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Appeal number: **T0186/18-3.3.08**

Communication of the Board of Appeal

The Rapporteur P. Julià
The Registrar L. Malécot-Grob
Tel.: 089 / 2399 - 3381

Registered letter

This document: 22 page(s) including this page

Annex(es):

Communication text

1. This communication is sent pursuant to Article 17 of the Rules of Procedure of the Boards of Appeal (RPBA 2020) (Supplementary publication 1 - OJ EPO, 2020, 42). Any opinions expressed herein are provisional and not binding on the board in arriving at its decision. The purpose of this communication is mainly to set out some of the issues to be discussed at the oral proceedings before the board, it is not an invitation to make further submissions generally. In this respect, the parties' attention is also drawn to Article 114(2) EPC and to Article 13(1) RPBA 2020.

2. European patent no. 2 328 918 is based on European patent application no. 09 781 633.4, originally filed under the PCT as International patent application PCT/EP2009/060299 and published as WO 2010/015714. The patent was granted with 15 claims.

3. An opposition was filed on the grounds set forth in Articles 100(a),(b) EPC. The opposition division considered the main request not to fulfil the requirements of Article 84 EPC and auxiliary request 1 to fulfil the requirements of the EPC. Both requests were filed on 14 November 2016 as auxiliary requests 1 and 2, respectively.

4. The opponent (appellant) lodged an appeal and, in the statement setting out its grounds of appeal, requested that the decision under appeal be set aside and the patent be revoked.

5. In response thereto, the patent proprietor (respondent) requested, as its main request, that the appeal be dismissed or, in the alternative, that the patent be maintained on the basis of any one of auxiliary requests 1 to 6 filed at first instance as auxiliary requests 3 to 8, respectively. Oral proceedings were requested as an auxiliary measure.

Main request

6. The main request is the auxiliary request 1 underlying the decision under appeal upheld by the opposition division. Thus, it already forms part of the present appeal proceedings.

7. In the statement setting out its grounds of appeal, the appellant maintained the objections raised under Article 53(a) EPC and Rule 28(1)(d) EPC against the subject-matter of claim 12. Neither did the appellant raise any other objection against the request upheld by the opposition division nor did the appellant attack any other claim of that request.

The subject-matter of claim 12 of the main request

8. Claim 12 is directed to "a non-human animal comprising the polynucleotide according to claim 10 or a non-yeast cell according to claim 11", wherein the specific non-human animal is thereafter further defined.

8.1 As a first observation, it is noted that the subject-matter of claim 12 is not limited to non-human transgenic animals but includes also non-transgenic animals comprising "the polynucleotide according to claim 10 or a non-yeast cell according to claim 11".

8.2 Claim 11 is directed to a cell comprising the polynucleotide or expression vector according to claim 10. Whilst the polynucleotide of claim 10 is characterised only by the feature "encoding the mutant alpha-synuclein or homologue thereof according to any of the preceding claims", the expression vector of claim 10 is defined only by "comprising said polynucleotide". No other features characterise the polynucleotide or the expression vector of claim 10, such as for instance the presence of a specific control sequence (e.g., promoter, transcriptional/translational stop signal, 3'-UTR sequence, etc.) or an attachment/ integration site.

8.3 The subject-matter of claims 10 and 11 is not limited to a polynucleotide (or an expression vector comprising said polynucleotide) encoding the specific alpha-synuclein A56P mutant with increased toxicity compared to the wild-type (human) alpha-synuclein (SEQ ID NO: 1). These claims are directed to a polynucleotide (or expression vector comprising said polynucleotide) encoding any alpha-synuclein mutant containing this specific A56P mutation, such as those defined in claims 2 to 9 (see "Case Law of the Boards of Appeal of the EPO", 9th edition 2019, II.A.6.2, 308, for the meaning of the term "comprising"). Thus, the subject-matter of claims 10 and 11 includes a mutant having the specific A56P mutation (at least) and potentially further mutations in 43 positions spread all over the N-terminal domain (N-terminal lipid binding alpha-helix), the core region (residues 61 to 95; amyloid binding central domain), and the C-terminal end domain (residues 96 to 140; with an acidic tail of 43 residues) of the alpha-synuclein. Further mutants having (at least) these mutations and a deletion of 1 to 40 amino acids of the C-terminus of alpha-synuclein are also contemplated (claim 8).

