Trial Decision

Invalidation No. 2015-800166

Demandant	TOKO YAKUHIN KOGYO CO., LTD.
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Intervener	KYORIN PHARMACEUTICAL CO., LTD.
Patent Attorney	UCHIYAMA, Tsutomu
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The case of trial regarding the invalidation of Japanese Patent No. 3480736, entitled "USE OF MOMETASONE FUROATE FOR TREATING AIRWAY PASSAGE AND LUNG DISEASES" between the parties above has resulted in the following trial decision.

Conclusion

The correction of the scope of claims of Japanese Patent No. 3480736 shall be approved for Claims 2 to 3 after the correction as the Corrected Scope of Claims attached to the Written Demand for Correction dated July 23, 2018.

The patent for the inventions according to Claims 1 to 3 of Japanese Patent No. 3480736 shall be invalidated.

The costs in connection with the trial including the costs due to intervention shall be borne by the Demandee and the Intervenor.

Reason

No. 1 History of the procedures

1 The application for Japanese Patent No. 3480736 (hereinafter, sometimes referred to also as the "Present Patent") was filed on January 26, 1995 (claim of priority under the Paris Convention, January 27, 1994, U.S.A.) as the international filing date, and the establishment of patent right was registered on October 10, 2003.

2 Against this, the Demandant, TOKO YAKUHIN KOGYO CO., LTD filed a demand for trial on August 24, 2015, seeking a trial decision for invalidating patent for inventions according to Claims 1 to 3 of the above patent. The Demandee, MERCK SHARP AND DOHME CORPORATION, filed a Written Reply of the Trial Case on December 8, 2015. Later, prior to oral proceedings on March 1, 2016, the Demandant filed an Oral Proceedings Statement Brief dated February 6, 2016, and the Demandee filed an Oral Proceedings Statement Brief on February 16, 2016. And, after the Oral Proceeding, the Demandant filed a Written Statement and a Written Statement 2 both dated March 11, 2016, and the Demandee filed a Written Statement on March 23, 2016.

Later, with respect to progress of trial examination, the Demandee filed a Written Statement on April 13, 2016, and, meanwhile, the Demandant filed two Written Statements, one dated April 15, 2016, and the other dated July 7, 2016, and furthermore, two additional Written Statements, one dated December 12, 2017, and the other dated March 14, 2018.

3 Later, the body made an Advance Notice of the Trial Decision dated April 13, 2018, and the Demandee filed a Written Demand for Correction and a Written Statement on July 23, 2018. Against these, the Demandant filed a Written Refutation of the Trial Case dated October 9, 2018.

4 The Intervenor, KYORIN PHARMACEUTICAL CO., LTD., lodged to intervene to

the present trial on the Demandee's side by filing an Application for Intervention on July 20, 2018 and was granted authorization to intervene by a Decision on Acceptance of Intervention dated September 4, 2018. The Intervenor filed three written statements respectively on July 20, 2018, September 5, 2018, and November 9, 2018.

No. 2 Request for correction

1 Object of the request for correction

The object of the request for correction made on July 23, 2018, is "to demand the correction of the scope of claims of Japanese Patent No. 3480736 for Claims 2 to 3 after the correction as in the corrected scope of claims attached to the written demand for correction."

2. Corrections

Correction A-1

"The dose is 25 to 200 micrograms" in Claim 2 of the scope of claims is corrected to "the dose is 100 to 200 micrograms."

Correction A-2

"Micrograms" in Claim 2 of the scope of claims is corrected to "micrograms, and the absolute bioavailability of unchanged mometasone furoate is less than about 1%."

Correction B

"For the treatment of seasonal allergic rhinitis" in Claim 3 of the scope of claims is corrected to "for the treatment of seasonal allergic rhinitis, and the dose is 200 micrograms administered once a day."

3 Adequacy of corrections

(1) Purpose of corrections

Since Correction A-1 further limits the matter specifying the invention of the invention according to Claim 2, "the dose is 25 to 1000 micrograms" by correcting it to the matter specifying the invention to "the dose is 100 to 200 micrograms," it is for the purpose of restriction of the scope of claims provided for in Article 134-2(1), proviso (i) of the Patent Act.

Since Correction A-2 further limits the invention according to Claim 2 by adding the matter specifying the invention, "the absolute bioavailability of unchanged

mometasone furoate is less than about 1%," it is for the purpose of restriction of the scope of claims provided for in Article 134-2(1), proviso (i) of the Patent Act.

Since Correction B further limits the invention according to Claim 3 by adding the matter specifying the invention, "the dose is 200 micrograms administered once a day," it is for the purpose of restriction of the scope of claims provided for in Article 134-2(1), proviso (i) of the Patent Act.

(2) Whether any new matter has been added

With respect to Correction A-1, since both of 100 micrograms that is deemed to be the lower limit of the dose and 200 micrograms that is deemed to be the upper limit of the dose are shown by the following descriptions in the detailed description of the invention of the specification attached to the application:

"The aqueous suspension of mometasone furoate has been found to be safe and effective in treating allergic rhinitis, e.g., seasonal allergic rhinitis, from 25 micrograms up to 1600 micrograms administered once-a-day; the preferred doses are 25-800 micrograms a day, although no further improvement in treatment is typically found above 400 micrograms a day. The most preferred doses are 25, 50, and 100 micrograms administered twice to each nostril, once-a-day for a total once-a-day dose of 100, 200 and 400 mcg" (Patent Publication, column 10, ll. 17 to 27), and,

"In a dose ranging safety and efficacy study, the mometasone furoate aqueous nasal spray formulation at doses of 50 mcg/day, 100 mcg/day, 200 mcg/day, and 800 mcg/day or placebo was administered to 480 patients with seasonal allergic rhinitis for 4 weeks. All treatments were well tolerated; results of statistical analysis indicated that all doses of mometasone furoate were effective relative to placebo. These results showed that administration of an aqueous suspension of mometasone furoate as a nasal spray to patients with seasonal allergic rhinitis was efficacious, and well tolerated with little potential for systemic side effects, and are consistent with the low oral bioavailability of mometasone furoate" (Patent Publication, column 14, ll. 36 to 48), in the relation with technical matters drawn by taking together all descriptions in the specification, the scope of claims, and drawing attached to the application, Correction A-1 does not introduce any new technical matter, is a correction within the scope of matters described in the specification attached to the application, the scope of claims, or drawings, and complies with the provisions of Article 126(5) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

With respect to Correction A-2, since the following descriptions in the detailed description of the invention of the specification:

"The substantial minimization of the systemic effect of mometasone furoate administered intranasally or by oral inhalation has been measured by High Performance Liquid Chromatography (HPLC) metabolite profiling of plasma radioactivity of mometasone furoate, its substantially complete (> 98%) first-pass metabolism in the liver and by a minimal reduction in cortisol secretion levels.

When mometasone furoate is administered orally (i.e., swallowed as an oral suspension) or by oral or nasal inhalation, there is substantial absence of absorption systemically into the bloodstream of mometasone furoate; i.e., there is essentially no parent drug (substantially, less than 1% of mometasone furoate) which reaches the bloodstream from the gastro-intestinal tract" (Patent Publication, column 5, ll. 34 to 46), "In addition, a single-dose absorption, excretion and metabolism study using 200 mcb of ^{3}H-mometasone furoate as the nasal spray formulation was conducted in 6 normal male volunteers. When systemic absorption (based on urinary excretion) was compared to an intravenously administered dose of ^{3}H- mometasone furoate, it was 8%. The plasma concentrations of parent drug could not be determined by metabolite profiling, because the levels of plasma radioactivity were below the limit of quantification. These data are consistent with substantially less than 1% of bioavailability of mometasone furoate" (Patent Publication, column 14, ll. 25 to 34), and,

"The results of these drug metabolism/clinical pharmacology studies indicate that:

1. Drug-derived radioactivity was completely absorbed when ^{3}H-MF was given orally as a solution to male volunteers. However, the absolute bioavailability of unchanged mometasone furoate was extremely low 1 (less than about 1%) due to extensive first pass metabolism" (Patent Publication, column, 25, l. 29 to column 26, l. 2), indicate that the absolute bioavailability of unchanged mometasone furoate is less than about 1%, in relation with technical matters drawn by taking together all descriptions in the specification, the scope of claims, and drawing attached to the application, Correction A-2 does not introduce any new technical matter, is a correction within the scope of matters described in the specification attached to the application, the scope of claims, or drawings, and complies with the provisions of Article 126(5) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

With respect to Correction B, since it is shown in the following descriptions:

"The aqueous suspension of mometasone furoate has been found to be safe and

effective in treating allergic rhinitis, e.g., seasonal allergic rhinitis, from 25 micrograms up to 1600 micrograms administered once-a-day; the preferred doses are 25-800 micrograms a day, although no further improvement in treatment is typically found above 400 micrograms a day. The most preferred doses are 25, 50, and 100 micrograms administered twice to each nostril, once-a-day for a total once-a-day dose of 100, 200 and 400 mcg" (Patent Publication, column 10, ll. 17 to 27),

"In a dose ranging safety and efficacy study, the mometasone furoate aqueous nasal spray formulation at doses of 50 mcg/day, 100 mcg/day, 200 mcg/day, 800 mcg/day, or placebo was administered to 480 patients with seasonal allergic rhinitis for 4 weeks. All treatments were well tolerated; results of statistical analysis indicated that all doses of mometasone furoate were effective relative to placebo. These results showed that administration of an aqueous suspension of mometasone furoate as a nasal spray to patients with seasonal allergic rhinitis was well tolerated with little potential for systemic side effects, and are consistent with the low oral bioavailability of mometasone furoate" (Patent Publication, column 14, ll. 36 to 48), and

"3. Drug - Each patient was given a metered nasal pump spray bottle containing either an aqueous suspension of mometasone furoate or placebo. Dosing instructions on the bottle informed the patient to deliver 2 sprays of drug (mometasone furoate 50 mcg/spray) or placebo into each nostril once-a-day, each morning" (Patent Publication, col. 16, ll. 12 to 17) in the detailed description of the invention of the specification attached to the application, that the dose is specified as 200 micrograms, in relation with technical matters drawn by taking together all descriptions in the specification, the scope of claims, and drawings attached to the application, Correction B does not introduce any new technical matter, is a correction within the scope of matters described in the specification attached to the application, the scope of claims, or drawings, and complies with the provisions of Article 126(5) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

(3) Whether there is any substantial expansion or modification of the scope of claims

Correction A-1 limits the range of dose in the invention according to Claim 2, does not substantially expand or modify the scope of claims, and complies with the requirement provided for in Article 126(6) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

Correction A-2 limits the absolute bioavailability of unchanged mometasone furoate in the invention according to Claim 2, does not substantially expand or modify

the scope of claims, and complies with the requirement provided for in Article 126(6) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

Correction B limits the dose in the invention according to Claim 3, does not substantially expand or modify the scope of claims, and complies with the requirement provided for in Article 126(6) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act.

(4) Independent requirements for patentability

Since Claims 1 to 3 do not include any claim for which no trial for invalidation is demanded, the provisions of Article 126(7) of the Patent Act applied mutatis mutandis by Article 134-2(9) of the Patent Act are not applied to Correction A-1, Correction A-2, and Correction B.

(5) Request for making correction for each group of claims

Between Claims 2 and 3 before the correction, since there is a relation that Claim 3 cites Claim 2, Correction A-1, Correction A-2, and Correction B for which objects of request for correction are Claims 2 and 3 were made for each group of claims.

(6) Summary

As stated in above (1) to (5), since corrections by the request for correction made on July 23, 2018, are for the purpose of the matter provided for in Article 134-2(1), proviso (i) of the Patent Act, and comply with the requirement provided for in Article 126(5) to (6) of the Patent Act cited mutatis mutandis by Article 134-2(9) of the Patent Act, the corrections are approved.

No. 3 Corrected inventions of the case

As a result of above corrections, inventions according to the scope of claims of Japanese Patent No. 3480736 are those shown below that are specified by matters described in Claims 1 to 3 of the scope of claims after the correction (hereinafter, referred to as "Present Corrected Invention 1," "Present Corrected Invention 2," and "Present Corrected Invention 3," respectively according to the order of the claims, and, sometimes, collectively as the "Present Corrected Inventions").

[Claim 1] A medicament for treating allergic or seasonal allergic rhinitis comprising an aqueous suspension of mometasone furoate to be administered intranasally once a day.

[Claim 2] The medicament of Claim 1, wherein the once-a-day dose is 100 to 200 micrograms, and the absolute bioavailability of unchanged mometasone furoate is less than about 1%.
[Claim 3] The medicament of Claim 1 or Claim 2, wherein the medicament is for treating seasonal allergic rhinitis and the once-a-day dose is 200 micrograms.

No. 4 Allegations of the parties
1 The Demandant's allegation

According to the Written Demand for Trial, the Oral Proceedings Statement Brief dated February 15, 2016, the First Oral Proceedings Record, the Written Statement, and the Written Statement 2 dated March 11, 2016, and the Written Refutation of the Trial Case dated October 9, 2018, filed by the Demandant, the Demandant seeks a trial decision to the effect that "The patent for the inventions according to Claims 1 to 3 of Japanese Patent No. 3480736 shall be invalidated. The costs in connection with the trial shall be borne by the Demandee," and alleges the following reasons for invalidation as reasons why the Present Patent should be invalidated and filed the following documents as means of proof.
(Hereinafter, Evidence A No. 1, Evidence B No. 1, etc. are described in abbreviated forms as A1, B1, etc.)

[Reason for Invalidation 1] (Lack of inventive step)

Since a person skilled in the art could have easily invented the Present Patented Inventions 1, 2, and 3 prior to the priority date of the patent application based on inventions described in Evidence A No. 1, Evidence A No. 2, and common technical knowledge, the Present Patented Inventions 1, 2, and 3 are not patentable under the provision of Article 29(2) of the Patent Act and the Present Patent falls under Article 123(1)(ii) of the Patent Act and should be invalidated (Written Demand for trial, p. 8, l. 3 from the bottom to p. 9, l. 2; it is recognized that "prior to the filing of the application for the patent," in the above excerpted part is an error of "prior to the priority date of the patent application," and "the Present Patented Inventions fall under Article 123(1)(ii) of the Patent Act," is an error of "the Present Patent falls under Article 123(1)(ii) of the Patent Act").

[Reason for Invalidation 2] (Violation of the enablement requirement)

With respect to "A medicament comprising an aqueous suspension of mometasone furoate to be administered intranasally" among the matters specifying the

invention described in Claim 1 of the present case, the present specification describes neither any concrete formulation nor any production method, and, since the present specification describes only vague operation, and a person skilled in the art could not have worked the Present Patented Invention, the detailed description of the invention of the present specification does not describe the Present Patented Inventions sufficiently clearly and completely so that a person skilled in the art can work the inventions, and does not comply with the requirement provided for in Article 36(4) of the Patent Act. Therefore, the Present Patent falls under Article 123(1)(iv) of the Patent Act and should be invalidated (Written Demand for trial, p. 9, ll. 3 to 10; it is deemed that "Article 36(4)(i) of the Patent Act" written in the above excerpted part in the Written Demand for trial is an error of "Article 36(4) of the Patent Act," and "the Present Patented Inventions fall under Article 123(1)(iv) of the Patent Act" is an error of "the Present Patent falls under Article 123(1)(iv) of the Patent Act").

<Means of proof>

A1: National Publication of International Publication No. 1993-506667

A2: Wang C-J. et al., Journal of Pharmaceutical & Biomedical Analysis, vol. 10, No. 7, 1992, pp. 473 to 479

A3: Kunihiro Odaguchi et al., THE CLINICAL REPORT, vol. 27, No. 9, 1993, pp. 3575 to 3591

A4: Shotaro Mitsui et al., J. Jpn. Bronchoesophagol. Soc., vol. 31, No. 1, 1980, pp. 51 to 64

A5: Shigenori Nakajima et al., J. Jpn. Bronchoesophagol. Soc., vol. 31, No. 5, 1980, pp. 375 to 385

A6: Ross, J.R.M., et al., Current Medical Research and Opinion, vol. 12, No. 8, 1991, pp. 507 to 515

A7: Bryson, H.M. et al., Drugs, vol. 43, No. 5, 1992, pp. 760 to 775

A8: Storms, W. let al, Annals of Allergy, vol. 66, 1991, pp. 329 to 334

A9: Atopic and allergic diseases, Latest internal medicine series, vol. 23, Nakayama Shoten Co., Ltd, 1992, pp. 311 to 315, cover, colophon

A10: Phillipps G.H., Respiratory Medicine, vol. 84 (Supplement A), 1990, pp. 19 to 23

A11: Test report (RE-QT-150501), dated May 25, 2015 (Copies of above-described Evidences A were attached to the written demand for trial as originals).

A12: Kunihiro Odaguchi et al., THE CLINICAL REPORT, vol. 24, No. 4, 1990, pp. 1985 to 2002

A13: Interview form: External use corticoid formulation Propaderum (R) ointment

0.025% Propaderum (R) cream 0.025%, revised in April 2010 (7th edition) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
A11-2: Test report (RE-QT-160201), February 12, 2016
A11-3: Document entitled at the top of the first page as "Supplement concerning enablement requirement"
(Copies of the above-described Evidences A were attached to the oral proceedings statement brief dated February 15, 2016, as originals).

