The examination is being carried out on the **following application documents**

Description, Pages

1-47 as published

Sequence listings, SEQ ID NO

1-14 as published

Claims, Numbers

1-19 filed in electronic form on 19-09-2012

Drawings, Sheets

1/4-4/4 as published

1 The amendments filed with the letter of 19.09.2012 are allowable under Art. 123(2) EPC.

2 Art. 137(5) EPC:

2.1 In respect of the present application only part of the claimed subject-matter has been searched, following an objection of lack of unity of the invention by the European Patent Office acting as International Searching Authority (see Article 17(3)(a) PCT).

The reasons were the following:

The application relates to the use of a substance which stimulates the expression of MC-1R, MC-2R or mu-opioid R, for the preparation of a cosmetic, nutraceutical or pharmaceutical composition and uses thereof for treating e.g ageing of the skin, to increase skin pigmentation or prevent skin depigmentation. The specific substances which are stimulators of the expression of MC-1R, MC-2R or mu-opioid R are claimed in claim 9. In claim 10 the use of these substances for treating the skin. e.g. improve the color of the skin or modify skin pigmentation, is claimed. Independent claim 17 is directed to nucleotides which are sense or antisense sequences of MC - 1R, MC - 2R, mu-opoid receptor or POMC.

The substance or plant extracts which are stimulators of the expression of MC - 1R, MC-2R, mu-opoid receptor (see claim 8) and which are subject-matter of independent claim 10 do not share a significant structural element, nor do they belong to a single class of chemical compounds in the art to which the invention pertains.

The common technical feature is the use of the stimulators of the expression of MC-R1, MC-2R or mu-opioid R for the preparation of cosmetic, nutraceutical or pharmaceutical compositions. This feature is not novel in view of the disclosure of the document US2004/0214851 (see [0020], [0047], claims 34 and 36) which discloses the use of compounds which induce expression of the mu-opioid receptor for reducing scarring of the skin. Furthermore, the prior art discloses the use of Achillea millefolium extracts for promoting wound healing (WO2007/030666: page 2 lines 21-30, claim 1) or reducing skin pigmentation (see EP1543825: [0007], claim 4).

2.2 With the communication dated 02.04.2012, the Applicant has been invited to limit the application to one invention covered by the international search report in accordance with Rule 164(2) EPC.

2.3 In response present claim 1-19 have been filed with the letter dated 19.09.2012.

These claims do not meet the requirements of Rule 137(5) EPC because they comprise non-searched subject-matter that does not combine with the originally claimed invention or group of inventions to form a single general inventive concept.

The reasons for that are the following:

Claim 1 as filed on the 19.09.2012 recites

"Use of at least one substance to stimulate the expression of a receptor of a neuromediator coded by the POMC gene chosen from among MC-1R, MC-2R, and mu-opioid R, in keratinocytes, as an active ingredient in a cosmetic composition to prevent or fight against cutaneous aging and/or against the effects of stress inducing the variations observed during the process of cutaneous aging, characterized in that the said substance is chosen from among:

- Extract of common yarrow plant (Achillea millefolium);
- **Extract of blackthorn (Prunus spinosa);**
- **Extract of sour cherry (Prunus cerasus);**
- **Extract of wild taro (Colocasia esculenta);**
- **Extract of wild hemp (Galeopsis ochroleuca);**

- Extract of Eburnamonine (Apocynacea Amsonia Abrenaemontan);

- (Z)-decahydro-6 ,8a-dihydroxy-l -isopropyl-3a, 6-dimethylazulen-5-yl 2-methylbut-2-enoate;
- Phenylacetic acid 3,6,9-trimethyl-2,7-dioxo-2,3,3a,4,5,7,9a,9b-octahydro- azuleno[4,5-b]furan-4-yl;
- 2.6 dimethyl-4(2-methyl butenoate) 5-6 (1-isopropyl-1 hydroxycyclopentane)) 1,2 epoxycycloheptane under CAS number 352220-52-1 and/or esters thereof
- 7-acetate-2.6 dimethyl-4(2-methyl butenoate) 5-6 (1-isopropyl-1 hydroxycyclopentane)) 1,2 epoxycycloheptane known under CAS number 86992-41-8
- Mango extract transformed with lactobacillus
- Date extract transformed with lactobacillus
- Papaya extract transformed with lactic bacteria
- Banana extract transformed with lactic bacteria
- and any mixture of these". (Emphasis added)

A search report has been established by the International search Authority for the first invention which is directed to the use of an extract of common yarrow plant (Achillea millefolium), as an active ingredient in a cosmetic, nutraceutical or pharmaceutical composition. The subject-matter of claim 1 in bold has not been searched as a consequence of he objection of lack of unity in the International Phase.

The extracts of various plants eventually transformed with lactic bacteria and the chemical compounds now listed in claim 1 do not share a significant structural element, nor do they belong to a single class of chemical compounds in the art to which the invention pertains. Hence there are a priori not unitary with the searched subject-matter.

The Applicant argues that the common inventive concept is the stimulation of the POMC chosen from MC-1R, MC-2R and mu-opioid R as an active ingredient in a cosmetic composition to prevent or fight against cutaneous ageing or against the effect of stress inducing variations observed during the process of cutaneous ageing.