9. Claim 12 further recites several specific non-human animals which may be divided into the following groups: (i) invertebrates selected from *C. elegans* and *D. melanogaster*; (ii) (non-mammal) vertebrates selected from lamprey, Japanese ricefish, pufferfish, zebrafish, and African clawed frog; (iii) vertebrates/mammals selected from zebra finch, chicken, cat and dog; (iv) (rodent) mammals selected from guinea pig, hamster, mouse, rat and *Sigmidon hispidus*; and (v) (non-human) primates selected from rhesus macaque, baboon, marmoset, and green monkey.

The scope of appellant's appeal against claim 12

10. Part 1 of the appellant's statement of grounds of appeal refers only to Rule 28(1)(d) EPC which excludes from patentability animals resulting from processes for modifying their genetic identity and which are likely to cause them suffering without any substantial medical benefit to man or animal. Thus, this rule applies only to transgenic animals and therefore, to the embodiments of claim 12 directed to those animals. This part of the statement of grounds of appeal refers to worms and flies as well as to mammals and primates in general.

11. Part 2 of the appellant's statement of grounds of appeal refers to Article 53(a) EPC which excludes from patentability inventions the commercial exploitation of which would be contrary to "ordre public" or morality. Although this part of the appellant's statement of grounds of appeal refers to ethical and moral problems arising from the experimental use of animals in general, reference is explicitly made only to vertebrates and mammals. The latter are the sole animals cited in part 3 of the statement of grounds of appeal, i.e. the conclusion. In part 2 of the statement of grounds of appeal, the appellant refers explicitly

to these animals as transgenic animals and to their suffering.

12. Thus, appellant's objections appear to be directed solely against embodiments of claim 12 directed to non-human, transgenic animals and, more particularly, to non-human transgenic vertebrates and mammals.

Relevant case law on the patentability of non-human animals

13. It is common ground between the parties and acknowledged also by the opposition division in the decision under appeal, that the two tests defined in decision T 315/03 (OJ EPO 2006, 15), namely the "Rule 28(d) EPC test" and the "real Article 53(a) EPC test", are relevant for assessing the patentability of the subject-matter of claim 12.

The first test - Rule 28(1)(d) EPC, the balancing test
The likelihood of animal suffering

14. The first condition of this test is a likelihood - and no more than a likelihood - of animal suffering (cf. T 315/03, *supra*, points 6.2 and 9.4 of the Reasons). In the case underlying that decision, the board considered that, due to the specific nature of the transgene (oncogene), animal suffering was "not just a likelihood but the inevitable consequence of the very purpose of the patent" (cf. T 315/03, *supra*, last sentence of point 12.2.1 of the Reasons). Likewise, in the present case, the claimed non-human animals are described as to "serve as a model system for synucleinopathies ... a group of diseases which have all a common involvement of alpha-synuclein" (cf. paragraph [0063] of the patent). The symptoms of these diseases are described in paragraphs [0070] to [0078] of the patent and referred to in the methods of claims 14 and 15, wherein non-human animals according to claim 12 are used. It is

worth noting that the polynucleotide according to claim 10 encodes alpha-synuclein mutants characterised by an increased toxicity - and decreased fibril formation ability (claim 9) - compared to the wild-type alpha-synuclein.

15. Moreover, as stated above, neither the polynucleotide nor the expression vector according to claim 10 are limited by any control sequence or integration site. There appears also to be no information in the patent on the effects of the expression of an alpha-synuclein mutant with increased toxicity - and decreased fibril formation ability (claim 9) - in cells, tissues or organs of non-human animals other than in (dopaminergic) neurons, let alone for alpha-synuclein mutants of increased toxicity having (at least) the substitutions and C-terminal end deletions contemplated in claims 2 to 8 of the main request.

16. In this context, the parties' attention is drawn to decision T 606/03 of 12 January 2005, wherein the claims underlying that decision were directed to a transgenic mouse. In this decision, the board considered that, since the claimed gene trapping construct was inserted in the genome in a mutagenic manner, the modification of the genetic identity of the animal - "in instances where the mutated gene is an essential one" - was likely to result in suffering of the mutated mouse (cf. T 606/03, *supra*, point 2 of the Reasons). In the present case, there is no limitation regarding the method for introducing "the polynucleotide according to claim 10 or a non-yeast cell according to claim 11" into the non-human animal of claim 12. Therefore, the scope of claim 12 allows for any possible method for introducing the polynucleotide according to claim 10 into the genome of the claimed non-human animals as well as the insertion

or integration of this polynucleotide at any possible genomic location, including into an essential gene.

