ANNEX 2: Comments of the EPO

QUESTIONNAIRE FOR COMPARATIVE STUDY ON REACH THROUGH CLAIMS

- EPO comments, summary

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Case 1:	Ind. Appln	Sufficiency	Clarity/Support
Claim 1 (Receptor)	-	+/-	+
Claim 2 (Screen.-meth.)	-	-	+/-
Claim 3 (Agonist)	-	-	-
Claim 4 (Use of agon.)	-	-	-
Claim 5 (MoAb)	-	+/-	+

Case 2:	Ind. Appln	Sufficiency	Clarity/Support
Claim 1 (Receptor)	+	+	+
Claim 2 (Screen.-meth.)	+	+	+
Claim 3 (Agonist)	+	-	-
Claim 4 (Use of agon.)	+	-	-
Claim 5 (MoAb)	+	+	+

Case 3:	Ind. Appln	Sufficiency	Clarity/Support
Claim 1 (Receptor)	-	+/-	+
Claim 2 (Screen.-meth.)	-	+/-	+
Claim 3 (Agonist)	-	-	-
Claim 4 (Use of agon.)	-	-	-
Claim 5 (use of spec. agon)	-	-	-
Claim 6 (MoAb)	-	+/-	+

Case 4:	Ind. Appln	Sufficiency	Clarity/Support
Claim 1 (Receptor)	+	+	+
Claim 2 (Screen.-meth.)	+	+	+
Claim 3 (Agonist)	+	+/-(scope)	+/-(scope)
Claim 4 (Use of agon.)	+	+/-(scope)	+/-(scope)
Claim 5 (use of spec. agon)	+	+	+
Claim 6 (MoAb)	+	+	+

+: no objection

- : objection(s) mainly **in addition to** **"**Lack of Inventive Step**"**!

QUESTIONNAIRE FOR COMPARATIVE STUDY ON REACH THROUGH CLAIMS

- EPO comments

1). THE RECEPTORS (claim 1 of cases 1-4)

1.1. In **cases 1-4**, the receptors are characterized by their sequence, and they have been expressed in animal cells.

1.2. In **cases 2 and 4**, the specific function has been described.

1.3. **=> no objection in cases 2 and 4;** the requirements of Arts. 56(Inventive Step), 57(Industrial Application), 83(Disclosure), 84(Clarity and Support) are met.

1.4. In **cases 1 and 3**, a rather vague function has been inferred from homology considerations: The claimed compounds are putative members of the vast family of "R-receptors" which are involved in a wide variety of physiological processes.

1.5. ==> Objections in cases 1 and 3:

Inventive Step (Art. 56): NO
Even though the outline for examples 1 and 3 states that the protein (SEQ ID NO:1) meets the inventive step and non-obviousness requirements, the EPO position is that such a claim cannot meet the requirements of **Inventive Step** (the other objections, as detailed further below, will however be made additionally if considered appropriate):

Prima facie, the routine provision of further sequences having the same general function as the known prior art sequences of closely related structure is **not inventive**. The **structural non-obviousness** is not a reason to accept an inventive step; sequences as well as all other chemical compounds should **solve a technical problem** in a non-obvious manner to be recognised as inventive.

Industrial application (~"utility"; Art. 57/R23(e)(3)/R27(1)(f)/Guidelines C-IV 4.6): NO
The function indicated in cases 1 and 3 is vague and heterogeneous: it includes a large variety of different physiological roles. Without the sequence (SEQ ID NO:1) being assigned to a particular (specific) function, it would not be suitable for industrial application.

Sufficiency of disclosure: (~"enablement"; Art. 83/Rule 27/Guidel. C-II 4ff): YES/NO
There is no doubt that the receptor protein can be prepared, in this respect it meets the requirements of sufficiency. However, since the specific function has not been disclosed in cases 1 and 3, it can be debated whether it would be an undue burden to perform the invention over the whole area (i.e. including the determination the specific function of the claimed receptor). This is however rather a problem that should be dealt with under "lack of inventive step" (supra).

Clarity and Support (Art. 84/Rule 29/Guidelines C-III): YES
The claims to the receptor are **clear and concise** (C-III 4ff and C-III 5), since the latter is identified by its sequence, which is a part of the description.
(NB: There is however no support in the description for the verification of assumptions

concerning the specific function, which would be necessary to overcome more straightforward objections under Arts. 56 and 57).

Possibilities to overcome the objections
Case 1: No obvious possibility; amendments are very likely to violate Art. 123(2) EPC.
Case 3: No obvious possibility, unless in the context of compounds X,Y,Z there is a more concrete indication of function.

2). THE METHODS FOR IDENTIFYING AGONISTS (claim 2 of cases 1-4)

2.1. In **cases 1 and 2**, there is only a general description of screening methods, but no working example.

2.2. In **cases 3 and 4**, ligands to the receptors have been isolated on the basis of the claimed method.

2.3. In **cases 2 and 4, but not 1 and 3**, the receptors have been found to meet the criteria of Arts. 56, 57, 83 and 84.

