including walls, floor and ceiling) should be inspected for general cleanliness, freedom from moisture, foreign materials, etc. which could cause product contamination or damage to the packages. The use of tent-covered vehicles should be avoided.

Vehicles bringing product to a storage area should be inspected for evidence of damage (including damage to internal vehicle lighting or other “brittle material”, e.g. glass, ceramic or hard plastic items), or of insect or rodent infestations, objectionable odours or other forms of contamination.

If damaged product is accepted on a vehicle, it must be kept separate from other product and handled in a manner that will not expose other products on the vehicle, or subsequently the storage area, to contamination or infestation.

A procedure should be set up to deal with consequences of accidents and damage occurring when goods are in storage or distribution, e.g. salvage or condemnation following damage to goods in a road traffic accident.

Security precautions should include means of deterring and preventing any tampering with goods in storage and distribution.

When feasible, if storage or transport is contracted out, the premises, vehicles and their internal conditions should be periodically checked for any risk of contamination or tainting. Procedures should be in place to prevent the transportation of raw materials, intermediate product or finished product in the presence of hazardous products.

To reduce the occurrence of physical changes in the product (for example, melting of soft gel capsules), instructions should be given when particular care is needed to reduce large temperature fluctuations during transport and delivery. Procedures for cold chain transportation should be followed where relevant.

Any docks, railway sidings, bays, driveways, etc. within the factory complex should be kept free from accumulation of debris and spillage.

Fire appliances should be easily accessible and suitable for use on the commodities concerned. A sufficient proportion of fire appliances should be capable of dealing with electrical and petroleum/fuel oil fires.

Fork lift and other trucks used within the storage areas should normally be battery driven or otherwise equipped to prevent fume or fuel contamination.

10 Hazard Analysis Critical Control Point (HACCP)

Definition: A Hazard analysis critical control point (HACCP) procedure, is a systematic approach to the identification and assessment of the hazards and risks associated with the manufacture, distribution and use of a particular product, and the definition of means for their control.

Hazard analysis critical control point (HACCP) is a science based and systematic technique which food supplement businesses must use to help satisfy all concerned that their products are consistently safe. It achieves product safety in an efficient, reliable and cost-effective way, by identifying and preventing hazards at each process step throughout the development and manufacturing process of food supplement products, instead of relying on end-product testing.

HACCP is a structured approach to the following:

- identifying the main risk areas in an operation;
- adopting the appropriate controls;
- ensuring the proper operation of these controls.

A HACCP system is designed to accommodate changes, whether in raw material supply, equipment design, processing procedures or technological developments.

It must be appreciated that HACCP is an integral part of Good Manufacturing Practice and should not be treated as a separate entity.

10.1 Requirement for HACCP

It is a legal requirement in the European Union, under the Food Hygiene Regulation, for all food supplement manufacturers to have a HACCP system in place, regardless of the size of their operation. HACCP is recognised as an integral part of GMP within the food supplement industry.

10.2 Setting up a HACCP system

HACCP can only be effectively implemented once all hygiene requirements and GMP for businesses are adhered to; i.e. all controls, systems and procedures are in place. The HACCP system can then be devised following the steps outlined below (see also Figure 1):

10.2.1 The HACCP team

The HACCP study should be carried out by a small multidisciplinary team, including e.g. a food technologist, microbiologist, production manager, quality assurance manager and engineer. Other specialists, e.g. from the purchasing department, may be co-opted as appropriate. The support and commitment of all staff is essential to the success of the exercise. The HACCP team members must be appropriately experienced in their field of expertise and must understand the products, their uses and the hazards and risks involved in their handling and processing. All team members must be suitably trained in the basic principles of HACCP.

The HACCP team should have a co-ordinator who must be fully trained in the principles of HACCP and in its operation and implementation.

It is permissible to include the services of an external HACCP resource, e.g. a consultant, as part of the HACCP team, but the following should be checked:

- the level of relevant experience in the food supplement industry
- appropriate references from existing clients.

10.2.2 Responsibilities

Responsibility must not be delegated to an external resource, if used.

- The ongoing review and management of the HACCP plan is the responsibility of the HACCP team.
- The management of the HACCP system and the development and implementation of the food supplement safety control system is the responsibility of the food supplement manufacturer.

10.2.3 Define Scope of Study

Limit the study to a specific product or process.

Define the type(s) of hazards to be included (e.g. microbial, chemical or physical).

Define the part of the food chain to be studied (e.g. development through to consumption).

10.2.4 Describe the product

In order to have a complete understanding of the product the HACCP team will need a broad overview of the raw material ingredients, processing conditions and finished product characteristics.

The team must consider whether raw material ingredients are likely to be contaminated; are susceptible to bacterial growth; interactions between active ingredients; composition; use of preservatives; packaging formats; method of storage and distribution; required shelf life; and instruction for use.

10.2.5 Identify intended use

A knowledge of how the product is treated and used after purchase is required. This will include how the consumer will normally be expected to store and consume the product, and the length of time taken to consume the product after the container is opened.

The normal consumer groups must be identified; detailing whom will be expected use the product and to determine if sensitive populations, e.g. infants, pregnant women and persons with sensitivity to specific allergens, are included.

If the product is unsuitable for some sensitive groups, the HACCP team must ensure appropriate labelling or change the product or process to ensure suitability.

10.2.6 Construct production flow diagram

A flow chart must be developed that clearly identifies every step in the process from the establishment of raw material specifications, receipt of raw material ingredients through manufacture, packaging and distribution, in accordance with the defined scope of the study. Each process step should be carefully considered. The flow chart should provide appropriate technical detail, including the conditions and controls at each stage, e.g. storage conditions, processing temperatures and times, cleaning and disinfection procedures, quality checks and consumer use instructions. The flow chart should also detail product recycle and rework systems.

A confirmation of the flow diagram should be performed by a person or persons with sufficient knowledge of the operations, who is not a member of the HACCP team.

10.2.7 Verification of flow diagram

A 'walk round' inspection throughout the whole operation at various times during the hours of operation is required to ensure that the identified steps are a true representation of the processes The flow diagram may need amendment if differences from it are observed.

10.2.8 List all hazards

The HACCP team should identify all hazards associated with each step and list any preventative measures. The physical, chemical, microbiological and foreign matter hazards must be identified. At each stage in the flow diagram the potential introduction, increase or survival of the hazard(s) must be considered.

10.2.9 List all preventative measures

Preventative measures are those actions and activities that are necessary to eliminate or reduce hazard occurrence to acceptable levels. It is possible that more than one preventative measure may be required to control a specific hazard. Conversely, a single preventative measure may eliminate more than one hazard.

10.2.10 Determine the critical control points (CCPs)

The determination of the CCPs is a key element of the HACCP process. The purpose of this stage is to determine the point, step or procedure at which control can be applied and a safety hazard can be prevented, eliminated or reduced to acceptable level(s).

In deciding which control points are critical, the critical control point decision tree may be used. The decision tree should be used with common sense by the team; each question should be answered in sequence at each step for each identified hazard.

The yes/no answers to the questioning sequence leads to the conclusion that each hazard is, or is not, a critical control point (see Figure 2).

10.2.11 Establish target levels and tolerances for each CCP

Target and tolerance levels need to be specified for each preventive measure, in order to be able to monitor the CCP in question and ensure that critical limits are not exceeded. A critical limit is the value that separates acceptability from unacceptability. Critical limits for one or more observable or measurable parameters must be set for each CCP. The parameters in relation to any preventative measure or process step are those that can readily demonstrate that the CCP is under control. Examples of commonly measured parameters include temperature, time, flow rate, moisture level, weight and pH for liquids, though it may not be possible or necessary to use a numerical limit in every situation. Where possible, critical limits should be based on substantiated evidence. Critical limits based upon subjective data, e.g. visual inspection, must be strengthened by clear specifications of what is acceptable and that is not.

The test methods selected for measuring the defined parameters must be appropriate and validated. They should be implemented at each required stage in the process to ensure control can be maintained or promptly regained.

10.2.12 Establish a monitoring system for each CCP

Monitoring is the scheduled measurement or observation of a CCP relevant to its established critical limits. The monitoring procedures must be able to detect any loss of control at the CCP.

Ideally, monitoring should be able to provide the required information in time to make adjustments to ensure control of the process to prevent deviation from the critical limits. Process adjustments should be made when deviation is detected.

The monitoring must be carried out, or evaluated by, a designated and trained person at predetermined frequencies.

For each CCP, the HACCP team will decide what form of monitoring is to be done, when it is to be done and who is responsible to maintain control.

It is essential that all monitoring and any adjustments are fully documented.

10.2.13 Establish corrective actions

It is important to plan and specify what actions are to be taken if a deviation from critical limits occur. The corrective action plan must include details of the specific actions to be taken, authorisation and responsibilities and the procedure for the management of defective materials or products manufactured when the deviation occurred. Deviation and product disposition procedures must be documented in the HACCP record keeping.

10.2.14 Verification of HACCP system

Verification must be carried out to ensure that the HACCP system is in compliance with the HACCP plan and that it is developed in accordance with the current process or product. Verification of the HACCP system should not be undertaken by the person who is responsible for the monitoring and corrective actions.

Where verification cannot be performed ‘in house’, verification should be performed on behalf of the business by external experts or qualified third parties.

Examples of verification activities include:

- review of the HACCP system plan and its records;
- validation of critical limits and parameters;
- review of any deviations from CCPs and the implemented corrective actions;
- review of product dispositions;
- confirmation that all CCPs are kept under control.

The verification activities must be fully documented and should be carried out at the completion of the HACCP study, as a result of newly identified hazards and at regular scheduled intervals.

10.2.15 Establish documentation system

A documented system is important for the effective implementation and control of HACCP. This requires good record keeping and a set procedure that is appropriate to the nature and size of the operation, which will ensure that HACCP activities keep pace with any proposed changes, e.g. formulation change, supplier change, process equipment change etc.

The documentation system should be sufficiently comprehensive to assist a defence of 'due diligence' in the event of prosecution. The documentation should include:

- a standard operating procedure detailing the implemented HACCP system;
- the information generated during the hazard analysis, including minutes of meetings etc.;
- test methods for the parameters of the critical limits and any appertaining standard operating procedure;
- records of the identification of the CCPs;
- deviation and corrective action records;
- audit reports.