17. In light of these considerations, the board agrees with the findings of the opposition division that, in the present case, the likelihood of suffering has been established for the non-human animals of claim 12.

The likelihood of substantial medical benefit

18. According to decision T 315/03, there is no difference in the level of proof required between animal suffering and substantial medical benefit - the difference is quite simply between, on the one hand, any likely suffering by animals however minor, and, on the other hand, the likely benefit to man or animal which must be substantial. The two integers of the Rule 28(1)(d) EPC test, namely the likelihood of suffering and of substantial medical benefit, require the same degree of proof; there is no need to provide evidence of an actual or real substantial medical benefit (cf. T 315/03, *supra*, points 9.2 and 9.3 of the Reasons).

19. In the decision under appeal, the opposition division referred to point 13.2.2 of the Reasons of decision T 315/03, *supra*, and to the recital 45 of the EU Biotech Directive as acknowledging that "the likely substantial medical benefit may result from the use in research or to prevent, diagnose or treat illnesses". In accordance with the disclosure of the patent, the non-human animal of claim 12 is understood to be "a model system for synucleinopathies", i.e. an animal model for synucleinopathies (cf. paragraph [0063] of the patent). As an animal model, it is intended for use in pharmaceutical and medical research and therefore, to mimic - as closely as possible - aspects of these synucleinopathies in humans. These animal models are used to obtain information on these diseases, their

prevention, diagnosis and treatment as well as for identifying substances that might prevent or reduce the toxicity of alpha-synuclein, such as those identified by applying the methods of claims 14 and 15 (cf. *inter alia*, paragraphs [0001], [0012] and [0013] of the patent).

20. Although a general statement in the description of the patent is normally not sufficient for establishing a likely substantial medical benefit, the opposition division considered that, in the present case, the invertebrate models exemplified in the patent, namely *C. elegans* and *D. melanogaster*, showed clear symptoms of neurological impairment and thus to be adequate disease models. However, the board observes that all the expression constructs used in Example 4 of the patent have specific (pan-neuronal, dopaminergic) promoters that direct the expression of the specific alpha-synuclein mutant in the dopaminergic neurons of *C. elegans* and *D. melanogaster*. Moreover, the expression vector used for the generation of the transgenic flies contains the attachment site attP which allows for a site-specific insertion of the polynucleotide encoding the alpha-synuclein mutant into the *D. melanogaster* genome. The experiments described in Example 6 with other alpha-synuclein mutants expressed in *C. elegans* used also the expression vectors disclosed in Example 4 and reference is made in Example 6 to "neurite defects" and to predictable changes in "neuronal toxicity and behavioral defects in neuronal cell cultures". None of these specific features is required for any of the non-human animals of claim 12. There is neither a limitation in claim 12 as regards the expression of the polynucleotide (or expression vector) according to claim 10 nor any requirement in claim 12 as regards the insertion or integration site of said polynucleotide (or expression vector). Likewise, the alpha-synuclein mutant is

broadly defined in claim 12 (by dependency on claims 1 to 9) and not limited to any of the specific alpha-synuclein mutants exemplified in the patent.

21. In response to the statement of grounds of appeal, the respondent filed Annex II which provides information on each of the non-human animals cited in claim 12. According thereto, these animals have all been used as animal models in studies of neurobiological diseases, in particular, for Parkinson's disease and related diseases. The respondent argues that each of these animals may provide a significant contribution to the studies of these diseases. Indeed, on the basis of the documents on file, the opposition division considered that the use of each of the animals listed in claim 12 as models for neurodegenerative diseases had already been disclosed in the art and that there was sufficient evidence in support of a likely substantial medical benefit for the non-human animals listed in that claim.