2 Demandee's and the Intervenor 's allegation

According to the Written Reply of the Trial Case, the Oral Proceedings Statement Brief filed on February 16, 2016, the First Oral Proceedings Record, the Written Statements filed by the Demandee on March 23, 2016 and July 23, 2018, as well as the Written Statements filed by the Intervenor on July 20, 2018, September 5, 2018, and November 9, 2018, the Demandee and the Intervenor seek for a trial decision to the effect that the demand for trial regarding the invalidation is groundless, and the costs in connection with the trial shall be borne by the Demandant, and allege that the above reason for invalidation alleged by the Demandant is groundless, and filed the following documentary evidences as means of proof.

<Means of proof>
B1: Expert's testimony by Prof. Stephan R. Durham, dated October 16, 2012
B2: How to use steroid formulations in each clinical department, published on May 10, 2001
B3: Feature article, Correct use of topical adrenal steroid, nasal allergy, published in August 2013
B4: Correct use of steroids depending on situations knowing differences between medicaments, published on February 15, 2010
B5: Interview form - Nazonex, published in July 2015
B6: Interview form - Furunase, published in August 2013
B7: Interview form - Aramist, published in April 2014
B8: Trial decision dated February 3, 2015, for the case of trail of invalidation No. 2014-800055
B9: Advances in Dermatology and Allergology XXVIII, 2011, pp. 107 to 119
B10: Print-out from Website (http://www.ncbi.nlm.nih.gov/pubmed/1867454) on August 18, 2015 (Annals of Allergy, 67(2 Pt 1), 1991, abstract from pp. 156 to 162)
B11: Acta Paediatr, No. 82, 1993, pp. 635 to 640

B12: PEDIATRICS, vol. 105, No. 2, February 2000, pp. 1 to 7
B13: THE JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY, vol. 44, No. 2, February 1993, pp. 141 to 145
B14: Interview form - Rinocote, published in June 2012
B15: Research report from Japan Association for International Chemical Information, SHIPS, October 27, 2014
B16: Table concerning anti-inflammation drugs for cutaneous diseases and nasal drops comprising corticosteroids as active ingredients, 2014
B17-1: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, pp. 209 to 210
B17-2: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, p. 216
B18-1-1: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 1007
B18-1-2: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 966
B18-1-3: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2133
B18-1-4: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 2155 to 2156
B18-1-5: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1010 to 1011
B18-1-6: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 972 to 973
B18-1-7: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1592 to 1593
B-18-1-8: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 1044
B18-1-9: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 864
B18-1-10: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 866
B18-1-11: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1438 to 1439
B18-1-12: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information p. 1504
B18-1-13: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2362

B18-1-14: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1633 to 1635
B18-1-15: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1007 to 1008
B18-1-16: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 2492 to 2493
B18-1-17: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2495
B18-1-18: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information pp. 1718 to 1719
B18-1-19: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 865
B18-1-20: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 974
B18-1-21: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2232
B18-1-22: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 691 to 692
B18-1-23: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 723
B18-1-24: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2362
B18-1-25: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 922
B18-1-26: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 1841
B18-1-27: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 921
B18-1-28: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 2496 to 2497
B18-1-29: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 2134 to 2135
B18-1-30: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 961 to 962
B18-1-31: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2127

B18-2-1: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 475 to 476
B18-2-2: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 2174 to 2176
B18-2-3: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1439 to 1440
B18-2-4: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, p. 2365
B18-2-5: 48 EDITION 1994 PHYSICIANS' DESK REFERENCE, Section 5 Product Information, pp. 1856 to 1857
B19-1: Print-out for item "Beconase" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-2: Print-out for item "Beconase AQ" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-3: Print-out for item "Vancenase" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-4: Print-out for item "Rhinocort" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B-19-5: Print-out for item "Nasalide" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-6: Print-out for item "Nasarel" from Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-7: Print-out from the item, "Flonase" on Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-8: Print-out from the item, "Nasonex" on Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.DrugDetails) on October 21, 2014
B19-9: Print-out from the item "Nasacort" on Website (http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?useaction=Search.Dr

ugDetails) on October 21, 2014
B20: Drugs, vol. 36, Supplement 5, 1988, pp. 15 to 23
(Copies of the above-described Evidences B were attached to the written reply of the trial case)

Reference 1: Pharmacy as you see, illustrated practical pharmacy, pp. 288 to 331
Reference 2: Expert's report by Dr. Petra Hegar, dated October 20, 2011
Reference 3: Encyclopedia of Pharmaceutical Additives, January 14, 1994, pp. 20 to 21, 30 to 31, 38 to 41, 78 to 79, 106 to 107, 114 to 115, 122 to 123, 148 to 151, 212 to 213, and colophon
(Copies of above Evidences were attached as the original to the oral proceedings statement brief filed by the Demandee filed on February 16, 2016)
B21: Judgment by the Intellectual Property High Court, 2015 (Gyo-Ke) 10054, rendered on March 30, 2016
B22: Ryoichi Mimura, Written opinion dated July 19, 2018
B23-1: Makoto Otsuka, Expert's written opinion, dated July 17, 2018
B23-2: Makoto Otsduka, Expert's written opinion, Appendix 1, List of research achievements
B23-3: Makoto Otsuka, Expert's written opinion, Appendix 2, Test report (RE-QT-160201), February 12, 2016 (copy of A11-2)
B23-4: Makoto Otsuka, Expert's written opinion, Appendix 3, a document marked at the uppermost part of the first page as "Supplement to enablement requirement" (copy of A11-3)
B23-5: Makoto Otsuka, Expert's written opinion, Appendix 4, written statement by the Demandant dated March 11, 2016
B23-6: Makoto Otsuka, Expert's written opinion, Appendix 5, package insert for MSD K.K. Nazonex (R) nasal drops, 50 μg, 56 spray Nazonex (R) nasal drops, 50 μg, 112 spray, revised in June 2012 (5th version) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
B24: Package insert of Shionogi & Co., Ltd., Furumeta (R) ointment, Furumeta (R) cream, Furumeta (R) lotion," revised in November 2015 (11th edition)
B25: Samir A. Shah, et al. "Regional deposition of mometasone furuate nasal spray suspension in humans," Allergy and Asthma Proceedings, Vol. 36, No. 1 (2015) pp. 48 to 57
(Among the above-described Evidences B, copies of B21 and B23-2 to B25 were attached to the Demandee's written statement filed on July 23, 2018, as originals, and

originals of B22 and B23-1 were attached to the above written statement).

C1: Takayuki Sawada, List of steroid formulations for skin and eye available in Japan in June 2018
C2: Information on "budesonide" shown in the database "New drugs for tomorrow" of Technomics, Inc. (Output on July 4, 2018)
C3-1: Package insert for Teijin Pharma "Rhinocort (R) capsule for nasal use 50 μg" (revised in September 2014) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
C3-2: CEOLIA Pharma Co., Ltd "Aruroiyer (R) nasal drops 50 μg" (revised in February 2015) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
C3-3: Package insert for GlaxoSmithKlein K.K. "Furunase (R) nasal drops 50 μg 28 spray furunase (R) nasal drops 50 μg 56 spray" (revised in December 2017) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
C4: "Clitic pharmacokinetics," 3rd revision, p. 32 to 33, published on March 15, 2005, Nankodo
C5: Mamoru Fukuda, Written Opinion, dated July 18, 2018
C6: Package insert for Toko-Yakuhin Kogyo "Skyron (R) nasal drops 50 μg 28 spray Skyron (R) nasal drops 50 μg 56 spray" (revised in October 2015) (In the original text, "(R)" is printed in the form, character "R" encircled in a circle).
C7: Japanese Unexamined Patent Application Publication No. 2013-64022
(Above evidences were attached to the intervenor's written statement filed on July 20, 2018, copies were attached as originals for C1 to C4, C6 and C7, and original was attached for C5.)
C8: "Final report: Test of properties of formulation with various suspending agents of mometasone furoate ester (mometasone furancarboxylic acid ester)" prepared by Mizuho Shibata and two others (Noted as "Person responsible for the test; date: August 31, 2018, signed: Mizuho Shibata" in the last line in the first page)
C9: Paul Kippax and three others, "Characterising a nasal spray formulation from droplet to API particle size," posted on "Research Gate" on March 20, 2016
C9-2: Print-out from http://www.pharmtech.com/characterizing-nasal-spray-formation-droplet-api-particle-size on August 30, 2018
(Copies of the above-described Evidences C were attached to the intervenor's written statement filed on September 5, 2018, as originals).

No. 5 Judgment of the body

The body judges that the Present Patent should be invalidated based on Reason for Invalidation 1 among Reasons for Invalidation 1 and 2.

1 Regarding Reason for Invalidation 1

(1) The point of the argument on Reason for Invalidation 1 alleged by the Demandant is as follows:

A Regarding Present Corrected Invention 1 of the case

Present Corrected Invention 1 has not been corrected by the correction by the demand for correction made on July 23, 2018.

(A) Comparison between Present Corrected Invention 1 and the invention described in Evidence A No. 1

The elements of Present Corrected Invention 1 is as follows:

(a) a medicament ... comprising an aqueous suspension of mometasone furoate,

(b) once-a-day,

(c) to be administered intranasally, and

(d) for treating allergic or seasonal allergic rhinitis.

(Written Demand for Trial, p. 21, ll. 3 to 7).

On the other hand, Evidence A No. 1 describes an invention related to "MOMETASONE FUROATE (furancarboxylic acid mometasone) MONOHYDRATE, PROCESS FOR MAKING SAME AND PHARMACEUTICAL COMPOSITIONS," and Exhibit A No. 1 describes that "mometasone furoate (furancarboxylic acid mometasone) is known to be useful in the treatment of inflammatory conditions," "aqueous suspension compositions ... , e.g. for nasal administration," and "aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate" (Written Demand for trial, p. 21, ll. 8 to 13).

It is common technical knowledge that mometasone furoate (furancarboxylic acid mometasone) is synonymous with mometasone furoate, and the present patent specification has a description, "mometasone furoate (mometasone furoate monohydrate ..." (the Present Patent Publication, p. 7, left column, ll. 43 to 44), and it is also described that mometasone furoate in Present Corrected Invention 1 includes mometasone furoate monohydrate or corresponds to mometasone furoate monohydrate. In addition, it was publicly known that mometasone furoate has a topical anti-inflammatory activity, and, furthermore, it is general knowledge that a medicament is

chemicals prepared for the purpose of treatment, etc. (including compositions). Therefore, "mometasone furoate (furancarboxylic acid mometasone) monohydrate aqueous suspension compositions known to be useful in the treatment of inflammatory conditions" in the invention described in Exhibit A No. 1 corresponds to (a) "a medicament comprising an aqueous suspension of mometasone furoate" of Present Corrected Invention 1 (Written Demand for trial, p. 21, ll. 14 to 30).

Meanwhile, "intranasal administration" in the invention described in Exhibit A No. 1 corresponds to (c) "to be administered intranasally" of Present Corrected Invention 1 (Written Demand for trial, p. 21, ll. 31 to 32).

In the invention described in Exhibit A No. 1, however, "frequency of administration" is not specified to "once-a-day," and "inflammatory conditions" are not specified to "allergic or seasonal allergic rhinitis" (Written Demand for trial, p. 21, l. 33 to p. 22, l. 1).

Judging from the above, Present Corrected Invention 1 and the invention described in Exhibit A No. 1 coincide with each other in that they relate to "a medicament (d') for treating inflammatory conditions (a) comprising (a) aqueous suspension of mometasone furoate useful for treating inflammatory conditions (c) to be administered intranasally," and differ from each other in that the invention described in Exhibit A No. 1 does not specify frequency of administration (Different Feature 1), and that inflammatory conditions are not specified (Different Feature 2) (Written demand for trial, p. 22, ll. 2 to 6).

(B) Regarding Different Feature 1

As shown in descriptions in Exhibit A Nos. 4 to 8 with respect to intranasal administration of corticosteroids having topical anti-inflammatory activity for treating allergic rhinitis, once-a-day, and 2 to 4 times a day were generally known frequencies of intranasal administration of corticosteroids for treating allergic rhinitis, and, in addition, since it was known that once-a-day medication regimen is more preferable than 2 to 4 times a day that was considered inconvenient from viewpoints of patient's preference and compliance, there was no difficulty in specifying once-a-day medication regimen as frequency of administration of aqueous nasal suspension of mometasone furoate described in Evidence A No. 1, and a person skilled in the art could have quite easily conceived it (Written Demand for trial, p. 22, l. 7 to p. 23, l. 19).

(C) Regarding Different Feature 2

Evidence A No. 2 describes that mometasone furoate was a promising candidate

for a new drug for treating asthma and allergic rhinitis by intranasal inhalation, and a person skilled in the art could have easily conceived to modify a "medicament to be administered intranasally for treating inflammatory conditions" in Evidence A No. 1 to a "medicament to be administered intranasally for treating allergic rhinitis" (Written Demand for trial, p. 23, ll. 20 to 26).

(D) Regarding effects

Both of effects by Present Corrected Invention 1, Present Effect 1 "allergic rhinitis can be effectively treated with once-a-day administration of mometasone furoate" and Present Effect 2 "undesired systemic side effects can be prevented," are such that could have been predicted from Evidence A Nos. 1 and 2 as well as common technical knowledge and are not particularly distinguishing features (Written Demand for trial, p. 23, l. 28 to p. 26, l. 32).

B Regarding Corrected Invention 2 of the case

Present Corrected Invention 2 is an invention according to a dependent claim that cites Claim 1, and, before the correction, it further included element (e) "the dose is 25 to 1000 micrograms administered once a day," but, the range of the dose is restricted by the correction to "100 to 200 micrograms" and, at the same time, a matter, "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" was added.

Evidence A No. 1 describes that "The aqueous suspension of the invention may contain from 0.1 to 10.0 mg of mometasone furoate monohydrate per gram of suspension," and that the concrete aqueous nasal suspension of mometasone furoate monohydrate comprises mometasone furoate monohydrate with "concentration 0.5 (mg/g)."

Since there are descriptions in Evidence A Nos. 6 to 8 with respect to intranasal dose of corticosteroid having a topical anti-inflammation effect, a person skilled in the art could have easily conceived to set the once-a-day dose to "100 to 200 micrograms" from the well-known ranges of dose of "intranasal fluticasone propionate once-a-day 200 μg against seasonal allergic rhinitis" (A7) and "triamcinolone acetonide once-a-day 110 μg, 220 μg against perennial allergic rhinitis" for the purpose of treating allergic rhinitis with once-a-day intranasal corticosteroid having topical anti-inflammation action.

In addition, the present specification does not disclose any additional efficacy by restriction of the once-a-day dose to "100 to 200 micrograms."

Furthermore, the matter added by the correction, "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" is not any action of the nature first delivered only after the range of once-a-day dose is restricted to "100 to 200 micrograms" but an action of the nature that can be delivered regardless of whether the dose is "25 to 100 micrograms" or "200 to 1000 micrograms." Namely, the matter is a nature proper to (inherent nature of) aqueous suspension of mometasone furoate and it has nothing to do with specifying dosage and administration.

Accordingly, Present Corrected Invention 2 could have easily been invented from Evidence A Nos. 1 and 2 as well as common technical knowledge (Written Demand for trial, p. 26, l. 33 to p. 27, l. 20; Written Refutation of the Trial Case dated October 9, 2018, p. 4, l. 11 to p. 5, l. 22).

C Regarding Corrected Invention 3 of the case

Present Corrected Invention 3 is an invention according to a dependent claim that cites Claim 1 or 2, and, before the correction, element (d) of Claim 1, "A medicament for treating allergic or seasonal allergic rhinitis" was further specified to element (f), "the medicament is for treating seasonal allergic rhinitis," and the matter, "the once-a-day dose is 200 micrograms" is added by the correction.

Both of Present Corrected Inventions 1 and 2 could have easily been invented from Evidence A No. 1 and Evidence A No. 2, as well as common technical knowledge. Furthermore, Evidence A No. 2 describes that mometasone furoate was a promising candidate for a new drug for treating allergic rhinitis by intranasal inhalation. In addition, it was publicly known art as described in Evidence A Nos. 6 and 7 that intranasal corticosteroid could be applicable to seasonal allergic rhinitis. From the description in Evidence A No. 9, it cannot be believed that element (f) of Present Corrected Invention 3, treatment of "seasonal allergic rhinitis", is discriminated from the treatment of "allergic rhinitis" described in Evidence A No. 2.

Since there are descriptions in Evidence A Nos. 6 to 8 with respect to intranasal dose of corticosteroid having a topical anti-inflammation effect, a person skilled in the art could have easily conceived to set, for the purpose of treating allergic rhinitis with once-a-day intranasal corticosteroid having a topical anti-inflammation effect, the once-a-day dose to "200 micrograms" from well-known ranges of dose, "intranasal fluticasone propionate once-a-day 200 μg against seasonal allergic rhinitis" (A7) and "triamcinolone acetonide once-a-day 220 μg against perennial allergic rhinitis."

