Trial decision

Invalidation No. 2012-800093

Tokyo, Japan
Demandant TAIHO PHARMACEUTICAL CO. LTD.

Osaka, Japan
Patent Attorney Saegusa and Partners.

Tokyo, Japan
Attorney UCHIDA, Hiroshi

Tokyo, Japan
Attorney SAMEJIMA, Masahiro

Tokyo, Japan
Attorney TAKAMI, Ken

Tokyo, Japan
Attorney TAKUMA, Hitoshi

USA
Demandee ANTICANCER, INC.

Tokyo, Japan
Patent Attorney SHIBATA, Fujiko

Tokyo, Japan
Attorney HAYASHI, Izumi

Tokyo, Japan
Patent Attorney SHIBATA, Itsuo

Regarding the trial decision made on October 4, 2013 for the case of patent invalidation trial of Patent No. 2664261, titled "ANIMAL MODEL FOR HUMAN DISEASE" between the parties, the IP High Court has made a court decision to rescind the trial decision (2013 (Gyo-Ke) 10311, sentenced on February 19, 2015). In response, as a result of a further proceeding, the body has made the following decision:

Conclusion

The correction of the description and the scope of the claims of Patent No.2664261, regarding Claims [1-10] and [11-19] after correction, shall be approved as the corrected description and the scope of claims attached the written demand for correction.

The patent with respect to the claimed invention of Patent No. 2664261 shall be invalidated.

The costs in connection with the trial shall be borne by the demandee.

Reason

No. 1 History of procedures

This application is an application with an international application date of October 5, 1989 (claiming priority with a Foreign Patent Office receipt date of October 5, 1988, United States, under the Paris Convention for the Protection of Industrial Property) in connection with the inventions according to Claims 1 to 19 of Patent No. 2664261. The history of procedure in the Invalidation Trial of the case is as follows.

In addition, the respective items of Evidence A and Evidence B are hereinafter collectively represented as like A1, etc. with A or B and a number of each evidence.

June 20, 1997 Establishment of the patent right
April 15, 1998 Written opposition to the grant of a patent (Opposition No. 1998-71767)
March 30, 1999 Written correction request
On May 14, 1999 Decision to the effect that the Correction is accepted, and the Patent should be maintained
On December 6,1999 Gazette of Decision on Opposition published
On June 1, 2012 Written Demand for Invalidation (from the demandant) (Evidence A No. 1 to A No. 8)
On September 20, 2012 (Posted on September 21, 2012) Written reply (from the demandee) (Evidence B No. 1 to B No. 24)
On September 20, 2012 (Posted on September 21, 2012) Written correction request (from the demandee)
October 2, 2012 Written amendment (from the demandee)
October 2, 2012 Written statement (from the demandee)
On November 29, 2012 Decision of dismissal of procedure with respect to the procedure according to the written correction request on September 21, 2012 (the Body)
On January 29, 2013 (Posted on January 30, 2013) Written statement (from the demandant)
On February 13, 2013 Notification of Matters to be examined (the Body)
February 26, 2013 Written amendment (from the demandee)
February 26, 2013 Written statement (from the demandee) (Evidence B No. 6)
On April 4, 2013 Oral proceedings statement brief (from the demandant) (A No. 9 to A No. 14)
April 4, 2013 Written statement (from the demandee)
April 4, 2013 Oral proceedings statement brief (from the demandee) (B No. 25 to B No. 51)
April 16, 2013 Written statement (from the demandee) (Evidence B No. 39-2)
April 18, 2013 Oral proceeding
April 24, 2013 Written statement (from the demandee)
April 24, 2013 Written statement (from the demandee) (Evidence B No. 52)
On June 7, 2013 Written statement (from the demandant) (Evidence A No. 15 to A No.18)
On June 7, 2013 Written statement (from the demandee) (Evidence B No. 53 to B No. 67)

On July 1, 2013 Written statement (from the demandant)
July 30, 2013 Written statement (from the demandee)
On August 5, 2013 Written statement (from the demandant)
August 13, 2013 Written statement (from the demandee) (Evidence B No. 68-1 to B No. 73-2)
On August 27, 2013 Written statement (from the demandant)
On October 4, 2013 Decision to the effect that the trial of the case was groundless (hereinafter referred to as "the original decision")
February 19, 2015 Rendition of Judgment to rescind the trial decision at the Intellectual Property High Court (2013 (Gyo-Ke) 10311)
June 10, 2016 Motion for correction request
July 21, 2016 Written correction request (From the demandee)
August 29, 2016 Written amendment (Formality) (from the demandee)
January 13, 2017 Written statement (from the demandee)
On January 17, 2017 Written statement (from the demandant)
February 13, 2017 Written amendment (Formality) (from the demandee)
February 24, 2017 Advance notice of a trial decision

No. 2 As for the Correction by the written correction request on July 21, 2016
1 Object of Correction request and the content of Correction

The correction requested by the demandee with the written correction request on July 21, 2016 (the object of the demand and the statement of the demand were amended by the written amendment (formality) on February 13, 2017) requests for the correction of the specification and the scope of claims of the Patent as per the corrected specification and the corrected scope of the claims attached to the written correction request in accordance with Claims 1 to 19 after the correction.

Here, the specification and the scope of claims of the Patent before the correction are specified by the matters described in the specification and the scope of claims of the gazette of a decision on opposition published on December 6, 1999 (hereinafter referred to as "Gazette of Decision on opposition").

Further, the content of the correction includes (1) the correction according to a unit of claims consisting of Claims 1 to 10 (Corrections 1 to 10), (2) the correction according to a unit of claims consisting of Claims 11 to 19 (Corrections 11 to 19) and (3) the correction of the Detailed Description of the Invention (Corrections 20 to 38) as set forth below (the underlined parts are the corrected parts).

(1) As for the Correction with respect to a unit of claims consisting of Claims 1 to 10
A. Correction 1

"Brain implanted into the corresponding organ" of Claim 1 of the scope of claims is corrected to "Brain orthotopically implanted into the corresponding organ", and "the obtained tumor tissue" is corrected to "the obtain human tumor tissue", and "animal model, having immunodeficiency," (Trial Decision's note: recognized as a typographical error of "animal model having immunodeficiency,") is corrected to "animal model, having immunodeficiency,".

B. Correction 2

"Animal" of Claim 2 of the scope of claims is corrected to "said animal".

C. Correction 3

"Human tumor tissue" of Claim 3 of the scope of the claims is corrected to "said human tumor tissue", and "obtained from" is corrected to "any tumor tissue obtained from the group consisting of".

D. Correction 4

"Tumor tissue" of Claim 4 of the scope of the claims is corrected to "said tumor tissue", and "obtained from a human kidney" is corrected to "is a human tumor renal tissue obtained from a human kidney,".

E. Correction 5

"Human tumor renal tissue" of Claim 5 of the scope of claims is corrected to "said human tumor renal tissue".

F. Correction 6

"Tumor cell" of Claim 6 of the scope of the claims is corrected to "said tumor tissue", and "obtained from a human stomach" is corrected to "is a human tumor stomach tissue obtained from a human stomach".

G. Correction 7

"Human tumor stomach tissue" of Claim 7 of the scope of claims is corrected to "said human tumor stomach tissue".

H. Correction 8

"Tumor tissue" of Claim 8 of the scope of the claims is corrected to "said tumor tissue", and "obtained from a human colon" is corrected to "is a human tumor colon tissue obtained from a human colon".

I. Correction 9

"Tumor colon tissue" of Claim 9 of the scope of claims is corrected to "said human tumor colon tissue".

J. Correction 10

"Tumor tissue" of Claim 10 of the scope of claims is corrected to "said human tumor tissue".

(2) As for the Correction with respect to a unit of claims consisting of Claims 11 to 19

A. Correction 11

"Implanted human tumor tissue" of Claim 11 of the scope of claims is corrected to "said orthotopically implanted human tumor tissue".

Further, "preparing an experimental animal with immunodeficiency;" of Claim 11 of the scope of claims is corrected to "preparing an experimental animal with immunodeficiency;".

B. Correction 12

"Experimental animal" of Claim 12 of the scope of claims is corrected to "said

experimental animal".

C. Correction 13

"Human tumor tissue" of Claim 13 of the scope of claims is corrected to "said human tumor tissue". Further, "obtained from" is corrected to "any tumor tissue obtained from the group consisting of".

D. Correction 14

"Tumor tissue" of Claim 14 of the scope of the claims is corrected to "said human tumor tissue", and "obtained" is corrected to "is a human tumor renal tissue obtained".

E. Correction 15

"Human tumor renal tissue" of Claim 15 of the scope of claims is corrected to "said human tumor renal tissue".

F. Correction 16

"Tumor cell" of Claim 16 of the scope of the claims is corrected to "said human tumor tissue", and "obtained" is corrected to "is a human tumor stomach tissue obtained".

G. Correction 17

"Human tumor stomach tissue" of Claim 17 of the scope of claims is corrected to "said human tumor stomach tissue".

H. Correction 18

"Tumor tissue" of Claim 18 of the scope of the claims is corrected to "said human tumor tissue", and "obtained" is corrected to "is a human tumor colon tissue obtained".

I. Correction 19

"Tumor colon tissue" of Claim 19 of the scope of claims is corrected to "said tumor colon tissue".

(3) Correction of the Detailed Description of the Invention

A. Correction 20

"Test the efficacy" on page 12, line 15 of the gazette of a decision on opposition is corrected to "test the effect", "chemical sensitivity testing" on page 12, line 16 of the gazette is corrected to "chemosensitivity testing".

B. Correction 21

"Attempts" on page 12, line 19 of the Gazette of Decision on opposition is corrected to "attempts", "developed in" on the same page, line 20 of the gazette is corrected to "developed in".

C. Correction 22

"In the animal system" on page 12, lines 22 to 23 of the gazette is corrected to

"in the animal system", and "Still other" on the same page, line 24 of the gazette is corrected to "Still, other". "Animal tumor models were ... spontaneously occurring tumors" on the same page, line 24 is corrected to "animal tumor models were, ... spontaneously occurring tumors".

