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Guideline on Good Agricultural and Collection Practice (GACP) for starting materials of herbal origin

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EXECUTIVE SUMMARY

This guideline on Good Agricultural and Collection Practice (GACP) for starting materials of herbal origin came into effect in August 2006 and is intended to provide guidance to ensure appropriate and consistent quality of herbal substances[1]. The current Revision 1 of the GACP guideline pertains to an update of the document to current standards taking into account advances over the last 10 years, as for instance, the increased development of indoor growing technologies, and also cover the established practice and legal interpretations published during this period.

1. INTRODUCTION

Herbal medicinal plants can be collected from the wild or cultivated. In most cases cultivation is performed on the land, indoor cultivation or in greenhouses. Nowadays indoor cultivation, where environmental factors such as light, temperature, and humidity can be controlled, is increasingly applied.

The cultivation, production and primary processing of the medicinal plant has a direct influence on the quality of the active pharmaceutical ingredient (API) used in herbal preparations[2]. Due to the inherent complexity of medicinal plants and herbal substances the quality of these starting materials requires an adequate quality assurance system for the collection and/or cultivation, harvest, and primary processing.

The choice of preferred conditions of obtention of the plants, for instance, wild collection or cultivation (either outdoor, indoor or in greenhouses) should be carefully considered, since each of the mentioned types could have several problems and advantages. The used cultivation method may be dependent on the final application of the herbal medicinal product. Collection in wild habitats for instance, may present special problems, especially with regard to confusion with similar plants, environmental damage, lack of control and poorly qualified personnel. Also, due to the possible non-uniformity between plants growing in the wild, variations in the composition can be a challenge exhibited by these plants. However, in situations where the agronomic requirements for a specific plant cannot be met by cultivation practices, manufacturers may opt for the collection of the specific herb from wild sources. This Guideline should be used as a basis for the establishment of an appropriate quality assurance system for the collection and/or cultivation, harvest and primary processing of herbal substances for use in the preparation of herbal medicinal products.

Information relating specifically to indoor cultivation is indicated in *"italics"*.

2. SCOPE

This guideline is intended to address the specific concerns related to the cultivation, collection, and primary processing of herbal substances that are used for the preparation of herbal medicinal products.

It addresses specific issues associated with outdoor, greenhouse and indoor cultivation, collection of medicinal plants/herbal substances in the wild and production facilities for the primary processing of medicinal plants/herbal substances.

[1] The term "herbal substance" should be considered as equivalent to the term "herbal drug" as defined in the European Pharmacopoeia

[2] The term "herbal preparation" should be considered as equivalent to the term "herbal drug preparation" as defined in the European Pharmacopoeia

These considerations should be read in connection with EudraLex Volume 4 GMP guidelines Part II for APIs[3] and Annex 7[4] Manufacture of Herbal Medicinal Products and should apply to all methods of production in accordance with regional and/or national regulations.

The operations that should fall under the scope of GACP, GMP part II (for APIs) or GMP part I (for medicinal products) depend on the application of the finished medicinal product. In general, the closer the preparation is to the final product, the stricter the requirements are. For instance, the requirements applicable to a comminuted herbal substance sold as a herbal tea should be higher than the requirements applicable for a herbal substance which will be subject to further processing steps, such as extraction. Manufacturers should ensure that all the steps are carried out in accordance with the marketing authorisation/registration and therefore establish an appropriate quality assurance system in different cultivation circumstances. This Guideline provides additional standards for the production and processing of medicinal plants/herbal substances insofar as they mainly focus on identifying those critical production steps that are needed to ensure good quality.

The main aim is to ensure patient safety by establishing adequate quality standards for obtaining medicinal plants and herbal substances, ensuring that they are handled appropriately throughout all stages of cultivation, collection, processing and storage.

The handling of the herbal substance should be in accordance with good hygiene practices, to ensure microbiological load is kept to a minimum. Therefore, care should be taken avoid agricultural inputs e.g. fertilisers, growth media/promoters etc being a source of contamination.

During cultivation, harvest, collection, and primary processing, medicinal plants, herbal substances and their preparations are exposed to a large number of environmental contaminants of both biotic and abiotic origin. This Guideline provides recommendations for producers to reduce contamination to a minimum.