22. In this context, the opposition division referred also to document (2) (J. Bailey, "Man or Mouse. Genetically Modified Animals in Medical Research. A Critical Review", Animal Aid, 2005) as showing that transgenic rats with altered alpha-synuclein expression were only marginally or not at all affected in their motor behaviour. However, the opposition division further stated that the deficiencies in these mice were due to the selection of an unsuitable promoter and that this problem was cured in document (12) (E. Masliah *et al.*, Science 2000, Vol. 287, 1265 to 1269). Indeed, the promoter used in the constructs described in this document "was chosen because it has been successfully used to target the expression of other human proteins to neurons in transgenic models of neurodegenerative diseases" (cf. page 1266, left-hand column of document (12)). It is worth noting also that document (12) describes the important differences

between low- and high-expresser lines of transgenic mice and, based on these differences, states that "[i]t is conceivable that a critical threshold of alpha-nuclein accumulation is required for dopaminergic and behavioral deficits to become detectable" (cf. page 1268, right-hand column of document (12)). As stated above, claim 12 requires the alpha-synuclein mutant neither to be expressed in neurons nor above any particular threshold level. Thus, claim 12 comprises non-human animals expressing any of the alpha-synuclein mutants of claims 1 to 9 at low levels and in cells other than neurons. These non-human animals certainly have the deficiencies referred to by the opposition division in the decision under appeal as regards document (2).

23. Moreover, the examples of non-human animals shown in the patent are invertebrates which are known to have no synuclein genes. Therefore, the interpretation of studies on the expression of (human) alpha-synuclein in these models is not complicated by any endogenous protein ortholog. This appears also to be the case for some of the fishes cited in claim 12 (zebrafish has genes only for beta and gamma-synucleins). Whilst it is questionable whether such simple non-human animals may be suitable and appropriate for modelling a disease as complex as Parkinson's disease, the interpretation of studies on the expression of (human) alpha-synuclein on a background expressing endogenous alpha-nuclein - as it is the case for most of the non-human mammals cited in claim 12 - seems to be much more complicated. The more so, in view of the possible presence of several isoforms and natural alpha-synuclein variants in these non-human animals as known from the art. In the board's view, the interpretation of these studies is also much more complicated when the alpha-synuclein mutants are expressed by (exogenous) promoters that fail to mimic the normal expression of the endogenous alpha-

synucleins (tissue-specificity, level of expression, etc.) and, even more so, when neither the physicochemical properties (except for those described in Examples 2 and 3 of the patent) nor the effects of these (heterologous) alpha-synuclein mutants are described in, and known from, the prior art.

24. Indeed, this appears to be the case for the alpha-nuclein mutants of claims 1 to 9 which, as stated above, may comprise mutations in all three domains of the alpha-synuclein, each of these domains being associated with, and playing different roles in, different cellular locations. There appears to be no information in the patent on the properties and effects of each of the specific alpha-synuclein mutants falling within the scope of claims 1 to 9 (except for those described in Examples 2 and 3 of the patent), let alone when they "comprise" further undefined mutations. The contribution and relevance of each of these alpha-synuclein mutants, which do not even appear to be found in nature, appears not to be directly derivable from the patent. Moreover, as stated above, the (random, unspecific) insertion-site of the polynucleotide encoding for these (heterologous) alpha-synuclein mutants (or expression vector comprising said polynucleotide) into the genome of the non-human animals may well further complicate the interpretation of these studies on synucleinopathies.

25. In the board's view, it cannot be contested that, at the very least for some exemplary applications, a non-human animal as defined in claim 12 may provide a substantial medical benefit. However, this is not the relevant question in the present case but whether, based on the whole content of the patent, it can be unambiguously and directly derived that, in case of suffering of any one of the claimed non-human animals, there is always a substantial medical benefit. In light

of all the considerations above, the board is of the opinion that a substantial part of the non-human animals falling within the scope of claim 12 may be suitable neither for use as models for synucleinopathies, in particular for Parkinson's disease, nor for obtaining information on any of these diseases. Therefore, the relevant question set out above is to be answered negatively.