D. Correction 23

"These rodent models, however, frequently responded to chemotherapeutic agents very differently than human subjects receiving the same agent." on page 12, lines 25 to 26 of the gazette is corrected to "These rodent models, however, frequently responded to chemotherapeutic agents, very differently than human subjects receiving the same agent.".

E. Correction 24

"Animal is" on page 12, line 27 of the gazette is corrected to "animal is", and "utilized mice" on the same page, lines 27 to 28 is corrected to "mice were utilized", and "cellular" on the same page, line 28 is corrected to "immune cells". "Therefore ... foreign transplant tissue" on line 28 on the same page is corrected to "therefore, ... foreign transplant tissue".

F. Correction 25

The term "clearly" on page 12, line 29 of the gazette is corrected to and "subcutaneously under the skin" on page 13, line 2 of the gazette is corrected to "subcutaneously, under the skin".

G. Correction 26

"Human tumors ... when implanted" on page 13, line 2 of the gazette is corrected to "human tumors ... , when implanted". "Tumors ... often ... to a great extent at the site of implant" on the same page, lines 5 to 6 is corrected to "Tumors ... often ... to a great extent at the implanted site", "even if ... highly metastatic in the donor" is corrected to "even if ... highly metastatic in the donor", and "model ... the previously described rodent model" on the same page, line 7 is corrected to "model ... already described rodent model". "The take rate or frequency ... the individual" on the same page, line 4 is corrected to "the take rate or frequency ... the individual", and "In these models, ... took" on the same page, line 5 is corrected to "In these models, ... took".

H. Correction 27

"the subcutaneous nude mouse human tumor model" on page 13, line 7 of the gazette is corrected to "the subcutaneous nude mouse human tumor model", and "had a ... drawback" on the same page, line 8 is corrected to "had a ... drawback", "lacked" on the same page, line 9 is corrected to "lacked", and "the above-mentioned deficiencies" on the same page, line 10 is corrected to "the above-mentioned drawback", and "the present invention ... in humans" on the same page, line 11 is corrected to "the present invention ..., in humans", "has the ability to truly mimic the progression" on the same page, line 11 is corrected to "has the ability to truly mimic the progression".

I. Correction 28

"primary object ... human" on page 13, line 14 of the gazette is corrected to

"primary object ..., human", "In accordance with the primary aspect of the present invention, a novel animal model for human neoplastic disease is provided having neoplastic tissue obtained from a human organ implanted into the corresponding organ of the animal and having sufficient immunodeficiency to allow the implanted tissue to grow and metastasize." on the same page, lines 16 to 18 is corrected to "In accordance with the primary aspect of the present invention, a novel nonhuman model for human neoplastic disease is provided having neoplastic tissue obtained from a human organ implanted into the corresponding organ of the animal and having sufficient immunodeficiency to allow the implanted tissue to grow and metastasize.".

J. Correction 29

"Another aspect of the invention ... a method of generating an animal model for human neoplastic disease" on page 13, line 19 of the gazette is corrected to "Another aspect of the invention ... a method of generating a nonhuman model for human neoplastic disease", "provides ..., the method ... implanted" on the same page, line 20 is corrected to "provides ..., the method ... implanted", "neoplastic tissue ... in said animal" on the same page, line 20 is corrected to "neoplastic tissue ... in said animal", and "sufficient ... to grow and metastasize" on lines 20 to 21 is corrected to "sufficient ... to grow and metastasize".

K. Correction 30

"Implantation of human neoplastic tissue into a laboratory animal having sufficient immunodeficiency to allow the implanted tissue to grow and metastasize" on page 13, lines 25 to 26 of the gazette is corrected to "implantation of human neoplastic tissue into a laboratory animal having sufficient immunodeficiency to allow the implanted tissue to grow and metastasize", and "laboratory animal ... T-cell immunity" on the same page, line 27 is corrected to "laboratory animal ... T-cell immunity", and "referred to as" on the same page, line 28 is corrected to "referred to as", "the human neoplastic tissue utilized herein comprises tissue from fresh surgical specimens which are pathologically diagnosed tumors occurring in, for example, human kidney, liver, stomach, pancreas, colon, breast, prostate, lung, testis and brain." on page 14, lines 6 to 9 of the gazette is corrected to "the human neoplastic tissue utilized herein comprises tissue from fresh surgical specimens which are pathologically diagnosed tumors occurring in, for example, human kidney, liver, stomach, pancreas, colon, breast, prostate, lung, testis and brain.".

L. Correction 31

"The placement ... is ... by means of orthotopic implantation" on page 14, line 3 of the gazette is corrected to "the placement ... is, ... by means of orthotopic implantation", and "the terminology" on the same page, line 5 is corrected to "the terminology", and "herein" on the same page, lines 6 and 10 is corrected to "herein", and "implantation thereof" on the same page, line 10 is corrected to "implantation thereof", and "include" on the same page, line 10 is corrected to "include".

M. Correction 32

"Such tumors include carcinomas" on page 14, line 9 of the gazette is corrected to "Such tumors include carcinomas", and "such as ... ten percent fetal calf serum and a

suitable" on the same page, lines 14 to 15 is corrected to "such as ... ten percent fetal calf serum and a suitable". "Antibiotic such as gentamycin" on the same page, line 15 is corrected to "antibiotic, such as gentamycin", and "The medium containing a tissue is then cooled to approximately 4 degrees C. A tissue" on the same page, lines 16 to 17 is corrected to "The medium containing the tissue is then cooled to approximately 4 degrees C. The tissue".

N. Correction 33

"Suitably" on the same page, line 18 of the gazette is corrected to "suitably", and "prepared for implantation by forming into a mass of suitable size." on the same page, lines 18 to 19 is corrected to "formed into a mass of suitable size, and prepared for implantation." "The specimen size may vary from about 0.1 x 0.5 cm to about 0.2 x 0.6 cm." on the same page, lines 19 to 20 is corrected to "The specimen size may vary from about 0.1 x 0.5 cm to about 0.2 x 0.6 cm.", and "The technique used to form a specimen of suitable size comprises teasing the tissue to size by pulling into pieces of the desired size with forceps or the like." on the same page, lines 20 to 22 is corrected to "The technique used to form a specimen of suitable size comprises teasing the , tissue to size by pulling into pieces of the desired size with forceps or the like.".

O. Correction 34

"Prior to implantation of neoplastic tissue, the selected immunodeficient animal is anesthetized with a suitable anesthetic." on page 14, line 28 of the gazette is corrected to "Prior to implantation of neoplastic tissue, the selected immunodeficient animal is anesthetized with a suitable anesthetic.", and "The implantations of all organ tissue mentioned herein, except lung tissue, is conveniently accomplished by conventional anesthesia using ethyl ether." on the same page, line 29 to page 15, line 1 is corrected to "the implantations of all organ tissue mentioned herein, except lung tissue, is conveniently accomplished by conventional anesthesia using ethyl ether.". "Implantation ... implantation site" on page 15, line 3 of the gazette is corrected to "implantation, ... implantation site", and "Several loose sutures are placed over a drug" on the same page, line 4 is corrected to "Several loose sutures are placed over the lobe", and "incision is made" on the same page, line 5 is corrected to "incision is made", "incision" is corrected to "incision", and "over the tumor" on the same page, line 6 is corrected to "over the tumor".

P. Correction 35

"The process ... recipient" on page 15, line 8 of the gazette is corrected to "The process ..., recipient", and "incision" on the same page, lines 18 and 20 is corrected to "incision", and "organ near" on the same page, line 9 is corrected to "the organ near", and "Implantation ... is ... penetrating the testis along the longitudinal axis with a number-18 gauge needle" on the same page, lines 23 to 25 is corrected to "implantation ... is, ... penetrating the testis along the longitudinal axis with a number-18 gauge needle", and "Tumor imaging is ... the animal with a labeled anti-tumor antibody such as ... a radioactive isotope" on page 16, line 20 of the gazette is corrected to "Tumor imaging is ... the animal with a labeled anti-tumor antibody such as ... a radioactive isotope".

Q. Correction 36

"Allowing the antibody time to localize within the tumor" on page 16, line 21 of the gazette is corrected to "allowing the antibody time to localize for certain time within the tumor", and "and then ... using a radiation detector" on the same page, lines 21 to 22 is corrected to "and then ... using a radiation detector", and "in the animal's body" on the same page, line 22 is corrected to "in the animal's body".

R. Correction 37

"The animal models of the present invention can also be used to screen new antineoplastic agents" on page 16, line 27 of the gazette is corrected to "The animal models of the present invention can also be used to screen new antineoplastic agents", and "The models will be also ... patient's tumors" on the same page, line 29 is corrected to "The models will be also ... patient's tumors". "Sensitivity" on page 17, line 1 of the gazette is corrected to "sensitivity", and "demonstration impact" on the same page, line 4 is corrected to "demonstrated impact", and "for surgery" on the same page, line 10 is corrected to "for surgery", and "An incision was made in each animal to access the kidney." is corrected to "An incision was made in each animal to access the kidney.", and "comprised" on the same page, lines 18 to 19 is corrected to "comprised".

S. Correction 38

"Mouse was incised to provide access to the stomach." on page 18, line 3 of the gazette is corrected to "mouse was incised to provide access to the stomach.", and "pocket" on the same page, lines 4 and 6 is corrected to "pocket", "with a suture" on the same page, line 17 is corrected to "with a suture", "None of ... appeared not have metastasized" on the same page, lines 20 to 21 is corrected to "None of ... appeared not to have metastasized", and "Although ... certain changes and modifications may be practiced within the scope of the appended claims" on the same page, lines 22 to 24 is corrected to "Although ... certain changes and modifications may be practiced within the scope of the appended claims".