It is noted that the original application was directed to the use of the claimed extracts or compounds for the preparation of neutraceutical, pharmaceutical and cosmetic compositions and the use thereof to fight against cutaneous ageing and/or against the effects of stress inducing the variations observed during the process of cutaneous ageing, **and also** to *prevent and/or fight*

against the diminishing of epidermal homeostasis, and/or to encourage epithelialization, and/or to improve cellular proliferation and differentiation, notably at the epidermal level, and/or to prevent or fight against a diminishing of cutaneous vascularization, and/or to improve skin vascularization, and/or to improve vascular hyperpermeability, and/or to improve angiogenesis during scarring of the skin, and/or to prevent and/or fight against a diminishing of skin innervation, and/or to improve skin innervation, or to generate a sensation of well-being and/or to improve the color of the skin and/or to modify skin pigmentation, notably when the pigmentation presents localized flaws, such as pigmentary spots.

Although present claims have been allegedly restricted to the prevention of cutaneous ageing it is considered that the claims comprise subject-matter that does not combine with the originally claimed invention or group of inventions to form a single general inventive concept since the common technical feature with the searched subject-matter is the use of the stimulators of the expression of MC-R1, MC-2R or mu-opioid R for the preparation of cosmetic, nutraceutical or pharmaceutical compositions. This feature is not novel in view of the disclosure of the document US2004/0214851 (see [0020], [0047], claims 34 and 36) which discloses the use of compounds which induce expression of the mu-opioid receptor for reducing scarring of the skin. The use of Achillea millefolium extracts for promoting wound healing (WO2007/030666: page 2 lines 21-30, claim 1) or reducing skin pigmentation (see EP1543825: [0007], claim 4). Furthermore, document D5 (DE20112636) discloses compositions comprising common yarrow extract for treating ageing skin (see page 1 lines 18-20, page 4 line 17).

Consequently, the subject-matter relating to the claimed use of **extract of blackthorn (Prunus spinosa); extract of sour cherry (Prunus cerasus); extract of wild taro (Colocasia esculenta); extract of wild hemp (Galeopsis ochroleuca); extract of Eburnamonine (Apocynacea Amsonia Abrenaemontan); (Z)-decahydro-6 ,8a-dihydroxy-l -isopropyl-3a, 6-dimethylazulen-5-yl 2-methylbut-2-enoate; Phenylacetic acid 3,6,9-trimethyl-2,7-dioxo-2,3,3a,4,5,7,9a,9b-octahydro- azuleno[4,5-b]furan-4-yl; 2.6 dimethyl-4(2-methyl butenoate) 5-6 (1-isopropyl-1 hydroxycyclopentane)) 1,2 epoxycycloheptane under CAS number 352220-52-1 and/or esters thereof, 7-acetate-2.6 dimethyl-4(2-methyl butenoate) 5-6 (1-isopropyl-1 hydroxycyclopentane)) 1,2 epoxycycloheptane known under CAS number 86992-41-8; mango extract transformed with lactobacillus; date extract transformed with lactobacillus; papaya extract transformed with lactic bacteria; banana**

extract transformed with lactic bacteria does not combine with the originally claimed invention or group of inventions to form a single general inventive concept contrary to the requirements of Rule 137(5) EPC.

3 Novelty (Art. 54 EPC):

3.1 Claim 1 is directed to the use of a substance in a cosmetic composition to prevent cutaneous ageing. It is noted that an intended cosmetic use is not a characterizing feature.

It is also stressed that the stimulation of the MC-1R, MC2-R and mu-opoid receptor is only the mechanism of action which accounts for the cosmetic effect of common yarrow which is disclosed in the prior art. This mechanism of action does not confer novelty to a claim directed to the use of the same common yarrow for the same activity as in the prior art.

Hence claim 1 lacks novelty in view of D2-D6 which disclose compositions comprising Achillea millefolium (see D2: claim 4; D3: claim 1; D4: col1 l71; D5: p1 l18-20, p4 l17; D6: p3 l1-9, example 5) and the use thereof for preventing skin ageing and hyperpigmentation in age (see D4 and D5). Claim 1 is thus not novel. The dependent claims 2-13 and 15-17 lack novelty. Since claim 17 comprises also an extract of common yarrow as additional substance it is also anticipated by D2-D5.

3.2 Claim 18 lacks novelty over D2-D5 for the reasons set forth under item 3.1 above.

3.3 Claim 19 seems to be anticipated by D4 since the diminishing of epidermal thickness is one of the signs of cutaneous ageing which is prevented by common yarrow extract in D4.

3.4 It seems that exhibit 1 filed pursuant to Art. 115 EPC in a third-party observation is still relevant for the novelty of claims 1 and 18 which are directed to compositions comprising extract of common yarrow.

4 Inventive step (Art. 56 EPC):

Although, present claims lack novelty the following can be noted with regard to inventive step:

Document D5 which can be considered as closest prior art discloses compositions for preventing skin ageing comprising an extract of Achillea millefolium. Claim 17 would differ in that it is combined with further substances that act on MC-1R or mu-opioid receptor in melanocytes to prevent

depigmentation spots. The problem to be solved can be seen as to provide a composition for preventing depigmentation spots in ageing skin. The application does not provide any evidence that the problem is solved. An inventive step is thus not acknowledged for claim 17.

5 The applicant is invited to file a new claims which take into account of the above comments.The applicant is informed that if the new claims were not allowable under the EPC, the next step would be appointment of Oral Proceedings.