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

Description, Pages

1-66	filed in electronic form on	04-10-2011

Claims, Numbers

1-14	filed in electronic form on	20-12-2013

The following documents are cited by the Examiner. A copy of the documents is annexed to the communication and the numbering will be adhered to in the rest of the procedure.

D36 TOKTON N ET AL: "Development of ellagic acid rich pomegranate peel extract loaded nanostructured lipid carriers (NLCs)", INTERNATIONAL JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES 2014 IJPPS IND, vol. 6, no. 4, 2014, pages 259-265, ISSN: 0975-1491

D37 Pomegranate provides ellargic acid and much more , 2013, Retrieved from the Internet: URL:http://www.becarre-natural.com/pomegranate.php [retrieved on 2014-10-22]

Allowability of the amendments (Articles 76 and 123(2) EPC)

The examining division considers that the claims do not comply with the requirements of articles 76 and 123(2) EPC at least for the following reasons.

1) the claimed pomegranade extract has been defined to be standardized to 40% ellagic acid. The applicant referred to three documents which describe some commercial pomegranade extracts which have been standardised to contain such amount of ellagic acid. However, the existence of said commercial products does not mean that, when reading paragraph 50 and the other sections of the originally filed parent and present divisional application, the skilled person would have clearly and unambiguously recognised a standardised the specific pomegranade extract which is now defined in the claims. This is only one of the possible standardised products which could have been envisaged by the skilled person. It is noted, for example, that pomegranade extracts standardised to contain different amounts of elagic acid are

also known and commercially available. D36 describes extracts standardised to containing 12% ellagic acid (see page 260, "methods") and D37 describes extracts standardised to contain grades of up to 98% of ellagic acid (see abstract). Accordingly, the feature "standardized to 40% ellagic acid" introduces new subject matter.

2) the combination of 1) the specific amounts expressed in absolute amounts of the relevant ingredients, namely 10-2000 mg of an extract of pomegranate and 35-250 mg of a grape seed extract and 2) their ratio of 10:1 is not disclosed in the parent and in the present divisional application as filed. The minimum value 10 mg of pomegranate and 35 mg of grape seeds is also not compatible with said ratio.

3) the combination of ingredients which is defined in claim 10 is not disclosed in the application as filed. It is noted that the paragraphs of the parent and of the present divisional application relating to similar combinations (92-94), refer to quercetin dihydrate or anhydrate and not to quercetin as such.

Inventive step (Article 56 EPC)

The inventive step objection raised in the earlier communications is maintained. The applicant arguments cannot be followed, because the experiments reported in the application do not show that a combination of ingredients as defined in the claims results in an unexpected technical effect associated to inhibition, decrease, or prevention of bone resorption or stimulation of bone growth.

As already mentioned in the earlier communications, all ingredients making up the claimed combinations have already been described in the prior art, as effective agents for improving bone metabolism, increasing bone density ond /or treating or preventing bone resorption. In some cases, this teaching was even present in documents reflecting traditional knowledge. Concerning pomegranade, reference is made to documents D22-D23, D27-D29 and concerning grape seeds extracts reference is made to documents D24, D25, D26. For the other additional ingredients reference is made to the documents cited in the earlier communications.

Starting from the prior art, the skilled person would have expected not only both these ingredients to induce these beneficial therapeutic effects, but their combinations to be active as well. The results reported in the application do not go beyond this expectation. There is no evidence that the combination results in something "special" or synergistic as submitted by the applicant. Actually, a comparison of the data reported in table 12, for example, indicates that the effect of a combination of pomegranade extract and grape seed extract is less pronounced than that which can be calculated adding the effects obtained when the two ingredients are administered individually.

Furthermore, the finding that the claimed ingredients alone or in combination, modulate certain mechanisms of action, involving *e.g.* RANK-L or of BMP does not, as such, confer inventiveness to the claimed solution. What matters is that the results of the experiments reported in the application do not show that the combination of the claimed ingredients results in any unexpected modulation of these mechanisms of action.

Conclusions

The examining division is still of the opinion that the claimed matter does not meet the requirements of Articles 123(2) and 56 EPC.

Without being bound to the present opinion, it would appear that:

- further limitations of the claimed compositions to specific amounts or ratios of the claimed ingredients would not overcome, or even give raise to new objections under article 123(2) EPC

- it is not disputed that the application presents new previously undisclosed technical information and that it provides new insight into the mechanism of action of the claimed ingredients on bone metabolism. However, what is still needed in order to overcome the inventive step objection, is a plausible evidence that the effects of claimed combinations translate into a practical therapeutic benefit which could not be expected on the basis of the prior art documents. Should it be plausibly shown that this effect is intrinsic of any combination of pomegranade and grape seed extracts, claims directed to such combinations, which are not limited to specific ratios of such ingredients, would also meet the requirements of the EPC.