2 Judgment of suitability of correction

(1) As for Correction 1

A. Purpose of Correction

Correction 1 corrects "implanted into the corresponding organ" before Correction with "orthotopically implanted into the corresponding organ" after Correction for the animal model of Claim 1, and "obtained tumor tissue" is limited to "obtained human tumor tissue" to confine the scope of "transplantation" and "tumor tissue". Thus these corrections are made for the purpose of the restriction of the scope of claims as provided in item (i) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alteration of the scope of the claims

Correction 1 serially adds matters specifying the invention to Claim 1 to restrict the scope of the claims, and it alters none of a category, a subject, and a purpose. Thus it does not correspond to the substantial enlargement or alteration of the scope of the claims, but complies with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Correction 1 was made on the basis of the following description on page 14, lines 3 to 6 of the gazette of a decision on opposition:

"The placement of neoplastic tissue in an immunodeficient laboratory animal according to the present invention is carried out by means of orthotopic implantation. This refers to an implant or graft transferred to a position formerly occupied by tissue of the same kind. In the present invention, the terminology orthotopic implantation is used to refer to the grafting of human neoplastic tumor tissue from a human organ into the corresponding organ of an immunodeficient laboratory animal.".

Therefore, Correction 1 does not introduce any new technical matter in relation to the technical matters derived from the whole disclosure of the specification and the scope of claims originally attached to the application, and thus it complies with the requirement as provided in Article 126(5) as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

D. Sufficiency of requirements for independent patentability

In the Patent invalidation trial case, all the claims are subjected to the trial for invalidation. Therefore, the provision of Article 126(7) of the Patent Act as applied mutatis mutandis by replacing certain terms pursuant to Article 134-2(9) of the Patent Act shall not apply to Correction 1.

(2) As for Corrections 2 to 10

A. Purpose of Correction

Corrections 2 to 10 respectively correct errors in the description to make Claims 2 to 10 definite. Thus they were made for the purpose of the correction of errors in the description as provided in item (ii) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alterationof the scope of the claims

Corrections 2 to 10 respectively clarify the recitation of Claims 2 to 10, and they alter none of a category, a subject, and a purpose. Thus they do not correspond to the substantial enlargement or alteration of the scope of the claims, but comply with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

The Corrections 2 to 10 respectively clarify the recitation of Claims 2 to 10, and thus do not introduce any new technical matter in relation to the technical matters derived from the whole disclosure of the specification and the scope of claims originally attached to the application, and thus they comply with the requirement as provided in Article 126(5) as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

D. Sufficiency of requirements for independent patentability

Similarly to "No. 2 2(1)D. Sufficiency of requirements for independent patentability", the provision of Article 126(7) of the Patent Act as applied mutatis mutandis by replacing certain terms pursuant to Article 134-2(9) of the Patent Act shall not apply to Corrections 2 to 10.

(3) As for Correction 11

A. Purpose of Correction

Correction 11 corrects "implanted human tumor tissue" before the Correction to "said orthotopically implanted human tumor tissue" after Correction with respect to the method of Claim 11.

Further, Correction 11 restricts "implantation". Thus it was made for the purpose of the restriction of the scope of claims as provided in item (i) of the proviso to Article 134-2(1) of the Patent Act, and further for the purpose of the clarification of the description of "human tumor tissue". Thus the Correction of the errors complies with item (ii) of the proviso to the same Article.

B. Regarding the substantial enlargement or alteration of the scope of the claims

Correction 11 serially adds matters specifying the invention to Claim 11 to restrict the scope of the claims and make the recitation of Claim 11 definite, and it alters none of a category, a subject, and a purpose. Thus it does not correspond to the substantial enlargement or alteration of the scope of the claims, but complies with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Similarly to "No. 2 2(1)C. Regarding addition of new matter", Correction 11 complies with the provision of Article 126(5) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

D. Sufficiency of requirements for independent patentability

Similarly to "No. 2 2(1)D. Sufficiency of requirements for independent patentability ", the provision of Article 126(7) of the Patent Act as applied mutatis mutandis by replacing certain terms pursuant to Article 134-2(9) of the Patent Act shall not apply to Correction 11.

(4) As for Corrections 12 to 19

A. Purpose of Correction

Corrections 12 to 19 respectively correct errors in the description to make Claims 12 to 19 definite. Thus they were made for the purpose of the correction of errors in the description as provided in the item (ii) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alteration of the scope of the claims

Similarly to "No. 2 2(2)B. Regarding the substantial enlargement or alteration of the scope of the claims", Corrections 12 to 19 comply with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Similarly to "No. 2 2(2)C. Regarding addition of new matter", Corrections 12 to 19 comply with the provision of Articles 126(5) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

D. Sufficiency of requirements for independent patentability

Similarly to "No. 2 2(2)D. Sufficiency of requirements for independent patentability", the provision of Article 126(7) of the Patent Act as applied mutatis mutandis by replacing certain terms pursuant to Article 134-2(9) of the Patent Act shall not apply to Corrections 12 to 19.

(5) As for Corrections 20 to 22, 25 to 26, 29, 31, and 33 to 38

A. Purpose of Correction

Corrections 20 to 22, 25 to 26, 29, 31, and 33 to 38 respectively correct errors in the description to make the Detailed Description of the Invention definite. Thus they were made for the purpose of the correction of errors in the description as provided in item (ii) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alteratione of the scope of the claims

Corrections 20 to 22, 25 to 26, 29, 31, and 33 to 38 respectively clarify the Detailed Description of the Invention, and they alter none of a category, a subject, and a purpose of the scope of the claims. Thus they do not correspond to the substantial enlargement or alteration of the scope of the claims, but comply with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Corrections 20 to 22, 25 to 26, 29, 31, and 33 to 38 respectively clarify the Detailed Description of the Invention, and thus do not introduce any new technical matter in relation to the technical matters derived from the whole disclosure of the specification and the scope of claims originally attached to the application, and thus they comply with the requirement as provided in Article 126(5) as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

(6) As for Corrections 23, 28

A. Purpose of Correction

Corrections 23, 28 respectively clarify an ambiguous description to make the Detailed Description of the Invention definite. Thus they were made for the purpose of the clarification of ambiguous statement as provided in the item (iii) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alteration of the scope of the claims

Similarly to "No. 2 2(5)B. Regarding the substantial enlargement or alteration of the scope of the claims", Corrections 23, 28 comply with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Similarly to "No. 2 2(5)C. Regarding addition of new matter", Corrections 23, 28 comply with the provision of Article 126(5) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

(7) As for Corrections 24, 27, 30, 32

A. Purpose of Correction

Corrections 24, 27, 30, 32 respectively correct errors in the description, and clarify an ambiguous description to make the Detailed Description of the Invention definite. Thus they were made for the purpose of the correction of errors in the description as provided in item (ii) and the clarification of ambiguous statement as provided in item (iii) of the proviso to Article 134-2(1) of the Patent Act.

B. Regarding the substantial enlargement or alteration of the scope of the claims

Similarly to "No. 2 2(5)B. Regarding the substantial enlargement or alteration of the scope of the claims", Corrections 24, 27, 30, 32 comply with the provision of Article 126(6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

C. Regarding addition of new matter

Similarly to "No. 2 2(5)C. Regarding addition of new matter", Corrections 24, 27, 30, 32 comply with the provision of Article 126(5) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act.

(8) Summary

As discussed in the above items (1) to (7), Corrections 1 to 38 are made for the purpose of the matters listed in items (i) to (iii) of the proviso to Article 134-2(1) of the Patent Act, and furthermore, they do not violate the provisions of Articles 126(5) and (6) of the Patent Act as applied mutatis mutandis to Article 134-2(9) of the Patent Act. Therefore, the Corrections shall be approved.

No. 3 The Invention

As discussed in "No. 2 As for the Correction by the written correction request on July 21, 2016", the Correction shall be approved. Thus, the inventions according to Claims 1 to 19 of the Patent No. 2664261 (hereinafter referred to as "Invention 1" to "Invention 19", respectively; further, they are collectively referred to as "Inventions 1 to 19" in some cases) should be specified by the matters recited in Claims 1 to 19 of the scope of the claims after the Correction as set forth below:

"[Claim 1] A non-human animal model for the metastasis of human neoplastic disease, said animal having neoplastic tissue obtained from a human organ, other than brain, implanted into the corresponding organ of said animal, and having sufficient immunodeficiency to allow said implanted neoplastic tissue to grow and metastasize.
[Claim 2] An animal model according to claim 1, wherein said animal is an athymic mouse.
[Claim 3] An animal model according to claim 2, wherein said human neoplastic tissue is obtained from the human liver, kidney, stomach, pancreas, colon, breast, prostate, lung, or testis.
[Claim 4] An animal model according to claim 3, wherein said neoplastic tissue is obtained from human kidney.
[Claim 5] An animal model according to claim 4, wherein said human neoplastic kidney

tissue is implanted in the renal cortex of the kidney of the mouse.
[Claim 6] An animal model according to claim 3, wherein said neoplastic tissue is obtained from human stomach.
[Claim 7] An animal model according to claim 6, wherein said human neoplastic stomach tissue is implanted in the stomach of the mouse between the inner mucosal lining of the stomach and the outer peritoneal coat of the stomach.
[Claim 8] An animal model according to claim 3, wherein said neoplastic tissue is obtained from human colon.
[Claim 9] An animal model according to claim 8, wherein said neoplastic colon tissue is implanted in the cecum of the large intestine of the mouse.
[Claim 10] A female animal model according to claim 3, wherein said human neoplastic tissue is obtained from a female human breast.
[Claim 11] A method of generating a non-human animal model for the metastasis of human neoplastic disease, said method comprising: providing a laboratory animal having sufficient immunodeficiency to allow orthotopically implanted human neoplastic tissue to grow and metastasize in said animal; and implanting a specimen of neoplastic tissue from a human organ other than brain into the corresponding organ of the immunodeficient animal.
[Claim 12] A method according to claim 11, wherein said laboratory animal is an athymic mouse.
[Claim 13] A method according to claim 12, wherein said human neoplastic tissue is obtained from human liver, kidney, stomach, pancreas, colon, breast, prostate, lung, or testis.
[Claim 14] A method according to claim 13, wherein said human neoplastic tissue is obtained from human kidney.
[Claim 15] A method according to claim 14, wherein said human neoplastic kidney tissue is implanted in the renal cortex of the kidney of the mouse.
[Claim 16] A method according to claim 13, wherein said human neoplastic tissue is obtained from human stomach.
[Claim 17] A method according to claim 16, wherein said human neoplastic stomach tissue is implanted in the stomach of the mouse between the inner mucosal lining of the stomach and the outer peritoneal coat of the stomach.
[Claim 18] A method according to claim 13, wherein said neoplastic tissue is obtained from human colon.
[Claim 19] A method according to claim 18, wherein said neoplastic stomach tissue is implanted in the cecum of the large intestine of the athymic mouse."