In addition, the present specification does not disclose any additional efficacy by restricting the once-a-day dose to "200 micrograms."

Accordingly, Present Corrected Invention 3 could have easily been invented from Evidence A Nos. 1 and 2 as well as common technical knowledge (Written Demand for trial, p. 27, l. 21 to p. 28, l. 4; Written Refutation of the Trial Case dated October 9, 2018, p. 5, l. 23 to p. 6, l. 14).

D Summary

Since a person skilled in the art could have easily invented Present Corrected Inventions 1, 2, and 3 based on Evidence A Nos. 1 and 2 as well as common technical knowledge, Present Corrected Inventions 1, 2, and 3 are not patentable under the provisions of Article 29(2) of the Patent Act, fall under the provisions of Article 123(1)(ii) of the Patent Act, and should be invalidated (Written Demand for trial, p. 31, ll. 26 to 31; Written Refutation of the Trial Case dated October 9, 2018, p. 6, ll. 15 to 17).

(2) Judgment by the body regarding Reason for Invalidation 1

A Matters described in each evidence A

Evidence A No. 1 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A1-a) to Description (A1-h).

Description (A1-a)

"MOMETASONE FUROATE (furancarboxcylic acid mometasone) MONOHYDRATE, PROCESS FOR MAKING SAME, AND PHARMACEUTICAL COMPOSITIONS" (p. 1, Title of the Invention)

Description (A1-b)

"Mometasone furoate (furancarboxcylic acid mometasone) is known to be useful in the treatment of inflammatory conditions" (p. 1, lower right column, ll. 8 to 9).

Description (A1-c)

"Of particular interest are aqueous suspension compositions of mometasone furoate (furancarboxcylic acid mometasone) monohydrate, e.g., for nasal administration. The aqueous suspensions of the invention may contain from 0.1 to 10.0 mg of mometasone furoate (furancarboxcylic acid mometasone) monohydrate per gram of suspension" (p. 3, upper left column, ll. 21 to 23).

Description (A1-d)

"Example 1

..... (Omitted) .... to afford 24.83 g of mometasone furoate (furancarboxcylic acid mometasone) monohydrate having an infrared spectrum and X-ray diffraction graph substantially the same as those in Figures 1 and 2" (p. 3, upper right column, ll. 14 to 24).

Description (A1-e)

"Example 2

..... (Omitted) ..... . Mometasone furoate (furancarboxylic acid mometasone) monohydrate, 316.5 g, weight yield 90%, is obtained having an infrared spectrum and X-ray diffraction graph substantially the same as those in Figures 1 and 2 " (p. 3, upper right column, l. 5 from the bottom to lower left column, l. 7).

Description (A1-f)

"Example 3

An aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate is prepared from the following.

Ingredient	Concentration (mg/g)	Representative Batch (g/12 kg)
Mometasone furoate (furancarboxylic acid mometasone) monohydrate	0.5	6.0
Avicel RC591*	20.0	240.0
Glycerin	21.0	252.0
Citric acid	2.0	24.0
Sodium citrate	2.8	33.6
Polysorbate 80**	0.1	1.2
Benzalkonium chloride	0.2	2.4
Phenylethyl alcohol	2.5	30.0
Purified water added in sufficient amount	1.0 g	12.0 kg

* Avicel RC591 is a trademark of FMC for a mixture of microcrystalline cellulose and sodium carboxymethyl cellulose.

** Polysorbate 80 is a tradename for a mixture of an oleate ester of sorbitol and its anhydride copolymerized with approximately 20 moles of ethylene oxide for each mole of sorbitol and sorbitol anhydride.

After dispersing the Avicel RC591 in 6 kg of purified water, glycerin is added thereto. The citric acid and sodium citrate are dissolved in 240 ml of water, and said solution is added to the Avicel-glycerin dispersion with mixing. In a separate vessel, Polysorbate 80 is dissolved in approximately 400 ml of purified water with stirring. The mometasone furoate (furancarboxylic acid mometasone) monohydrate is dispersed in the aqueous Polysorbate 80 solution, and said slurry is then added with stirring to the Avicel-glycerin citric acid mixture. After dissolving benzalkonium chloride and phenylethyl alcohol in purified water, said solution is added to the suspension mixture with stirring. The suspension is added to the suspension mixture with stirring. The suspension is brought to 12 kg with purified water with mixing. The final pH of the suspension is 4.5±0.5" (p. 3, lower left column, l. 8 to lower right column, l. 9).

Description (A1-g)

"Example 4

The following compositions were prepared without the suspending agent, Avicel RC591, to prevent interference in X-ray diffraction studies:

Ingredient	Concentration (mg/g)		
	4A	4B	4C
Micronized mometasone furoate (furancarboxylic acid mometasone) monohydrate	0.5	0.5	0.5
Citric acid monohydrate	2.0	2.0	2.0
Sodium citrate dihydrate	2.8	-	2.8
Sodium phosphate	-	4.0	-
Polysorbate 80	0.1	0.1	0.1
Benzalkonium chloride	0.2	0.2	0.2
Phenylethyl alcohol	2.5	-	-
Potassium sorbate	-	3.4	-
Propylene glycol	-	-	100.0
Glycerin	21.0	21.0	21.0
Purified water (USP) added in sufficient amount	1.0 g	1.0 g	1.0 g

These compositions were prepared according to the procedure described in Example 3" (p. 3, lower right column, l. 10 to the last line).

Description (A1-h)

"Example 5

The following compositions were prepared and tested to determine thermal stability of said compositions.

Ingredient	Concentration (mg/g)		
	5A	5B	5C
Micronized mometasone furoate monohydrate	0.5	0.5	0.5
Citric acid monohydrate	2.0	2.0	2.0
Sodium citrate dihydrate	2.8	-	2.8
Sodium phosphate	-	4.0	-
Polysorbate 80	0.1	0.1	0.1
Benzalkonium chloride	0.2	0.2	0.2
Phenylethyl alcohol	-	2.5	-
Potassium sorbate	-	-	3.4
propylene glycol	100.0	-	-
Glycerin	21.0	21.0	21.0
Avicel RC591	20.0	20.0	20.0
Purified water (USP q.s.ad)	1.0 g	1.0 g	1.0 g

The compositions were prepared according to the procedure described in Example 3" (p. 4, upper left column, l. 6 to l. 4 from the bottom).

Evidence A No. 2 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A2-a) to Description (A2-h) (As A2 is written in English language, a translation by the body is shown).

Description (A2-a)

"Competitive enzyme immunoassay for direct quantification of mometasone furoate (SCH32088) in human plasma" (p. 473, Title)

Description (A2-b)

"A highly sensitive competitive enzyme immunoassay (EIA) for measuring unextracted SCH32088 in human plasma has been developed" (p. 473, Abstract, ll. 2 to 3).

Description (A2-c)

"For thus-developed EIA, 1 pg of SCH32088 per assay, or 25 pg per ml of human plasma can be detected. This can reliably quantify 50 pgml-1 to 2.5 ngml-1 of SCH32088 in human plasma with excellent linearity, accuracy, and precision" (p. 473, Abstract, ll. 6 to 8).

Description (A2-d)

"Mometasone furoate (SCH32088) is a synthetic corticosteroid that has a topical anti-inflammatory activity, and, on the other hand, exhibits a potential capability to suppress hypothalamic-pituitary-adrenal (HPA) function to the minimum [1,2]." (p. 473, left column, ll. 3 to 8).

Description (A2-e)

"SCH32088 is a promising candidate for a new drug for treating asthma and allergic rhinitis by oral inhalation and intranasal inhalation. SCH32088 has so far exhibited promising biological and pharmacological activities, but, because of lack of an analytical method that is sufficiently highly sensitive and is necessary for remedy with very small dose of the drug, its metabolism, pharmacokinetics, and toxicokinetics have not been evaluated" (p. 473, left column, ll. 8 to 17).

Description (A2-f)

"Based on studies using radioactivity-labeled materials, after intra-abdominal administration to male rats, SCH32088 seems to be distributed into various tissues and widely metabolized (undisclosed data). Because of this, it is surmised that the plasma concentration of parent drug is within the domain of $pgml^{-1}$ and cannot be quantified by normal chromatography" (p. 473, left column, ll. 17 to 25).

Description (A2-g)

"Specificity

Cross reactivity of anti-SCH32088 antiserum was examined by testing competitive binding of SCH32088-3-CMO-HRP with various structurally associable steroids and known or potentially possible metabolites of SCH32088, intrinsic steroid hormone, and general steroidal drugs. As shown in Table 1, as measured with the 50% replacement level of SCH32088-3-CMO-HRP, no significant cross reactivity was observed" (p. 477, right column, ll. 15 to 5 from the bottom).

Description (A2-h)

"Application

This EIA method was applied for analyzing SCH32088 in ... clinical samples. As shown in Figure 5, plasma concentration of SCH32088 in human reached a peak of about 150 $pgml^{-1}$ (Cmax) at 30 minutes (Tmax) after oral administration of 1 mg of SCH32088 solution to a male volunteer, and then rapidly dropped. This result clearly proves that this EIA method is suitable for pharmacokinetic evaluation of SCH32088 in human and, probably, animal.

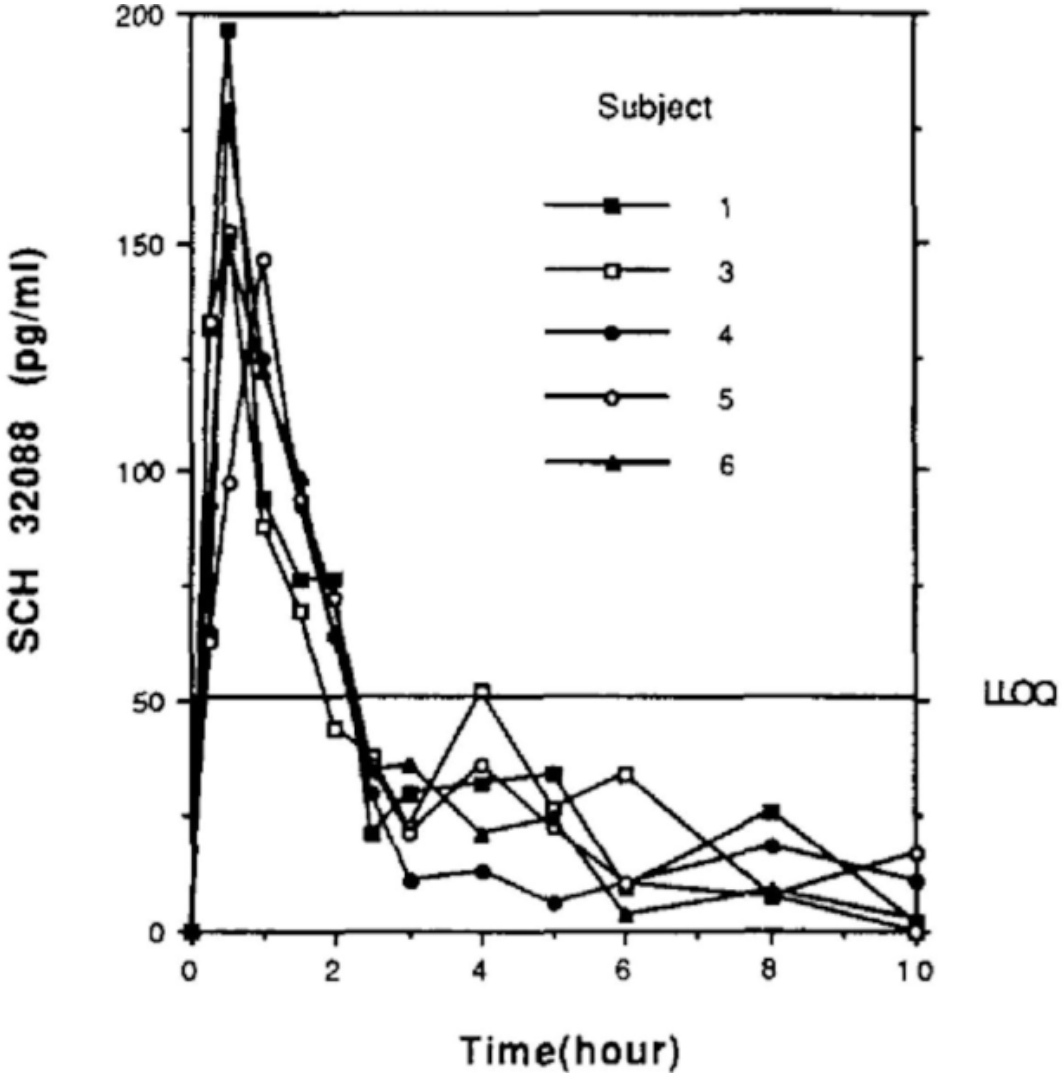

Figure 5

Concentration of SCH32088 in human plasma. Single dose of 1 mg of SCH32088 solution was administered by oral swallowing to each healthy male volunteer ....

Blood samples were collected at each indicated time, and plasma was assayed for concentration of SCH32088. Procedures are shown in "Materials and Method" (p. 478,

right column, ll. 1 to 14, Figure 5, Explanation of the figure)

Evidence A No. 3 that was distributed prior to the priority date of the present patent application includes the following Description (A3-a) to Description (A3-h).

Description (A3-a)

"Mometasone furoate (MF) is a corticoid agent for external application developed by Schering-Plough, U.S.A., and it has been made clear that, while it exhibits very strong topical anti-inflammation effect, it is weak in terms of side effects[1, 2)]." (p. 131, left column, ll. 3 to 7).

Description (A3-b)

"This time, topical anti-inflammation effect, systemic action, and skin atrophy by continuous application of diflorasone diacetate (DDA), difluprednate (DFBA), dexamethasone dipropionate (DDP) and budesonide (BDS), whose strength of clinical efficacy is very strong or higher, were compared to MF using mice. Deviation between principal action and side effects is compared from these results, and positioning of efficacy and safety of the drug was carried out" (p. 131, left column, l. 2 from the bottom to right column, l. 7).

Description (A3-c)

"2) Relative titer of MF to control medication

..... (Omitted) ..... .Relative titers indicate that the topical anti-inflammation effect of MF is 4.63 times that of DDA, 1.16 times that of DFBA, 1.88 times that of DDP, and 0.99 times that of BDS, and MF exhibited the largest activity together with BDS" (p. 134, left column, ll. 3 to 16).

Description (A3-d)

"2. Systemic action and skin atrophy (7-day continuous application test)

First, dose-action relationship of thymus atrophy and skin atrophy caused by DDA, DFBA, DDP, and BDS as systemic actions was examined, and relative titer of MF to these actions was obtained within the dose range for which regression lines can be obtained" (p. 134, right column, ll. 11 to 17).

Description (A3-e) (As the original text is written in English language, a translation by the body is shown).

"

表8　マウスにおけるＭＦおよび対照化合物の相対力価および治療係数の比較

パラメーター	MF	DDA	DFBA	DDP	BDS	BD[3]
抗炎症作用	(A) 1.00	0.22 (0.12～0.40)	0.86 (0.43～1.71)	0.53 (0.28～1.01)	1.01 (0.62～1.62)	0.16 (0.10～0.26)
胸腺萎縮	(B) 1.00	3.03 (1.74～5.23)	2.00 (1.04～3.56)	1.49 (0.78～2.69)	1.28 (0.64～2.33)	4.34 (2.26～8.11)
皮膚萎縮	(C) 1.00	0.93 (0.58～1.50)	1.64 (0.73～3.20)	0.71 (0.27～2.09)	3.33 (2.00～5.33)	0.22 (0.13～0.38)
治療係数	(A/B) 1.00 (A/C) 1.00	0.07 0.24	0.43 0.52	0.36 0.75	0.79 0.30	0.04 0.73

（　）：95%　信頼限界

表 8　マウスにおける MF および対照化合物の相対力価および 治療係数の比較

Table 8　Comparison of relative titer and therapeutic index in mice between MF and control chemicals

パラメータ　　Parameter
抗炎症作用　　Anti-inflammation effect
胸腺委縮　　Thymic atrophy
皮膚委縮　　Skin atrophy
治療係数　　Therapeutic index
信頼限界　　Confidence limit

" (p. 142).

Description (A3-f)

"2) Systemic action and skin atrophy

Systemic action indicated with thymus atrophy as an index is, when MF is 1.00, 4.34 for BD, 3.03 for DDA 3.03, 2.00 for DFBA, 1.49 for DDP, and 1.28 for BDS, and MF exhibited the weakest action compared to control drugs" (p. 143, right column, ll. 9 to 4 from the bottom).

Description (A3-g)

"3) Therapeutic index

In order to evaluate deviation of principal action from side effects, therapeutic indices were calculated. When MF is 1.00, deviation of the topical anti-inflammation effect to thymus atrophy is 0.79 for BDS, 0.43 for DFBA, 0.36 for DDP, 0.07 for DDA,

and 0.04 for BD" (p. 144, left column, ll. 1 to 6).