The correspondence principle

26. According to the criteria established in decision T 315/03 for assessing the evidence in the Rule 28(1) (d) EPC test, a necessary correspondence is required between suffering and medical benefit, i.e. Rule 28(1) (d) EPC "should be applied to ensure that the patent should only extend to those animals whose suffering is balanced by a medical benefit" (cf. T 315/03, *supra*, point 9.2 of the Reasons). As regards the nature of the evidence, the board stated in that decision that the evidence as to the relevant matter, i.e. the likelihood of both, suffering and substantial medical benefit, and the necessary correspondence between the two, must be directed to those matters at the effective date. The assessment of such evidence is made analogously to that regarding evidence of sufficiency of disclosure under Article 83 EPC (cf. T 315/03, *supra*, points 9.5 and 9.6 of the Reasons).

27. It is derivable from all the considerations above that, in the present case, the correspondence principle does not apply for each of the non-human animals cited in claim 12.

28. The claims of the main request underlying the decision T 315/03 were directed to a transgenic rodent (cf. T 315/03, *supra*, point 12 of the Reasons). The request embraced all animals within the taxonomic order

Rodentia and the suffering was considered to be present in the case of every such animal, not just mice but also squirrels, beavers, porcupines and every other rodent (cf. T 315/03, *supra*, point 12.2.1 of the Reasons). In that case, the board considered that there was "quite simply no evidence to show that **all** the various animals in the category of rodents are so different that **each of them** would provide a contribution to cancer studies, such as being specifically suited as a model for studying a specific type of cancer". Therefore, the board considered the main request to fail the balancing test of Rule 28(1)(d) EPC and refused it under Article 53(a) EPC (cf. T 315/03, *supra*, points 12.2.2 to 12.2.4 of the Reasons).

29. In the present case, claim 12 refers to the selected invertebrates by their genus and species, namely *C. elegans* (*Caenorhabditis elegans*) and *D. melanogaster* (*Drosophila melanogaster*). This is also true for the mammal *Sigmidon hispidus* (hispid cotton rat) but not for all other vertebrates, in particular not for the selected mammals and non-human primates. Contrary thereto, paragraph [0062] of the patent refers to most of these non-human animals by genus, species and subspecies, such as for chicken (*Gallus gallus domesticus*), cat (*Felis cattus*), and dog (*Canis lupus familiaris*). However, according to the established case law, there is no reason to use the description to interpret an excessively broad claim more narrowly (cf. "Case Law", *supra*, I.C.4.8, 122; II.A.3.3, 295; and II.A.6.3.4, 312). Therefore, if the selected vertebrates referred to in claim 12, in particular the selected mammals, are understood in their broadest possible interpretation, such as for example the term "dog" as referring to the dog family/subfamily (*Canidae*, *Caninae*), and likewise for the terms "cat" (*Felidae*, *Felinae*) and "chicken" (*Phasianidae*,

Gallus), the considerations made in points 12.2.1 to 12.2.4 of the Reasons of decision T 315/03 apply also directly to the subject-matter of claim 12 of the main request.

30. Thus, the board is of the opinion that the evidence on file does not support, and is not enough to demonstrate, that for each of all possible non-human animals of claim 12, when suffering occurs, a substantial medical benefit is necessarily provided for the purpose of the balancing test of Rule 28(1)(d) EPC.

Conclusion

31. It follows from the above considerations that the subject-matter of claim 12 fails the balancing test of Rule 28(1)(d) EPC.

The second test - the "real" Article 53(a) EPC test

32. Although, in view of the above conclusion on the Rule 28(1)(d) EPC test, there is no further need for the board to carry out the "real" Article 53(a) EPC test, the parties' attention is nevertheless drawn to the following points:

33. In line with decision T 315/03 (*supra*, points 10.5 to 10.10 of the Reasons), the starting point for carrying out the "real" test is the test suggested in decision T 19/90 (OJ EPO 1990, 476; see also T 356/93, OJ EPO 1995, 545). It is however worth noting that, in decision T 315/03, the board referred to the introduction of other considerations in the starting test, either by way of adapting it or broadening its framework (cf. point 10.7 of the Reasons), and, accordingly, the board further referred to the nature and extent of the evidence required and to the

effective date for carrying out this test (cf. point 10.9 of the Reasons).