2.4. ==> no objections in cases 2 and 4

2.5. ==> objections in cases 1 and 3:

Inventive Step:
Cases 1 and 3: NO
logical consequence of item 1.5: no technical problem is solved if the specific function of the receptor and the agonists is unknown.
analogous to item 1.5
Cases 2 and 4: YES

Industrial Application:
Cases 1 and 3: NO
The receptor itself is not industrially applicable, because it has no specific function. It follows that there can be no industrial applicability for the methods of identifying agonists that are supposed to stimulate an unknown function.
Cases 2 and 4: YES
In view of the proven pharmaceutical relevance of the receptor, methods for identifying agonists are obviously industrially applicable.

Sufficiency:
Case 1: NO
The specific function of the receptor has not been disclosed. It would be an undue burden to determine the specific function that is to be stimulated by the agonist, which is a prerequisite for the identification of agonists.
Case 3: YES/NO
3 candidate compounds have been isolated that bind to the receptor and trigger a cascade of second messenger signals. It can therefore be accepted that compounds X,Y and Z are agonists, and that the method is suitable to detect agonists.
However, since the specific function has not been disclosed, it can be debated whether it

would be an undue burden to perform the invention over the whole area. This is however a problem that should be dealt with under "lack of inventive step" (see item 1.5).
Cases 2 and 4: YES
In both cases, the receptor has been obtained in pure and active form; it would appear that methods for measuring the function of the receptor have also been disclosed in the application. On this basis, there appears to be no known obstacle to setting up a method for identifying agonists, either on the basis of routine procedures as described in the application (case 2), or by following the examples of case 4.

Clarity and Support:
- Clarity:
Cases 1-4: YES
- Support:
Case 1: NO
In case 1, there is no sufficient support for the function of the receptor, its activation, and the measurement of the activation.
Case 3: YES
A screening method has been performed, and 3 candidate compounds have been isolated that are very likely to be aginists, although the specific function is unknown.
Cases 2 and 4: YES

Possibilities to overcome the objections
Cases 1 and 3: As under item 1.5: No obvious possibility; amendments are very likely to violate Art. 123(2) EPC.

3). THE AGONISTS IDENTIFIED BY THE METHOD OF CLAIM 1 (claim 3 of cases 1-4)

3.1. In **cases 1 and 2**, no agonist has been isolated.
3.2. In **cases 3 and 4**, only three compounds that bind to the receptor of claim 1 have been isolated and characterized.

3.3. **==> objections in cases 1-4**:
All claims No. 3 will already be objected to at the **search stage**:
no search will be carried out for compounds which are **only** defined by the method for their identification (Guidelines B-III 3.7): No special search effort for unduly wide or speculative claims, for subject-matter which is not sufficiently disclosed (Art. 83 EPC) or not supported by the description (Art. 84 EPC). A meaningful search is not possible (B-VIII, 6), since it would require a minimum of structural information: The functional feature "binding to a receptor" may be an inherent known or unknown feature of any known and unknown organic or inorganic compound (in cases 3 and 4, a partial search for the compounds X,Y,Z is of course possible).

Industrial application:
Case 1: NO
An objection under Lack of Industrial Application is possible (a compound that has not been disclosed cannot be made and used in any kind of industry), but the main objection will be under Lack of Support.
Case 2: YES
Although the same argument ("a compound that has not been disclosed cannot be made and used in any kind of industry") could also be made in case 2, it can also be argued

here that the person skilled in the art would know that there is a potential application of agonists in the treatment of obesity. The question "Industrial application, yes or no" has however no practical relevance in this case, since the Lack of Support is so striking.
Case 3: NO
Analogous to item 2.5.
Case 4: YES
For the assessment of industrial application, the scope is not taken into consideration.
The compounds of examples X,Y,Z fulfil the requirements.

Sufficiency:
Cases 1-2: NO
(Note however that Art. 83 will mainly be used if Art. 84 is no longer available, i.e. in opposition):
There is no sufficient disclosure of the technical solution to the problem, i.e. the structurally defined compounds (Rule 27(1)(c); Guidelines C-II 4.1, 4.5). It would be an undue burden to isolate and to characterize possibly binding compounds without any clue to their chemical structure (Guidelines C-II 4.9), or to test each and every known and future compound from all areas of organic and inorganic chemistry whether it falls within the scope of the claim.
Case 3:
Compounds X,Y,Z: NO
Although the compounds as such are sufficiently disclosed to be prepared, there is no sufficient indication of the specific function of the agonists. The term "agonist" implies that the claim to the compound is linked to a functional definition. In such a case, the specific function has to be indicated, in order to fulfill the requirements on sufficiency of disclosure.
General scope: NO
In the absence of any indication of a general formula for a larger group of compounds that plausibly act as agonists, the motivation for cases 1 and 2 applies.
Case 4:
Compounds X,Y,Z: YES
General scope: NO
In the absence of any indication of a general formula for a larger group of compounds that plausibly act as agonists, the motivation for cases 1 and 2 applies for the general scope of claim 3.