Description (A3-h)

"Compared to 5 control drugs whose clinical efficacy is very strong or higher, activity of MF was strongest in principal action but weak in side effects, and its deviation was the largest" (p. 144, right column, ll. 2 to 5).

Evidence A No. 4 that was distributed prior to the priority date of the Present Patent Application describes the following Description (A4-a) to Description (A4-b).

Description (A4-a)

"Study on clinical efficacy of nasal beclomethasone dipropionate to patients with bronchial asthma complicated with nasal allergy" (p. 51, Title)

Description (A4-b)

"(2) Dose

Daily spray amount of 400 μg of beclomethasone dipropionate was administered continuously for 1 week with bilateral spray (1 spray/side each time) 4 times a day (morning, noon, evening, and night) " (p. 53, right column, ll. 16 to 12 from the bottom).

Evidence A No. 5 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A5-a) to Description (A5-c).

Description (A5-a)

"Study of influences of nasal and oral inhalation of beclomethasone on endocrine function - especially centering on a sound case and a case of bronchial asthma complicated with nasal allergy -" (p. 375, Title)

Description (A5-b)

"Therefore, influence of combined use of nasal and oral inhalation on endocrine function was studied using nasally inhaled beclomethasone dipropionate (hereinafter, abbreviated as BDN) and orally inhaled beclomethasone dipropionate (hereinafter, abbreviated as BDI)" (p. 376, left column, ll. 25 to 30).

Description (A5-c)

"Method for inhalation was each of BDN and BDI 4 times a day, 2 sprays each

time for group A and group of patients, and BDN 4 sprays a time, 4 times a day for group B" (p. 376, right column, ll. 5 to 7).

Evidence A No. 6 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A6-a) to Description (A6-e) (As Evidence A No. 6 is written in English language, a translation in Japanese language by the body is shown).

Description (6-a)

"Budesonide administered once-a-day against seasonal allergic rhinitis " (p. 507, Title)

Description (6-b)

"Use of glucocorticoid topically administered for symptom relief for seasonal allergic rhinitis and perennial rhinitis is now an established form of treatment.[3] It was revealed by studies that budesonide (200 μg) nasally administered twice a day is effective, and well tolerated by a patient in the above-described condition[4,5]" (p. 507, ll. 6 to 3 from the bottom).

Description (6-c)

"From viewpoints of patient's preference and compliance, however, once-a-day intranasal application of budesonide can provide an advantage better than that of regiment of twice-a-day" (p. 507, l. 3 from the bottom to the last line).

Description (6-d)

"Comparison between once-a-day and twice-a-day intranasal budesonide (400 μg/day) by metered-dose pressurized aerosol to perennial rhinitis patients proved equal efficacy and tolerance between these two treatment regimens[2]. A similar test in which nasal aqueous budesonide ('Rhinocort Aqua') delivered with a pump-type spray is used in treating seasonal allergic rhinitis showed equal efficacy and tolerance between two regimens (400 μg/day), once-a-day and twice-a-day[1]" (p. 508, ll. 1 to 7).

Description (6-e)

"Thus, in the present test, once-a-day treatment with budesonide gave the same efficacy as that of twice-a-day treatment. This confirms the result obtained from the test for perennial rhinitis[3] and the result 1 obtained from the test for seasonal allergic rhinitis

in which aqueous budesonide was used" (p. 514, ll. 6 to 4 from the bottom).

Evidence A No. 7 that was distributed prior to the priority date of the Present Patent Application describes the following Description (A7-a) to Description (A7-b) (As Evidence A No. 7 is written in English language, a translation in Japanese language by the body is shown).

Description (7-a)

"Intranasal fluticasone propionate

Review of its pharmacodynamic properties and pharmacokinetics properties, as well as treating capability in allergic rhinitis" (p. 760, Title).

Description (7-b)

"A large-scale test with placebo using a large number of patients established efficacy of intranasal fluticasone propionate 200 μg/day in both of adults and children with seasonal allergic rhinitis. In addition, according to the results of 5 tests in which over 1,000 patients were used, fluticasone propionate 200 μg by once-a-day administration has efficacy nearly equal to that of 100 μg twice-a-day" (p. 762, ll. 2 to 5).

Evidence A No. 8 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A8-a) to Description (A8-e) (As Evidence A No. 8 is written in English language, a translation in Japanese language by the body is shown).

Description (8-a)

"Once-a-day intranasal spray of triamcinolone acetonide is effective for treating perennial allergic rhinitis" (p. 329, Title).

Description (8-b)

"Randomized double blind trial placebo-controlled parallel-group trials were carried out in 11 facilities, and, in relief for symptoms of rhinitis in 305 adults, and children in late elementary grades with perennial allergic rhinitis, safety and efficacy of intranasal aerosol of triamcinolone acetonide with regimens of once-a-day, 110 μg, 220 μg, and 440 μg compared to placebo were evaluated" (p. 329, ll. 1 to 4).

Description (8-c)

"No noteworthy significant side effects or abnormality in examination findings was observed in this trial. Intranasal triamcinolone acetonide 220 μg and 440 μg used for 12 weeks by once-a-day regime was superior clinically and statistically to placebo with respect to treatment of perennial allergic rhinitis" (p. 329, ll. 9 to 12).

Description (8-d)

"Currently available aerosol preparations, beclomethasone and flunisolide, have been proved to be effect by research tests and clinical use for 10 years in the U.S.A. Currently recommended medication regimen for these preparations is 2 to 4 times of administration a day, and they are approved for use in adults and children of the age of 6 years" (p. 329, left column, l. 7 from the bottom to p. 329, middle column, l. 4).

Description (8-e)

"For currently available intranasal steroids, beclomethasone and flunisolide, it is recommended to administer by regimen of 4 times a day at the maximum, which is an inconvenient regimen compared to once-a-day administration" (p. 333, right column, ll. 5 to 10).

Evidence A No. 9 that was distributed prior to the priority date of the Present Patent Application includes the following Description (A-a).

Description (9-a)

"Allergic rhinitis allergic is synonymous with nasal allergy, and the cause of disease is nasal mucosa type I allergy. Depending on the timing of onset, it is classified into perennial allergic rhinitis and seasonal allergic rhinitis. In Japan, for the former, house dust (ticks) is the primary antigen. The latter is mainly caused by allergy by pollens called pollinosis. Historically, allergic rhinitis was clarified from pollinosis, and often occurs as a complication with allergic conjunctivitis and is called pollinosis, or hay fever, giving an impression that it is different from allergic rhinitis. Different from Japan, especially in Europe and America, perennial seasonal allergy, namely pollinosis, is dominant in many countries. Since they are equivalent to each other in symptoms, diagnostic method, and therapeutic method, however, discriminating them rather hinders understanding of the disease and may cause misunderstanding" (p. 311, left column, l. 2 to right column, l. 2).

B Invention described in Evidence A No. 1

Judging from Description (A1-a) to Description (A1-h), it is recognized that Evidence A No. 1 describes the following invention.

"An aqueous nasal suspension of mometasone furoate monohydrate for treating inflammatory conditions" (hereinafter, sometimes referred to also as "Invention A-1").

C Comparison between Present Corrected Invention 1 and Invention A-1

(A) In the industry, "mometasone furoate (furancarboxylic acid mometasone)," is synonymous with "mometasone furoate."

In addition, since the present patent specification has the following descriptions: "The aqueous suspension compositions of the present invention may be prepared by admixing mometasone furoate or mometasone furoate monohydrate (preferably mometasone furoate monohydrate) with water and other pharmaceutically acceptable excipients. ... . The aqueous suspensions of the invention may contain from about 0.01 to 10.0 mg, preferably 0.1 to 10.0 mg of mometasone furoate monohydrate per gram of suspension" (Patent Publication, column 8, ll. 33 to 41), "Mometasone furoate (intranasally in the form of an aqueous suspension of mometasone furoate monohydrate) has been used for treating patients with seasonal allergic rhinitis" (Patent Publication, column 13, ll. 43 to 45), "Several Phase I studies have been completed using the aqueous nasal spray suspension formulation of mometasone furoate monohydrate" (Patent Publication, column 13, l. 49 to column 14, l. 1), "In a follow-up multiple dose study, ..., ...: A) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate, ...; B) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate, ... All treatments were administered as once-daily dosing in the morning" (Patent Publication, column 14, ll. 10 to 19), and "The objectives of these studies in male volunteers were to determine the absorption, metabolism, and excretion of ^{3}H-labeled mometasone furoate ("^{3}H-MF") following administration by oral swallowing as a solution and as an aqueous suspension of the monohydrate, ..., by nasal inhalation as an aqueous suspension of the mometasone furoate monohydrate from a nasal spray unit" (Patent Publication, column, 18, ll. 18 to 27), "mometasone furoate" in Present Corrected Invention 1 encompasses "mometasone furoate monohydrate."

Accordingly, "mometasone furoate monohydrate" in Invention A-1 corresponds to "mometasone furoate" in Present Corrected Invention 1.

In addition, "aqueous nasal suspension" in Invention A-1 corresponds to "A medicament ... comprising an aqueous suspension ... to be administered intranasally ..."

in Present Corrected Invention 1.

Then, since both of allergic and seasonal allergic rhinitis are diseases that cause inflammatory conditions to noses, "inflammatory conditions" in Invention A-1 and "allergic and seasonal allergic rhinitis" in Present Corrected Invention 1 mean the same thing, inflammatory conditions.

Then, Present Corrected Invention 1 and Invention A-1 coincide with each other in that they relate to "a medicament comprising an aqueous suspension of mometasone furoate to be administered intranasally for treating inflammatory conditions," and differ from each other in the following two points:

· While dosage and administration of the medicament is specified as "once-a-day" in Present Corrected Invention 1, it is not specified in Invention A-1 (hereinafter, referred to as "Different Feature 1"), and

· While the target of treatment, inflammatory conditions is specified as "allergic or seasonal allergic rhinitis" in Present Corrected Invention 1, it is not specified in Invention A-1 (hereinafter, referred to as "Different Feature 2").

(B) Different Feature 1 is examined below.

Description (A4-a) to Description (A4-b), and Description (A5-a) to Description (A5-c) indicate that beclomethasone dipropionate is administered nasally 4 times a day to patients with bronchitis with nasal allergy.

Description (A6-a) to Description (A6-d) indicate that, with respect to intranasal application of budesonide to patients with seasonal allergic rhinitis, the regimen of once-a-day has a similar symptom relief function to that of the regiment for twice-a-day, and the regimen for once-a-day is preferable from viewpoints of patients' preference and compliance.

Description (A7-a) to Description (A7-b) indicate that, in intranasal application of fluticasone propionate to patients with seasonal allergic rhinitis, the regimen of once-a-day has equal efficacy to the regimen of twice-a-day.

Description (A8-a) to Description (A8-e) indicate that intranasal application of triamcinolone acetonide with the regimen of once-a-day to patients with perennial allergic rhinitis was carried out and effective, and, at the same time, it is recommended to administer aerosol preparation of beclomethasone and flunisolide, steroids for intranasal administration with a regimen of 2 to 4 times a day, but they are less convenient compared to the regimen for once-a-day.

In actually using a medicament of Invention A-1 in treatment, it is indispensable to determine appropriate dosage and administration, and, in the case in which no

publicly known dosage and administration for a drug for intranasal application comprising mometasone furoate exists, a person skilled in the art would naturally examine and adopt dosage and administration of publicly known similar drugs; and, since all of beclomethasone dipropionate, budesonide, fluticasone propionate, and triamcinolone acetonide had been widely known as corticosteroids having topical anti-inflammatory activity used against allergic rhinitis, etc. as of the priority date of the Present Patent Application, a person skilled in the art who read Description (A4-a) to Description (A8-e) would understand that, from viewpoints of patient's preference and compliance, once-a-day among once to four times a day indicated in those Descriptions is most preferred as the frequency of intranasal administration.

Then, since "mometasone furoate (furancarboxylic acid mometasone)-hydrate" of A1 invention, namely, "mometasone furoate" of Present Corrected Invention 1, not need to wait for Description (A2-a) and Description (A3-a), was known as of the priority date of the Present Patent Application as a corticosteroid that has topical anti-inflammatory activity, and Evidence A No. 1 also discloses that, it can be deemed that a person skilled in the art could have easily conceived by examining dosage and administration of the above corticosteroids that are similar drugs to mometasone furoate to make frequency of administration of aqueous nasal suspension in A1 invention "once-a-day."

(C) Different Feature 2 is examined below.

Since Description (A2-a) to Description (A2-h) indicate that mometasone furoate has a topical anti-inflammatory activity and, on the other hand, exhibits a potential capability to suppress hypothalamic-pituitary-adrenal (HPA) function only at the minimum, and that mometasone furoate was a promising candidate for a new drug for treating asthma and allergic rhinitis by intranasal inhalation, and it is recognized that it was common technical knowledge as of the priority date of the Present Patent Application that allergic rhinitis is nasal inflammation as its name suggests and, although allergic rhinitis is classified into perennial and seasonal depending on the time of onset, symptoms, diagnostic method, and treating method are absolutely identical for both of them, as shown also in Description (A9-a), it can be deemed that a person skilled in the art who read Description (A2-a) to Description (A2-h) could have easily conceived to select "allergic and seasonal allergic rhinitis" as "inflammatory conditions" mentioned in Invention A-1 that relates to a medicament to be intranasally administered.

D Comparison between Present Corrected Invention 2 and Invention A-1

(A) Present Corrected Invention 2 is the invention which is further added with "the once-a-day dose is 100 to 200 micrograms" and "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" to Present Corrected Invention 1 to the matters specifying the invention.

Then, Present Corrected Invention 2 and Invention A-1 differ from each other, in addition to above Different Feature 1 and Different Feature 2 between Present Corrected Invention 1 and Invention A-1, in that, while "the once-a-day dose is 100 to 200 micrograms" in Present Corrected Invention 2, it is not specified in Invention A-1 (hereinafter, sometimes referred to also as "Different Feature 3-1"), and that, while "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" in Present Corrected Invention 2, it is not specified in Invention A-1 (hereinafter, sometimes referred to also as "Different Feature 3-2"), and coincide with each other in other points.

(B) Different Feature 3-1 is examined below.

Description (A6-d) indicates that a regimen of intranasal aqueous budesonide once-a-day (400 μg/day) delivered efficacy against seasonal allergic rhinitis, and Description (A7-b) indicates that a regimen of intranasal fluticasone propionate once-a-day 200 μg delivered efficacy against seasonal allergic rhinitis, and Description (A8-b) indicates that a regimen of triamcinolone acetonide once-a-day 110 μg, 220 μg, 440 μg intranasal aerosol delivered efficacy against perennial allergic rhinitis.

Then, it can be deemed that a person skilled in the art who learned of Invention A-1 could have easily conceived, in addition to examining its dosage and administration and set to once-a-day based on Evidence A Nos. 4 to 8, to set the dose, taking Description (A6-d), Description (A7-b) and Description (A8-b) into consideration, to the range of "the once-a-day dose is 100 to 200 micrograms."

(C) Different Feature 3-2 is examined below.

As indicated by the following descriptions in the detailed description of the invention of the specification attached to the application:

"The substantial minimization of the systemic effect of mometasone furoate administered intranasally or by oral inhalation has been measured by High Performance Liquid Chromatography (HPLC) metabolite profiling of plasma radioactivity of mometasone furoate, its substantially complete (> 98%) first-pass metabolism in the liver, and by a minimal reduction in cortisol secretion levels.

When mometasone furoate is administered orally (i.e., swallowed as an oral

suspension) or by oral or nasal inhalation, there is substantial absence of absorption systemically into the bloodstream of mometasone furoate; i.e., there is essentially no parent drug (substantially, less than 1% of mometasone furoate) which reaches the bloodstream from the gastro-intestinal tract" (Patent Publication, column 5, ll. 34 to 46),

"In addition, a single-dose absorption, excretion and metabolism study using 200 mcb of ^{3}H-mometasone furoate as the nasal spray formulation was conducted in 6 normal male volunteers. When systemic absorption (based on urinary excretion) was compared to an intravenously administered dose of ^{3}H-mometasone furoate, it was 8%. The plasma concentrations of parent drug could not be determined by metabolite profiling because the levels of plasma radioactivity were below the limit of quantification. These data are consistent with substantially less than 1% of bioavailability of mometasone furoate" (Patent Publication, column 5, ll. 34 to 46),

"In addition, a single-dose absorption, excretion, and metabolism study using 200 mcb of ^{3}H-mometasone furoate as the nasal spray formulation was conducted in 6 normal male volunteers. When systemic absorption (based on urinary excretion) was compared to an intravenously administered dose of ^{3}H- mometasone furoate, it was 8%. The plasma concentrations of parent drug could not be determined by metabolite profiling because the levels of plasma radioactivity were below the limit of quantification. These data are consistent with substantially less than 1% of bioavailability of mometasone furoate" (Patent Publication, column 14, ll. 25 to 34), and

"The results of these drug metabolism/clinical pharmacology studies indicate that:

1. Drug-derived radioactivity was completely absorbed when ^{3}H-MF was given orally as a solution to male volunteers. However, the absolute bioavailability of unchanged mometasone furoate was extremely low (less than about 1%) due to extensive first pass metabolism" (Patent Publication, column 25, l. 29 to column 26, l. 2), it is recognized that "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" can be automatically achieved by making the dose in Present Corrected Invention 1 100 to 200 micrograms.