10.2.16 Review of HACCP system

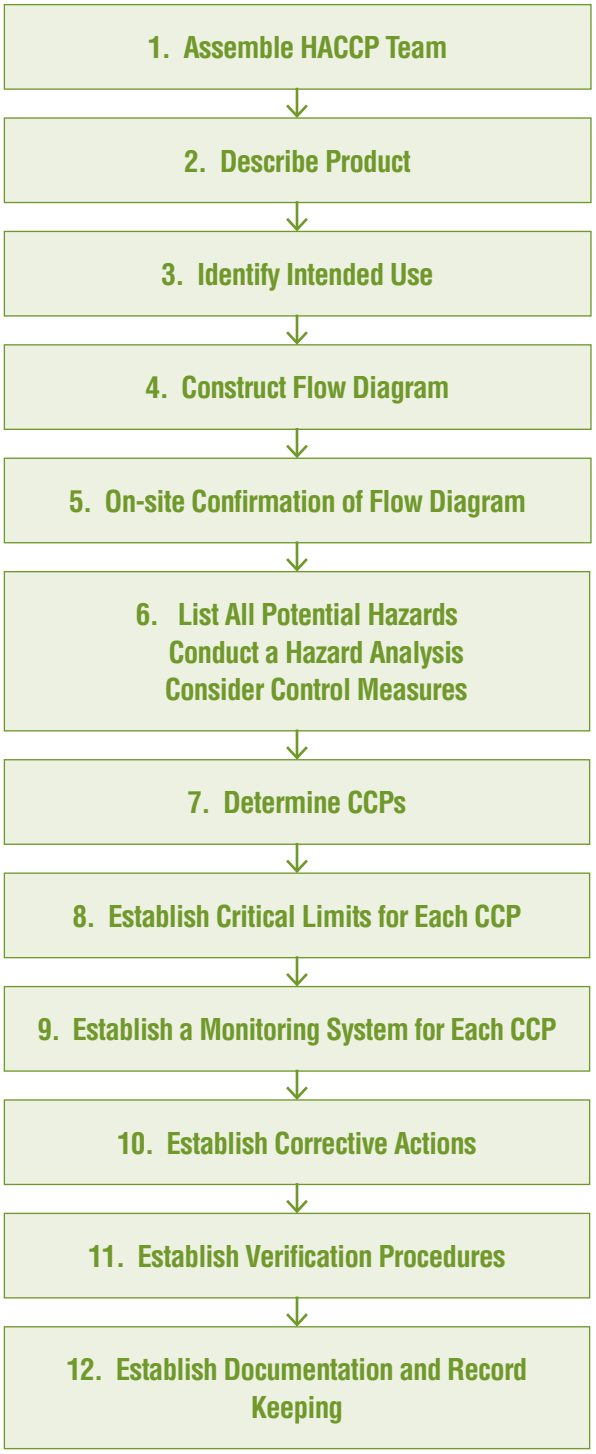
A review of the HACCP plan should take place whenever changes to processes and formulations are made, or as need is identified during verification. As a minimum, a review of the HACCP procedure should be undertaken once a year. Regular review of the HACCP plan is necessary to ensure that it remains flexible and accommodating to change, such as technological developments, formulation changes or advances in equipment design, while providing a means of preventing errors in hazard management which can be prejudicial to consumer safety and company survival

An example of a HACCP Control Chart for food supplement tablets or capsules is given in Annex III.

10.3 Training

The training of all personnel in HACCP principles and applications is an essential element for the effective implementation of HACCP. As an aid in developing specific training to support a HACCP plan, working instructions and procedures should be developed which define the tasks of the operating personnel to be stationed at each Critical Control Point.

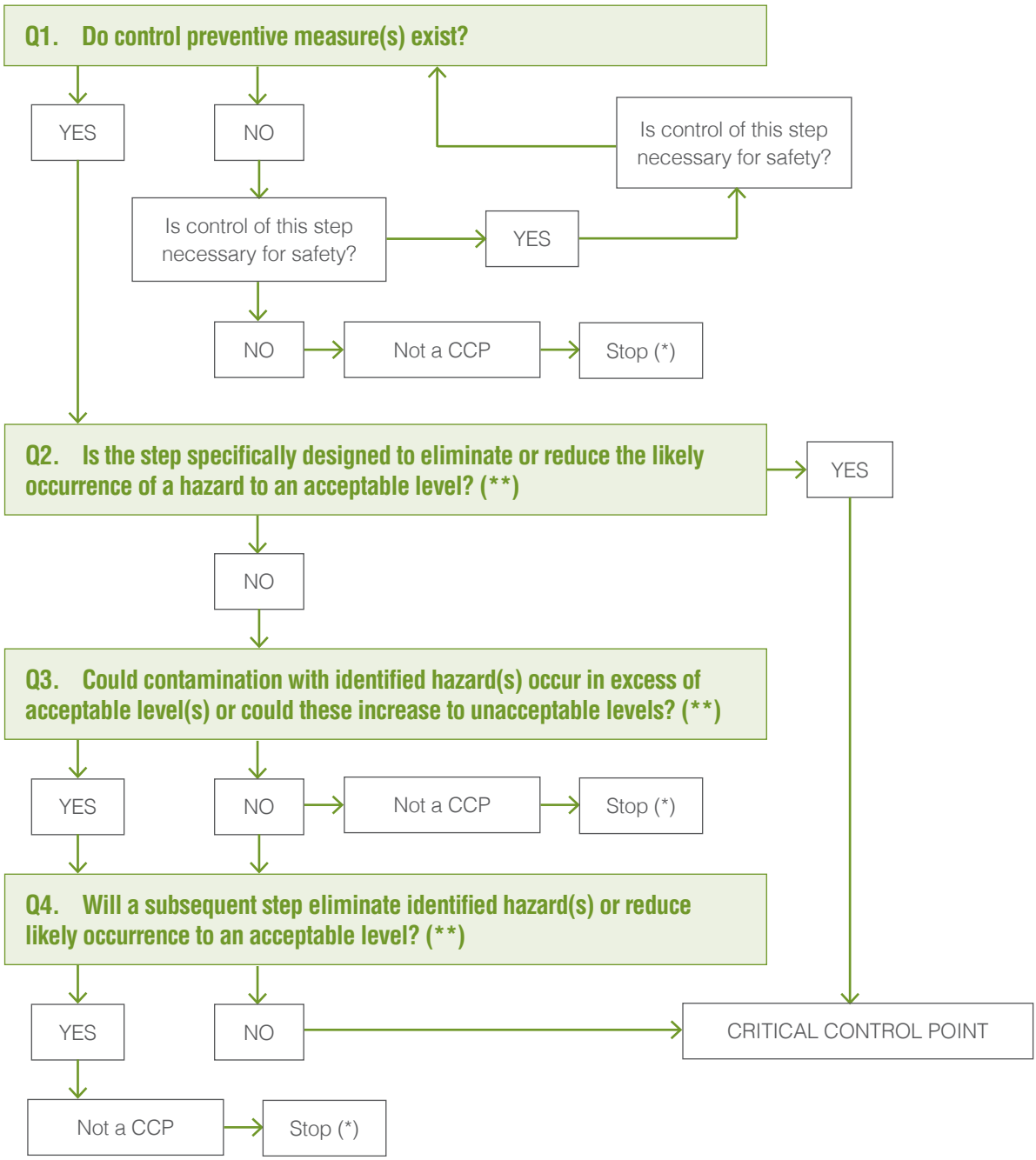
Figure 1: Logic sequence for application of HACCP



Adapted from Codex Alimentarius CAC/RCP 1-1969, Rev. 4-2003 - Annex

Figure 2: Example of a Decision Tree to identify CCPs

(answer questions in sequence)



(*) Proceed to the next identified hazard in the described process

(**) Acceptable and unacceptable levels need to be defined within the overall objectives in identifying the CCPs of HACCP

Adapted from Codex Alimentarius CAC/RCP 1-1969, Rev. 4-2003 - Annex

11 Stability and shelf life

11.1 Product Stability

It is part of Good manufacturing Practice that a product should meet qualitative and quantitative specifications and quantitative label claims for all ingredients throughout the product's shelf life.

It is a requirement in EU food law that the date of the product's durability (i.e. Best Before End) is declared on the packaging.

For food supplements, assurance of product stability is related to the quality of the product and consumer confidence, and product safety is a relatively minor concern as the ingredients and additives have already been assessed for safety.

Some common ingredients in food supplements or their declared constituents are inherently unstable. The degree of instability is dependent on a number of factors, including their chemical structure.

In some cases, such as vitamins, the quantity in the product reduces with time. Where this happens in a product with multiple active ingredients, such as a multivitamin supplement, the active components can degrade at different rates. In such cases the shelf life has to be based on the ingredient with the fastest decline in declared levels.

The essential requirements of stability for supplements are:

a) To ensure that the product meets quantitative label claims for all ingredients at the end of the proposed shelf life.
b) To ensure that no untoward organoleptic changes take place during the proposed life of the product. Such changes could relate to the colour, flavour or texture of a product.

The primary requirement of stability testing for supplements is to confirm that the product can sustain a commercially realistic shelf life; in other words, it should confirm that all label claims can still be met at the end of shelf life and that there are no obvious or unacceptable organoleptic changes during the declared shelf life of the product.

The main objective of stability assessments for supplements and fortified foods is related to consumer protection, in terms of their expectation, in addition to consumer safety. In simple terms, it is to assure the consumer that the product will be organoleptically acceptable and that the content is consistent with the label claim.

11.2 Objectives of Stability Testing

Stability studies can be carried out for two purposes:

a) To estimate the chemical and physical stability of the product and to ensure that the claimed levels of ingredients are retained during the intended shelf life of the product.
b) To confirm packaging protection and integrity. This is to ensure that the packaging is suitable for the product for the intended shelf life and that it is not permeable to oxygen, moisture and ultra-violet light.

These objectives are inter-related as any deficiencies in packaging integrity can have a detrimental effect on the product stability. A product can be more stable in one package than in another.

It is recommended that consideration is given to the suitability of the packaging before a product stability study is undertaken.

11.3 Principles of Stability Testing

As mentioned above, some common ingredients in supplements, or their declared constituents, are inherently unstable. When a shelf life expiry date is provided on labelling, the product manufacturer is responsible for ensuring its accuracy, based on a realistic assessment of relevant data obtained under conditions similar to those under which the product is likely to be distributed, stored and used.