34. In the present case, the subject-matter to be tested is the morality and "ordre public" of the exploitation of the non-human animals defined in claim 12 and not of a particular transgenic mouse, as it was the case for the subject-matter underlying decisions T 315/03 and T 606/03 (cf. T 315/03, *supra*, point 13.2.2 of the Reasons; T 606/03, *supra*, points 14 and 15 of the Reasons). The different scope of the claimed subject-matter must certainly be taken into account when assessing the relevance of all issues that must be considered when carrying out the "real" test, such as, for instance, non-animal alternatives, environmental risks, threat to evolution, and public attitudes and perception of genetic manipulation of animals in general and (non-human) primates in particular, for the purpose of medical research (cf. T 315/03, *supra*, points 13.2.7 to 13.2.21 *et seq*. of the Reasons). It is in this context that appellant's arguments on the exploitation of the invention and the incentive of patents for increasing the commercial use of (non-human, transgenic) animals, with reference to the decisions T 1213/05 of 27 September 2007 (cf. points 52 and 53 of the Reasons; cited in the decision under appeal by the opposition division) and G 2/06 (OJ EPO 2009, 306), may be of relevance.

35. In the board's view, the effort required to assess the broad subject-matter of claim 12 for the purpose of the "real" Article 53(a) EPC test is much more demanding and challenging than that carried out for the narrower subject-matter underlying decisions T 315/03 and T 606/03 (*supra*). The arguments and considerations that may apply to, and be relevant for, the two specific invertebrates mentioned in claim 12, may certainly be different from those applying to, and arising from, the

four non-human primates, namely rhesus macaque, baboon, marmoset, and green monkey, mentioned in this claim. There is no doubt that public attitudes and perception for the latter have nothing in common with those for the former. However, appellant's argumentation in the statement of grounds of appeal appears neither to go beyond general statements and considerations that were already made in much detail in decision T 315/03 (*supra*) nor to address the problems and deficiencies arising from each of the specific non-human animals mentioned in claim 12.

36. In any case, the board is of the opinion that, in the present case, the question arises as regards the morality of a commercial exploitation of each of the non-human animals cited in claim 12 which are characterised only by the presence in their genome of a polynucleotide (with undefined expression system and insertion-site) encoding at least one of all possible alpha-synuclein mutants falling within the broad definition ("comprising") of claims 1 to 9 and for which neither the properties nor the effects are directly derivable from the patent. In the board's view, non-human transgenic animals are one of the last tools or systems used in the studies carried out for elucidating the biological and physiological role(s), function(s) and/or effect(s) of a particular product(s) (protein, polypeptide, polynucleotide, etc.). Indeed, numerous and detailed *in vitro* experiments - such as the effects on several cell/tissue culture(s) of different sources and with different expression systems and insertion-sites, etc. - are usually required for arriving at a meaningful and technically sensible interpretation of the results obtained with studies using non-human transgenic animals, the more so when the non-human transgenic animal is a complex one, such as a non-human primate. None of these experiments appears to have been carried out for most of the alpha-

synuclein mutants defined in claims 1 to 9, in particular not for those mutants "comprising" a large number of substitutions and C-terminal end deletions, let alone in complex background systems with (several) endogenous alpha-synucleins.

37. As stated in decision T 356/93 (*supra*, points 18.1 to 18.3 of the Reasons), a patent confers on its owner(s) for a specified time an exclusive right to exploit the subject-matter of the claims, and to prevent others from doing the same. This protection is accorded in exchange for a full disclosure of the claimed invention. As established in the case law, the purpose of granting a patent is not to reserve an unexplored field of research for an applicant (cf. T 870/04 of 11 May 2005, point 21 of the Reasons). In the present case and in light of the disclosure of the patent, the board is of the opinion that the subject-matter of claim 12 represents nothing more than an attempt to reserve several non-human animals - including non-human primates - that may or may not represent appropriate models or systems for carrying out further research on synucleinopathies and for further identifying substances for preventing or reducing the toxicity of alpha-synucleins (claims 14 and 15). The granting of exclusive rights for the commercial exploitation of all these non-human animals, including those for which the likelihood of suffering is well established (*supra*) but for which such appropriate use can be neither directly anticipated nor foreseen, appears to contravene Article 53(a) EPC.

Conclusion

38. If, contrary to the provisional opinion expressed above, the board came to a different conclusion on the Rule 28(1)(d) EPC test, it would become necessary to assess whether the subject-matter of claim 12 fails the

"real" Article 53(a) EPC test. In light of the actual scope of this claim, the board is of the opinion that it does not pass this test.