Then, Different Feature 3-2 cannot be deemed to be any new different feature that is substantially different from Different Feature 3-1. Since it can be deemed with respect to Different Feature 3-1 as shown in above (B) that a person skilled in the art who learned of Invention A-1 could have easily conceived, in addition to examining its dosage and administration and setting to once-a-day based on Evidence A Nos. 4 to 8, to set the dose taking Description (A6-d), Description (A7-b), and Description (A8-b) into consideration to the range of "the once-a-day dose is 100 to 200 micrograms," it

can also be deemed that, in line with the above, the matter according to Different Feature 3-2, "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" is achieved as a matter of course.

E Comparison between Present Corrected Invention 3 and Invention A-1

(A) Present Corrected Invention 3 is such that "a medicament" in Present Corrected Invention 1 or Present Corrected Invention 2 is defined as "the medicament is for treating seasonal allergic rhinitis" and the matter, "the once-a-day dose is 200 micrograms" is further added.

Then, Present Corrected Invention 3 and Invention A-1 differ from each other, in addition to above Different Feature 1 and Different Feature 2 between Present Corrected Invention 1 and Invention A-1, and above Different Feature 3-1 and Different Feature 3-2 between Present Corrected Invention 2 and Invention A-1, in that, while "the medicament is for treating seasonal allergic rhinitis" in Present Corrected Invention 3, the medicament is "for treating inflammatory conditions" in Invention A-1 (hereinafter, sometimes referred to also as "Different Feature 4-1"), and that, while "the once-a-day dose is 200 micrograms" in Present Corrected Invention 3, it is not specified in Invention A-1 (hereinafter, sometimes referred to also as "(Different Feature 4-2 "), and coincide with each other in other points.

(B) Different Feature 4-1 is examined below.

Since Description (A2-a) to Description (A2-h) indicate that mometasone furoate has a topical anti-inflammatory activity and, on the other hand, exhibits a potential capability to suppress hypothalamic-pituitary-adrenal (HPA) function only at the minimum, and that mometasone furoate was a promising candidate for a new drug for treating asthma and allergic rhinitis by intranasal inhalation, and it is recognized that it was common technical knowledge as of the priority date of the Present Patent Application that allergic rhinitis is nasal inflammation as its name suggests and, although allergic rhinitis is classified into perennial and seasonal depending on the time of onset, symptoms, diagnostic method, and treating method are absolutely identical for both of them, as shown also in Description (A9-a), it can be deemed that a person skilled in the art who read Description (A2-a) to Description (A2-h) could have easily conceived to make the "medicament" as "the medicament is for treating seasonal allergic rhinitis" by selecting the "seasonal allergic rhinitis" as the "inflammatory conditions."

(C) Different Feature 4-2 is examined below.

Description (A6-d) indicates that a regimen of intranasal aqueous budesonide once-a-day (400 μg/day) delivered efficacy against seasonal allergic rhinitis, and Description (A7-b) indicates that a regimen of intranasal fluticasone propionate once-a-day 200 μg delivered efficacy against seasonal allergic rhinitis, and Description (A8-b) indicates that a regimen of triamcinolone acetonide once-a-day 110 μg, 220 μg, 440 μg intranasal aerosol delivered efficacy against perennial allergic rhinitis.

Then, it can be deemed that a person skilled in the art who learned of Invention A-1 could have easily conceived to examine the dosage and administration, and, in addition to setting the regimen to once-a-day based on Evidence A Nos. 4 to 8, to make the "medicament" as "the medicament is for treating seasonal allergic rhinitis" by selecting "seasonal allergic rhinitis" as "inflammatory conditions" of Invention A-1, and, at the same time, to set the dose to "once-a-day 200 micrograms" taking Description (A6-d), Description (A7-b), and Description (A8-b) into consideration.

F Regarding effects

(A) Effects of Present Corrected Inventions

The Present Patent Specification has the following descriptions.

Description (P-a)

"Mometasone furoate (intranasally administered in the form of an aqueous suspension of mometasone furoate monohydrate) has been used for treating patients with seasonal allergic rhinitis. ...

Several Phase I studies have been completed using the aqueous nasal spray suspension formulation of mometasone furoate monohydrate. In a randomized, third party-blinded, placebo-controlled rising single-dose safety and tolerance study, the aqueous nasal spray suspension formulation was administered to eight healthy male volunteers. Doses were administered at 11 pm, and plasma cortisol concentrations were measured during the following 24-hour period. Compared to placebo, mometasone furoate at doses of 1000 mcg, 2000 mcg, and 4000 mcg did not significantly affect the 24-hour area under the curve plasma cortisol profile (AUC 0-24).

In a follow-up multiple dose study, 48 normal male volunteers were empaneled in ... parallel group study. Twelve volunteers in each of four groups received one of the following treatments for 28 days: A) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate 400 mcg/day; B) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate, 1600 mcg/day; C) Intranasal placebo; D) Oral prednisone, 10 mg/day. All treatments were

administered as once daily dosing in the morning. ... Neither of the 2 doses of the mometasone furoate aqueous nasal spray formulation were associated with any changes in cortisol secretion compared to placebo.

In addition, a single-dose absorption, excretion, and metabolism study using 200 mcg of ^{3}H-mometasone furoate as the nasal spray formulation was conducted in 6 normal male volunteers. When systemic absorption (based on urinary excretion) was compared to an intravenously administered dose of ^{3}H-mometasone furoate, it was 8%. The plasma concentrations of parent drug could not be determined by metabolite profiling because the levels of plasma radioactivity were below the limit of quantification. These data are consistent with substantially less than 1% of bioavailability of mometasone furoate. See Tables 1 to 2 herein below. In a dose ranging safety and efficacy study, the mometasone furoate aqueous nasal spray formulation at doses of 50 mcg/day, 100 mcg/day, 200 mcg/day, 800 mcg/day, or placebo was administered to 480 patients with seasonal allergic rhinitis for 4 weeks. ...results of statistical analysis indicate that all doses of mometasone furoate were effective relative to placebo. These results show that administration of an aqueous suspension of mometasone furoate as a nasal spray to patients with seasonal allergic rhinitis was efficacious and well tolerated with little potential for systemic side effects and are consistent with the low oral bioavailability of mometasone furoate" (Present Patent Publication, column 13, l. 43 to column 14, l. 48)

Description (P-b)

"... 'rapid onset of action in treating allergic or seasonal allergic rhinitis' ... means that there is a clinical and statistically significant reduction in the total nasal symptom score from baseline for seasonal allergic rhinitis patients treated with mometasone furoate nasal spray with medium onset to moderate or complete relief at about 3 days (35.9 hours) compared to 72 hours for the patients treated with a placebo nasal spray. These results were obtained in a randomized, double-blind, multicenter, placebo-controlled, parallel group study to characterize the period between initiation of dosing with mometasone furoate nasal spray and onset of clinical efficacy as measured by the total nasal symptom score in symptomatic patients with seasonal allergic rhinitis. The study lasted 14 days in length. Data from 201 patients were used for analysis.

... Clinical Evaluations

... Each patient was given a metered nasal pump spray bottle containing either an aqueous suspension of mometasone furoate or placebo ... informed patient to deliver 2 sprays of drug (mometasone furoate 50 mcg/spray) or placebo into each nostril once a

day, each morning. ...

RESULTS

The primary efficacy results are based on a survival analysis of the onset times of relief ... for the mometasone furoate nasal spray and placebo groups. ...

Data from 201 patients were used in the survival analysis. There were 101 patients in the mometasone furoate nasal spray group and 100 patients in the placebo group. ...

Survival analysis results suggest that mometasone furoate nasal spray group had a median onset time to relief of 35.9 hours as compared to 72 hours for the placebo group ... From a plot of the survival distribution for the two groups, it was seen that proportion reporting slight or no relief with increasing duration ... in the placebo group was higher compared to the mometasone furoate nasal spray group. Using log-rank data showed a statistically significant difference between the two treatment groups (p-value < 0.001).

Analysis of morning & evening averaged diary data showed that (for the 15-days average) reduction in the total nasal symptom score from baseline for the mometasone furoate nasal spray group was statistically significantly higher than that for the placebo group" (Present Patent Publication, column 14, l. 49 to column 17, l. 39).

Description (P-c)

"DRUG METABOLISM/CLINICAL PHARMACOLOGY STUDY

A drug metabolism and clinical pharmacology study was conducted by administering ... tritium-labeled mometasone furoate ("^{3}H-MF") to 6 groups of 6 normal male volunteers in each group. Blood and urine samples were collected for measurement of total drug (including metabolites).

... The objectives of these studies ... were to determine the absorption, metabolism, and excretion of ^{3}H-MF ... following administration by oral swallowing as a solution and as an aqueous suspension of the monohydrate, by oral inhalation as a suspension from a standard metered dose inhaler (MDI) and from a metered dose inhaler containing a spacer device (Gentlehaler), by nasal inhalation as an aqueous suspension of the mometasone furoate monohydrate from a nasal spray unit and by intravenous injection as a solution.

... Study Design

Six volunteers in each of the six treatment groups received one of the following ^{3}H-MF dosage forms listed in Table 1:

Plasma, urine, ... and fecal samples were collected and assayed for radioactivity

content. The limit of quantitation (LOQ) for plasma radioactivity ranged from 0.103 to 0.138 ng eq/ml., except for the nasal spray treatment where the LOQ was 0.025 ng eq/ml. Selected plasma, urine, and fecal samples were analyzed for metabolite profiles.
RESULTS

... Pharmacokinetics - The mean (n= 6) plasma concentrations of total radioactivity are illustrated collectively in Figures 1 and the mean (n= 6) pharmacokinetic parameters derived from total plasma radioactivity are presented in Table 2.

Comparison of plasma radioactivity illustrated in Figure 1 and/or urinary excretion data and presented in Table 2 after the various formulations with plasma radioactivity with those after intravenous treatment indicated that drug-derived radioactivity was completely absorbed when ^{3}H-MF was administered orally as a solution. In contrast, systemic absorption of drug-derived radioactivity following administration of ^{3}H-MF as an oral suspension or as a nasal spray suspension was approximately 8% of the dose. ...

Radioactivity was predominantly excreted in the feces regardless of dosage form and route of administration. Excretion of radioactivity in the urine was approximately 25% for the intravenous and oral solution formulations, ... and 2% or less for both the nasal spray and oral suspension formulations. These data thus indicate that the drug was well absorbed when orally administered as a solution formulation but poorly absorbed following oral or intranasal application as a suspension formulation.

Selected plasma, urine, and fecal extracts were analyzed by ... HPLC ... with radio-flow monitoring to determine metabolite profiles. The results of these analyses indicate that, following administration of the oral solution, most of the plasma radioactivity was associated with metabolites .... Approximately 1.5% of the 3 hr. plasma radioactivity was associated with parent drug indicating extensive first past metabolism and rapid inactivation by the liver. In contrast, following intravenous administration, approximately 39% of the 3 hr. plasma radioactivity was associated with parent drug. ... In general, the plasma concentrations of radioactivity following the nasal and oral suspension routes of administration were too low for metabolite profiling.
... The results of these drug metabolism/clinical pharmacology studies indicate that:
1. Drug-derived radioactivity was completely absorbed when ^{3}H-MF was given orally as a solution to male volunteers. However, the absolute bioavailability of unchanged mometasone furoate was extremely low (less than approximately 1%) due to extensive first pass metabolism.
...

3. The absorption of drug-derived radioactivity following administration of ^{3}H-MF nasal spray and oral suspension formulations was approximately 8%.
4. The plasma concentrations of unchanged mometasone furoate could not be determined ... because of the plasma concentrations of total radioactivity were too low for metabolite profiling.
5. Mometasone furoate was extensively metabolized following all routes of administration. As shown in Table 2, ^{3}H-MF-derived radioactivity suggests that systemic absorption was greater from an orally swallowed solution (about 100%) than from an orally swallowed suspension or an intranasally inhaled suspension (8%). Mometasone furoate was detectable in plasma by ... after administration of the drug by intravenous injection or oral administration as solution dosage forms, but not after administration of the oral or nasal suspensions. Similarly, the excretion of radioactivity in urine after dosing with the solution formulation was greater (25%) than after dosing with the nasal spray or oral suspension (2%). The total recovery or radioactivity in urine and feces was 87% and 75% respectively, with most of the radioactivity being excreted in the feces. After intravenous dosing, the total radioactivity excreted was 78%, with 24% being excreted in the urine and 54% being excreted in the feces" (Present Patent Publication, column 18, l. 11 to column 26, l. 31).

Description (P-d)
"

表1

投与形態	用量* mg/被検体	μCi/被検体	投与形式
経口用溶液	1.03	209	経口嚥下により33.3ml(0.031mg/ml)
MDI（計量用量吸入器）	0.86	163	MDIキャニスターから4回吸入(215μg/作動)
鼻腔スプレー	0.19	197	鼻腔スプレーボトルから4回スプレー（47μg/スプレー）
Gentlehaler	0.40	79	間欠器を含有するMDIキャニスター（Gentlehalerという）から4発射（101μg/発射）
静脈用溶液	1.03	204	1ml/分の速度で1.03mg/ml投与
経口用懸濁液（水和物）	0.99	195	1.6ml（経口嚥下により0.62mg/ml）

*研究開始前の投与形態の分析に基づく用量

表１　Table 1
容量　Dose
投与形態　Dosage form
ｍｇ／被検体　mg/Subject
μＣｉ／被検体　μCi/Subject
投与形式　Mode of Administration
経口用溶液　Oral Solution
ＭＤＩ（計量用量吸入器）　MDI (metered-dose inhaler)
鼻腔スプレー　Nasal Spray
静脈用溶液　Intravenous Solution
経口用懸濁液（水和物）　Oral Suspension (hydrated)
傾向嚥下により３３．３ｍｌ（０．０３１ｍｇ／ｍｌ）　33.3 ml (0.031 mg/ml) by oral swallowing
ＭＤＩキャニスターから４回吸入（２１５μg／作動）　4 puffs from an MDI canister (215 μg/actuation)

鼻腔スプレー ボトルから４回スプレー（４７μg／スプレー） 4 sprays from a nasal spray bottle (47 μg/spray)
間欠器を含有するＭＤＩキャニスター（Ｇｅｎｔｌｅｈａｌｅｒという）から４発射（１０１μg／発射） 4 bursts from an MDI canister containing a spacer (referred to as Gentlehaler) (101 μg//burst)
１ｍｌ／分の速度で１．０３ｍｇ／ｍｌ投与 1.03 mg/ml administered at a rate of 1 ml/min
１．６ｍｌ（経口嚥下により０．６２ｍｇ／ｍｌ） 1.6 ml (0.62 mg/ml by oral swallowing)
＊研究開始前の投与形態の分析に基づく用量 * Doses based on analysis of dosage forms prior to start of study

" (Present Patent Publication, p. 10)

Description (P-e)
"

表2

男性ボランティアにおける^{3}H-MFの投与後の

総放射能の薬物動態学パラメータ

	投与形態					
パラメータ	静脈	経口溶液	MDI	Gentlehaler	鼻腔スプレー	経口懸濁液
Cmax	23.7	4.8	0.80(0.93*)	0.69(1.71*)	BQL**	BQL
AUC(1)	401	488	81(94*)	110(275*)	BQL	BQL
尿	24	25	7	16	2	2
(%用量)						
糞便	54	62	86	89	78	73
(%用量)						
U+F	78	87	94	105	80	75
(%用量)						
%吸収						
AUC	--	122	23*	69*	--	--
尿	--	104	30	67	8	8

*用量標準化データに基づく

**BQL=定量限界以下

パラメータ	単位	定義
Cmax	ng eq/ml	最大血漿濃度、但し静脈処置は除くC_{0min}
AUC(1)	ng eq 時/ml	最後までの血漿濃度-時間曲線下面積。
尿 (%用量)	%	168時間を通して尿中に排泄された投与放射能のパーセント。
糞便 (%用量)	%	168時間を通して糞便中に排泄された投与放射能のパーセント。
U+F (%用量)	%	168時間を通して尿および糞便中に回収された総パーセント用量。
%吸収 (AUC)	%	静脈内データに対して標準化された用量に基づく吸収された投与放射能のパーセント。
処置データ	%	吸収された投与放射能のパーセント
%吸収(尿データ)		(静脈内用量と比較した尿排泄に基づく)

表２　Table 2

男性ボランティアにおける ^{3}H-MF の投与後の総放射能の薬物動態学パラメータ

PHARMACOKINETIC PARAMETERS OF TOTAL RADIOACTIVITY FOLLOWING ADMINISTRATION OF ^{3}H-MF IN MALE VOLUNTEERS

投与形態　Dosage Form

パラメータ　Parameter

静脈　Intravenous

経口溶液　　Oral Solution
鼻腔スプレー　　Nasal Spray
経口用懸濁液　　Oral Suspension
尿　　Urine
（%用量）　　(% dose)
糞便　Feces
%吸収　% Absorbed
用量標準化データに基づく　　Based on dose normalized data
ＢＱＬ＝定量限界以下　　BQL = Below Quantifiable Limit
処置データ　　Treatment data
%吸収（尿データ）　　% Absorbed (Urine data)
単位　Units
定義　Definition
最大血漿濃度、但し静脈処置は除く C_{5min}　　Maximum plasma concentration, except for the intravenous treatment which is C_{5min}
無限までの血漿濃度＝時間曲線下面積。　　Area under the plasma concentration-time curve to infinity
１６８時間を通して尿中に排泄された投与放射能のパーセント。　　Percent of administered radioactivity excreted in the urine through 168 hr.
１６８時間を通して糞便中に排泄された投与放射能のパーセント。　　Percent of administered radioactivity excreted in feces through 168 hr.
１６８時間を通して尿および糞便中に回収された総パーセント用量。　　Total percent dose recovered in the urine and feces through 168 hr.
静脈内データに対して標準化された用量に基づく吸収された投与放射能のパーセント。　　Percent of administered radioactivity absorbed based on dose normalized versus intravenous data
吸収された投与放射能のパーセント（静脈内用量と比較した尿排泄に基づく）
Percent of administered radioactivity absorbed (based on urinary excretion compared to the intravenous dose)

" (Present Patent Publication, p. 12)

According to Description (P-a) to Description (P-e), it can be deemed that the Present Patent Specification describes the following matters as the effects of the Present Corrected Inventions.