The ideal way a shelf life can be confidently estimated is to conduct a 'real-time' study exceeding the time of the required shelf life at a temperature and humidity simulating the conditions to which the product is likely to be exposed. In most cases, however, real-time studies before a product launch are not commercially viable, and shorter studies are utilised. These are commonly designated 'accelerated studies'.

Accelerated studies utilise the fact that, in general, the rate of a chemical reaction can double with every 10°C rise in temperature. Therefore, accelerated studies involve storage of the product at temperatures considerably above the expected ambient storage in the market place. Thus, if the ambient average temperature is 30°C, the accelerated storage must be at temperatures of 40°C and above. The accelerated studies should be carried out at two or more elevated temperature points, particularly where extended shelf life is required. For example, a study where there is only one temperature point at 10°C above the ambient may in some cases only give confidence of 2 x accelerated storage time. That is, if the accelerated storage time for certain products is 6 months, the confidence for the shelf life is only 12 months.

The accuracy of both real-time and accelerated shelf life studies depends on the selection of representative product ingredients or constituents, or specific product attributes, that can be examined qualitatively or tested quantitatively in relation to the product matrix.

Well-characterised quantitative test methods are available from the literature and various compendia for all the vitamins and many other supplement ingredients. For botanical products that do not declare specific levels of naturally-occurring constituents, qualitative review of such attributes of taste, odour, and colour may be appropriate to review product stability. On the other hand, when a botanical constituent is declared, a significant amount of analytical work may be needed on the product before a stability study can commence if scientifically valid methods are not readily available. It is expected that this analytical work would be undertaken prior to manufacturing and packaging to ensure label accuracy.

For products containing two or more ingredients, different ingredients may degrade at different rates so reliance cannot necessarily be placed on one single ingredient or constituent; instead multiple assays may be needed. For such products, a single accelerated study may only be able to give a rough approximation of the shelf life and should be accompanied by real-time studies and/or other data whenever possible. Other data can consist of real-time experience on similar products or other information on the stability of the ingredients and constituents. In other words, undue reliance should not be placed on an accelerated study alone.

Particularly in cases where there are a number of active ingredients in the product, the estimation of the shelf life may have to be based on a variety of data sources such as:

- data from an appropriate stability study on the specific product;
- extrapolation of data from stability studies on similar products (similar products are those with similar matrices and containing the same or very similar combinations of ingredients);
- bibliographical references from scientific literature relating to the stability of the ingredients;
- combinations of the above.

Flexibility is needed when determining the shelf life for products containing two or more ingredients, so that all available and relevant data can be used to indicate the stability of such products.

11.4 Overages

As mentioned above, some ingredients in supplements and fortified foods can be inherently unstable and their levels can reduce over the life of a product. Such substances do not deteriorate at the same rate. In, for example, a multivitamin product containing all 13 recognised vitamins, some of the vitamins will be more stable than others and the rate of loss under specified conditions will vary greatly from vitamin to vitamin.

In order that commercially realistic products can be produced, a well established technique is to add an 'overage' to the more stability-sensitive vitamins to ensure that all claimed levels are still met at the end of the declared shelf life.

The 'overage' is defined as the difference between the formulated and declared levels and is normally expressed as a percentage of the declared value. Thus, an input level of 45mg of vitamin C and a declared level of 30mg would give an overage of 50%.

The amount of 'overage' that needs to be added will vary according to the known stability of the vitamins in the product matrix. The stability of a given ingredient can also vary depending on the product matrix (for example, tablet, capsule, liquid, powder).

It is a fundamental requirement of Good Manufacturing Practice (GMP) that the total amount of the declared level of the vitamin (or any other ingredient) per recommended daily intake should be well below any known safety concerns. If the product is correctly formulated, within the generally accepted safe limits as defined by Codex Alimentarius, there will be no safety issues with the product.

11.5 Environmental Storage Conditions

Storage conditions used for stability trial samples need to reflect the temperature and humidity conditions to be found in the intended market for the product. In some cases, notably where storage conditions are specified on product packaging, it may be adequate to store only in the specified conditions, unless accelerated studies are required.

Accelerated stability testing, as the name implies, is intended to give early indication of potential problems in product stability. This is usually achieved by stressing the product in terms of storage temperature and/or humidity.

For the European market the accepted room temperature is 20-25°C. Real time storage for the duration of the product shelf life is needed at this temperature. The ambient humidity recommended by the International Committee for Harmonisation (ICH) is 60% rh for 25°C; if this is not fixed then the humidity needs to be monitored and recorded along with the temperature.

For supplement products it should be adequate to commence stability studies shortly before product launch provided ingredients are known to be stable or there is a supporting scientific rationale for the formulation. If challenged, data could then be made available and some action could be seen to have been taken to establish stability of the product.

For entirely new formulations for which it is not possible to extrapolate data or apply previous experience it may be wise to instigate accelerated stability studies 3-6 months prior to product launch to provide confidence on stability.

For accelerated testing, samples are typically stored at either 30°C ± 2°C / 65% RH ± 5% RH and / or at 40°C ± 2°C / 75% RH ± 5% RH, where appropriate to the product being tested. Accelerated testing of refrigerated materials is typically conducted at 25°C ± 2°C / 60% RH ± 5% RH.

In all cases the product being stored should be in its final marketed pack.

Further stability storage and assays should be carried out for all products, particularly liquid products and emulsions, for the 'in use' period, replicating the gradual loss of product from its packaging.

Storage times for 'in use' trials should equate to the pack size and the recommended daily serving i.e. 300ml of a liquid product at 10ml per day gives an 'in use' storage requirement of 30 days minimum.

Storage facilities can be of various types, ovens, incubators, cabinets, or rooms both with and without humidity control, but all with temperature control. All should, however, have the means to monitor and record the temperature and humidity of the storage facility.

Assay periods should reflect the intended shelf life of the product. A typical schedule for a product with 3 years shelf life should be an assay initially and then again after 1, 3, 6, 12, 18, 24 and 36 month intervals for the 25oC storage condition. If only 24 months shelf life is envisaged, more frequent assays may be considered, in order to give the same quantity of data as for the three year example. Storage at elevated temperatures and humidities for accelerated storage trials may be of shorter duration.

11.6 Microbiological Testing

Testing should be carried out on syrups, tonics and emulsions and other formulations having a high moisture content. Such testing should be carried out over the shelf life period of the product. Microbiological testing should also be carried out as part of the 'in use' trials and if necessary as a challenge test to prove preservative efficacy in new formulations.

Microbiological testing should always be considered where it is known that raw materials carry a high microbial load.

Where microbiological testing is carried out on tablets or capsules it is probably only necessary to conduct this work at the beginning and end of shelf life, due to the low risk associated with these presentations.

Microbiological 'in use' trials should also be carried out on microbiologically sensitive products, particularly liquid products. These trials should attempt to simulate sources of microbial contamination that could be introduced during product usage.

11.7 Suggested Analytical Requirements for Stability Studies

The following recommendations should be taken in context and only appropriate tests under any particular section heading should be applied.

i) Organoleptic Assessment

e.g. Appearance, odour, taste and colour

ii) Physical Testing

Tablets (including chewable and effervescent)
weight
friability
disintegration
hardness
solubility (chewable tablets)

Capsules
weight
disintegration/dissolution
hardness (soft gel only)
seal integrity

Liquids (including oils and emulsions)
pH
viscosity
refractive index
weight per ml
stability to centrifugation (emulsions)
microscopic examination (syrups & emulsions)

Powders (including effervescent)
bulk density
moisture content
particle size
microscopic examination
solubility
agglomeration/lumping

Appropriate physical testing should be carried out to ensure that the quality and aesthetic properties of the product are maintained. A significant change in the appearance of a product often indicates a deterioration in quality.

iii) Chemical Testing

Vitamins and Minerals

Assay of individual vitamins or minerals by an appropriate validated and stability indicating method.

Herbal Products

Qualitative assessment such as Thin Layer Chromatography (TLC) or Infra Red Spectroscopy (IR) and/or quantitative assay for claimed active constituents. Where possible assay should be performed by an appropriate validated and stability indicating method.

Oil Based Products

e.g. Tests for peroxide value and free fatty acids.

Assay for claimed active ingredients (eg EPA, DHA, GLA and oil soluble vitamins) should be carried out by an appropriate validated and stability indicating method.

Syrups

Preservatives should be assayed by an appropriate validated stability indicating method where their presence is required for antimicrobial effect in the product.

Emulsions

Applicable chemical testing, as for oil based products and syrups.

12 Documentation

Good and effective documentation is an essential and integral part of GMP and the essential basis of an effective HACCP system. The purposes of documentation are:

- to define the materials, operations, activities, control measures and products;
- to record and communicate information needed before, during or after manufacture;
- to reduce the risk of error arising from oral communication; and
- to permit investigation and tracing of defective products.

The system of documentation should be such that, as far as is practicable, the history of each lot of product may be ascertained. In order to maintain traceability, as required under EU law, the documentation should include the utilisation and disposal of raw materials, intermediates and bulk or finished products (see Annex IV).

12.1 Documentation design

To facilitate proper and effective use of documents they should be designed and prepared with care, be free of errors and pay particular attention to the following points:

a. The title of each document should be unambiguous.
b. The title, nature and purpose of the document should be clearly stated.
c. The document should be laid out in an orderly fashion, and be easy to check.
d. It is an advantage if it is possible to revise part of a document without necessarily completely rewriting the whole.
e. The way the document is to be used, and by whom, should be clearly apparent from the document itself. Other means provided to explain its use are of less value.
f. Documents which bear instructions should:
    i. be written in the imperative, as numbered steps;
    ii. be clear, precise, unambiguous and in language the user can understand;
    iii. be readily available to all personnel who have to carry out the instructions.
g. Documents which require the entry of data should:
    i. provide sufficient space for the entry, including sufficient space to note preventive and / or corrective actions that may have been taken following inspection, as applicable;
    ii. allow adequate spacing between the entries;
    iii. show headings clearly indicating what is to be entered.
h. The size and shape of documents and the quality and colour of the paper used should be considered in relation to the typing/printing, reproduction and filing facilities available.
i. Reproduced documents should be clear and legible.

Documents should contain all necessary, but no superfluous, data. Any headings, or places for entries, which cease to be used should be removed at the earliest opportunity.