Considerations and recommendations in this Guideline are intended for all participants from cultivators, harvesters, collectors, producers, traders, and processors of medicinal plants and herbal substances. Therefore they each should comply with these considerations, document all relevant activities in batch documentation and demand that their partners do likewise, unless it can be justified. The manufacturer of medicinal product should ensure that regular audits of the primary producers (cultivators, harvesters, and collectors) are performed.

Growers and collectors of medicinal plants and herbal substances must ensure that they avoid damage to existing wildlife habitats and must adhere to CITES (Convention on International Trade in Endangered species of Wild Fauna and Flora).

3. QUALITY MANAGEMENT

Agreements between producers (cultivators, harvesters, collectors) and buyers of medicinal plants/herbal substances should make reference to the GACP quality assurance system and should be laid down in written form.

GACP quality assurance system compliance should be verified through regular audits of the cultivation or collection sites and processing facilities by expert representatives of producers and buyers.

[3] https://health.ec.europa.eu/document/download/bd537ccf-9271-4230-bca1-2d8cb655fd83_en?filename=2014-08_gmp_part1.pdf
[4] https://health.ec.europa.eu/document/download/fd318dd6-2404-4e67-82b0-2324825e4d90_en?filename=vol4_an7_2008_09_en.pdf

4. PERSONNEL AND TRAINING

All primary processing procedures should fully conform with regional or national guidelines on hygiene and personnel entrusted with handling of medicinal plants/herbal substances. The personnel should be required to have a high degree of personal hygiene (including personnel working in the field) and have received adequate training regarding their hygiene responsibilities.

1. Personnel must be protected from contact with toxic or potentially allergenic medicinal plants/herbal substances via skin, eyes or inhalation, by means of adequate protective clothing or other adequate measures.

2. Persons suffering from known infectious transmittable diseases, must be suspended from areas where they are in contact with medicinal plants/herbal substances, according to regional and/or national regulations.

3. Persons with open wounds, inflammations and skin-infections should be suspended from areas where the plant processing takes place or should have to wear appropriate protective clothing/gloves until their complete recuperation. Special care should be applied when the herbal material is intended to be used in a further unprocessed state (irrespective to the route of administration).

4. There should be an adequate number of personnel qualified by appropriate education, training and/or experience to perform and supervise all related operations. Training should be regularly conducted by qualified individuals and should be periodically assessed. Records of training should be maintained, as required by the manufacturer.

5. Collectors must have sufficient knowledge of the plant they have to collect. This includes identification, characteristics and habitat requirements. The collectors must be able to differentiate between the collected species and botanically related and/or morphologically similar species to avoid any risk to public health and environmental damage. Collectors must have sufficient knowledge about the presentation of plant pests to recognize diseased plants/plant parts in order not to collect them. Collectors should have sufficient knowledge about the best time to harvest and harvesting technique, and the importance of primary processing to guarantee the best possible quality. Collectors should be instructed on all issues relevant to the protection of the environment and conservation of plant species, including information on regulations related to protected species. If collectors are lacking the adequate knowledge, a local supervisor should guarantee the training, supervision and documentation.

6. Personnel dealing with the medicinal plant and all those engaged in its cultivation should receive adequate botanical and agronomical training before performing particular cultivation steps (e.g., pruning) and regarding cultivation techniques, including appropriate use of herbicides and pesticides or beneficial arthropods and microorganisms. Personnel should receive adequate training in handling the plants (e.g., under controlled climate circumstances in case of indoor cultivation). Personnel must have sufficient knowledge about the presentation of plant pests to recognize diseased plants/plant parts in order not to harvest them. Harvesters should have sufficient knowledge about the best time to harvest and harvesting techniques and the importance of primary processing to guarantee the best possible quality.

7. Personnel should be trained in the maintenance and cleaning of equipment and schedules and procedures (including assignment of responsibility) should be established for the equipment maintenance and cleaning as a preventive measure against contamination.

8. In general, personnel should be trained not to engage in activities such as smoking, eating, drinking, eating and storing food in the direct proximity of the plants to avoid contamination. *For indoor cultivation these activities should be restricted to separate designated areas.*

5. BUILDING AND FACILITIES

Buildings used in the processing of harvested medicinal plants/herbal substances must be clean, as well as thoroughly aerated and must never be used for housing livestock.

Buildings must provide adequate protection for the harvested medicinal plants/herbal substances against birds, insects, rodents and domestic animals. In all storage and processing areas suitable pest control measures such as rodent traps, baits and electric insect killing machines must be operated and maintained by professionally qualified staff or contractors.