1) Namely, first, with respect to efficacy in treatment, it is described, as a result of

analysis concerning 101 allergic rhinitis patients to whom mometasone furoate aqueous suspension (mometasone furoate 100 μg dose) was administered intranasally once a day, and 100 allergic rhinitis patients to whom placebo was administered, that they exhibited statistically significant difference, and that reduction in the total nasal symptom score from baseline for allergic rhinitis patients to whom mometasone furoate was statistically significantly larger than that from then placebo group (Description (P-b)).

Namely, it can be deemed that it is described that intranasal application of mometasone furoate once a day has efficacy in treatment of allergic rhinitis compared to placebo.

2) Next, with respect to systemic absorption and metabolism, it is described that assay on the content of radioactivity in samples such as plasma, urine, and feces collected after administration of ^{3}H-MF as oral solutions, oral aqueous suspensions, nasal spray suspensions, intravenous solutions, etc. to groups consisting of 6 volunteers revealed that, while systemic absorption of drug-derived radioactivity was 100% of the dose when 1.03 mg (1030 μg) dose was administered as oral solution, it was only 8% of the dose when 0.99 mg (990 μg) dose as oral suspensions, or nasal spray suspension or 0.19 mg (190 μg) dose as nasal spray suspensions were administered, and mometasone furoate itself could be detected in plasma when administered as an oral solution, but it could not be detected in plasma when administered as an oral suspension or a nasal spray suspension (Description (P-c), Description (P-d), Description (P-e)).

Namely, it can be deemed that it is described that, compared to oral solution, oral suspension and nasal spray suspension have lower systemic absorption of mometasone furoate, and there is an effect that mometasone furoate itself exists in plasma below the limit of quantification.

3) Furthermore, with respect to systemic side effects, it is described that aqueous nasal spray suspension of mometasone furoate monohydrate was administered to 8 volunteers, and, compared to placebo, mometasone furoate at doses of 4000 μg did not significantly affect the 24-hour area under the curve plasma cortisol profile (AUC 0-24) (Description (P-a)), and that 12 volunteers in each of 4 groups received one of the following treatments for 28 days: A) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate 400 μg/day; B) Intranasal aqueous nasal spray suspension formulation of mometasone furoate monohydrate, 1600 μg/day; C) Intranasal placebo; D) Oral prednisone, 10 mg/day, and neither of the 2 doses of the mometasone furoate aqueous nasal spray formulation were associated with any changes in cortisol secretion compared to placebo (Description (P-a)).

Namely, it can be deemed that it is described that, compared to placebo, there is

no systemic side effect caused by suppression of HPA function.

(B) Effects of Invention A-1

According to Description (A1-a) to Description (A1-c) and Description (A1-f), Invention A-1 describes that intranasal application of aqueous suspension of mometasone furoate is effective against inflammation, and it can be deemed that there is a therapeutic effect.

(C) Efficacy of mometasone furoate read from Evidence A No. 2

In Evidence A No. 2, Literature 1 and Literature 2 referred to when it was mentioned that mometasone furoate is a corticosteroid with little suppression of HPA function only describe the case in which mometasone furoate was topically administered to skin, and do not describe anything about intranasal application. However, as of the priority date of the present case, it was believed that drug absorbability differs between dermal tissue and nasal mucous tissue, and that nasal mucosa has larger absorbing ability. In addition, in the case in which a drug researcher describes in an article as "a promising candidate for a new drug," it is understood, if the article relates to basic research, that it means that something interesting as a candidate for a new drug has been found and, in many cases, the degree or details of side effects when actually administered are not concretely considered, and, on the other hand, if the article relates to any research in the stage of clinical study, it is considered to some extent that serious side effects that may force the researcher to give up administration will not occur. Judging from the fact that Evidence A No. 2 describes that 1 mg of mometasone furoate solution was actually orally administered to human male volunteers and that mometasone furoate was approved in Japan in 1993, Evidence A No. 2 that is an article published in 1992 can be deemed to have been prepared in situations regarding mometasone furoate in which studies in the clinical stage had remarkably progressed.

Then, a person skilled in the art can read efficacy of mometasone furoate in a) to c) below from descriptions in Evidence A No. 2.

a) Based on an assumption that mometasone furoate has a topical anti-inflammatory activity to skin, it is described that therapeutic efficacy of oral inhalation and intranasal inhalation against asthma and allergic rhinitis can be expected, and it can be read that mometasone furoate has therapeutic efficacy of certain anti-inflammation activity against allergic rhinitis compared to placebo not only by oral inhalation but also by intranasal inhalation.

b) It is surmised that, after intra-abdominal administration to male rats, mometasone furoate is distributed into various tissues and widely metabolized, and, therefore, the plasma concentration of mometasone furoate is in the domain of $pgml^{-1}$ that cannot be quantified by normal chromatography, and, on the other hand, by oral administration of 1 mg of mometasone furoate solution to male volunteers, the plasma concentration reached the peak of about 150 $pgml^{-1}$ (Cmax) in 30 minutes (Tmax), and then rapidly dropped. Accordingly, it is possible to read effects that the amount of intra-abdominally or orally administered mometasone furoate that remains in plasma is not large, and that it disappears within a comparatively short period of time.
c) It can be read that Evidence A No. 2 describes not only that mometasone furoate has sufficient therapeutic efficacy against asthma and allergic rhinitis by oral inhalation and intranasal inhalation, but also that its side effects are small enough to allow practical use. Reference in a portion that described that potential capability to suppress HPA function is exhibited at minimum mentions only a case of local administration on skin, but, from the context of Evidence A No. 2 as a whole, the effect that the risk of suppressing HPA function is sufficiently small even with other administering method, and the risk of systemic side effects caused by HPA suppression is also small can be read.

(D) Comparison between effects of Invention A-1, efficacy of mometasone furoate read from Evidence A No. 2, and the effects of the Present Corrected Inventions

As indicated in (A), the effects of the Present Corrected Inventions exist in the following 3 points:
1) Once-a-day intranasal application of mometasone furoate has therapeutic efficacy against allergic rhinitis compared to placebo,
2) Compared to oral solution, oral suspension and nasal spray suspension have efficacy that systemic absorption of mometasone furoate is lower and mometasone furoate itself exists in plasma below the limit of quantification, and
3) Compared to placebo, no systemic side effect caused by suppressed HPA function.

However, a person skilled in the art could have predicted the effect of 1) from the effects of Invention A-1, the effect of a) indicated in (C) as readable from descriptions in Evidence A No. 2, and the descriptions in Evidence A Nos. 6 to 8 in which it is indicated that, in other corticosteroids, once-a-day regimen has efficacy equivalent to that of twice-a-day regimen. In addition, the effect of 2) can be a proof of existence of advantageous effects of the Present Corrected Inventions with respect to the reason for invalidation related to inventive step based on a cited invention for oral solution of mometasone furoate, but, since the cited invention for the Reason for

Invalidation 1 in the present case relates to intranasal suspension of mometasone furoate, the effect of 2) cannot be any proof of existence of advantageous effect of the Present Corrected Inventions with respect to Reason for Invalidation 1 of the present case. Finally, a person skilled in the art could have predicted the effect of 3) from the results of Invention A-1, the effects of b) and c) indicated in (C) as readable from descriptions in Evidence A No. 2, and descriptions in Evidence A Nos. 6 to 8 in which it is indicated that, in other corticosteroids, once-a-day regimen has efficacy equivalent to that of twice-a-day regimen.

G With respect to allegations by the Demandee and the Intervenor

The Demandee made the following allegations in the Written Reply of the Trial Case, the Oral Proceedings Statement Brief filed on February 16, 2015, the Written Statement filed on March 23, 2016, and the Written Statement filed on July 23, 2018, and the Intervenor made the following allegations in the Written Statement filed on July 20, 2018 and the Written Statement filed on September 5, 2018, and the Written Statement filed on November 9, 2018, but none of the allegations can be accepted.

(A) Allegations by the Demandee and the Intervenor with respect to the invention described in Evidence A No. 1 and judgment on the allegations

(i) Allegations by the Demandee and the Intervenor with respect to the invention described in Evidence A No. 1

With respect to the invention described in Evidence A No. 1, the Demandee and the Intervenor allege as outlined below.

In the Advance Notice of the Trial Decision, it was judged that "aqueous nasal suspension" of A1 corresponds to "A medicament ... comprising an aqueous suspension ... to be administered intranasally" in Present Corrected Invention 1, but A1 merely describes that "mometasone furoate (furancarboxylic acid mometasone) is effective in treating inflammatory conditions" (P. 473, left column, ll. 8 to 10), and A1 does not disclose use of mometasone furoate for treating "allergic or seasonal allergic rhinitis." Furthermore, there is no disclosure of the method for pharmacological test and the results of pharmacological test in the case in which mometasone furoate (furancarboxylic acid mometasone) monohydrate is administered for treating allergic or seasonal allergic rhinitis. Furthermore, although A1 describes the term, "pharmaceutical compositions," A1 does not disclose anything about the method for pharmacological test or the results of pharmacological test for the pharmaceutical compositions in which any mometasone furoate is used. Thus, Advance Notice of the

Trial Decision that determined Common Feature reasoning that A1 discloses "a medicament" is not correct .
(Written Statement filed by the Demandee on July 23, 2018, p. 9, l. 6 to p. 10, l. 13; Written Statement filed by the Intervenor on July 20, 2018, p. 3, l. 5 to p. 4, l. 4)

(ii) Judgment on allegations by the Demandee and the Intervenor with respect to the invention described in Evidence A No. 1

Above Description (A1-c) has a description that "Of particular interest are aqueous suspension compositions of mometasone furoate monohydrate, e.g. for nasal administration," and Description (A1-f) has a description that "An aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate is prepared," and A1 indicates "an aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate." It cannot be deemed in the light of common technical knowledge that this "aqueous nasal suspension" does not fall under "medicaments," and, furthermore, the above Description (A1-b) has a description that "Mometasone furoate is known to be useful in the treatment of inflammatory conditions" and the above Description (A1-a) has a description, "MOMETASONE FUROATE MONOHYDRATE, PROCESS FOR MAKING SAME AND PHARMACEUTICAL COMPOSITIONS." Considering the above, the determination in the above "B Inventions described in A1" to the effect that Evidence A No. 1 describes Invention A-1, "Aqueous nasal suspension of mometasone furoate monohydrate for treating inflammatory conditions," is not erroneous.

(B) Allegations by the Demandee and the Intervenor with respect to Different Feature 1 and the judgment on the allegations

(i) Allegations by the Demandee and the Intervenor with respect to Different Feature 1

With respect to Different Feature 1, the Demandee and the Intervenor allege as outlined below.

Even if compounds belong to corticosteroids, the levels of therapeutic efficacy against allergic rhinitis differ. Therefore, it is not possible to predict therapeutic efficacy of a specific corticosteroid from therapeutic efficacy of another corticosteroid just because both of them belong to corticosteroids. Similarly, since properties of a specific corticosteroid cannot be surmised from properties of another corticosteroid, corticosteroids for which nasal administration has not been tried like mometasone furoate require unique safety evaluation. And, since dose and frequency of administration of a drug are closely related to the degree of therapeutic efficacy of the

drug against the target illness and safety, even if dose regiment of a specific corticosteroid against allergic rhinitis is "once-a-day," it cannot be deemed that a dose regiment of "once-a-day" is sufficient for another type of corticosteroid (Written Reply of the Trial Case, p. 30, l. 13 to p. 32, l. 11).

It cannot be known from A1 and A4 to A8, how far intranasal inhalation of mometasone furoate is effective against allergic rhinitis. Since dose regimen of a drug closely relates to the degree of the effect of treatment against the target illness (strength, endurance, etc.), and it is impossible to select a dose regiment in a situation in which therapeutic efficacy and the degree of safeness cannot be predicted. Even if it is known that once-a-day is most preferable from the viewpoints of patient's preference and compliance, it is ideal and whether an actual medicament with active ingredient that is the object delivers efficacy by once-a-day administration and has safety cannot be predicted without carrying out a pharmacological test and it cannot be deemed easy to adopt the dose regiment just because such fact is known (Written Reply of the Trial Case, p. 32, l. 12 to p. 33, l. 3).

As pharmacokinetics differ between application to skin and intranasal application, even if a medicament is safe and effective when topically applied to skin, it cannot be known what behavior the medicament shows when administered by nasal spray and its safeness and/or effectiveness cannot be surmised. Since some medicaments can deliver efficacy equally as a topical skin liniment and as a nasal preparation, and some cannot, the example of budesonide cannot be simply applied to the present case.

As aforementioned, a person skilled in the art never applies dose regimen for using budesonide, fluticasone, or triamcinolone acetonide for treating allergic rhinitis to mometasone furoate just because they are corticosteroids, and there is no reason to use the administration method of once-a-day as a matter of course. Since it was not known as of the priority date of the present case whether intranasally inhaled mometasone furoate is effective in treating allergic rhinitis, the fact that both of budesonide and mometasone furoate have a strong action for treating cutaneous inflammation cannot be any ground to apply the dose regimen for budesonide to mometasone furoate. Right from the beginning, a person skilled in the art never set the dose regimen to "once-a-day" in situations that the degree of therapeutic efficacy of intranasally inhaled mometasone furoate to allergic rhinitis cannot be concretely known.

Accordingly, there is no motivation to combine Invention A-1 with the administration method, "once-a-day" described in A6 to A8 (Written Reply of the Trial Case, p. 33, l. 17 to p. 34, l. 13); Written Statement filed by the Intervenor on July 20,

2018, p. 5, l. 14 to p. 8, l. 11; and Written Statement filed by the Intervenor on November 9, 2018, p. 4, l. 23 to p. 5, l. 9).

The Advance Notice of the Trial Decision judged that there was a motivation to refer to these doses based on the reason that corticosteroids other than mometasone furoate have topical anti-inflammatory activity to be used against allergic rhinitis (Written Statement filed by the Demandee on July 23, 2018, p. 12, l. 18 to p. 13, l. 5).

However, it is hindsight to read into A1, in combining with another publicly known example, that aqueous suspension of mometasone furoate is used as a medicament against allergic rhinitis, notwithstanding that A1 does not disclose that aqueous suspension of mometasone furoate is used as a medicament against allergic rhinitis. Furthermore, this can be deemed to combine dosage and administration of A4 to A8 based on publicly known virtual examples in which A1 is combined with A2, and it is clear that such judging technique denies inventive step based on "two-easy-step" technique and it should not be allowed (Written Statement filed by the Demandee on July 23, 2018, p. 13, l. 6 to p. 14, l. 18).

In the Advance Notice of the Trial Decision, it was judged that a person skilled in the art who read A4 to A8 understands that once-a-day is most preferable and it is easy to adopt once-a-day in Invention A-1.

However, A1 has a description that mometasone furoate is "known to be useful in the treatment of inflammatory conditions," but nothing has been shown about whether mometasone furoate is effective against allergic rhinitis and safe. Pharmacological action and side effects differ for each corticosteroid, and it was not possible to predict therapeutic efficacy of a specific corticosteroid from therapeutic efficacy against allergic rhinitis of another corticosteroid just because both are compounds that belong to corticosteroids. Similarly, since properties of a specific corticosteroid cannot be surmised from properties of another corticosteroid, corticosteroids for which nasal administration has not been tried like mometasone furoate require unique safety evaluation. Moreover, since dose and frequency of administration of a drug are closely related to the degree of therapeutic efficacy of the drug against the target illness and safety, even if dose regiment of a specific corticosteroid against allergic rhinitis is "once-a-day," it cannot be deemed that a dose regiment of "once-a-day" is sufficient for another type of corticosteroid.