12.2 Types of documents

Manufacturing formulae and processing and packaging instructions

These state all the starting materials used and lay down all processing and packaging operations.

Specifications

These describe in detail the requirements with which the products or materials used or obtained during manufacture have to conform. They serve as a basis for quality evaluation.

Procedures

These give directions for performing certain operations, e.g. cleaning, clothing, environmental control, sampling, testing, equipment operation.

Records

These provide a history of each lot of product, including its distribution, and also of all other relevant circumstances pertinent to the quality of the final product.

12.3 Classes of documents

The following lists are not exhaustive but do give an indication of the types of documents which are advisable:

a) Specifications, Instructions and Procedures:
   - Ingredient specifications;
   - Packaging materials specifications;
   - Copy of order and/or terms of conditions of purchase;
   - Master manufacturing instructions (including standard recipes);
   - Intermediate specifications;
   - Bulk product specification;
   - Finished product specifications;
   - Quality control (including analytical and microbiological) procedures and methods;
   - Standard procedure for product recall;
   - Plant operating instructions;
   - Cleaning instructions, good housekeeping and pest control schedules;
   - Plant maintenance schedules;
   - HACCP plans;
   - Quality Assurance programme.

b) Records and reports
   - Records of receipt, test reports, approval and issue for use of raw materials and packaging materials;
   - Records of the testing and release of intermediates, bulk products and finished products;
   - Records of process control tests;

- In-process recording instruments charts;
- Weight or volume control charts;
- Lot manufacturing records;
- Records of authorisation of distribution of the product;
- Contracts held for the subcontracting of production, distribution, analysis etc.;
- Customer complaint records;
- Quality control summaries and surveys;
- Quality audit reports and records;
- HACCP review reports;
- Self-assessment records;
- Training records;
- Superseded documents.

c) Programmes
- Production programmes;
- Calibration programmes;
- Validation/verification programmes;
- Training programmes;
- Quality audits.

12.4 Documentation system

The documentation system should include procedures for issue, authorisation, distribution, periodic review and revision.

Relevant personnel should be given appropriate training on how to complete the documents and the effectiveness of this training should be regularly checked. It should be ensured that personnel using and/or completing the documents are literate in the language used in the documentation (see also 3.1).

Only those personnel who have been previously authorised by the manufacturer should enter data on the documents. Hand-written entries should be made in clear legible writing, using ink or other indelible medium, and be confirmed by the addition of the writer's initials or signature. A signed recorded observation is preferable to simply ticking in a box.

Documents should be kept up to date. Any amendments should be formally authorised and signed by the previously authorised responsible person. In the case of permanent amendments, the amended document should be replaced at the earliest opportunity by a newly prepared document.

If an error is made or detected on a document it should be corrected in such a manner that the original entry is not lost and the correction initialled and dated. Where appropriate, the reason for the correction should be recorded. The use of correction fluid, tape or pens is not permitted.

An outdated or superseded document should be removed from active use, and a copy, marked that it has been superseded, retained for reference. Regular internal reviews should be undertaken to verify that the correct versions of documents are in use.

It may be beneficial to prepare a manual that describes the overall Quality Assurance system, the procedures employed and the documents used. This manual should be fully integrated with the HACCP documentation and should be accessible to all relevant personnel.

12.5 Electronic documentation

Certain additional requirements are needed in the case of electronic documentation, as follows:

- sufficient protection should be put in place to ensure correct entry of the data;
- a back-up system should be created to ensure that the original data can be retrieved in the event of file alteration, corruption or deletion;
- adequate protection should be in place to prevent unauthorised access to the data;
- procedures should be established outlining the issue, cancellation or amendment of authorisation;
- procedures should also be established defining the action to be taken in the event of system failure or breakdown;
- all safeguards, back-up systems and procedures should be regularly checked and updated as necessary.

Any electronic system that is used to control critical operations such as quarantine / release status should be restricted to allow access and 'change control' only by authorised personnel.

12.6 Retention of documents

The retention period for documents is dependent upon their function. When determining a suitable period of retention, any legal requirements must be taken into consideration, including the potential provision of evidence of due diligence in the event of an investigation by the authorities. As a general guide, records should be stored for the shelf life of the product plus an additional year. Any national legal requirements must be observed for the retention of particular documents (for example, packaging records).

Retention of personnel data should be in accordance with national data protection laws.

An ongoing and continuously monitored system, known as a Controlled Records List, should be used for removing the files of redundant data.

Due consideration should be given to fire risk. It is recommended that a fireproof safe be used for the storage of electronic backups and, in the case of paper-only systems, master copies and key documents.

13 Complaints procedure, product withdrawal and recall and emergency procedure

13.1 Legal requirements

The EU Regulation on general food law places full responsibility on food business operators for ensuring that the food products they place on the market do not pose any risk to the consumer. Under the requirements of this Regulation, if a food supplement company considers, or has reason to believe, that a food supplement which it has imported, produced, manufactured or distributed is not in compliance with the food safety requirements, it must immediately initiate procedures to withdraw the product in question from the market. The company must also inform the appropriate competent authorities in the country(ies) where the product(s) is marketed of the problem and collaborate with the authorities on action taken to avoid or reduce the hazards posed by the product.

If the product has already reached the consumer, the company must effectively and accurately inform consumers of the reason for its withdrawal, possibly by way of public announcement. If deemed necessary, affected products should be recalled from the consumers.

The relevant competent authorities must also be informed if a company considers, or has reason to believe, that a product placed on the market may be injurious to health. The company must cooperate with the relevant authorities on action taken to prevent, reduce or eliminate risks posed by the product.

Adequate records must be retained to ensure the traceability of the products, in order to enable rapid and effective withdrawal or recall, if required (see Annex IV).

13.2 Complaints

Procedures should be put in place for receiving, assessing and managing all consumer complaints received by the company. These should include procedures for handling complaints relating solely to manufacturing issues, with no potential health impact, and also procedures for handling complaints of adverse events and quality complaints that may additionally have a potential health impact. The procedures should indicate the relevant responsible person(s) through whom the complaints must be channelled.

All company personnel should be appropriately trained to ensure the proper recognition, communication and recording of received complaints.

13.2.1 Quality complaints

Complaints with no potential health impact and relating solely to manufacturing issues (e.g. short-weights or counts, packaging complaints etc.) should be forwarded directly to the Quality department.

Where possible, product quality complaints should be thoroughly investigated by appropriately qualified personnel, who have an understanding of the full significance of a complaint and who may also have knowledge of other related complaints. Each complaint received should be recorded and reports should be prepared as a basis for action. The Quality Control Manager should be kept fully informed and closely consulted.

13.2.2 Adverse event complaints

A suitably experience and qualified accountable person should be responsible for implementing and monitoring the adverse event complaints procedure and for reviewing the records of all adverse event complaints received. The day to day recording and reviewing of incoming adverse event complaints may be delegated to suitably experienced and trained personnel, but overall control and overview of the adverse event complaints should be maintained by the nominated accountable person.

Company personnel should be given appropriate training in the adverse event complaints procedure, to ensure that all such complaints are referred to the accountable person or their delegate(s) in an efficient and timely manner.

All adverse event complaints should be recorded with as much detail as possible. It is recommended that a standard questionnaire be used to obtain information from the consumer in response to a complaint. Sufficient information should be obtained to ensure that the complaint can be confirmed as genuine and, where necessary, to enable an investigation of the adverse event. Records of adverse event complaints should be retained in a central records system, which should be easily accessible by the accountable person.

The IADSA global guide for supplement companies on the Handling of Adverse Event Complaints provides detailed guidelines on the creation of an adverse events complaints procedure (see Annex V).

13.2.3 Action following receipt of complaints

Action should include responding to the complainant and, where relevant, must include responding to any enforcement authority involved. Where the complaint is justified, steps to remove or overcome the cause and thus prevent recurrence should be taken; and the defective material which the complaint sample might represent should be dealt with, including possibly a product withdrawal or recall.

Records of complaints should be regularly analysed, summarised and reviewed for any trends or indication of a need for a product recall or of any specific problem requiring attention. This is particularly important in relation to complaints of adverse events.

It is strongly recommended that appropriate summaries are regularly distributed to and reviewed by senior management.

13.3 Product withdrawal and recall

13.3.1 General

The withdrawal of a product is the action taken to have the product returned to the manufacturer from the customer/retailer but not from the final consumers. Withdrawal of a product may be a voluntary action by the company, following concerns of product quality but not necessarily product safety.

The recall of a product is the action taken to have a product returned to the manufacturer from the customer/retailer and also from the final consumers. Product recalls are generally made in response to safety concerns.

Product withdrawals or recalls may arise in a variety of circumstances which typically fall into three main categories:

a) where the national or local authorities become aware of a hazard or suspected hazard, and information and co-operation from the manufacturer or importer is necessitated;
b) where the manufacturer, importer, distributor or retailer becomes aware of a hazard or suspected hazard;
c) where there is no hazard or suspected hazard involved, but there is some circumstance (e.g. sub-standard quality, mislabelling) which has come to light and which prompts the manufacturer, importer or retailer to decide to withdraw or recall the affected product.

In case (c), the company will itself have to organise the withdrawal or recall operation. In cases (a) and (b), consideration may be given to issuing a public food hazard warning. Generally this would be done in consultation with the manufacturer or importer, the distributor or retailer, and any relevant enforcement authority interest. Normally any arrangements for withdrawal would be discussed so that the most appropriate methods could be effected or endorsed by the authorities.

Manufacturing records systems, distribution records systems and the marking of outer cartons and of individual packs should be designed in a way that will facilitate effective withdrawal or recall, if necessary. A good system of lot / identification marking throughout the production process will pinpoint the suspect material and help avoid excessive recall.

Although a defect or a suspected defect leading to withdrawal or recall may have come to light in respect of a particular lot or lots or a particular period of production, urgent consideration should be given to whether other lots may also have been affected (e.g. through use of a faulty material or a plant or processing fault), and whether these should also be included in the withdrawal or recall.

13.3.2 Withdrawal and recall procedures

Procedures should be in place for the withdrawal or recall of product when required, and these should be capable of being put into operation at short notice, at any time, inside or outside working hours.

A responsible person, with appropriate named deputies, should be appointed to initiate and co-ordinate all withdrawal and recall activities, and to be the point of any contact with the nominated competent authority on withdrawal and recall matters. A crisis procedure and management team should also be established.