Auxiliary requests 1 to 6

39. Auxiliary requests 1 to 3 are identical to auxiliary requests 3 to 5, respectively, filed on 14 November 2016 at first instance. Auxiliary requests 4 to 6 are identical to auxiliary requests 6 to 8, respectively, filed on 27 July 2017 at first instance.

40. According to the case law, the mere fact of filing an auxiliary request at the first instance cannot serve as a justification for automatically admitting it into the appeal proceedings, especially when its admission has not even been examined at first instance (cf. T 217/15 of 14 March 2019, point 39.2 of the Reasons; T 105/14 of 12 April 2019, points 3 to 12 of the Reasons). There are no submissions on file from the appellant as regards the admission and patentability of any of these auxiliary requests. Should the board maintain its provisional opinion on the main request, the admission of auxiliary requests 1 to 6 into the appeal proceedings will have to be discussed.

41. For the sake of efficiency and without prejudice to any decision on the admission of any of these auxiliary requests into the appeal proceedings, the parties' attention is drawn to the following issues:

41.1 The vertebrate Japanese ricefish and the mammals cat and dog have been deleted in claim 12 of auxiliary request 1. Claim 12 of auxiliary request 2 is identical to claim 12 of auxiliary request 1, except for the deletion of the four non-human primates, namely rhesus macaque, baboon, marmoset, and green monkey. The scope

of claim 12 in auxiliary request 3 has been limited to the two invertebrates *C. elegans* and *D. melanogaster* and the rodent species selected from guinea pig, hamster, mouse, rat, and *Sigmidon hispidus*. Whilst in auxiliary request 4, the rodent species is selected from a mouse or a rat, the rodent is a mouse in claim 12 of auxiliary request 5. There is no claim directed to a non-human animal in auxiliary request 6.

41.2 Since auxiliary request 6 does not contain any claim with subject-matter attacked by the appellant in appeal proceedings, this auxiliary request overcomes all grounds of opposition and therefore, it may be a basis for the maintenance of the patent. The subject-matter of auxiliary request 5 appears to be the closest to that of the cases underlying the decisions T 315/03 and T 606/03 (*supra*), even though in the present case the claimed mouse is characterised neither as a transgenic mouse nor as comprising a specific transgene and expression system. Thus, the claimed subject-matter of this auxiliary request appears to be broader than that underlying decisions T 315/03 and T 606/03 (*supra*). The same deficiencies are also present for claim 12 of auxiliary requests 3 and 4 for which, additionally, there appears to be no evidence on file to show that the specific claimed non-human animals are so different that each of them provides a relevant contribution to studies on synucleinopathies (cf. T 315/03, *supra*, point 12.2.3 of the Reasons). However, there are also no submissions on file from the appellant attacking the specific subject-matter of any of these auxiliary requests.

41.3 Thus, except for auxiliary request 6, the problems and deficiencies described above for the main request, or at least some of them, appear to apply also to the subject-matter of claim 12 of all other auxiliary requests.

Summary and conclusion

42. For convenience, the main points of this communication can be summarised as follows:

i) the main request already forms part of the appeal proceedings and appears to contravene Article 53(a) EPC in combination with Rule 28(1)(d) EPC;

ii) if necessary, the admission of auxiliary requests 1 to 6 into the appeal proceedings will be discussed at the oral proceedings;

iii) the problems and deficiencies described for the main request, or at least some of them, appear to apply also to the subject-matter of claim 12 of auxiliary requests 1 to 5;

iv) auxiliary request 6 overcomes all grounds of opposition and may provide basis for the maintenance of the patent.

43. Since the respondent has requested oral proceedings, summons to these proceedings were issued and oral proceedings were scheduled for 12 March 2021. There is a request from the respondent to reschedule the date of these proceedings because he had been already summoned pursuant to Rule 115(1) EPC on 4 August 2020.
The board will decide on the respondent's request as soon as possible and inform the parties accordingly.

44. The parties are asked to inform the board, and also the other party, as early as possible and in unambiguous way, if they intend not to attend the oral proceedings.

45. The appellant's attention is drawn to Rule 103 EPC, in particular to Rule 103(3) EPC, (as amended from

1 April 2020; see decision of the Administrative Council of 12 December 20 December 2019 CA/D 14/19, OJ EPO, 2020, A5).