Even if it is known that once-a-day is most preferable from the viewpoints of patient's preference and compliance, it is ideal, and whether an actual medicament with

active ingredient that is the object delivers efficacy by once-a-day administration and has safeness cannot be predicted without carrying out a pharmacological test and it cannot be deemed easy to adopt the dose regiment just because such fact is known (Written Statement filed by the Demandee on July 23, 2018, p. 14, l. 19 to p. 16, l. 18).

In situations that the degree of therapeutic efficacy of intranasally inhaled mometasone furoate to allergic rhinitis cannot be concretely known, there is no rational reason for a person skilled in the art to set the using method for it to "once-a-day."

Accordingly, there is no motivation to combine A1 with the administering method of "once-a-day" described in A6 to A8 (Written Statement filed by the Demandee on July 23, 2018, p. 16, l. 19 to p. 17, l. 10).

(ii) Judgment on allegations by the Demandee and the Intervenor with respect to Different Feature 1

As described in above (2), B, Evidence A No. 1 describes "aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate for treating inflammatory conditions" (Invention A-1) and, as described in above (2), C, (B), it is a matter a person skilled in the art would naturally carry out to examine dosage and administration of similar drugs of Invention A-1, and, since a person skilled in the art understands from Description (A4-a) to Description (A8-e) that once-a-day is most preferable as the frequency of intranasal application for corticosteroid that is a similar drug to Invention A-1, it can be deemed that there was motivation to set the frequency of administration of aqueous nasal suspension of "mometasone furoate" to once-a-day in Invention A1.

Accordingly, Demandee's allegation with respect to Different Feature 1 cannot be accepted.

(C) Allegations by the Demandee and the Intervenor with respect to Different Feature 2 and the judgment on the allegations

(i) Allegations by the Demandee and the Intervenor with respect to Different Feature 2

With respect to Different Feature 2, the Demandee and the Intervenor allege as outlined below.

A1 does not have any description on the problem to be solved by the present invention; namely, a medicament that is effective for treating allergic and seasonal allergic rhinitis, and, when administered by intranasal application, has low systemic bioavailability and suppresses onset of systemic side effects, and there is no suggestion that actively bind "aqueous suspension" of mometasone furoate for intranasal inhalation

with treatment of allergic rhinitis.

Nasal inflammations include in addition to allergic rhinitis and seasonal allergic rhinitis, acute and chronical rhinitis, acute and chronical sinusitis, etc., and nasal administration for easing inflammatory conditions does not directly mean treatment of allergic rhinitis. A1 just states without any supportive evidence such as pharmacological experiment that mometasone furoate is "effective for inflammatory conditions," and does not disclose even "a medicament for treating" inflammatory conditions (Written Reply of the trial case, p. 34, l. 22 to p. 36, l. 9; Written Statement filed by the Demandee on July 23, 2018, p. 17, l. 20 to p. 18, l. 26).

A2 describes that mometasone furoate "is a promising candidate for a new drug for treating asthma and allergic rhinitis through oral and intranasal inhalation." However, in A2, this sentence is the only one that states the relationship between mometasone furoate and allergic rhinitis, and the "candidate for a new drug" in A2 means merely that it is one of a large number of compounds whose efficacy or safety as a therapeutic agent for allergic rhinitis has not been made sure through a clinical trial. It will never be concluded that, even if there is no data such as pharmacokinetics on mometasone furoate, it can be expected to be effective for treating nasal inflammations, because it has been made sure that it exhibits anti-inflammation activity in topical skin application.

A "promising candidate for a new drug for treating ... allergic rhinitis" in A2 has no pharmacological data, etc. that proves its therapeutic efficacy and it merely means that there is a possibility to become an object of development of therapeutic agent for allergic rhinitis in the future. Normally, a "candidate for a new drug" means a compound that has possibility to become a material for a drug, but a "medicament" means a compound for which safety and efficacy as a medicine has been made sure through objective experiments. Therefore, "mometasone furoate as a promising candidate for a new drug for treating ... allergic rhinitis through ... intranasal inhalation" disclosed by A2 differs from "A medicament for treating allergic or seasonal allergic rhinitis" according to the Present Invention (Written Reply of the Trial Case, p. 36, l. 10 to p. 38, l. 13; and Written Statement filed by the Demandee on July 23, 2018, p. 19, l. 1 to p. 21, l. 19).

The problem to be solved by A1 is to obtain mometasone furoate monohydrate in which crystals do not easily grow during storage for an extended period of time in the form of suspension, and the problem to be solved by A2 is to obtain a method for measuring plasma concentration of mometasone furoate. A1 and A2 have a different problem to be solved and have nothing to do not only with problems to be solved by the

Present Invention to provide a medicament that is effective in treating allergic and seasonal allergic rhinitis and, when administered by intranasal application, to have low systemic bioavailability and to suppress onset of systemic side effects, but also with the problem "to provide a medicament," and, therefore, there is no motivation to combine A1 and A2 together (Written Reply of the Trial Case, p. 38, ll. 14 to 25; Written Statement filed by the Demandee on July 23, 2018, p. 21, l. 20 to p. 22, l. 19).

A1 and A2 do not have any description or suggestion with respect to problems related to systemic bioavailability, side effects, etc. when aqueous suspension of mometasone furoate is intranasally inhales, and do not disclose any "medicament." In addition, there was no knowledge that indicates that, as of the priority date of the present case, a person skilled in the art could have easily recognized that, if intranasally applied, mometasone furoate is effective for treating allergic and seasonal allergic rhinitis, and systemic bioavailability is low and there are substantially no side effects even to children.

Accordingly, it cannot be deemed that a person skilled in the art could have easily conceived the element of the invention, "a medicament for treating allergic and seasonal allergic rhinitis," according to Different Feature 2 (Written Reply of the Trial Case, p. 39, ll. 1 to 13; Written Statement filed by the Intervenor on July 20, 2018, p. 4, l. 5 to p. 5, l. 13; and Written Statement filed by the Intervenor on November 9, 2018, p. 4, l. 23 to p. 5, l. 9).

(ii) Judgment on allegations by the Demandee and the Intervenor with respect to Different Feature 2

Even if safety and efficacy as a drug have not been ensured through objective experiments for a "promising candidate for a new drug" different from "a medicament," as described in above (2), C, (C), Description (A2-a) to Description (A2-h) do not describe, without showing any ground, that mometasone furoate is a promising candidate for a new drug, and it is described as a ground that mometasone furoate has a topical anti-inflammatory activity and, on the other hand, potential capability to suppress hypothalamic-pituitary-adrenal (HPA) function is exhibited at the minimum.

In addition, as describe in above (2), C, (C), since it is recognized that it was common technical knowledge as of the priority date of the present patent application that, although allergic rhinitis is classified into perennial and seasonal depending on the time of onset, symptoms, diagnostic method, and treating method are absolutely identical for both of them, as shown also in Description (A9-a), even if safety and efficacy as a drug have not been ensured through objective experiments for "promising

candidate for a new drug," different from "a medicament," it can be deemed that a person skilled in the art who read Description (A2-a) to Description (A2-h) could have easily conceived to select "allergic and seasonal allergic rhinitis" as "inflammatory conditions" mentioned in Invention A-1.

Accordingly, Demandee's allegation with respect to Different Feature 2 cannot be accepted.

(D) Demandee's allegation with respect to Different Feature 3-1 and judgment thereon

(i) Demandee's allegation with respect to Different Feature 3-1

(Different Feature 3-1 corresponds to "Different Feature 3" in the Written Statement filed by the Demandee on July 23, 2018.)

As the dose for once-a-day, A6 discloses Budesonide 400 μg, A7 discloses fluticasone propionate 200 μg, and A8 disclosed triamcinolone acetonide 110 μg, 220 μg, and 440 μg. However, there is no motivation to refer to dose of other corticosteroid than mometasone furoate, and there is no motivation to combine these doses with A1, which has no disclosure of allergic rhinitis.

In fact, it cannot be predicted what degree of dose of mometasone furoate exhibits efficacy and safety with once-a-day administration unless pharmacological tests are carried out.

It cannot be predicted from A1 to A10 that 100 to 200 micrograms of mometasone furoate once-a-day is effective, and the element of the invention according to Different Feature 3-1 is not easily conceivable (Written Statement filed by the Demandee on July 23, 2018, p. 31, ll. 1 to 15; Written Statement filed by the Intervenor on November 9, 2018, p. 5, l. 18 to p. 6, l. 5).

(ii) Judgment on the Demandee's allegation with respect to Different Feature 3-1

In actually using a medicament of Invention A-1 in treatment, it is indispensable to determine appropriate dosage and administration, and, in the case in which no publicly known dosage and administration for a drug for intranasal application comprising mometasone furoate exists, a person skilled in the art would naturally examine and adopt dosage and administration of publicly known similar drugs, and all of budesonide, fluticasone propionate, and triamcinolone acetonide had been widely known as corticosteroids having topical anti-inflammatory activity used against allergic rhinitis, etc. as of the priority date of the Present Patent Application.

As shown in above D, (B), Description (A6-d) indicates that a regimen of intranasal aqueous budesonide once-a-day (400 μg/day) delivered efficacy against

seasonal allergic rhinitis, Description (A7-b) indicates that a regimen of intranasal fluticasone propionate once-a-day 200 μg delivered efficacy against seasonal allergic rhinitis, and Description (A8-b) indicates that a regimen of triamcinolone acetonide once-a-day 110 μg, 220 μg, 440 μg intranasal aerosol delivered efficacy against perennial allergic rhinitis.

Then, it can be deemed that a person skilled in the art who learned of Invention A-1 could have easily conceived to examine the dosage and administration, and, in addition to setting the regimen to once-a-day based on Evidence A Nos. 4 to 8, to set the dose to the range of "once-a-day 100 to 200 micrograms" taking Description (A6-d), Description (A7-b), and Description (A8-b) into consideration.

Accordingly, Demandee's allegation with respect to Different Feature 3-1 cannot be accepted.

(E) Demandee's allegation with respect to Different Feature 3-2, and judgment thereon

(i) Demandee's allegation with respect to Different Feature 3-2

(Different Feature 3-2 corresponds to "Different Feature 4" in the Written Statement filed by the Demandee on July 23, 2018.)

The Present Corrected Inventions have technical significance in that, after checking not only the plasma concentration of cortisol that is an index of side effects of adrenal suppression, but also measurement of absorption rate of mometasone furoate and drug metabolism, a result that bioavailability that indicates how much of administered drug arrives to systemic bloodstream and acts is as low as below 1% was obtained and it has been ensured that there is hardly any influence of side effects.

A1 and A2 do not disclose that "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" when aqueous suspension of mometasone furoate is intranasally administered.

In addition, A2 does not disclose that, since mometasone furoate was administered by "oral administration" in the form of "aqueous solution," A2 does not disclose that the absolute bioavailability of unchanged mometasone furoate is less than about 1% when "aqueous suspension" of mometasone furoate is administered "in the nasal cavity." It cannot be read from the peak of plasma concentration of the parent compound of mometasone furoate when the solution of A2 is orally administered, and the description, "potential capability to suppress HPA function is exhibited at the minimum," that "the absolute bioavailability of unchanged mometasone furoate is less than about 1%."

Side effects of mometasone furoate described in A3 are from the case of topical

application to skin, and it does not state side effects when aqueous suspension of mometasone furoate is intranasally administered. Since pharmacokinetics significantly differ between application to skin and intranasal administration, side effects of corticosteroid when intranasally administered cannot be predicted from side effects of corticosteroid when dermally administered.

Present Corrected Invention 2 achieved "the absolute bioavailability of unchanged mometasone furoate is less than about 1%" by causing suspension of mometasone furoate to act, and this point cannot be predicted from A3 that discloses only ointment.

A4 to A10 describe corticosteroids other than mometasone furoate, and do not disclose that "the absolute bioavailability of unchanged mometasone furoate is less than about 1%."

The element of the invention according to Different Feature 3-2 cannot be easily conceived even by combining A1 with A2 to A10 (Written Statement filed by the Demandee on July 23, 2018, p. 31, l. 16 to p. 36, l. 4; and Written Statement filed by the Demandee on November 9, 2018, p. 6, ll. 6 to 15).

(ii) Judgment on the Demandee's allegation with respect to Different Feature 3-2

As shown in above D, (C), it is recognized that the requirement, "the absolute bioavailability of unchanged mometasone furoate is less than about 1%," can be naturally achieved by setting the dose of Present Corrected Invention 1 to 100 to 200 micrograms.

Then, as indicated in above D, (B) and (D), as far as it can be deemed that a person skilled in the art who learned of Invention A-1 could have easily conceived by examining the dosage and administration to set the dose to the range of "the once-a-day dose is 100 to 200 micrograms," in addition to setting the dose to once-a-day by examining dosage and administration taking Description (A6-d), Description (A7-b), and Description (A8-b) into consideration and, based on Evidence A Nos. 4 to 8, it can also be deemed that a person skilled in the art could have easily achieved the matter, "the absolute bioavailability of unchanged mometasone furoate is less than about 1%," that is naturally achieved by setting the dose to the range of "the once-a-day dose is 100 to 200 micrograms."

Accordingly, Demandee's allegation with respect to Different Feature 3-2 cannot be accepted.

(F) Allegations by the Demandee and the Intervenor with respect to Different Feature 4-

1 and judgment on the allegations

(i) Allegations by the Demandee and the Intervenor with respect to Different Feature 4-1

According to the Written Reply of the Trial Case, the Oral Proceedings Statement Brief filed by the Demandee on February 16, 2015, the Written Statements filed by the Demandee on March 23, 2016 and July 23, 2018, and the Written Statements filed by the Intervenor on July 20, 2018, September 5, 2018, and November 9, 2018, it is recognized that allegations by the Demandee and the Intervenor with respect to Different Feature 4-1 are included in the allegations by the Demandee and the Intervenor with respect to the above (C), (i) Different Feature 2.

(ii) Judgment on the allegations by the Demandee and the Intervenor with respect to Different Feature 4-1

It is recognized that allegations by the Demandee and the Intervenor with respect to Different Feature 4-1 are included in the above allegations by the Demandee and the Intervenor with respect to Different Feature 2, and judgment on the allegations is as shown in the judgment on the allegations by the Demandee and the Intervenor with respect to the above (C), (ii) Different Feature 2.

Accordingly, Demandee's allegation with respect to Different Feature 4-1 cannot be accepted.

(G) Demandee's allegation with respect to Different Feature 4-2 and judgment on the allegation

(i) Demandee's allegation with respect to Different Feature 4-2

(Different Feature 4-2 corresponds to what the Demandee points out in the Written Statement filed on July 23, 2018, as "Different Feature 5." The Intervenor did not make any allegation with respect to Different Feature 4-2).

There is no motivation to refer to dose of corticosteroids other than mometasone furoate, and there is no motivation to combine doses of them with A1, which does not have any disclosure with respect to allergic rhinitis.

It cannot be predicted from A1 to A10 that 200 micrograms once-a-day of mometasone furoate is effective, and the element of the invention according to Different Feature 4-2 cannot be easily conceived.

(ii) Judgment on the Demandee's allegation with respect to Different Feature 4-2

In actually using a medicament of Invention A-1 in treatment, it is indispensable

to determine appropriate dosage and administration, and, in the case in which no publicly known dosage and administration for a drug for intranasal application comprising mometasone furoate exists, a person skilled in the art would naturally examine and adopt dosage and administration of similar publicly known drugs, and all of budesonide, fluticasone propionate, and triamcinolone acetonide had been widely known as corticosteroids having topical anti-inflammatory activity used against allergic rhinitis, etc. as of the priority date of the Present Patent Application.

As shown in above D, (B), Description (A6-d) indicates that a regimen of intranasal aqueous budesonide once-a-day (400 μg/day) delivered efficacy against seasonal allergic rhinitis, and Description (A7-b) indicates that a regimen of intranasal fluticasone propionate once-a-day 200 μg delivered efficacy against seasonal allergic rhinitis, and Description (A8-b) indicates that a regimen of triamcinolone acetonide once-a-day 110 μg, 220 μg, 440 μg intranasal aerosol delivered efficacy against perennial allergic rhinitis.

Then, it can be deemed that a person skilled in the art who learned of Invention A-1 could have easily conceived to examine the dosage and administration, and, in addition to setting the regimen to once-a-day based on Evidence A Nos. 4 to 8, to set the dose to the range of "once-a-day 100 to 200 micrograms" taking Description (A6-d), Description (A7-b), and Description (A8-b) into consideration.

Accordingly, the Demandee's allegation with respect to Different Feature 4-2 cannot be accepted.

(H) Allegations by the Demandee and the Intervenor with respect to the effects of the Present Corrected Inventions, and judgment on the allegation

(i) Allegations by the Demandee and the Intervenor with respect to the effect of the Present Corrected Inventions

With respect to the effects of the Present Corrected Inventions, the Demandee and the Intervenor allege as outlined below.