Out of hours contact details of key personnel and competent authorities should be kept in an accessible form and regularly updated.

The withdrawal and recall procedures should be shown to be practicable and operable within a reasonable time by carrying out suitable testing of the procedure. The procedures should be reviewed regularly to check whether there is need for revision in the light of changes in circumstances or of the responsible person.

The withdrawal or recall procedures should lay down precise methods for notifying and implementing a recall from all distributive channels and retailers where the affected product might be, as well as affected goods in transit, and of halting any further distribution of affected goods. The recall procedures should additionally lay down the process for recalling product from consumers.

Notification of withdrawal or recall should include the following information:

- name, pack size and adequate description of the product;
- identifying marks of the lot(s) concerned;
- the nature of the defect;
- action required, with an indication of the degree of urgency involved;
- name of contact and telephone number of contact who can supply further information.

Procedures should also be in place to ensure the proper treatment of withdrawn or recalled material or product, which should be quarantined, pending a decision as to appropriate treatment or disposal. Quantities of the withdrawn or recalled lot of product, at their identified locations, should be reconciled with the total lot quantity in question.

13.4 Emergency procedure

Regrettably, the possibility of real or threatened hazard arising from the actions of second or third parties must be faced (e.g. deliberate contamination or poisoning of product or ingredient by extremists or otherwise misguided persons). Although some of the additional action that might be taken in such circumstances could be considered outside the scope of this Guide, it is included because those concerned in the manufacturing operation would very probably become involved.

The first intimation of a problem in this area could come from a whole variety of sources, e.g. consumer complaint, from a retailer, the media, the police, the enforcement authorities, employees, or by telephone, post or personal contact with any company location or any employee at any time.

It is therefore essential that any personnel engaged in manufacture should be aware of company action to be followed in dealing with such threats both within and outside of normal working hours, and that suitable arrangements exist for calling in key personnel out of hours in such an emergency. The extent to which any such emergency procedures may override normal lines of management should be explicitly stated. The emergency procedures should be formally documented.

Faced with an emergency situation, the withdrawal and recall procedures described in section 13.3 above will apply, while the expertise of those involved in Quality Control and other relevant functions should be put at the disposal of the crisis management team responsible for handling the emergency.

The possibility of such sabotage and even site invasion may indicate a need for particular security precautions in vulnerable areas, e.g. locked rooms, use of seals, etc.

The relevant national police authority should be informed and consulted regarding any cases of deliberate or malicious contamination.

Any emergency or recall situation is likely to involve retailers or wholesalers, and a smooth and effective interface with their procedures should be achieved as early as possible during the crisis.

14 Self-inspections

A food supplement company should undertake regular self-inspections, particularly in those departments that are performing quality- and safety-relevant activities, in order to check the implementation and compliance with GMP principles and to propose any required remedial actions. These should cover:

- personnel matters;
- premises;
- equipment;
- production;
- quality control;
- distribution of the products;
- documentation, including the HACCP system;
- systems for dealing with complaints, withdrawals and recalls.

Self inspections should be conducted at intervals, at least once a year, or more frequently dependent on the extent and criticality of the quality- and safety-relevant activities that are performed in specific departments. Self inspections should follow a prearranged programme, in order to verify their conformity with the principles of Quality Assurance.

Designated competent person(s) from the company should conduct the self-inspection in an independent and detailed way. It may also be helpful to have an independent audit by external experts.

The person(s) conducting the self-inspection should call the attention of the relevant manager(s) of the company to the result of the inspection and any necessary corrections. The agreed corrections should be completed within a specified period of time.

Records should be kept of the observations made during the inspection, the actions proposed and taken, the relevant time frames for completion and any statements made on the actions taken. These records should be retained for a pre-determined period of time and should be periodically reviewed by the company's senior management.

15 Sub-contracting operations

Where complete or part manufacture is carried out as an own-label, private label, distributor's own-brand, contract packing or similar operation, the obligation is on the Contract Acceptor/Consignee (manufacturer) to ensure that production is carried out in accordance with GMP in the same way that would be expected were he manufacturing for distribution and sale on his own account, except where responsibility is specifically excluded by mutual agreement between the Contract Giver/Consignor (customer) and the Contract Acceptor.

15.1 Terms of contract

The Contract Acceptor should ensure that the terms of the contract are clearly stated in writing. This should include a Technical Agreement between the two parties (see 15.2 below).

It is essential to ensure that raw materials, intermediates and end products are covered by sufficiently detailed specifications (as outlined in other chapters). Any special GMP requirements should be clearly emphasised, and quality control, record transfer, coding, rejection, dispute and complaint procedures should be identified and agreed.

It is normal practice for Contract Givers to impose contractual conditions that ensure quality standards and good manufacturing practice. This is frequently achieved in the first instance by a visit to the manufacturing unit, whether at home or abroad, by the Contract Giver's auditors. The visit should include the following objectives:

a) to ensure that the food supplement can be produced safely within the manufacturing environment;
b) to agree on a detailed product specification that covers all aspects of product, process, pack and delivery; this should include the parameters to be used for acceptance or rejection, and any legal requirements relating thereto;
c) to agree on levels of sampling of finished products by the Contract Giver and sample plans to be used in case of dispute;
d) to agree on the methods for determination of dates of expiration and the confirmatory documents that should be provided to the Contract Giver;
e) to evaluate the adequacy of the control resources, systems, methods and records of the manufacturer;
f) to agree, wherever possible, objective methods of examination; subjective measurements should conform to recognised and accepted standards if possible;
f) to agree the period for record keeping.

Agreement in all six areas is generally essential for any manufacturer/Contract Giver trading relationship and should benefit both parties.

When the Contract Giver requests amendments or improvements by the Contract Acceptor, these changes should be well documented and confirmation of acceptance of the completed work should be recorded.

15.2 Technical agreement

A technical agreement is a useful method of clearly defining the responsibilities of each party with regard to the above.

Attention should especially be given to clarifying the responsibilities of each party in relation to key/critical activities, such as:

- the scope of the instructions given by the Contract Giver to the Contract Acceptor;
- approval and release of raw materials;
- changes to the formulation and processes;
- release specification;
- release of the finished product and its transportation;
- the complaints and withdrawal and recall procedures;
- the procedure for notifying the Contract Giver of any abnormalities during the contracted process.

Any agreement may also include a section on the ownership of intellectual material (e.g. formulae, specific processing techniques), together with any restrictions on the transfer of information to third parties. Items of possible confidentiality should be identified and any appropriate safeguards be mutually agreed.

16 Laboratory testing

A Quality Control laboratory should have appropriate premises, facilities, equipment and staff and be so organised as to enable it to fulfil GMP and good laboratory practice (GLP) requirements (see Annex V). The laboratory should complement the scale of the manufacturing operations

Both personnel and facilities will depend on the nature of the product range and the amount of testing required. It is essential that the facilities are appropriate to the needs of the tests.

16.1 Laboratory personnel

Laboratory personnel should be appropriately trained. High standards of work should be set and maintained by rigid adherence to approved and agreed methods and method checks.

All personnel should wear clean protective clothing appropriate to the tasks being carried out, especially eye protection.

See also Chapter 3.

16.2 Laboratory facilities and equipment

Quality Control laboratories should be designed and equipped to suit the operations required. Space should be made available for writing and the storage of documents and records and for any special provisions such as the storage of samples etc. at the appropriate temperature.

All laboratory equipment and instrumentation should be appropriate to the approved test procedures, and should be regularly serviced and calibrated by assigned persons or organisations.

Written operating procedures should be available for each instrument or piece of equipment. All personnel operating the equipment should be trained and familiar with the operating procedures.

Records of each service and calibration must be maintained for each piece of equipment. These records should also identify when the next service or calibration is due.

Where necessary, analytical methods should include a control step to verify that the instrument or piece of equipment is functioning accurately. Defective instruments or equipment should be withdrawn from the possibility of use until the fault has been rectified.

All equipment should be maintained to a high standard of cleanliness in accordance with written procedures.

Suitable facilities should be provided for the placement of laboratory waste material prior to disposal. Procedures should be in place to ensure the careful and responsible disposal of all such waste material.

16.3 Sampling

Whether or not there is an official method required to be used for sampling (e.g. in EU contaminants legislation), written procedures should be developed for sampling and should specify the following:

- the method and frequency of sampling;
- the sampling equipment and type of sample container to be used;
- the quantity of sample required;
- any special precautions to be taken to maintain homogeneity of sample;
- instructions for any subdivision of the sample;
- sample storage and handling requirements prior to testing, e.g. to minimise separation of mixed powders;
- the cleaning and storage of sampling equipment and reusable containers.

Sample containers should be clearly labelled with the contents, sample identification number, lot number and date sampled.

Any tables or notes used for calculation of the sample requirements should be validated.

16.4 Analysis

Written procedures should be created for the preparation of the reagents to be used in the analyses. Reagents should be clearly labelled with the date of receipt or preparation, their concentration, standardisation factor, shelf life and storage conditions, as applicable.

Reference standards, and any secondary standards prepared from them, should be stored, handled and used according to instructions. Reference standards and secondary standards should be clearly labelled with the date of receipt or preparation, their concentration, standardisation factor, storage conditions and shelf life, as applicable.

Samples should be analysed according to written procedures, using test methods which are either legally required or are internationally accepted, or other methods that have been scientifically validated for the required sample matrix. Validation generally includes the following parameters:

- specificity / selectivity;
- recovery;
- precision;
- linearity and range;
- accuracy;
- Limit of Detection (LOD) / Limit of Quantitation (LOQ).

Details of the validation should be recorded and retained.

Results of any sample analysis should be within the validated range of the method used.

16.5 Laboratory documentation

Detailed records should be maintained of all tests and analyses performed in the laboratory. These should be signed or initialled and dated by the analyst responsible for the analysis and countersigned by a second responsible person from Quality Control (or Quality Assurance).

Procedures should be in place so that the data for all sampling, analyses and calculations for each sample are correctly identified in order to ensure traceability (see Annex IV).

Laboratory documents, records and retained samples should be stored for a time period that is consistent with the requirements for the manufacturing records (see Chapter 12).

16.6 External laboratories

Where necessary, in-house testing can be supported by external laboratories who are accredited by an official national or international authority for the specific analysis required. The accredited analysis should cover the sample matrix, that is, the relative combination of the components and form of the sample. If not, a sample specific validation should be carried out and applied.