Clarity and Support
- Clarity:
Cases 1-2: NO
Claim 3 does not include the technical feature (i.e. the structure) which is essential for the technical effect (binding to the receptor, T32/82).
Characterisation of a compound only by parameters is not allowed, as no meaningful comparison with the prior art can be made (Guidelines C-III 4.7a).
Attempts to define an invention by the result to be achieved (i.e. here: the results of a ligand-binding experiment) are not allowed (C-III 4.7)
Case 3:
X,Y,Z: NO
Although the compounds themselves are clearly identified, the functional aspect "agonist" is not clear. The selective binding of a compound to a receptor, without indicating the specific function of the agonist does not allow to assess the contribution to the state of the art (see the recent decision T241/95).

General scope: NO
In the absence of any indication of a general formula for a larger group of compounds that plausibly act as agonists, the motivation for cases 1 and 2 applies.
Case 4:
X,Y,Z: YES
Compounds X,Y,Z are clearly defined by their formula.
General scope of claim 3: NO
See the discussion of cases 1 and 2.

- <u>Support:</u>
Cases 1-3: NO
In order to comply with the requirement of Art. 84, there must be sufficient support of technical character in the description that allows to extend the particular teaching of the description to the whole field claimed (C-III 6.3).
The functional feature "binding" is not a technical feature that allows to distinguish the claimed group of compounds from prior art compounds. It is not possible for the person skilled in the art to recognize the members of the claimed group, because the functional feature only indicates what the compound does, and not what it is. The definition by the function only is therefore merely the definition by a result, and not as required the indication of the technical feature that is necessary to achieve the result (supra, C-III 4.7).
Art. 84 and Rule 27(1)(c, e) require a technical description of the invention, and not the indication of a functional property that one might observe if he made that invention.
Case 4:
X,Y,Z: YES
General scope of claim 3: NO
see the discussion of cases 1 - 3.

<u>Possibilities to overcome the objections</u>
Cases 1 - 3: no obvious possibility
Case 4: Restriction to X,Y,Z

4). MEDICAL APPLICATION OF AGONISTS IN GENERAL, OBTAINED BY THE METHOD OF CLAIM 3 (claim 4 of cases 1-4)

Cases 1-4:
Motivation as under item 3: if a compound is not industrially applicable (or sufficiently supported, or disclosed), the medical application of said compounds suffers *a fortiori* from the same deficiencies.

5). MEDICAL APPLICATION OF DEFINED AGONISTS (claim 5 of cases 3 and 4)

Case 3: Motivation in line with items 3 and 4. Unless a specific disease is known, claims relating to the treatment of the disease do not fulfil the requirements of industrial application, clarity, support in the description, and disclosure.
Case 4: no objection

6). MONOCLONAL ANTIBODIES AGAINST THE RECEPTORS OF CLAIM 1 (claim 5 in

cases 1 and 2; claim 6 in cases 3 and 4)

Inventive step:
Cases 1 and 3: NO
logical consequence of item 1
Cases 2 and 4: YES

Industrial Application :
Cases 1 and 3: NO
logical consequence of item 1. There seems to be no industrial application for an antibody against a target which has itself no industrial application.
Cases 2 and 4: YES
The industrial application of an antibody against a receptor with known properties is obvious.

Sufficiency of disclosure:
cases 1 and 3: YES/NO
There is no doubt that an antibody can be made, once the receptor protein has been prepared, in this respect it meets the requirements of sufficiency. However, since the specific function of the receptor has not been disclosed in cases 1 and 3, it can be debated whether it would be an undue burden to determine the specific function for the antibody.
Cases 2 and 4: YES
The general process of obtaining antibodies has become routine. The person skilled in the art knows what to do with an antibody against a receptor with specific function.

Clarity and Support
Cases 1-4: YES
The claims to an antibody are clear and concise, if the target has been sufficiently defined. The term "antibody" implies a structural information and selects a certain genus of compounds. Antibodies are traditionally defined by their target. The combination of target-specificity with the restriction to a certain genus of compounds makes the claim searchable and clear. The general process for obtaining antibodies has become routine. The support in the description would be considered as sufficient.
(There is however no support in the description for the verification of assumptions concerning the specific function of the receptor and consequently of the antibody, see item 1).

CONCERNING THE CLAIMS DRAFTED TO ANTIBODIES:
Note however that in all four cases there appear to exist receptor families of closely related structure. In order to distinguish the antibodies of cases 1-4 from potentially existing prior art antibodies against related compounds, which may cross-react with the present antibodies, it may become necessary to restrict the scope of the claims to **specific** antibodies, in order to overcome a novelty objection. There seems to be no basis in the description as filed for such an amendment.