The Present Corrected Inventions have an effect to effectively treat allergic rhinitis with once-a-day intranasal application of mometasone furoate, but neither A1 nor A2 discloses any result of confirmation of the effect of treatment of allergic rhinitis with mometasone furoate. Therapeutic efficacy of treatment differs depending on the type of the drug, and, even if drugs belong to corticosteroid, therapeutic efficacy against allergic rhinitis may differ, and, since therapeutic efficacy against allergic rhinitis when intranasally administered cannot be predicted from the action of mometasone furoate to

skin, it cannot be predicted with respect to mometasone furoate that allergic rhinitis can be effectively treated with dose regimen of once-a-day (Written Reply of the Trial Case, p. 39, l. 14 to p. 48, l. 23; Oral Proceedings Statement Brief filed by the Demandee on February 16, 2016; Written Statement filed by the Demandee on March 23, 2016, p. 10, l. 1 to p. 11, l. 17; Written Statement filed by the Demandee on July 23, 2018, p. 22, l. 20 to p. 24, l. 17).

While Present Corrected Inventions have effects that there is substantially no systemic absorption of mometasone furoate in bloodstream, and that undesired systemic side effects can be prevented, neither A1 nor A2 discloses the result of checking of systemic side effects when mometasone furoate is administered to nasal cavities. Pharmacokinetics differ between skin and nasal cavity, and, different from application to skin, since a part of medicament is swallowed and systemically absorbed when intranasally administered, side effects when mometasone furoate is intranasally administered cannot be predicted from side effects when mometasone furoate is applied to skin, and, the effects of the Present Corrected Inventions that systemic absorption of mometasone furoate in bloodstream substantially does not exist, and undesired systemic side effects can be prevented cannot be predicted from A1 to A10, which do not disclose anything about side effects when mometasone furoate is intranasally administered (Written Reply of the Trial Case, p. 48, l. 24 to p. 52, l. 2; Oral Proceedings Statement Brief filed by the Demandee on February 16, 2016, p. 8, l. 24 to p. 13, l. 21; Written Statement filed by the Intervenor on July 20, 2018, p. 8, l. 12 to p. 9, l. 17).

The effects that systemic absorption of mometasone furoate in bloodstream does not substantially exist, and undesired systemic side effects can be prevented are effects that can be obtained only after carrying out tests described in the Present Patent Specification and cannot be predicted from A1. In addition, the description in A2, "potential capability to suppress HPA function is exhibited at the minimum" is for the case in which mometasone furoate is applied to skin for treating a corticosteroid-responsive cutaneous disease, and not for the case in which it is intranasally inhaled. Therefore, it cannot be read from the description in A2 that "systemic absorption ... does not substantially exist." A6 to A8 describe corticosteroids other than mometasone furoate. Properties of a specific corticosteroid cannot be surmised from properties of another corticosteroid just because they are compounds that belong to corticosteroids. In addition, A6 to A8 do not disclose that there is no substantial systemic absorption of corticosteroid (Written Statement by the Demandee filed on July 23, 2018, p. 24, l. 17 to p. 28, l. 12).

The Present Corrected Inventions clear up apparently conflicting problems; namely, while effectively treating allergic rhinitis with once-a-day intranasal administration, to prevent undesired systemic side effects once for all with the means of intranasal administration of aqueous suspension, and such especially prominent effect as such cannot be predicted from A1 to A10 (Written Reply of the trial case, p. 52, l. 3 to p. 52, l. 16).

(ii) Judgment on the allegations by the Demandee and the Intervenor with respect to the effects of the Present Corrected Inventions

Indeed, although Evidence A Nos. 1 to 2 do not disclose any result of checking therapeutic efficacy of mometasone furoate against allergic rhinitis, since the efficacy of mometasone furoate as shown in above F can be read, a person skilled in the art could have predicted the effects of the Present Patented Invention from the effects of Invention A-1, the effects that could be read from the description in Evidence A No. 2 and the description in Evidences A6 to A8, as indicated in the above F.

Therefore, allegations by the Demandee and the Intervenor concerning the effect of the Present Patented Invention cannot be accepted.

H Summary

As aforementioned, the patent for Present Corrected Inventions 1 to 3 should be invalidated due to Reason for Invalidation 1 alleged by the Demandant.

2 Regarding Reason for Invalidation 2

(1) Point of the argument of Reason for Invalidation 2 alleged by the Demandant is as follows:

A The present specification does not disclose anything about concrete formulation and production method with respect to "A medicament ... comprising an aqueous suspension of mometasone furoate to be administered intranasally" among matters specifying the invention of Present Corrected Invention 1. According to the explanation of the clinical trial in the Present Patent Publication, page 8, right column, line 4 and after, in the section, "A. Clinical Evaluations," it is stated that "Each patient was given ... either an aqueous suspension of mometasone furoate or placebo," and the result of the clinical trial is shown in Table 2, but, with respect to aqueous solutions of mometasone furoate of the Present Corrected Inventions, it does not concretely describe compositions comprising what kind of formulation can be used. Particularly, with respect to suspending agent in "A medicament ... comprising an aqueous suspension of

mometasone furoate to be administered intranasally ..." that can significantly affect (i) suspension stability, (ii) redispersibility, (iii) retentivity in mucosa, and (iv) nasal mucosa irritating property of the suspension solution to be intranasally administered, the present specification only describes as "suspending agents (e. g., microcrystalline cellulose, sodium carboxymethyl cellulose, and hydroxypropylmethylcellulose" (Present Patent Publication, p. 4, right column, ll. 43 to 45), and there is no concrete guideline what suspending agent should be selected on what occasion, and the aqueous suspension should be prepared to what value of what properties (for example, viscosity) of the aqueous suspension as a target.

Accordingly, the detailed description of the invention of the present specification does not describe any formulation and production method of "A medicament ... comprising an aqueous suspension of mometasone furoate to be administered intranasally ..." among matters specifying the invention of Present Corrected Invention 1, and there is no concrete description how the medicament can be prepared; therefore, the present specification does not describe Present Corrected Invention 1 sufficiently clearly and completely so that a person skilled in the art can work it and does not comply with the requirement provided for in Article 36(4)(i) of the Patent Act (Written Demand for Trial, p. 28, l. 5 to p. 29, l. 8).

B The present specification describes as "See International Application No. PCT/US91/06249, especially Examples 1 to 5 for preparation of mometasone furoate monohydrate and aqueous suspension containing same" (Present Patent Publication, p. 4, right column, ll. 37 to 39), and it can also be understood that the compositions described in Examples 1 to 5 of the international patent application are compositions that may be used in the Present Corrected Inventions. This international patent application is an international application that corresponds to Evidence A No. 1.

Examining those descriptions, it is understood that, among Examples 1 to 5 of A1 (aqueous suspension is described in Examples 3 to 5), Example 3 falls under the intranasally administered aqueous suspension. However, working examples described in A1 show only example of use of Avicel RC591 (mixture of microcrystalline cellulose and sodium carboxymethyl cellulose) as a suspending agent that significantly affects suspension stability, re-dispersibility, retentivity in mucosa and nasal mucosa irritating property, and it is not clear whether hydroxypropylmethylcellulose that is a remaining suspending agent out of 3 types of suspending agents described in the present specification (microcrystalline cellulose, sodium carboxymethyl cellulose, and hydroxypropylmethylcellulose) and other publicly known suspending agents can be

used similarly (Written Demand for Trial, p. 29, l. 9 to p. 30, l. 9).

C From the results of comparison test in which the suspending agent is changed in the aqueous suspension of mometasone furoate of the Present Corrected Inventions (Evidence A No. 11), with respect to "A medicament ... comprising an aqueous suspension of mometasone furoate to be administered intranasally" among the matters specifying the invention of Present Corrected Invention 1, since desired aqueous suspension could be prepared when the preparation was carried out in accordance with the method described in working examples in Evidence A No. 1, but desired aqueous suspension could not be obtained in the cases in which suspending agents other than the suspending agents used in Example 3 of Evidence A No. 1 (Avicel RC591) were used, it is recognized that, in preparing "A medicament ... comprising an aqueous suspension of mometasone furoate to be administered intranasally," in a situation in which there is no guideline what kind of suspending agent should be selected, and what numerical value for properties of aqueous suspension comprising the suspending agent (e.g., pH and viscosity) should be targeted, working Present Corrected Invention 1 requires trial and error, and/or complicated and sophisticated experimentation beyond the extent to which a person skilled in the art should be reasonably expected to conduct.

In addition, since the composition and guideline described in Example 3 of Evidence A No. 1 are not concretely described in the present specification, it is recognized that the present specification places excessive burdens to a person skilled in the art in working Present Corrected Invention 1.

The above matters also apply to the Present Corrected Inventions 2 and 3 that cite Claim 1 of the present case (Written Demand for Trial, p. 30, l. 10 to p. 31, l. 21).

D Accordingly, since it cannot be deemed that the detailed description of the invention of the present specification is described sufficiently clearly and completely so that a person skilled in the art can work the Present Corrected Inventions and does not satisfy the provisions of the requirement provided for in Article 36(4)(i) of the Patent Act, the present patent falls under the provisions of Article 123(1)(iv) of the Patent Act and should be invalidated (Written Demand for Trial, p. 31, ll. 22 to 24; p. 31, l. 32 to p. 32, l. 2).

(2) Judgment of the body on Reason for Invalidation 2

A Present Corrected Inventions 1 to 3 have a matter specifying the invention, "A medicament ... comprising an aqueous suspension of mometasone furoate to be

administered intranasally" and, with respect to the preparation method thereof, the detailed description of the invention of the Present Patent Specification has a description, "An aqueous suspension compositions of the present invention may be prepared by admixing mometasone furoate or mometasone furoate monohydrate (preferably, mometasone furoate monohydrate) with water and other pharmaceutically acceptable excipients. See International Application No. PCT/US91/06249, especially Examples 1-5 for preparation of mometasone furoate monohydrate and aqueous suspensions containing same. The aqueous suspension of the invention may contain from about 0.01 to 10.0 mg, preferably 0.1 to 10.0 mg of mometasone furoate monohydrate per gram of suspension. The aqueous suspension compositions according to the present invention may contain, inter alia, water, auxiliaries, and/or one or more of the excipients, such as: suspending agents, e.g., microcrystalline cellulose, sodium carboxymethyl cellulose, hydroxpropyl-methyl cellulose; humectants, e.g. glycerin and propylene glycol; acids, bases, or buffer substances for adjusting the pH, e.g. citric acid, sodium citrate, phosphoric acids, sodium phosphate as well as mixtures of citrate and phosphate buffers; surfactants, e.g. Polysorbate 80; and antimicrobial preservatives, e.g., benzalkonium chloride, phenylethyl alcohol, and potassium sorbate" (Present Patent Publication, column 8, l. 33 to column 9, l. 3). Therefore, although concrete formulation and preparation condition of the suspension composition are not described, it is described that Examples 1 to 5 of the above international application should be referred to.

B "International Application No. PCT/US91/0624" cited in this description indicates an international application number, but not any number of International Publication. However, it is widely known that a specification, scope of claims, and drawings are published in the International Publication, and that, if International Publication is written in any language other than Japanese language, translation thereof is published in National Publication of International Patent Application, and technique to search International Publication and National Publication of International Patent Application is also widely known. Since a person skilled in the art can understand that International Publication that corresponds to "International Application No. PCT/US91/0624" is International Publication 92/04365 and National Publication of International Patent Application that publishes the translation thereof is National Publication of International Patent Application No. H5-506667, it can be deemed that the content of "International Application No. PCT/US91/0624" can be known from the description in National Publication of International Patent Application No. H5-506667 (Evidence A No. 1).

Therefore, Examples 1 to 5 of Evidence A No. 1 are examined below.

As shown in Description (A1-d), Example 1 of A1 does not relate to any aqueous suspension, and it cannot be recognized to indicate concrete formulation and preparation condition of suspension compositions according to the Present Corrected Inventions.

As shown in Description (A1-e), Example 2 of A1 does not relate to any aqueous suspension, and it cannot be recognized to indicate concrete formulation and preparation condition of suspension compositions according to the Present Corrected Inventions.

As shown in Description (A1-g), Example 4 of A1 relates to an aqueous suspension for X-ray diffraction experiment prepared "without using suspending agent Avicel RC591," and it cannot be recognized to indicate concrete formulation and preparation condition of suspension compositions according to the Present Corrected Inventions.

In contrast, since Description (A1-f) has a description, "An aqueous nasal suspension of mometasone furoate (furancarboxylic acid mometasone) monohydrate is prepared from the following," Example 3 of Evidence A No. 1 can be recognized to relate to an aqueous nasal suspension of mometasone furoate monohydrate. In addition, as shown in above 1, (2), C, "mometasone furoate (furancarboxylic acid mometasone)" is a synonym of "mometasone furoate" in the industry, and, since it is recognized that "mometasone furoate (furancarboxylic acid mometasone) monohydrate" in Exhibit A No. 1 corresponds to "mometasone furoate" in the Present Corrected Inventions, and "aqueous nasal suspension" in Exhibit A No. 1 corresponds to "A medicament ... comprising an aqueous suspension ... to be administered intranasally" in the Present Corrected Inventions, a person skilled in the art can understand that Example 3 of Exhibit A No. 1 describes something that corresponds to "A medicament ... comprising an aqueous suspension of mometasone furoate to be administered intranasally" in the Present Corrected Inventions is described.

As described in Description (A1-f), aqueous nasal suspensions indicated in Example 3 of Evidence A No. 1 include "Avicel RC591" (a trademark of FMC for a mixture of microcrystalline cellulose and sodium carboxymethyl cellulose), and a person skilled in the art could have prepared the above aqueous nasal suspension in accordance with the production method described in Description (A1-f), and, from Description (A1-g), it can be understood that this "Avicel RC591" was used as suspending agent.

In addition, since Description (A1-h) describes that "these compositions were produced by the method described in Example 3," a person skilled in the art can

understand that Example 5 of Evidence A No. 1 is an aqueous nasal suspension prepared according to the production method described in Description (A1-f), the same as Example 3 of Evidence A No. 1, and, from Description (A1-g), that "Avicel RC591" contained in the aqueous nasal suspension is used as a suspending agent.

Based on the facts that the detailed description of the invention of the Present Patent Specification has a description, "suspending agents (e.g., microcrystalline cellulose, sodium carboxymethyl cellulose, and hydroxpropyl-methyl cellulose)" (Present Patent Publication, column 8, ll. 43 to 45) (It is recognized that "hydroxpropyl-methyl cellulose" is an error of "hydroxypropylmethylcellulose"), and that Description (A1-f) indicates that "Avicel RC591" is a mixture of microcrystalline cellulose, sodium carboxymethyl cellulose, and hydroxpropyl-methyl cellulose, a person skilled in the art can understand that the medicaments of the Present Corrected Inventions can be prepared by using hydroxypropyl-methyl cellulose or a suspending agent normally used for aqueous nasal suspensions other than "Avicel RC591."

In addition, even if properties such as suspension stability and retentivity in mucosa of an aqueous suspension for intranasal application prepared by using a suspending agent normally used for aqueous nasal suspensions other than "Avicel RC591" are inferior to some extent to those of the case in which "Avicel RC591" is used as a suspending agent, since it is clear that, as far as certain viscosity of the medicament is ensured, the medicament stays in the nasal cavity, a person skilled in the art can understand usefulness of the Present Corrected Inventions as medicaments in the light of common technical knowledge regarding intranasal medicaments.

C Then, it can be deemed, with respect to the Present Corrected Inventions in which a suspending agent normally used for aqueous nasal suspensions, other than "Avicel RC591" is used, that the type and the compounding amount of suspending agent as well as preparation condition for preparing a medicament containing an aqueous nasal suspension with desired properties can be determined by a person skilled in the art, in the light of common technical knowledge as of the time of filing the application for the present patent, without needing trial and error beyond the extent to which a person skilled in the art should be reasonably expected to conduct.

D Accordingly, the detailed description of the invention of the Present Patent Specification is described so that, in the light of common technical knowledge as of the date of filing the application for the present patent, a person skilled in the art could have

produced and used a medicament that has usefulness as the medicament according to the Present Corrected Inventions.

E Summary

As explained above, Reason for Invalidation 2 alleged by the Demandant with respect to Present Corrected Inventions 1 to 3 is groundless.

No. 5 Closing

As aforementioned, the patent for Present Corrected Inventions 1 to 3 should be invalidated due to Reason for Invalidation 1.

The costs alleged by the Demandant in connection with the trial including costs caused by intervention shall be borne by the Demandee and its Intervenor under the provisions of Article 61 of the Code of Civil Procedure which is applied mutatis mutandis in the provisions of Article 169(2) of the Patent Act.

Therefore, the trial decision shall be made as described in the conclusion.

December 5, 2018

Chief administrative judge: TAKIGUCHI, Naoyoshi
Administrative judge: MURAKAMI, Kimitaka
Administrative judge: MAEDA, Kayoko