The selected external laboratory should be contractually required to divulge all details of the analysis when requested by the client.

Trend analyses should be carried out periodically on all analyses carried out by external laboratories, to ensure that there are no major trends or variations developing.

Annex 1
Glossary of terms

Adverse Event Complaint: **Complaint** of any untoward physiological occurrence that is reported as being experienced following the ingestion of a **food supplement** or combination of products and is suspected by the reporter to be related to the product intake.

Analytical Method: a detailed description of the procedures to be followed in performing tests for assessing conformity with the **specification**.

Analyte: the component of a sample that is being analysed.

Audit: Systematic, independent and documented **process** for obtaining **audit evidence** and evaluating it objectively to determine the extent to which **audit criteria** are fulfilled[1].

Audit Criteria: Set of policies, **procedures** or **requirements** used as a reference[1].

Audit Evidence: Relevant information (e.g. physical observation, **records**, results of tests) obtained by the **auditor** in order to assess the extent to which the **audit criteria** are fulfilled and are verifiable.

Auditor: Appropriately experienced and **competent** person who conducts an **audit**.

Batch: see **Lot**.

Buffer Area: An enclosed space between the **storage area** and the manufacturing area, often with positive pressure system, with the aim of reducing the contamination of processes and materials.

Bulk Product: Any **product** that has completed all processing stages up to, but not including, final **packaging**[2].

Central Records System: A group of **records** that is stored and maintained in one location or facility and from which (on electronic versions) information is retrieved by an individual's name, identifying number, or other identifier assigned to that individual.

Change Control: a systematic approach to managing all changes made to a **product** or **system**, ensuring that no unnecessary changes are made, that all changes are documented, that services are not disrupted unnecessarily and that resources are used efficiently.

Characteristic: A feature or attribute that helps to distinguish one thing from another.

Competent: Having suitable or sufficient skill, knowledge and experience for a specific task.

Complaint: Any expression of dissatisfaction, whether oral, written or electronic, and whether justified or not, from or on behalf of a consumer related to a **food supplement product** or group of **products**.

Compound ingredient: an ingredient that is itself the **product** of more than one **ingredient**.

Conformity: Compliance with a particular **specification** or **requirement**.

Contract: A formal written agreement between two or more parties that is enforceable by law.

Contract Manufacture: **Manufacture** or partial **manufacture** of **product** by one person or **organisation** (the contract acceptor) ordered by another person or **organisation** (the contract giver). Services may be provided to several (even competing) organisations based on their own or the contract giver's designs, formulae and/or specifications.

Control Point: Any point, step or **procedure** at which microbiological, physical or chemical factors can be controlled.

Corrective Action: Action to eliminate the cause of a detected **nonconformity** or other undesirable situation in order to prevent recurrence[1].

Critical Control Point (CCP): A step in a **process** or **procedure** which, if controlled, will eliminate or reduce a **hazard** to an acceptable level.

CCP Decision Tree: A sequence of questions to determine whether a **control point** is or is not a **CCP**.

Critical Limit: A criterion which separates acceptability from unacceptability.

Customer: An individual or **organisation** that purchases the services or **product** produced by another **organisation**.

Defect: Non-fulfilment of a requirement related to an intended or specified use[1].

Documentation: The collection of all written or diagrammatic information, whether produced and stored on paper or electronically, that relates to the **manufacture** of a **food supplement**, including instructions, **procedures**, **specifications** and **records**.

Effectiveness: Extent to which planned activities are successful in producing the desired end result.

Finished Product: Any **product** that has completed all processing stages including final **packaging**.

Flow Chart/Diagram: The detailed sequence of operations involved with a particular **product** or **process**, usually from the **raw material** through to the end user.

Food Supplements: Foodstuffs the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form, namely forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles, and other similar forms of liquids and powders.

Hazard Analysis Critical Control Point (HACCP): A systematic and documented approach to **hazard** identification, assessment and control.

HACCP deviation: Failure to meet a **critical limit.**

HACCP Plan: The written document which is based upon the principles of **HACCP** and which delineates the **procedures** to be followed to assure the control of a specific **process** or **procedure**.

HACCP Validation: Obtaining evidence that the elements of the **HACCP plan** are effective.

HACCP Verification: The application of methods, **procedures**, tests and other evaluations, in addition to **monitoring** to determine compliance with the **HACCP plan**.

Hazard: A biological, chemical or physical agent in, or the condition of, a **product** with the potential to cause harm to the consumer.

Hazard Analysis: The process of collecting and evaluating information on **hazards** and conditions leading to their presence to decide which are significant for **product** safety and therefore should be addressed in the plan.

Information: Specific data or details about a subject.

Ingredient: any substance, including flavourings, food additives and food enzymes, and any constituent of a compound ingredient, used in the **manufacture** of a **food supplement** and still present in the **finished product**, even if in an altered form.

Inspection: Examination of **conformity** by appropriate methods.

Intermediate Product: Any material or mixture of materials that have to undergo further stages of processing before becoming a **bulk product** or **finished product.**

Legislation: the law, or group of laws, which apply in the country or region of **manufacture** or intended market.

Lot: A defined quantity of raw **material, packaging material** or **finished product** processed in one process or series of processes so that it could be expected to be homogenous, i.e. uniform in composition and quality.

Lot Manufacturing Record: A comprehensive document that is based on the **Master Manufacturing Instructions**, which is created and developed during the manufacturing process of each **lot** and which provides a full and authoritative record of the manufacturing history of each **lot** of every **product**. It should include details of the **product** name, **lot number**, date(s) of processing, quantity, in-process controls, their results and signature of person who performed these and details of authorisation of any **deviation**, if any was made.

Lot Number: A distinctive combination of numbers and/or letters which specifically identifies a **lot** and allows for full **traceability** of all details relating to the **lot**.

Management: The coordination of the activities of an **organisation** in order to achieve defined objectives.

Management System: A set of interrelated or interacting elements to establish policy and objectives and to achieve those objectives. *(ISO 9000:2000)*

Manufacture: The complete cycle of production and **quality control** of a **food supplement** from the purchase of all materials through all stages of subsequent processing, **packaging** and storage to the distribution or release of the **finished product**.

Manufacturer: The person or **organisation** that is involved in the **manufacture** of a **food supplement**.

Master Manufacturing Instructions: Detailed document(s) that covers all aspects of the **manufacture** of a **food supplement,** including the identification and quantity of all **raw materials** and **packaging materials** and a comprehensive description of the manufacturing operations and procedures (e.g. designation of the equipment and facilities to be used, processing conditions, in-process controls and procedures for the transfer of **finished product** to storage).

Measuring Equipment: Measuring instrument, software, measurement standard, reference material or auxiliary apparatus or combination thereof necessary to realise a **measurement process**[1].

Measurement process: Set of operations to determine the value of a quantity[1].

Monitoring: The planned observations and measurements of targets and tolerances of control points to confirm that the **process** is under control.

Nonconformity: Non-fulfilment of a **requirement**[1].

Objective Evidence: Data supporting the existence or authenticity of something[1].

Operator: The owner or person responsible for a manufacturing business.

Organisation: Group of people and facilities with an arrangement of responsibilities, authorities and relationships[1].

Packaging: All operations, including filling, sealing and labelling, that a **bulk product** has to undergo in order to become a **finished product.**

Packaging Materials: All materials of any nature to be used for the containment, protection, handling, delivery and preservation of a **food supplement** from the manufacturer to the consumer, e.g. containers, closures, bags, packing, label materials (labels, inserts, etc.), seals, binding materials, adhesives and tapes.

Pass Box: box providing a **buffer area** for material pass through.

Potable water: water meeting the minimum requirements as laid down in EU legislation on the quality of water intended for human consumption.

Preventive action: Action to eliminate the cause of a potential **nonconformity** or other undesirable potential situation[1].

Preventative Measure: Any factor that can be used to control an identified **hazard**.

Process: Set of interrelated or interacting activities that transform one or more of the properties (physical, chemical, microbiological, sensory) of the **raw materials.**

Procedure: Specified way to carry out an activity or a **process**[1].

Product: Result of a **process**[1].

Quality: Degree to which a set of inherent **characteristics** fulfils **requirements**[1].

Quality Assurance: Part of **quality management** focussed on providing confidence that quality requirements will be fulfilled. Mainly focussed on intended product[1].

Quality Control: Part of **quality management** focussed on fulfilling **quality** requirements. Includes all measures undertaken during **manufacture** designed to ensure the uniform output of **food supplements** that conform to established **specifications** of identity, purity, strength and other characteristics[1].

Quality Management: Coordinated activities to direct and control an **organisation** with regard to **quality**[1].

Quality Management System: **Management system** to direct and control an **organisation** with regard to **quality**[1].

Quality Manual: **Document** specifying the **quality management system** of an **organisation**[1].

Quality Plan: **Document** specifying which **procedures** and associated resources shall be applied by whom and when to a specific **product, process** or **contract**[1].

Quarantine: The status of any materials or product set aside (physically or by system) while awaiting a decision on their suitability for processing, **packaging** or distribution.

Raw Materials: All materials, whether active or inactive, that are used for the manufacture of **food supplements**.

Recall: The action taken to have a **product** returned to the **manufacturer** from the **customer**/retailer and from the final consumers. Recalls are often made due to safety concerns.

Record: **Document** stating results achieved or providing evidence of activities performed[1].

Recovery: the introduction of all or part of a previous **lot** of the required **quality** into another **lot** at a defined stage of **manufacture**.

Released: The status of **raw materials**, intermediate, **bulk** or **finished products** which are accepted for use in processing, **packaging** or distribution.

Rejected: The status of **raw materials**, intermediate, **bulk** or **finished products** which are not permitted to be used for processing, **packaging** or distribution and which should be discarded in a safe manner.

Reprocessing: using, in the manufacture of a **food supplement**, clean, uncontaminated materials or **product** that have been previously removed from manufacturing and that have been made suitable for use in the **manufacture** of a **food supplement.**

Requirement: Need or expectation that is stated, generally implied or obligatory[1].

Review: Activity undertaken to determine the suitability, adequacy and effectiveness of the subject matter to achieve established objectives[1].

Rework: Action on a **nonconforming product** to make it conform to the **requirements**[1].

Sample Matrix: the components of a sample other than the **analyte**.