No. 4 The demandant's argument
1 Gist of reasons for invalidation

The demandant seeks for the trial decision to the effect that the Inventions 1 to 19 should be invalidated, and the costs in connection with the trial shall be borne by the demandee, and submits means of proof as shown in the following "2 Means of Proof" in the written demand for trial, the oral proceeding (including oral proceedings statement brief and record) and the written statement, and presents the following allegation of reasons for invalidation: The allegation of the reasons for invalidation may be summarized as set forth below.

(1) Reason for invalidation 1 [Violation of Article 29(1), main paragraph of the Patent Act (Incomplete Invention)]

Inventions 1 to 19 are not configured specifically and objectively to the extent that the technical content can bring about a targeted technical effect through the repetitive implementation by a person skilled in the art, and thus these inventions are incomplete inventions, and do not comply with the requirement as provided in Article 29(1), main paragraph of the Patent Act. Therefore, the patents with respect to Inventions 1 to 19 correspond to Article 123(1) of the Patent Act, and thus should be invalidated. (Written demand, page 11, lines 11 to 20)

(2) Reason for Invalidation 2 [Violation of Article 36(3) of the Patent Act (Violation of enablement requirement)]

The specification after Correction (hereinafter referred to as "the specification") fails to confirm the occurrence or non-occurrence of metastasis of tumor, which is a purpose and an effect of the Invention, and fails to describe what constitution can achieve the purpose of the Invention and bring the effects of the Invention. Specifically, it cannot be said that the Detailed Description of the Invention of the specification describes the purpose, the constitution, and the effects of the invention to the extent that allows a person who has ordinary knowledge in the art to which the invention belong to easily implement the invention. Thus the invention does not conform to the requirement as provided in Article 36(3) of the Patent Act. Therefore, the patents with respect to Inventions 1 to 19 correspond to Article 123(1) of the Patent Act, and thus should be invalidated. (Written demand, page 11, line 21 to page 12, line 8)

(3) Reason for Invalidation 3 [Article 36(4)(i) of the Patent Act (Violation of supporting requirement)]

The specification fails to confirm the occurrence or non-occurrence of metastasis of tumor, which is a purpose and an effect of the Invention, and fails to describe what constitution can achieve the purpose of the Invention and bring the effects of the Invention. Specifically, the specification is totally silent about the description supporting the function and effect of "an implanted neoplastic tissue metastasizing". Thus it fails to describe or suggest to the extent that allows a person skilled in the art to recognize that the problem to be solved by the Invention would be solved, nor could it be recognized by a person skilled in the art from the common general knowledge as of the filing that the problem would be solved. Therefore, the recitation of the claims goes beyond the scope of the technical matter described and disclosed in the Detailed Description of the Invention of the specification, and thus the Detailed Description of the Invention does not conform to the requirement as provided in Article 36(4)(i) of the Patent Act. Therefore, the patents with respect to Inventions 1 to 19 correspond to Article 123(1) of the Patent Act, and thus should be invalidated. (Written demand, page 12, lines 9 to 21)

(4) Reason for Invalidation 4 [Violation of Article 36(4)(ii) of the Patent Act (Violation of description requirement with regard to constituent elemental function of claim)]

The specification fails to describe a method for solving a technical problem on "metastasis"; i.e. the technical matter essential for inducing metastasis, and it is highly

likely that the examples of the specification comprising all the constituent elements of the Invention did not induce the metastasis of tumor, which was a purpose and an effect of the Invention. Therefore, it is recognized that the recitation of the scope of claims of the specification on the premise that a non-human animal model of the Invention has an ability to metastasize does not recite all the indispensable constituent features of the invention for which a patent is sought. Thus the scope of claims does not conform to the requirement as provided in Article 36(4)(ii) of the Patent Act. Therefore, the patents with respect to Inventions 1 to 19 correspond to Article 123(1) of the Patent Act, and thus should be invalidated. (Written demand, page 12, line 22 to page 13, line 7)

(5) Reason for invalidation 5 [Violation of Article 29(1)(iii) of the Patent Act (Novelty) or Violation of Article 29(2) of the Patent Act (Inventive step)]

All of Inventions 1 to 19 correspond to the provision of Article 29(1)(iii) of the Patent Act, or violate the provision of Article 29(2) of the Patent Act, which are both reasons for invalidation as set forth below. Therefore, these Inventions correspond to Article 123(1) of the Patent Act, and thus should be invalidated. (Written demand, page 13, lines 8 to 13)

(5-1) Reason for invalidation 5-1

Inventions 1 to 3, 10 to 13 are the invention described in A1, or were at least easily conceivable by a person skilled in the art on the basis of the invention described in A1, and Inventions 4 to 9, 14 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A1 and the common technical knowledge. (Written demand, page 13, last line to page 14, line 3)

(5-2) Reason for invalidation 5-2

Inventions 1 to 3, 6, 11 to 13, 16 are the invention described in A2, or were at least easily conceivable by a person skilled in the art on the basis of the invention described in A2, and Inventions 4 to 5, 7 to 10, 14 to 15 and 17 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A2 and the common technical knowledge. (Written demand, page 14, lines 5 to 8)

(5-3) Reason for invalidation 5-3

Inventions 1 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A3 and each technique described in A1 and A2 (and common technical knowledge). (Written demand, page 14, lines 11 to 13)

(5-4) Reason for invalidation 5-4

Inventions 1 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A4 and each technique described in A1 and A2 (and common technical knowledge). (Written demand, page 14, lines 15 to 17)

If the "neoplastic tissue obtained from a human organ" of Claim 1 is construed as including one that has undergone subcutaneous passage, the following reasons for Invalidation (5-5) and (5-6) are added. (Written demand, page 14, line 3 from the bottom to page 15, line 2)

(5-5) Reason for invalidation 5-5

Inventions 1 to 3, 11 to 13 are the invention described in A3, or were at least easily conceivable by a person skilled in the art on the basis of the invention described in A3, and Inventions 4 to 10, 14 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A3 and the common technical knowledge. (Written demand, page 15, lines 5 to 9)

(5-6) Reason for invalidation 5-6

Inventions 1 to 3, 11 to 13 are the invention described in A4, or were at least easily conceivable by a person skilled in the art on the basis of the invention described in A4, and Inventions 4 to 10, 14 to 19 were easily conceivable by a person skilled in the art on the basis of the invention described in A4 and the common technical knowledge. (Written demand, page 15, lines 10 to 14)

(5-7) Reason for invalidation 5-7

There are the same reasons for invalidation as the above Reason for invalidation 5-1 and Reason for Invalidation 5-2. (Written demand, page 15, line 15 to page 16, line 2)

2 Means of Proof (Evidence A No. 1 to A No. 18)

Evidence A No. 1: Journal of the National Cancer Institute, vol. 55, no. 6, December 1975, pp. 1461-1466, and the translation thereof

Evidence A No. 2: Article of the 35th Annual Meeting of the Japanese Cancer Association, October 1976, page 171, Subject 624

Evidence A No. 3: Journal of Clinical and Experimental Medicine, Vol. 104, January 7, 1978, pages 31 to 33

Evidence A No. 4: Kanzo, Vol. 21, No. 3, March 25, 1980, pages 303 to 315

Evidence A No. 5: English-Japanese Dictionary, Kenkyusha, 4th Edition, 1977, page 66

Evidence A No. 6: Tokyo District Court The case of 1999 (Wa) 15238 (Judgment on December 20, 2001)

Evidence A No. 7: Tokyo High Court The case of 2002 (Ne) 675 (Judgment on October 10, 2002)

Evidence A No. 8: Tokyo District Court, The case of 2009 (Wa) 31535 (Judgment on April 27, 2012)

Evidence A No. 9: Excerpt of law available from e-Gov (http://www.e-gov.go.jp/)

Evidence A No. 10: A website of Legislative Bureau House of Councillors, Columns of legislative work, "Transitional provision and the effect of old law - 'the provisions then in force remain applicable' and 'the provisions remain in force' -" A print out of http://houseikyoku.sangiin.go.jp/coluinn/coluran051.htm

Evidence A No. 11: CANCER RESEARCH, vol. 38, 1978, pp. 2651 to 2652, and the translation

Evidence A No. 12: Journal of Clinical and Experimental Medicine, Vol. 96, No. 5, January 31, 1976, pages 288, 289, and 291

Evidence A No. 13: Kanzo, Vol. 21, No. 3, March 25, 1980, pages 303 to 304

Evidence A No. 14: Human cancer and Nude mouse, April 20, 1982, page 319

Evidence A No. 15: LONGMAN Advanced AMERICAN DICTIONARY, 2000, pages xviii to xix and pages 54 to 55

Evidence A No. 16: Journal of JAPAN ASSOCIATION FOR PRACTICAL ENGLISH, No. 15, September 2009, pages 29 to 38
Evidence A No. 17: An A-Z of English Grammar and Usage, 1996, pages 638 to 639
Evidence A No. 18: Intellectual property High Court case of 2012 (Ne) 10054, Brief on appeal on July 26, 2012 (Part 1: Patent Infringement Discussion), page 1, pages 47 to 48

No. 5 The demandee's allegation
1 Object of the reply

The demandee seeks for the trial decision to the effect that the demand for trial should be dismissed, and the costs in connection with the trial shall be borne by the demandant, and submits means of proof as shown in the following "2 Means of Proof" in the written reply, the oral proceeding (including oral proceedings statement brief and record), and the written statement, and counter-argues that the demandant's allegation of reasons for invalidation is groundless and the patents according to the Invention should not be invalidated under the provision of Article 123(1) of the Patent Act:

2 Means of proof (Evidence B No. 1 to B No. 73-2)
Evidence B No. 1: MEDICAL VIEW CO., LTD., Stedman's Medical Dictionary 3rd Edition, Fifth printing, March 10, 1995, pages 630 to 631
Evidence B No. 2: Jikken Igaku Bessatsu BioScience Term library Immunology, YODOSHA CO., LTD., First printing, November 1, 1995, pages 14 to 17
Evidence B No. 3: Jikken Igaku Bessatsu BioScience Term library Immunology, YODOSHA CO., LTD., First printing, November 1, 1995, pages 18 to 19
Evidence B No. 4: English-Japanese Dictionary, Kenkyusha Co., Ltd., 28th Printing, 1997, pages 866 to 867
Evidence B No. 5: Edited by Science editorial desk, additional volume: Science Cancer, NIKKEI SCIENCE Inc., November 20, 1981, pages 98 to 110
Evidence B No. 6: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 8 to 11
Evidence B No. 7: MEDICAL VIEW CO., LTD., Stedman's Medical Dictionary 3rd Edition, Fifth printing, March 10, 1995, pages 738 to 739
Evidence B No. 8: MEDICAL VIEW CO., LTD., Stedman's Medical Dictionary 3rd Edition, Fifth printing, March 10, 1995, pages 752 to 753
Evidence B No. 9: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 24 to 28
Evidence B No. 10: Cancer Res., vol.48, December 1, 1988, pp. 6863 to 6871, and the translation
Evidence B No. 11: Introduction of Modern Biology 3 Structural Function Biology, Iwanami Shoten Publishers, First printing, January 27, 2011, pages 112 to 119
Evidence B No. 12: Jikken Igaku Additional Volume, BioScience Term library Immunology, YODOSHA CO., LTD., November 1, 1995, pages 62 to 63
Evidence B No. 13: Edited by Yoshimi Takai and Tohru Akiyama, Cancer Research Today, 2 Cancer Cell Biology, University of Tokyo Press, First Edition, February 21, 2006, page 5
Evidence B No. 14: Edited by Science editorial desk, additional volume: Science

Cancer, NIKKEI SCIENCE Inc., November 20, 1981, pages 85 to 97
Evidence B No. 15: The Japanese Journal of Gastroenterological Surgery, Vol. 22, No. 11, 1989, pp. 2563 to 2568
Evidence B No. 16: The Atlas of Human Diseases, Kodansha Ltd., 13th printing, January 9, 1998, page 60
Evidence B No. 17: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 57 to 59
Evidence B No. 18: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 42 to 45
Evidence B No. 19: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 3 to 7
Evidence B No. 20: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 12 to 17
Evidence B No. 21: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 29 to 33
Evidence B No. 22: Edited by Noriyuki Kasai, Yasuhiro Yoshikawa, Takashi Agui, Modern Laboratory Animal Science, Asakura Publishing Co., Ltd., first edition, 4th printing, published on February 20, 2011, page 111
Evidence B No. 23: Edited by Nobuo Saiki and Takashi Aikoh, "Experimental method of cancer metastasis study", KINPODO, INC., First Edition, First Printing, August 1, 2008, pages 18 to 23
Evidence B No. 24: Chemistry Today, 11, 1980, page 62
Evidence B No. 25: Examination Guideline Part IV, pages 1 to 12
Evidence B No. 26-1: Cancer Res., vol. 41, October 1981, pp. 3995 to 4000
Evidence B No. 26-2: A translation of B No. 26-1 provided by the demandee's representative
Evidence B No. 27-1: Cancer Res, vol.48, April 1, 1988, pp. 1946 to 1948
Evidence B No. 27-2: A translation of B No. 27-1 provided by the demandee's representative
Evidence B No. 28-1: Cancer and Metastasis Reviews, vol. 5, 1986, pp. 29-49
Evidence B No. 28-2: A translation of B No. 28-1 provided by the demandee's representative
Evidence B No. 29-1: Update Series Comprehensive Textbook of Oncology, volume number 3, issue number 1, 1996, pp. 1 to 10
Evidence B No. 29-2: A translation of B No. 29-1 provided by the demandee's representative
Evidence B No. 30-1: Cancer Res, vol.48, December 1, 1988, pp. 6863 to 6871
Evidence B No. 30-2: A translation of B No. 30-1 provided by the demandee's representative
Evidence B No. 31-1: Cancer Res, vol. 46, August 1986, pp. 4109 to 4115
Evidence B No. 31-2: A translation of B No. 31-1 provided by the demandee's representative

Evidence B No. 32-1: Br. J. Cancer, vol. 37, 1978, pp. 199-212
Evidence B No. 32-2: A translation of B No. 32-1 provided by the demandee's representative
Evidence B No. 33-1: Cancer Res, vol. 40, December 1980, pp. 4682-4687
Evidence B No. 33-2: A translation of B No. 33-1 provided by the demandee's representative
Evidence B No. 34-1: Eur. J. Cancer. Clin. Oncol., Vol. 21, No. 10, 1985, pp. 1253-1260
Evidence B No. 34-2: A translation of B No. 34-1 provided by the demandee's representative
Evidence B No. 35-1: Declaration prepared by Sheldon Penman, August 24, 2001
Evidence B No. 35-2: A translation of B No. 35-1 provided by the demandee's representative
Evidence B No. 36: Edited by Katsuharu Kato, reduced edition of Kato's Integrated English-Japanese Medical Dictionary, 10th Edition, 10th printing, September 20, 1980, p. 120 the item of "appearance"
Evidence B No. 37: Shin Ogawa, English-Japanese Plastic Industry Dictionary, 5th Edition, 2nd printing, May 25, 1992, p. 47, the item of "appearance"
Evidence B No. 38: THE NEW SHORTER OXFORD ENGLISH DICTIONARY ON HISTORICAL PRINCIPLES, VOLUME 1 A-M, Clarendon Press-Oxford, 1993, pp .97-98, the item of "appear"
Evidence B No. 39-1: Taiichiro Egawa, A NEW GUIDE TO ENGLISH GRAMMAR -Revised New Edition-, KANEKOSHOBO, Revised new edition, 55th printing, February 25, 1981, pp. 146 to 147
Evidence B No. 39-2: Taiichiro Egawa, A NEW GUIDE TO ENGLISH GRAMMAR -Revised New Edition-, KANEKOSHOBO, Revised new edition, 55th printing, February 25, 1981, pp.150 to 151
Evidence B No. 40: A drawing illustrating a syntax of a sentence of the patent specification prepared by the demandee's representative, 2013
Evidence B No. 41: Supervised by Tadahiko ITOH, ESSENTIALS OF DRAFTING U.S. PATENT SPECIFICATIONS AND CLAIMS, Japan Institute for Promoting Invention and Innovation, 2nd Edition, 2nd printing, July 14, 2005, pp. 17 to 28
Evidence B No. 42: Examination Guideline Part I, Chapter 1, 3.2, pages 14 to 15
Evidence B No. 43: Written by Kosaku Yoshifuji, revised by Kenichi Kumagai, Tokkyohou Gaisetsu [13th Edition], YUHIKAKU PUBLISHING CO., LTD., 13th Edition, First printing, December 10, 1998, pages 110 to 111
Evidence B No. 44: A result of Internet search by the demandee's representative, Output date: February 15, 2013
Evidence B No. 45: A result of Internet search by the demandee's representative, Output date: February 15, 2013
Evidence B No. 46: Nobuyuki Miyagi et al., Journal of Japanese Society of Gastroenterology, Vol. 79, No. 10, October 1982, pages 1911 to 1917
Evidence B No. 47: Heizaburo Ichikawa et al., Bessatsu Science Cancer, NIKKEI SCIENCE Inc., November 20, 1981, pages 138 to 151
Evidence B No. 48: Written by Kosaku Yoshifuji, revised by Kenichi Kumagai, Tokkyohou Gaisetsu [13th Edition], YUHIKAKU PUBLISHING CO., LTD., 13th Edition, First printing, December 10, 1998, pages 62 to 63