It is recommended that the packaged medicinal plant/herbal substance be stored:

- in buildings with concrete or similar easy to clean floors;
- on pallets;
- with a sufficient distance from the wall;
- well separated from other herbal substances to avoid cross-contamination.

Buildings where plant processing is carried out, must have changing facilities as well as toilets including hand-washing facilities, according to regional and/or national regulations.

Indoor cultivation facilities should contain adequate systems for air, climate and humidity control, light, ventilation and air filtration systems. They are designed to:

- *minimize potential contamination;*
- *facilitate cleaning, maintenance and other operations;*
- *be impermeable to cleaning and disinfecting agents.*

Designated areas for different stages of cultivation may be assigned.

6. EQUIPMENT

Equipment used in plant cultivation and processing should comply with the following points:

- Equipment should be clean, regularly serviced and maintained to ensure good working order and mounted, where applicable, in an easily accessible way. Furthermore, equipment used in fertiliser and pesticide application, or other operations must be qualified and regularly calibrated.
- Those machine parts that are in direct contact with the harvested medicinal plant, must be cleaned after use to ensure that remaining residue does not result in subsequent cross-contamination.
- The equipment should be made from appropriate materials so that cross-contamination of medicinal plants/herbal substances with chemicals and other non-desirable substances is prevented.

Equipment and other supportive systems used in the critical steps of cultivation, processing, packaging and storage, should be shown to be appropriate for the intended use, and this process should be documented.

7. DOCUMENTATION

The following should be documented as agreed with the manufacturer:

- All processes and procedures that may impact the quality of the product e.g. training, personal hygiene, cleaning and maintenance activities, irrigation, fertilisation, applications of pesticides and herbicides, harvesting, processing, packaging, residual plant material and management (if relevant).
- Any extraordinary circumstances occurring during the cultivation period that may influence the chemical composition of the medicinal plant, e.g., extreme weather conditions, pests and plant diseases (particularly in the harvest period).
- For cultivated medicinal plants: the geographical location i.e. exact country and region/ area/ province. The type, quantity, and the date of harvest as well as the chemicals and other substances used during production. Site records showing previous crops, varieties and/ or cultivars and plant protection products used.
- For wild collection of medicinal plants: the geographic location i.e. exact country and region/ area/ province. The type, quantity, and the date of collection.
- The use of fumigant products.
- Batches of herbal substances should be unambiguously and unmistakeably traceable to their sources. Therefore, appropriate labelling and batch assignment should take place as early as possible in the process. Wild collected and cultivated material should be assigned different batch numbers.
- Single and combination batches of the same plant species harvested from different geographical location, i.e. exact country and region/ area/ province, and/ or subject to different cultivation conditions.
- All agreements between each producer or collector and the manufacturer, e.g., production guidelines, contracts etc. should be in written form.
- The audit reports, including those by or on behalf of the GMP licensed manufacturers or other parties. Copies of all documents, audit reports, analysis reports etc. should be stored.

For indoor cultivation (and greenhouse, if applicable) the agronomic conditions and all materials used during cultivation should be fully documented. If applicable, acceptance criteria for all cultivation conditions to obtain the specified quality should be laid down and documented for each batch. All documents related to the cultivation and production should be prepared, reviewed, approved and distributed according to written procedures. A procedure should be established for retaining all appropriate documents. All the specifications related to the process and product should be documented. All cleaning activities should be recorded in the batch records and appropriate logbooks. For indoor cultivation daily records of critical process parameters must be kept and reviewed.

8. SEEDS AND PROPAGATION MATERIAL

Seeds should originate from plants that have been accurately identified in terms of genus, species, variety/ cultivar/ chemotype and origin and should be traceable. The same applies to vegetatively propagated medicinal plants. Seeds and/ or vegetatively propagated medicinal plants used in organic production must be certified as organic. The starting material should be free from pests and diseases in order to guarantee healthy plant growth. Where possible, stable varieties and cultivars naturally

resistant or tolerant to disease should preferably be used. Seeds should be free from seeds of other species, especially seeds of plants that contain toxic components, like pyrrolizidine alkaloids.

The presence of different species, varieties, or different plant parts must be controlled during the entire production process, and such adulteration should be avoided. The use of genetically modified medicinal plants or seeds must comply with regional and/or national regulations.

Suppliers of materials used in cultivation must be evaluated and qualified according to established procedures. Changing the source of supply of materials should be handled through the Change Control procedure.