Serious Adverse Event Complaint: **Complaint** of an **adverse event** that is reported to have resulted in death, a life-threatening experience, inpatient hospitalisation, a persistent or significant disability or incapacity, a congenital anomaly or birth defect, or if it was required, based on reasonable medical judgment, a medical or surgical intervention to prevent one of these outcomes.

Specification: A **document** giving the description of a **raw material, intermediate, bulk** or **finished product** in terms of its chemical, physical and (if any) biological characteristics. A specification describes in detail the **requirements** with which the products or materials used or obtained during **manufacture** have to conform and normally includes descriptive clauses and numerical clauses, stating standards and permitted tolerances. It serves as a basis for quality evaluation.

Storage Area: designated area within the manufacturing premises where all **raw materials** and/or **quarantined material/product** and/or **finished product** can be kept safe until utilised, disposed of or distributed as applicable.

Supplier: **Organisation** or person that provides a **product**[1].

System: Set of interrelated or interacting elements[1].

Test: Determination of one or more characteristics according to a **procedure**[1].

Tolerance: The specified degree of latitude for a control measure which if exceeded would render the **process** or **product** unsafe.

Traceability: Ability to trace and follow **food supplements** and **raw materials** through all stages of production, processing and distribution.

Validation: Confirmation, through the provision of **objective evidence**, that the specific intended use or application of a **procedure, process**, equipment, material, activity or **system** leads to the expected results[1].

Verification: Confirmation, through the provision of **objective evidence**, that the specified requirements for any **procedure, process**, equipment, material, activity or **system** have been met[1].

Warehouse: **storage area** that may be located either within or away from the manufacturing premises.

Waste: any substance or object which the holder discards or intends or is required to discard.

Withdrawal: The action taken to have a **product** returned to the **manufacturer** from the **customer**/ retailer but not from the final consumers. Withdrawals may be a voluntary action by the company, following concerns of product quality but not necessarily product safety.

1 Sourced or adapted from http://www.qualitytimes.co.in/definitions.htm
2 Sourced or adapted from WHO Technical Report Series, No. 902, 2002

Annex II

Questions to pose to suppliers when deciding on ingredients

Ingredients that have not previously been used in a formulation must be evaluated to ensure that the current legislation within the European Union (EU) is met, alongside any national Member State legislation. In addition, if new suppliers are used or changes in the supplied ingredient are proposed, there are certain issues that must be considered.

1. Are the proposed ingredients considered to be Novel within the EU?

It should be checked as to whether proposed new ingredients would be classified as novel foods, i.e. they have not been in general use in foods or food supplements since May 1997. This classification, which is defined in the legislation, includes ingredients that are completely new and also ingredients that have been used previously in a certain form but that are now manufactured using a novel process. The use of such materials in foods is only permissible where the materials have received full novel foods approval.

Following the introduction of ingredients produced by nanotechnology, the European Commission has stated that all such ingredients are to be considered as novel foods which thus require approval under the conditions of the novel foods legislation. Generally, when considering food ingredients, 'nano' is taken to be a dimension of the order of 100 nm and below. Nanotech ingredients of concern are those that have been deliberately created such that they are composed of discrete functional and structural parts, either internally or at the surface, many of which will have one or more dimensions of the order of 100 nm or less. This is one area where the 'sieve dimensions' in ingredient specifications can be of importance.

2. Have the ingredients been irradiated?

Under current legislation, only certain categories of foods are permitted to be irradiated at approved irradiation facilities and up to specific maximum levels. All irradiated foods have to be labelled as such. Very few supplement ingredients are permitted to be irradiated, but a number of illegally irradiated ingredients are known to come in from countries outside of the EU. In general, irradiation is not permitted for botanicals or products of animal origin in supplements.

3. Have all the components of compounded ingredients been revealed?

A large number of ingredients used in food supplements are compounded, in that they have other substances added as technological or organoleptic aids. All sub-components of an ingredient have to be declared in the ingredients listing, regardless of quantity, unless they fall within one of the following categories:

a. the constituents of an ingredient which have been temporarily separated during the manufacturing process and later reintroduced but not in excess of their original proportions;
b. food additives and food enzymes:
    i. whose presence in the food supplement is solely due to the fact that they were contained in one or more ingredients of that food supplement, in accordance with the carry-over principle referred to within the Regulation on food additives, provided that they serve no technological function in the finished product; or
    ii. food additives which are used as processing aids;
c. carriers and substances which are not food additives but are used in the same way and with the same purpose as carriers, and which are used in the quantities strictly necessary;
d. substances which are not food additives but are used in the same way and with the same purpose as processing aids and are still present in the finished product, even if in an altered form;

e. water:
   i. where the water is used during the manufacturing process solely for the reconstitution of an ingredient used in concentrated or dehydrated form; or
   ii. in the case of a liquid medium which is not normally consumed.

Care has to be taken to ensure that all sub-components have been declared by the ingredient manufacturer or supplier. As the rule on compounded ingredients does not apply to many countries outside of the EU, many manufacturers do not voluntarily declare the whole composition of their ingredients. It is essential that certification of their composition is obtained from the supplier.

Care must also be taken to ensure that, if the ingredient contains a substance that appears on the allergen listing set in EU legislation, this is clearly labelled within the ingredients list on the final product. The name as indicated in the allergen listing must be used and, from 13 December 2014, it will be mandatory that the allergen is highlighted in the ingredients list in some manner, e.g. by bold text or text of another colour.

4. Have the ingredients been checked for potential contaminants and are these compliant with EU levels?

4.1 Heavy Metals/Trace Elements

Specific limits are set in the EU for food supplements for lead, cadmium and mercury.

4.2 Microbiological Contamination

Although official limits have not been set in the legislation for all possible ingredients of food supplements, care should be taken that raw materials have been assessed for microbiological contamination. Unprocessed botanical ingredients in particular have a potential for relatively high microbiological loadings. When agreeing a specification with the supplier, realistic levels should be set. However, if suspiciously low microbiological values are found in botanical ingredients or some ingredients of animal origin, it may be necessary to further check that the material has not been subjected to irradiation or gaseous sterilisation.

4.3 Dioxins, Furans and Polychlorinated Biphenyls (PCBs)

Limits are set in the EU for dioxins, furans and dioxin-like PCBs in foods, including components of food supplements such as oils.

4.4 Polycyclic aromatic hydrocarbons (PAHs)

Limits are set in the EU for Benzo(a)pyrene and the sum of benzo(a)pyrene, benz(a)anthracene, benzo(b) fluoranthene and chrysene in certain foods. This is of particular note for oils and fats that may be used in food supplements.

4.5 Mycotoxins (e.g. aflatoxin)

Maximum levels are set in EU legislation for certain foods that may be used as ingredients in food supplements. Fungal attack and the possibility of aflatoxin residues should be particularly considered for botanical products, for which some specific limits are set.

4.6 Pesticides and Herbicides

This is of particular concern with botanical materials. Maximum residue levels of pesticides are set within EU legislation.

4.7 Extraction solvent residues

Maximum residue limits in the extracted food or food ingredient are set within EU legislation, as are the actual extraction solvents that may be used during the processing of raw materials, foods, food components or ingredients. These include limits for extraction solvents used in the preparation of flavourings.

4.8 Botanical Products

Many botanical products contain both biologically active compounds responsible for their action, and undesirable compounds, which are also natural constituents of the plant species used. The EU has set prohibitions and controls on certain substances found in botanical powders and extracts. In particular, there are certain substances listed in the legislation that must not be added as such to food. These substances, which include capsaicin, can not be added to any foods regardless of whether they are being included for flavouring or not. Where botanical extracts have been standardised by the addition of isolated substances, care must be taken that this addition complies with the legislation.

5. Are all the ingredients from a non-genetically modified (GM) source?

Legislation is in place in the EU that controls the use of genetically modified organisms in foods and food ingredients. It is essential to have specifications from the supplier confirming that the ingredient is obtained from a non-GM source as defined in the legislation. If GM ingredients are used, or the ingredients are from GM sources, this must be stated on the label in accordance with the legislation.

6. Is there consistency of production of the ingredient?

It must be confirmed whether the supplier can prove consistency of production of the ingredient. Documentation should be requested that shows that there is no significant variation between the batches, which could affect the quality of the finished products.

Annex III

Example of a HACCP Control Chart

The example of a HACCP control chart for food supplement tablets or capsules, as outlined on the following pages, is kindly provided by the Council for Responsible Nutrition (UK).

CONTROL CHART								
STEP NO.	PROCESS	HAZARD	CONCERN LEVEL	PREVENTATIVE CONTROL	CCP?	CRITICAL	RESPONSIBILITY	ACTION OUTSIDE CONTROL LIMITS
1	Raw material delivered	Dirty / damaged container	L	All goods inspected on delivery	CP	Each delivery checked	Warehouse	Do not accept delivery & investigate.
		Wrong material delivered	M	Material name, code no. and quantity checked on delivery vs delivery note	CP	Every delivery	Warehouse	Do not accept delivery & investigate.
		Microbiological	H	Susceptible material tested	CCP	Raw material	QC	Material placed in Quarantine.
2	Sampling & Testing	Contamination during sampling	L	Raw material sampling booth Sampling procedure Staff training	CP	Sampling procedure & test method	QC	Material Rejected. Retrain staff member.
		Material not to specification	M	Tested by QC to raw material spec. CofA / CofC for each batch delivered	CCP	Each batch delivered tested against raw material spec	QC	Material placed in Quarantine pending completion of tests.
3	Transferred to passed stock	Forklift truck damage	L	Training	QP	Each Transfer	Warehouse	Damaged containers repaired / rejected.
4	Stored	Pests	H	Contract with pest control company	CCP	Reports issued	Warehouse	Recommendations by Contractor completed in timely manner.
		Temperature	L	Temperature monitored	QP	Recorded	Warehouse	Segregated storage.
		Degradation	L	All materials labelled with shelf-life FIFO principles are followed.	QP	Limits specified on raw material spec.	QC and warehouse	Materials placed in Quarantine & re-tested by lab.
5	Transfer of materials to production	Forklift truck damage	L	Training	QP	Each Transfer	Warehouse	Damaged containers repaired/ rejected.
		Wrong Material transferred	M	Materials checked against works order	CP	Name, code no. and quantity checked	Warehouse	Isolate incorrect materials and immediately return to storage.
6	Cleaning of room and equipment	Contamination from previous product	M	Cleaning schedules in place Cleaning checked by supervisor and QA	CP	Procedure Recorded	Production and QA	Room re-cleaned and re-inspected.
		Microbiological contamination	M	Sanitiser used for cleaning Monitoring of cleaning	CP	Hygiene test method	Production and QA	Re-cleaned and rechecked. Investigate if result is out of specification.
				Environmental monitoring performed		Test method		Review cleaning procedures and methods.
				COSHH exercised	CP	Procedure	Production	COSHH audit.
		Residues of cleaning agents	L	Cleaning standards verified.	N		Production	Review cleaning procedures and agents.