Evidence B No. 49: Written by Kosaku Yoshifuji, revised by Kenichi Kumagai, Tokkyohou Gaisetsu [13th Edition], YUHIKAKU PUBLISHING CO., LTD., 13th Edition, First printing, December 10, 1998, pages 84 to 86
Evidence B No. 50: A real scale drawing of implanting needle for cancer cells and mouse prepared by the demandee's representative, March 2013
Evidence B No. 51: Edited by Sei Nakagama, Muteki no Biotechnical series mouse/rat experimental note, YODOSHA CO., LTD., 3rd printing, July 25, 2011, pages 104 to 106 and 158
Evidence B No. 52: A page of "Injection/Injector" prepared by Natsume Seisakusho Co., Ltd. via Internet search, Output date: April 17, 2013
Evidence B No. 53: Edited by Yukio Shimozato et al., Human cancer and nude mouse, Ishiyaku Publishers, Inc., First Edition, First printing, April 20, 1982, iii-x, pages 1 to 353
Evidence B No. 54-1: Int. J. Cancer, Vol. 49, 1991, pp. 938-939
Evidence B No. 54-2: A Translation of B No. 54-1 provided by the demandee's representative
Evidence B No. 55: Written by Kenji Uemura et al., Introduction of biological statistics, Ohmsha, Ltd., First Edition, First printing, August 25, 2008, pages 216 to 217
Evidence B No. 56: Written by Kenji Uemura et al., Introduction of biological statistics, Ohmsha, Ltd., First Edition, First printing, August 25, 2008, pages 2 to 5
Evidence B No. 57-1: Proc. Natl. Acad. Sci. USA, Vol. 88, October 1991, pp. 9345-9349
Evidence B No. 57-2: A translation of B No. 57-1 by the demandee's representative
Evidence B No. 58: Written by Kosaku Yoshifuji, revised by Kenichi Kumagai, Tokkyohou Gaisetsu [13th Edition], YUHIKAKU PUBLISHING CO., LTD., 13th Edition, First print, December 10, 1998, pages 52 to 57
Evidence B No. 59: Edited by Yoshimi Taka et al., Cancer Research Today 2 Cancer Cell Biology, University of Tokyo Press, First Edition, February 21, 2006, pages 94 to 95
Evidence B No. 60: Edited by Hiroyasu Esumi, Jikken Igaku, Vol. 27, No. 2 (special number), YODOSHA CO., LTD., 2nd printing, February 15, 2010, 198(326) page
Evidence B No. 61-1: Cancer Research, Vol. 19, June 1959, pp. 515-520 (It should be noted that a drawing without page number is attached hereto.)
Evidence B No. 61-2: A translation of B No. 61-1 provided by the demandee's representative
Evidence B No. 62-1: Journal of Clinical and Experimental Medicine, vol. 201, No. 10, June 8, 2002, pp. 790 to 798
Evidence B No. 62-2: Journal of Clinical and Experimental Medicine, vol. 201, No. 11, June 15, 2002, pp. 863 to 867
Evidence B No. 63-1: A copy of a webpage of Journal of Clinical and Experimental Medicine, http://www.ishiyaku.co.jp/magazines/ayumi/corrigenda.aspx, errata from October 2003 to January 2013 Edition, Output date: May 10, 2013
Evidence B No. 63-2: "Radiation Chemistry", Guide for paper submission, Published date unknown
Evidence B No. 63-3: Journal of Nuclear and Radiochemical Science Submission Guide, http://www.radiochem.org/publ/guidepj.html, Output date: May 10, 2013
Evidence B No. 63-4: Japanese Journal of Applied Physics vol. 49 (2010) Typo

correction page 069201-1, 019201-1, 089202-1
Evidence B No. 64: Journal of Clinical and Experimental Medicine, Vol. 136, No. 6, February 8, 1986, pages 393 to 399
Evidence B No. 65: The plaintiff's second brief of 2012 (Ne) 10054, April 30, 2013
Evidence B No. 66: The plaintiff's fourth brief of 2012 (Ne) 10054, May 2, 2013
Evidence B No. 67: Sambrook, Joseph Fritsch, T. Maniatis, Molecular Cloning A LABORATORY MANUAL SECOND EDITION, Cold Spring Harbor Laboratory Press, 1989, pp. 16.45 to 16.46
Evidence B No. 68-1: Int. J. Cancer, Vol. 51, 1992, pp. 989-991
Evidence B No. 68-2: A translation of B No. 68-1 provided by the demandee's representative
Evidence B No. 69-1: Int. J. Cancer, Vol.51, 1992, pp. 992-995
Evidence B No. 69-2: A translation of B No. 69-1 provided by the demandee's representative
Evidence B No. 70-1: Int. J. Cancer, Vol. 52, 1992, pp. 987-990
Evidence B No. 70-2: A translation of B No. 70-1 provided by the demandee's representative
Evidence B No. 71-1: ANTICANCER RESEARCH, Vol. 13, 1993, pp. 901 to 904
Evidence B No. 71-2: A translation of B No. 71-1 provided by the demandee's representative
Evidence B No. 72-1: ANTICANCER RESEARCH, Vol. 13, 1993, pp. 1999 to 2002
Evidence B No. 72-2: A translation of B No. 72-1 provided by the demandee's representative
Evidence B No. 73-1: Cancer Research, vol. 53, March 1993, pp. 1204-1208
Evidence B No. 73-2: A Translation of B No. 73-1 provided by the demandee's representative

No. 6 Judgment by the body
1 The Invention
It is as found in "No. 3The Invention".

2 Reason for invalidation 5 -1 [violation of Article 29(2) of the Patent Act (Inventive step)]
(1) Ruling in the Intellectual Property High Court
The Intellectual Property High Court ruled as follows in a decision handed down on February 19, 2015 (2013 (Gyo-Ke) 10311) with regard to "No. 4 1(5-1) Reason for invalidation 5-1".

"1 The Invention
According to the description of the specification, the Invention is recognized as set forth below.
Although an animal model in which a human tumor is implanted subcutaneously into a mouse without a thymus and its ability to reject foreign transplant tissue (nude mice, athymic mice, athymic nude mice) brought a better result than a conventional rodent model, it showed a varied take rate or frequency with which such human tumor tissue actually formed a tumor in the mouse, depending on the individual donor and the tumor type, and had a substantial drawback of tumors that took growing to a great

extent at the site of implant and rarely metastasized, even if the original tumor had been highly metastatic in the donor; i.e., the subcutaneous transplant lacked the ability to metastasize (page 3, lines 6 to 15). There is a problem to prepare an animal model which has the ability to truly mimic the progression of neoplastic disease as it occurs in humans; i.e., an animal model with a human tumor tissue that can metastasize as well as grow (page 3, lines 18 to 20). Further, in order to solve the above problem, the Invention has adopted the constitution to maintain a "three-dimensional structure" of a lump of an original tumor tissue without separating individual cells from a human tumor tissue obtained from a human organ other than brain and implant the tissue in the corresponding organ of an immunodeficient animal (orthotopic implantation) (page 4, lines 3 to 20), and prepare a non-human animal model having the ability to truly mimic the progression of neoplastic disease as it occurs in humans; i.e., a non-human animal model for metastasis with a human tumor tissue that can metastasize and grow (page 3, line 22 to page 4, line 1).

2 Reason for rescission 5 (Lack of Inventive Step or Novelty on the basis of A1 invention)

In view of the nature of the case, the reasons for rescission 5 is firstly considered in the following.

(1) Reason for rescission 5-1 (Errors in the determination of Reasons for invalidation 5-1-Errors in the finding of the Invention)

Plaintiff argues that "metastasis" in the Invention is an effect of the invention, not a constitution of the invention.

In the technical field to which the Invention pertains, however, an animal model is to reproduce human diseases in animal, and to be used in an experimentation for confirming the function and effect of a drug. The Invention is as found in the above item 1. Thus "a non-human animal model for the metastasis of human neoplastic disease" of Inventions 1 and 11 specifies "a non-human animal model" as one capable of reproducing "the metastasis of human neoplastic disease". Further, "sufficient immunodeficiency to allow said implanted neoplastic tissue to grow and metastasize" of Invention 1 and "sufficient immunodeficiency to allow said implanted neoplastic tissue to grow and metastasize" of Invention 11 specify the extent of immunodeficiency as being "sufficient to allow said implanted neoplastic tissue to grow and metastasize".

Therefore, it can be said that the "metastasis" of the Invention is a matter necessary for specifying the Invention, and thus a constitution of the invention.

As seen above, Plaintiff's argument is not acceptable.

Therefore, reason for rescission 5-1 is groundless

(2) Reason for rescission 5-2 (Errors in the judgement of Reasons for invalidation 5-1-Errors in the finding of the identical features and different features)

Plaintiff argues that, even if "metastasis" were a constitution of the Invention, the "metastasis" of the Invention has only a technical significance at a similar level to "take" or "infiltrate".

The term "metastasis" means, however, that malignant cells separate from an original tumor move to a distant site therefrom and spread systemically via blood vessels and lymph channels to multiply form colonies (A23, A39, A41, A44), which is a general technical term, and the meaning of the term is not unambiguous.

The term "take" means that a tumor tissue becomes colonized at an implantation site, and the term "infiltrate" means that a tumor tissue grows while destroying an adjacent tissue, and the boundary is unclear. The Detailed Description of the Invention of the specification discloses that "In these models, tumors that took, often grew to a great extent at the site of implant and rarely metastasized, even if the original tumor had been highly metastatic in the donor." (page 3, lines 13 to 15), "The five mice of this example are still alive six months later. Approximately one month following implantation of the tissue, the mice were surgically opened and the implanted tumors were observed. In each case, the tumor was found to have taken. This means that the implanted neoplastic tissue had invaded adjacent tissue." (page 7, lines 18 to 21), "Four of the five mice which underwent this implant surgery have survived for three to four months and appear to be in good health. Approximately one month following tissue implantation, the mice were surgically opened and the tumors were observed to have taken. None of the tumors appeared not to have metastasized to other organs at this time." (page 8, lines 21 to 24). It can be seen from the above description that the terms "take" and "infiltrate" are used to have almost the same meaning; however, the term "metastasize" is definitely distinguished from "take" or "infiltrate", and it is obvious that "take" or "infiltrate" is not expressed as "metastasize".

Consequently, it cannot be said in the Invention that "metastasize", and "take" or "infiltrate" are used to have a similar level of technical significance. Further, it should be noted that this point is a matter of the description of the specification, which has nothing to do with whether or not the metastasis is actually confirmed in Example III.

Further, the A1 invention is recognized as "a nude mouse, wherein the #4 inguinal mammary fat pads of germfree female nude mice 20-25 days of age were cleared of host epithelium by surgical extirpation of the nipple rudiment and adjacent portions of the fat pad up to the site of the inguinal lymph node, and wherein a human breast tissue diagnosed as infiltrating ductal carcinoma is implanted into said cleared portion, and wherein sections of the fat pad 2 months after transplantation showed the tumor to be healthy and beginning to infiltrate the fat pad." Therefore, comparing Inventions 1 to 19 with the A1 invention, they are at least different from each other in that the A1 invention cannot be said to be "a non-human animal model for metastasis model".

Therefore, the finding of the identical features and the different features is not erroneous, nor is the judgement in the trial decision that Inventions 1 to 19 are not identical to the A1 invention on the premise of this different feature erroneous.

As seen above, Plaintiff's argument is not acceptable.

Therefore, reason for rescission 5-2 is groundless.

(3) Reason for rescission 5-3 (Errors in the judgement of Reasons for invalidation 5-1 - Errors in the judgement of the different features)

A Description of Publicly Known Document

(A) Evidence A No. 1

A1 has the following descriptions (the translation is derived from B13. Obvious errors have been corrected.).