9. CULTIVATION

The chosen method of cultivation should be described in a standard operating procedure (SOP), taking care to avoid any negative environmental impact. The principles of good crop husbandry must be followed and include appropriate rotation of crops if applicable.

- Soil and fertilisation:
    - Medicinal plants should not be grown in soil or substrate contaminated with sludge, heavy metals, residues, plant protection products or other chemicals. Any products used in the growth or protection of the crop should be kept to a minimum and its use should be justified.
    - In cases where the area considered for the cultivation of the medicinal plant is potentially contaminated or is in close proximity to contaminated areas, the responsible person should take suitable measures (including testing) prior to the commencement of the cultivation process.
    - Manure should be thoroughly composted and should be void of human faeces. The use of compost containing toxic plants must be avoided.
    - All other fertilising agents should be applied sparingly and in accordance with the needs of the particular plant species. Fertilisers should be applied in such a manner as to minimise leaching.
    - All fertilising agents should be appropriated in order to avoid contamination with heavy metals and organic contaminants, such as PCBs and PAHs.
- Irrigation:
    - Irrigation should be controlled and carried out according to the needs of the medicinal plant.
    - Water used in irrigation should comply with the country of destination's regional/ national quality standards.
- Crop maintenance and plant protection:
    - Tillage should be adapted to plant growth and requirements. During the cultivation season, any toxic weeds should be removed from the field and not composted.
    - Pesticide and herbicide applications should be avoided as far as possible. When necessary, approved plant protection products should be applied at the minimum effective level in accordance with the recommendations from the manufacturer and approved by the authorities of the country of destination. Consideration should be given to exclude their application to those plants that rapidly uptake and retain them.

The application should be carried out only by qualified staff using approved equipment. The minimum interval between such treatment and harvest time must be stipulated by the buyer or be consistent with recommendations from the manufacturer of the plant protection product. Regional and/or national regulations on maximum residue limits in the European Pharmacopoeia, European Directives, Codex Alimentarius etc. should be complied with.

- In situations where the cultivation site is located in an area of other cultivation activities, the risk for possible contamination with pesticides and herbicides not approved for the concerned species should be assessed.
- The cultivated plant should be monitored for signs of defects, regardless of whether these are of biotic or abiotic origin. Suitable rogueing should be carried out to maintain the plant in good growing conditions.
- *In case of indoor cultivation* (and if applicable to greenhouse setups)*, and if the following aspects should also be considered. There should be written procedures describing the receipt, identification, storage, handling, sampling and approval or rejection of materials. The company's overall policy, intentions, and approach to validation, including the validation of production processes, cleaning procedures and persons responsible for design, review, approval and documentation of each validation phase, should be documented. All the equipment involved in the cultivation process must be calibrated according to the established procedure and schedule. Before a new cultivation cycle, all materials used should be checked and approved by the person responsible for quality.*
- *For indoor cultivation critical quality attributes and critical process parameters should be identified. Appropriate in-process acceptance criteria and controls must be established. Cultivation process must be standardised in order to ensure reproducible results. Qualification of critical equipment and ancillary systems should be completed.*

10. COLLECTION

Designated individuals should supervise the collectors of the medicinal plants/herbal substances and also identify and verify the collected material (see 4.5, 4.6 and 4.7).

Collection must be carried out in compliance with existing regional and national and/or national species conservation legislation. Collection methods must not damage the growth environment ensuring optimum conditions for regeneration of the medicinal plant.

Medicinal plants/herbal substances from species that are listed as endangered (CITES, Convention on International Trade in Endangered Species of Wild Fauna and Flora) must not be collected unless the relevant competent authority has given its authorisation.

Medicinal plants/herbal substances from species that are not yet listed as endangered (section 10.3) should undergo a risk assessment prior to collection to ensure that the species is not pushed towards extinction.