CONTROL CHART								
STEP NO.	PROCESS	HAZARD	CONCERN LEVEL	PREVENTATIVE CONTROL	CCP?	CRITICAL	RESPONSIBILITY	ACTION OUTSIDE CONTROL LIMITS
7	Raw material transferred to dispensary	Materials not Passed	M	Each container checked for PASS label before use	QP	Procedure	Production	Place materials in quarantine. Retrain.
8	Raw material dispensed	Wrong quantity weighed out	M	All quantities double checked Balance calibrated	CCP	Specified on production Document Calibration Procedure	Production QC	Corrective action taken and recorded on the production document. Retrain. Balance calibrated.
		Wrong material weighed out	M	All material name and code numbers double checked	CCP	Specified on production document	Production	Incorrect material returned and material re-weighed. Retrain. Recorded on production document
		Contamination during dispensing	M	Clean scoops for each material Protective clothing worn by operators Filtered air supplied to manufacturing area Dust extraction used	CP	Dispensary procedure Hygiene procedure SP1	Production	Material placed in Quarantine. Filters checked – investigated
9	Sieved	Metal contamination from broken sieve	M	Integrity of sieves inspected	CCP	Mesh must be intact	Production	Material placed in Quarantine and metal detected.
10	Transferred to mixing vessel	Contamination from vacuum transfer system	L	Filters checked Regularly	CP	Inspection Recorded	Production	Change filters.
11	Materials mixed	Mixing time set wrong	L	Specified on production document	CP	Timer set as per process	Production	Investigation and corrective actions recorded on production document.
		Contamination during mixing	L	Materials mixed in closed system	CP	No foreign bodies	Production	Investigation & Materials placed in Quarantine.
		Not adequately mixed	M	Mixing validated to verify mixing time	CCP	Test against product specification	QC	Remix. Retest & record results on production document.
12	Transfer of mixed materials	Drums mixed up	L	Drums numbered and labelled and kept together Each pallet labelled	CP	Each batch	Production	Investigate & materials placed in Quarantine.

CONTROL CHART								
STEP NO.	PROCESS	HAZARD	CONCERN LEVEL	PREVENTATIVE CONTROL	CCP?	CRITICAL	RESPONSIBILITY	ACTION OUTSIDE CONTROL LIMITS
13	Compression Encapsulation	Foreign body Contamination	M	Protective clothing is worn. Materials kept covered. Materials are metal detected.	CP	Visually checks. Metal detection test pieces	Production and QA Production	Investigate. Check filters and investigate. Place material ON-HOLD metal detect product. Reject tablets.
		Product not to specification	M	1st Sample checks In process checks Samples taken throughout manufacture	QP	Finished product specification In process testing specified on production document	QA / QC Production	Place material in Quarantine. Rework if required.
14	Coating	Microbiological	L	Water heated	CP	> 65°c	Production	Not used unless reaches >65°c
		Foreign bodies	L	Kept covered	CP	No foreign bodies	Production	Investigate.
	Add coating ingredients	Wrong ingredients or quantities	M	Check vs production document	CP	Production document	Production	Place materials in Quarantine.
	Mix	Foreign bodies	L	Kept covered	CP	No foreign bodies	Production	Investigate per Procedure.
	Make up to volume	Incorrect volume	L	Checked vs production document	N	Production document	Production	Investigate per Procedure.
		Microbiological	L	Water checked for Ecoli coliforms and TVC	CP	No Ecoli or coliforms Test method	QA	Re-test and investigate
	Cool and store	Foreign bodies	L	Kept covered during cooling	CP	No foreign bodies	Production	Procedure
		Microbiological	M	All containers cleaned following cleaning schedules	CP	Visual check	Production	Re-clean and reinspect
		Microbiological	L	Stored for 72 hours max labelled with shelf-life	CP	Shelf-life checked before use	Production	If >72 hours reject.
	Label	Incorrect labels	L	Checked vs production document	QP	Production document	Production	Reject & dispose of incorrect label and re-label with accurate label.
	Transfer to spray vessel	Wrong solution used	L	Checked vs production document	QP	Production document	Production	Place materials in Quarantine & Investigate.
	Add plasticer and colour	Incorrect material / quantity	L	All materials code numbers checked vs production document	QP	Process sheet	Production	Place materials in Quarantine & Investigate.
	Mix	Foreign body	L	Vessel closed, solution passes fine atomiser.	CP	No foreign bodies	Production	Investigate

CONTROL CHART								
STEP NO.	PROCESS	HAZARD	CONCERN LEVEL	PREVENTATIVE CONTROL	CCP?	CRITICAL	RESPONSIBILITY	ACTION OUTSIDE CONTROL LIMITS
14	Pre heat coating vessel	Incorrect temperature	L	All settings checked vs production document. Accelacota temperature calibrated	CP	Specified on production document Calibration control	Production QC	Investigate & record on production document. Service and recalibrate.
	Add bulk tablets to pan	Wrong tablets	M	Checked vs production document	CCP	Specified on production document	Production	Investigate & record action taken on production document.
	Spray tablets with coating solution	Uneven coating	L	Product checked during coating	QP	Checked vs sample if supplied	Production	Check spray nozel, re-spray and reinspect.
	Cool	Foreign body contamination	L	All air to manufacturing area filtered Operators wear protective clothing Metal detection	CP CCP	Procedure Hygiene procedure Metal detection test pieces	Production Production Production	Check filters and investigate. Investigation.
15	Pack into bulk cartons	Foreign body contamination	L	All bags sealed immediately	CP	No foreign bodies	Production	Place material in Quarantine & Investigate.
		Condensation	L	Tablets cooled before packing	CP	Heat is turned off whilst tablets waxed and passed through metal detector temp <40oC.	Production	Re-dry, cool and pack.
16	Reconciliation	Incorrect final quantity	M	Reconciliation when batch complete	CCP	Target Limits	Production	Investigate and document findings. Reconciliation verified by Q.C before batch release.

Annex IV
Traceability

‘Traceability’ means the ability to trace and follow a food supplement, or a raw material that is intended to be incorporated into a food supplement, through all stages of production, processing and distribution.

All businesses in the food supplement supply chain, including importers, should be able to identify the business from which the food supplement, or the raw material that is to be incorporated in the food supplement, has been supplied. All businesses in the supply chain should also be able to identify the other businesses to which their products have been supplied (excluding to the final consumer). In simple terms, the very minimum requirement is that the documentation retained by a food supplement business should establish ‘one step back and one step forward’ in the supply chain.

Systems and procedures should be in place to ensure that records of traceability are maintained and are readily available in the event of the information being requested by the authorities.

It is a legal requirement that food supplements that are placed on the EU market, or that are likely to be placed on the EU market, be adequately labelled or identified in order to facilitate their traceability through the relevant documentation.

A comprehensive system of traceability enables targeted, rapid and accurate withdrawals to be undertaken, or specific information to be given to consumers or the authorities, thereby avoiding the potential for unnecessary wider disruption in the event of a safety concern.

Annex V
Useful resources

Further information on EU food law, with links to the relevant pieces of legislation, can be found on the European Commission's website at:

http://ec.europa.eu/food/food/foodlaw/index_en.htm

Chapter 2

European Organisation for Quality

http://www.eoq.org/

Chapters 3 and 4

Recommended International Code of Practice-General Principles of Food Hygiene. Codex Alimentarius CAC/RCP 1-1969, Rev. 4-2003:

http://www.codexalimentarius.org/standards/list-of-standards/ http://www.codexalimentarius.org/)

Chapter 5

Chemical and Microbiological Contaminants in Supplements and their Ingredients: A Guide to Encourage Good Practice. 2009. Council for Responsible Nutrition, London, United Kingdom.

http://www.crnuk.org/

CRN Technical Guide to the development, manufacture and compliance of quality food supplements (3rd edition) 2009. Council for Responsible Nutrition, London, United Kingdom.

http://www.crnuk.org/

Chapter 10

Annex to the Recommended International Code of Practice-General Principles of Food Hygiene. Codex Alimentarius CAC/RCP 1-1969, Rev. 4-2003.

http://www.codexalimentarius.org/standards/list-of-standards/ http://www.codexalimentarius.org/

Chapter 11

Shelf-Life Recommendations for Supplements

http://www.iadsa.org/publications/1390199690_Shelf_Life_Recommendations_fo.pdf

http://www.iadsa.org/

Chapter 13

EU Commission guidance document on the implementation of the General Food law main requirements, including responsibility of food businesses, withdrawal of unsafe food from the market and notification to the authorities. (26 January 2010).

http://ec.europa.eu/food/food/foodlaw/guidance/docs/guidance_rev_8_en.pdf
http://ec.europa.eu

Global Guide to The Handling of Adverse Event Complaints: Guidelines for Supplement Companies. International Alliance of Dietary / Food Supplement Associations. 2012.

http://www.iadsa.org/publications/1350552619_Global_Guide_to_the_Handling_.pdf

http://www.iadsa.org/

Chapter 16

Organisation for Economic Co-operation and Development (OECD) Environmental Health and Safety Publications Series on Principles of Good Laboratory Practice and Compliance Monitoring No. 1: OECD Principles of Good Laboratory Practice (as revised in 1997) (ENV/MC/CHEM(98)17).

http://www.oecd.org/

Annex IV

EU Commission guidance document on the implementation of the General Food law main requirements, including Traceability (26 January 2010).

http://ec.europa.eu/food/food/foodlaw/guidance/docs/guidance_rev_8_en.pdf

http://ec.europa.eu

The European food supplement sector brings together many of the most innovative and dynamic companies in the food area, making a substantial contribution to Europe's public health goals.

Food Supplements Europe combines the unique expertise of associations and companies committed to building partnership with regulatory, scientific and consumer bodies to help shape the future regulatory and policy framework in this area and to ensure that consumers can benefit from safe and high quality products.

food supplements europe

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