"Brief Communication: Growth of Human Normal and Neoplastic Mammary Tissues in the Cleared Mammary Fat Pad of the Nude Mouse

H.C. Outzen and R.P. Custer"

"SUMMARY

Dysplastic and malignant human breast tissues were grown successfully in the cleared mammary fat pads (CFP) of nude mice. The mammary fat pads were cleared while the mice were in a germfree isolator. Prepared mice were removed from the germfree environment to facilitate transplantation of the human mammary tissue into their CFP and subsequently were maintained in sterile laminar flow racks.

The experimental investigation of neoplastic progression in humans has been limited by ethical and moral restrictions. A means to expand such studies may be provided by the nude mouse which, due to its hereditary thymic dysplasia, lacks all cell-mediated immunologic reactivity; the nude mouse is potentially valuable as a "test tube" in which human tumors can be grown. A previous difficulty was the short life-span of nude mice. However, when raised under germfree conditions, they have a virtually normal life-span, and this major drawback to their use is thereby removed.

We wanted to determine whether the cleared mammary fat pad(s) (CFP) of the nude mouse would be as receptive to the growth of human mammary tissues, normal or neoplastic. If so, the site would be ideal for growth of human breast samples, and a model would be useful for investigation of the growth potential of variously diseased human mammary tissues such as lobular carcinoma in situ, fibrocystic disease, and primary stage I carcinoma."

"MATERIALS AND METHODS

Mice.-Female nude mice were raised and maintained in a germfree environment until they received a human tissue transplant. These mice were obtained from brother X sister matings in our germfree colony.

When the recipients were 6-8 weeks of age, 3-4 weeks after their #4 mammary fat pads had been cleared, they were removed from the germfree environment, and a human mammary tissue fragment was transplanted into each CFP. All transplantations were performed under sterile conditions in a vertical, sterile, air-flow hood (Biogard hood; The Baker Co., Inc., Sanford, Me.).

After receiving transplants, the mice were housed in laminar sterile air flow animal racks (Carworth Farms, New City, N.Y.) until they either were killed or became sick. Either the human tissue in the CFP was transferred into another nude mouse CFP or the entire fat pad containing the human tissue was removed and prepared for whole mounting and/or histologic sectioning.

Preparation of recipient gland-free mammary fat pads. -The procedures described by Slemmer were followed, all within a germfree isolator. The #4 inguinal mammary fat pads of germfree female nude mice 20-25 days of age were cleared of host epithelium by surgical extirpation of the nipple rudiment and adjacent portions of the fat pad up to the site of the inguinal lymph node. When cleared in this manner, the mammary fat pads have been shown to completely lack any mammary epithelial outgrowth from the host. An improperly cleared fat pad is readily recognized: Growth of any residual mammary gland originates at the excisional margin from which the proximal portion of the fat pad has been removed, adopting a distinctive branching pattern that reaches beyond the inguinal limph node.

...

Transplantation.- Generally, the procedure described by Slemmer was followed, with minor modifications required to maintain the mice in an environment as sterile as possible. The prepared germfree mice were removed from the isolator, placed in a

vertical laminar sterile air-flow hood, anesthetized with pentobarbital sodium (0.01 mL/kg body wt; solution of 6.7 mg pentobarbital sodium/ml in 9% ethanol), and pinned on sterile operating boards. By an aseptic technique, the #4 CFP were exposed through a midline ventral incision. Sharpened watchmaker's forceps were used to create a defect in the CFP through which the tissue transplants could be introduced. The transplants ranged in size from 1x2x2 to 1x2x10 mm. The ventral skin incision was closed with 7.5-mm wound clips. Any CFP showing growth of residual mammary tissue from the host was discarded; thus epithelial proliferation within the remaining CFP clearly originated from the implanted human breast tissue."

"RESULTS

Gross Morphology and Histomorphology of the Nude Mouse Mammary Gland

...

Growth of Human Mammary Tissue in CFP of Nude Mice

Three samples of nonmalignant but abnormally proliferating mammary tissue and one sample of a mammary adenocarcinoma were obtained from human biopsy specimens.

...

4) Tissue for the fourth transplantation was obtained from a biopsy specimen of human breast tissue diagnosed as infiltrating ductal carcinoma (FIG. 9). Sections of the fat pad 2 months after transplantation showed the tumor to be healthy and beginning to infiltrate the fat pad. Occasional mitotic figures were seen. The basic appearance of the mouse CFP was essentially the same as that of the original human biopsy specimen. Thus the human tumor and its transplant in the nude mouse CFP had a similar histologic pattern, e.g., ducts lined with multiple layers of abnormal epithelium, strands of infiltrating tumor cells, and abundant fibrous stroma. This human mammary carcinoma has been successfully propagated through five transplant generations in the CFP of our nude mice. In the serial transplants, the human tissue from one fat pad was bisected and transplanted into two other CFP. This resulted in an increase in the human tissue volume of approximately 32 times that of the original transplant."

"DISCUSSION

These preliminary observations on the growth of human hyperplastic and neoplastic mammary tissues in the CFP of nude mice contradict past experimental conclusions that it is extremely difficult to grow human mammary tissues, even highly malignant ones, either in vitro or in vivo in immunologically crippled xenogeneic hosts. Growth of human mammary tumors transplanted sc into nude mice has also had limited success. Therefore, the simple demonstration that three benign human mammary hyperplasias (e.g., fibrocystic disease) and a human mammary adenocarcinoma grew in the CFP of nude mice may be a technologically important step in the maintenance of human mammary tissues beyond the original host.

Prior failure of human mammary tissues to develop and continue growth in nude mice is probably due to the fact that the tissues were transplanted sc. The subcutaneous transplantation site is not receptive to the growth of most mammary tissue, at least in the isologous mouse model.

...

These preliminary observations offer a potential for future studies in the nude mouse CFP, to yield data concerning the growth and behavioral characteristics of human breast tissues, both normal and diseased."

(B) Evidence A No. 3

A3 has the following descriptions:

"Transplantation of human hepatoma in nude mice" (page 31, title)

"Animal bearing human cancer is an ideal model in studying biological properties of the tumor and various therapeutic effects. Implanted human cancer is required to have unchanged original nature in the host animal, and it is desirable to grow in an original organ." (page 31, left column, lines 1 to 5)

"Since then, there have been attempts to implant various human cancers into nude mice, and one of the authors has achieved success in implanting pancreatic cancer. However, all of them are implanted in a subcutaneous tissue.

We have been mainly trying to implant hepatoma in a nude mouse since 1976, and recently achieved success in the transplantation of human hepatoma into a nude mouse liver for the first time, and thus report herein." (page 31, left column, lines 9 to 15)

"Experimental Methods

In eight cases of hepatoma for which our trauma unit conducted a surgery from October 1976 to July 1977, pieces of hepatoma tissue of three cases for which an excision was conducted and four cases which only resulted in a test excision were implanted. The mice used were male or female nude mice with a genetic background of BALB/C, which were supplied from Central Institute for Experimental Animals. ...

The transplantation was conducted by cutting out a hepatoma tissue sampled by excision or a needle into a piece of tissue with 2 mm square in saline, and transplanting this with a needle in both sides of abdominal region and dorsal region under the skin with the right side one being located close to a liver lateral segment." (page 31, left column, lines 16 to 28)

"Experimental result

Seven hepatoma tissues ever implanted were obtained from six cases, with one case of hepatoblastoma and five cases of liver cells cancer. Three of six cases have taken and become capable of serial transplantation: the samples before and after chemotherapy for cirrhotic liver with hepatoma (Hc-3,4) of a 45-year-old male, differentiated hepatoma (Hc-5) of a 70-year-old male, and hepatoblastoma (Hb-1) of a three-year-old male infant, which have been in a sixth passage, a second passage, and a fourth passage, respectively." (page 31, left column, line 31 to right column, line 3)

"AFP value of Hc-4 was 8.2 μg/ml in patient's serum, and there are a positive one and negative one in implanted rat by the SRIA method. In the positive case, AFP values were detected only in the second and third passages of Hb-4, which were 10.1 μg/ml and 9 μg/ml, respectively." (page 31, the right column, lines 11 to 14)

"Remarkably, the second passage rat (it is recognized as a typographical error of "mouse") formed a tumor mass with a size of about 1.5 cm as a result of the implantation of a piece of tumor mass into the liver at a deep right flank region. The tumor mass was a massive type, which had spread across the lobes with only a left lateral lobe being left. No ascites fluid or lymph node metastasis to hepatic portal region was observed, but a spherical metastasis with a diameter of about 2 mm was observed in the right lower lobe.

Histological appearance of tissue grown in the liver showed a thin fibrous capsule surrounding a tumor, and it was somewhat hemorrhagic, having a number of

mitosis differing from that of hypodermal tissue.

The capsule of lung metastatic foci was only one layer of fibrous cells, and almost no reactive change was found in the surrounding lung tissue. The central part became the site of necrosis." (page 31, right column, line 18 to page 32, right column, line 7)"

"Conventionally, a subdermal region of dorsal region or lower extremity, etc. is used for an implanted site. These sites might change a type of reaction of surrounding tissue of tumor from an original organ. Specifically, hepatocellular tumor grown under the skin usually shows a spherical shape covered with a relatively thick fibrous capsule, but almost no fibrous capsule formation in our case of liver transplantation, bleeding in some region, somewhat differing from a manner grown under the skin, and furthermore involves lung metastasis.