11. HARVESTING

Medicinal plants/herbal substances should be harvested when they are at the best possible quality for the proposed use. The following should be noted:

- Damaged plants or plant parts need to be excluded or limited in accordance with a specific pharmacopoeia monograph, where relevant.
- Ensure the best possible conditions avoiding wet soil, dew, rain, or exceptionally high air humidity. Harvesting in wet conditions can have adverse effects on the medicinal plant/herbal substance. (e.g., postharvest spoilage).
- Cutting devices or harvesters must be appropriately cleaned and adjusted so that contamination from foreign matter, leaking lubricants, and other extraneous agents and/ or particles is reduced to a minimum. Such devices should always be maintained in good working order. Recommendations in section 6. Equipment must be followed and documented.
- The harvested medicinal plant/herbal substance should not come into direct contact with the soil or floor. It must be promptly collected in suitable containers and transported in dry, clean conditions.
- Care should be taken to ensure that no toxic weeds are co-harvested with medicinal plants/herbal substances.
- All containers used during harvesting must be clean and free of contamination from previous harvests. When containers are not in use, they must be kept in dry conditions free of pests and inaccessible to rodents, livestock and domestic animals.
- Mechanical damage and compacting of the harvested medicinal plant/herbal substance that would result in undesirable quality changes must be avoided. In this respect, attention must be paid to:
    - overfilling of the sacks;
    - stacking up of sacks.
- Freshly harvested medicinal plants/herbal substances must be delivered as quickly as possible to the processing facility to prevent physical or chemical degradation or microbial growth.
- The harvested crop must be protected from pests, rodents, livestock and domestic animals. Any pest control measures taken must be documented.

12. PRIMARY PROCESSING

Primary processing may include washing, cutting before drying, microbial decontamination, freezing, distillation, primary and secondary drying, etc. Where applicable, all these processes must conform to the competent authority regulations and should be carried out as soon as possible after harvesting.

In some circumstances drying and cutting should be performed according to EudraLex Volume 4 GMP part I or II (refer the GMP Table[5] in Annex 7).

In exceptional circumstances, which must be justified in the marketing authorisation/registration, some of these steps, like expression and distillation, may be performed in the field, only if it is necessary for these activities to be an integral part of harvesting in order to maintain the quality of the product within the approved specification (see note to the Table of GMP Annex 7).

- On arrival at the processing facility, the harvested medicinal plant/herbal substance must be promptly unloaded and unpacked. Prior to processing, the material should not be exposed

[5] The Table illustrating the application of Good Practices to the manufacture of herbal medicinal products is found in EudraLex Vol. 4 Annex 7, page 3.

directly to the sun (except in cases where there is a specific need) and must be protected from rainfall, insect infestation, etc.

- In the case of natural open-air drying, the medicinal plant/herbal substance must be spread out in a thin layer. To secure adequate air circulation, the drying frames must be located at a sufficient distance from the ground. Drying directly on the ground or under direct exposure to the sunlight should be avoided unless specifically required. Attempts must be made to achieve uniform drying of the medicinal plant/herbal substance and thus avoid mould formation and to maintain quality.
- The drying conditions such as maximum temperature, duration and air circulation must be selected taking into consideration the medicinal plant part to be dried, such as root, leaf or flower, and the nature of its active constituent, such as essential oils. Individual conditions must be recorded in detail. In case of artificial drying, gas or electrical ovens should be considered, and the use of wood and petrol ovens minimised, to reduce to possible contamination with polycyclic aromatic hydrocarbons (PAHs).
- In case of distillation in the field (refer the GMP Table[5] in Annex 7), this can be performed at a small plant in the field, which should be audited by the finished product manufacturer and validated according to GMP principles, and may be subject to inspections by Regulatory Authorities to assess compliance.
- All materials must be inspected and where necessary sieved to eliminate sub-standard product and foreign matters. Sieves must be maintained in a clean state and should be serviced regularly.
- Clearly marked waste-bins should be available, emptied daily and cleaned. The waste plant material must be segregated from growing media and the materials for the cultivation of plants. The waste plant material may require incineration for destruction.
- Fumigation should be limited as far as possible and only be used when a real need is identified. In such cases, treatment should be carried out at the earliest possible stage, according to the specific recommendations for use[6].
- Fumigation against pest attack should be carried out only where necessary and must be carried out exclusively by licensed personnel. Only registered chemicals must be used. The use of ethylene oxide and 1,3-dichloropropene is prohibited. Any fumigation against pests must be documented (see section 7).
- For fumigation of warehouses, only substances permitted by the regional and/or national regulations should be used and documented (see section 7).
- When frozen storage or saturated steam is used for pests and microbial contamination control, the humidity of the material must be controlled after treatment.

13. PACKAGING

To protect the product and to reduce the risk of pest attacks, early packaging is advisable.

Following processing monitored by in-process controls, the product should be packaged in clean and dry, preferably new sacks, bags or cases. The label must be clear, permanently fixed and made from

[6] Reflection paper on the use of fumigants (EMEA/HMPC/125562/2006)

non-toxic material. Information must conform with regional and/or labelling regulations of the country of destination.

Reusable packaging material should be well cleaned and properly dried prior to use. No contamination should occur through reusing of bags.

Packaging materials must be stored in a clean and dry place that is free of pests and inaccessible to livestock and domestic animals. It must be guaranteed that the packaging materials do not cause contamination of the product, particularly in the case of fibre bags.

14. STORAGE AND DISTRIBUTION

Packaged dried medicinal plants/herbal substances and essential oils, should be stored in a dry, well-aerated building, in which daily temperature fluctuations are defined and limited and good ventilation is ensured.

In the case of bulk transport, it is important to secure dry conditions. Furthermore, to reduce the risk of mould formation or fermentation it is advisable to use aerated containers. As a substitute, the use of sufficiently aerated transport vehicles and other aerated facilities is recommended. Essential oil transport must conform with appropriate regulations. Regional and/ or national regulations on transport must be respected.

15. DEFINITIONS

Abiotic:	Physical instead of biological factors or compounds. Examples are sunlight, water, air, type of soil, minerals, etc.
Adulteration:	The illegal and fraudulent mixing of ingredients that are not declared.
Agricultural inputs:	Any incoming material (e.g. seeds, fertilizers, including compost, water, agricultural chemicals, plant support) used for the primary production of herbal substances.
Biotic:	Relating to living organisms.
CITES:	Convention on International Trade in Endangered species of Wild Fauna and Flora.
Collection:	The gathering of plant species from wild/spontaneous sources.
Fumigation:	The process of disinfecting a batch in a closed container with the fumes of certain chemicals.
Greenhouse:	A facility designed for the cultivation of plants under automated and/or manually semi-controlled climate conditions. They can be of glass or other light transparent materials. They can be open and in contact with the external environment if needed, depending on the internal/external climate conditions.
Habitat:	The natural home or environment of a plant species.
Harvesting:	The gathering of plant species from cultived sorces.
Herbal substances:	Are mainly whole, fragmented or cut, plants, parts of plants, algae, fungi, lichen in an unprocessed state, usually in dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are

	also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binominal system (genus, species, variety and author).
Herbal preparations:	Are obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.
Indoor cultivation:	Cultivation in a closed environment equipped with air filtration to avoid cross-pollination, pollutants, insects etc.
Outdoor cultivation:	Live plants growing in an area (open field) exposed to natural sunlight and environmental conditions including variable temperature, precipitation, and wind.
Olfactory:	Relating to the sense of smell.
Organic production:	A sustainable agricultural system that uses ecologically based pest controls and biological fertilizers derived largely from animal and plant wastes and nitrogen-fixing cover crops. For further information see Regulation (EU) 2018/848.
Postharvest spoilage:	The presence of moulds and other organisms that may impact negatively on the quality of the herbal material.
Pyrrolizidine alkaloids:	PAs are a group of naturally occurring alkaloids in certain plants that are based on the structure of pyrrolizidine that are toxic to the liver.
Residual plant materials:	Are crop materials such as stems, leaves, and roots, that are left on the field after the harvest. There are different ways to manage crop residues. They can be used for tillage prior to planting when plant residues are incorporated into the soil. Another farming practice is reduced tillage or no-till farming, where crop residues are left on the surface and planting is carried out without soil tillage. The residues can also be used for composting and, in some cases, like Cannabis, they need to be destroyed.
Rogue/rogueing:	The removal of inferior or defective plants or seedlings from a crop.
Tillage:	Agricultural preparation of the soil by mechanical agitation in preparation for growing crops.

16. REFERENCES

1. EudraLex Volume 4 Part II "Basic Requirements for Active Substances used as Starting Materials". Good Manufacturing Practices (GMP) for medicinal products, Volume 4, The rules governing medicinal products in the European Union, current version

2. EudraLex Volume 4 Annex 7 "Manufacture of herbal medicinal products" of Good Manufacturing Practices (GMP) for medicinal products, Volume 4, The rules governing medicinal products in the European Union, current version

3. European Pharmacopoeia General Monograph "HERBAL DRUGS" 07/2017:1433

4. Reflection paper on the use of fumigants (EMEA/HMPC/125562/2006)

5. Reflection paper on quality of essential oils as active substances in herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/84789/2013)

6. REGULATION (EU) 2018/848 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 May 2018 on organic production and labelling of organic products and repealing Council Regulation (EC) No 834/2007