Most of the reports did not recognize metastasis in a nude mouse transplantation of human tumor, whereas only a few report of metastasis of A. Microscopic metastatic foci has been found in local limph nodes for the case of a second passage hepatocellular tumor, but there is no report of the case of metastasis to the lung." (page 32, right column, line 26 to page 33, left column, line 10)

"Human tumor implanted in a nude mouse showed almost no metastasis. This is supposed to be the animal used is immunosuppressive animal, a change of biological nature of implanted tumor, or a death prior to metastasis due to a few case of long-term survival since it was not conducted under an SPF environment. One possible major factor may be that the implanted site was a hypodermal tissue. Specifically, if implanted in an original organ, it might possibly show a similar metastasis. We would like to believe that the induction of lung metastasis by our liver-implanted hepatocellular tumor had clearly demonstrated this." (page 33, left column, lines 11 to 19)

"Summary

We have report the successful transplantation of human hepatoma in nude mouse. Somewhat differing in a manner of growing from the one implanted subcutaneously, no fibrous capsule of tumor was found, but the metastasis to the lung was observed." (page 33, the right column, lines 1 to 4)

(C) Evidence A No. 4

A4 has the following descriptions:

"A method of cellular culture or animal implantation is used for studying biological characteristics of human tumor or various anticancer studies, but these methods are not always feasible depending on kinds of tumors. ... In particular, animal bearing human cancer is an ideal model in studying biological characteristics of tumor and various therapeutic effects. Implanted human cancer is required to have unchanged intrinsic nature in the host animal." (page 303, left column, lines 2 to 11)

"On the other hand, studies of human hepatoma have been conducted by clinical studies and animal-generated hepatoma due to the difficulty of the establishment of the cell cultivated strain." (page 303, left column, line 20 to right column, line 2)

"From such a viewpoint, the author implants human hepatoma into a nude mouse to try subculturing. At this time, the first passage implanted system could be established. Accordingly, we report the finding obtained by a consideration given to the biological characteristics of human hepatoma implanted in a nude mouse and the appropriateness

for the subject of human hepatoma study as well as the other 14 cases in which a serial transplantation was conducted but systematization failed." (page 303, the right column, lines 3 to 8)

"1. Experimental Animals

Male and female BALB/c nude mouse (nu/nu) raised under a specific pathogen free condition in Central Institute for Experimental Animals at 5 to 7 weeks old were used." (page 303, the right column, lines 10 to 13)

"2. Experimental Methods

Hepatoma patients were sixteen cases who were hospitalized in the First Surgery Department of Hokkaido University and underwent laparotomy from November 1976 to May 1978, of which there were 14 cases in which 15 pieces of liver tumor tissue implantable into a nude mouse were sampled from surgical or excised specimens. These tissue pieces were subjected to primary implantation into a nude mouse, and tissue samples that took were further subjected to serial transplantation.

...

Note that the implantation system is described as Hc for hepatocellular tumor, and Hb for hepatoblastoma, which are respectively numbered in the order of implantation." (page 303, right column, line 19 to page 304, line 9)

"(a) Primary implantation

A hepatoma tissue was aseptically sampled from the partial excision of tumor or from a liver excision sample, and this was cut out in a 2 mm square or less after removing a necrotic zone and a blood constituent in saline by use of a knife and a pincette. Subsequently, one or several pieces of the tissue were implanted subcutaneously into a lateral region or a dorsal region of a nude mouse by use of a needle." (page 304, left column, lines 11 to 17)

"(b) Serial transplantation

When tumors that have undergone first passage or serial transplantation reached a certain size, the nude mouse was cardiopunctured under anesthesia with ether, was followed by blood drawing, and then tumors were aseptically isolated. This tumor was immediately put into a physiological saline, and cut out into about 2 mm square, and one or several pieces thereof were implanted subcutaneously into a lateral region or a dorsal region of another new nude mouse by use of a needle ... These serial transplantations were conducted at a time point when a diameter exceeds about 1 cm, where the bleeding, central necrosis and exulceration of tumor rarely took place." (page 304, left column, lines 23 to 33)

"(c) Transplantation into nude mouse

A nude mouse was laparotomized under anesthesia with ether, and a piece of tissue of 1 to 2 mm square prepared by the aforesaid method was implanted into a liver middle lobe by use of a needle with an outer diameter of 2.5 to 1.5 mm. Further, a needle was inserted into a right flank region of a nude mouse subcostally, so that a piece of tumor tissue might contact the right lateral segment of the right hepatic lobe." (page 304, left column, lines 34 to 39)

"It was 10 mice which were subjected to the subcostal insertion of a needle into a right flank region thereof to implant into a liver, but only two mice consisting of a second passage of Hc-3 and a third passage of Hc-5 achieved success. Implantation into the liver was conducted by opening the abdominal cavity for two of the sixth passage of Hc-4. Both have taken, but one contracted wasting disease 18 days after the

implantation, the other 38 days after the implantation, and both have been killed. After killing, the presence of hepatoma was observed for all four mice. Further, a lung metastasis was observed in the second passage of Hc-3 implanted into the right subcostal region." (page 306, left column, lines 16 to 23)
"All six cases that established the primary implantation were subcultured, and also achieved success in the implantation of the second passage, and serial transplantation was further continued" (page 306, right column, lines 1 to 2)
"Further, it is interesting that the direct implantation into the liver showed an AFP value 10 times or higher than the otherwise. The correlation between the tumor occurrence origin and the AFP value should be considered hereinafter. It is assumed that there are some differences in terms of take rate and biological characteristics of implanted tumor between subcutaneous implantation and implantation into liver of hepatoma."
(page 312, left column, lines 26 to 31)
"Fifteen tumor tissues sampled from fourteen cases were subjected to serial transplantation into nude mice. As a result, the following conclusions were obtained. 1) Primary implantation achieved success in five cases of thirteen cases for hepatocellular tumors, and one case of two cases for hepatoblastoma. ... 4) AFP was detected from all six cases that took. 5) Implanted hepatocellular tumor showed an image analogous to an original tumor, except that the alveolar formation was not significant. 6) Metastasis was observed in only one mouse where an infiltrative tumor was formed in the liver. The mouse was found to have a metastasis to lung. 7) Karyotype analysis, serum absorption test, and precipitation reaction caused by anti-human AFP serum, etc. identified the metastasis to the lung to be of human origin." (page 312, the right column, lines 4 to 18)
"3) Macroscopic findings

After removing a tumor for serial transplantation and necropsying a deceased one due to another cause, the nature of the tumor and the presence or the absence of distant metastasis, etc. were observed macroscopically." (page 304, the right column, lines 13 to 16)

Regarding the origin of hepatoma to be implanted in a nude mouse, Table 1 of page 305 discloses that Hc-3 was derived from a 45-year-old male before chemotherapy and obtained by a centesis biopsy.

B Easy Conceivability

1 (Trial Decision's note: 1 in a circle) It was found that a human tumor implanted under the skin of a nude mouse had almost no infiltration or metastasis (Evidence A No. 50 [1986]). As seen above, in connection with the difference between a tumor grown under the skin of a nude mouse and a tumor grown in an original organ, there are the following descriptions: [1] "Conventionally, a subdermal region of the dorsal region or lower extremity, etc. is used for an implanted site. These sites might change a type of reaction of surrounding tissue of tumor from an original organ. Specifically, human hepatocellular tumor grown under the skin usually shows a spherical shape covered with a relatively thick fibrous capsule, but almost no fibrous capsule formation in our case of liver transplantation, bleeding in some region, somewhat differing from a manner grown under the skin, and furthermore involves lung metastasis. ... Specifically, if implanted in an original organ, it might possibly show a similar metastasis. We would like to believe that the induction of lung metastasis by our liver-implanted

hepatocellular tumor had clearly demonstrated this." (A3 [1978], page 32, right column, line 26 to page 33, left column, line 19); and "Tumors are formed subcutaneously with a definite boundary without any infiltrative growth, but once a tumor invades a muscle, it exhibits infiltrative growth." (B28 [1982], page 2, lines 2 to 4). In view of these descriptions, it was recognized as of the priority date of the Patent that human tumor grown under the skin of nude mouse forms a tumor with a definite boundary surrounded by a fibrous capsule when observed, and thus infiltration and metastasis would rarely occur.

2 (Trial Decision's note: 2 in a circle) According to the description of the above A(A) (in particular, the column of "Consideration"), A1 uses orthotopic implantation as a means for investigating the progression or behavior of human malignant tumors. As the trial decision finds as an A1 invention,

human infiltrating ductal breast cancer implanted into an excised fourth mammary fat pad was active and beginning to invade the fat pad 2 months after the implantation.

3 (Trial Decision's note: 3 in a circle) Further, it was supposed as of the priority date of the Patent that malignant tumor became advanced in a living body as in the order of [1] tumor growth, [2] infiltration to adjacent tissue, and [3] the metastasis to other tissue via blood vessels and lymph channels (A23, 41, 43). It is recognized that it was generally known as a matter of common general knowledge of the process of cancer progression that the metastasis would occur with some level of probability (frequency) in a stage where the infiltration of tumor was observed if the spread of infiltration was wide, or the metastasis was likely to occur due to a future spread of infiltration as time passed (A39, A44 to A48).

4 (Trial Decision's note: 4 in a circle) Further, as in the above items (B) and (C), the A3 invention and the A4 invention describe the formation of infiltrative tumor with almost no fibrous capsule formation and the occurrence of the metastasis when a human neoplastic tissue that has been subjected to serial cultivation under the skin of a nude mouse is implanted (orthotopically implanted) into an original organ, differing from the case of subcutaneous cultivation.

5 (Trial Decision's note: 5 in a circle) On the premise of the aforesaid items 1 (Trial Decision's note: 1 in a circle) to 4 (Trial Decision's note: 4 in a circle), [1] Regarding the A1 invention where the infiltration occurs as a result of implementing orthotopic implantation by use of a tumor that has not undergone subcutaneous passage, [2] in view of the A3 invention and the A4 invention where the infiltration and the metastasis occur as a result of implementing orthotopic implantation similar to the A1 invention by use of a tumor that has undergone subcutaneous passage, [4] a person skilled in the art could only have easily [3] expected that it is highly likely to cause metastasis in a similar manner to the A3 invention and the A4 invention should the infiltration further spread as time goes by in the A1 invention, and at most would have been motivated for attempts within an ordinary creativity.

Consequently, a person skilled in the art could have easily conceived of applying the findings of the A3 invention and the A4 invention to a nude mouse (athymic mouse) of the A1 invention to obtain an animal model for the metastasis of human tumor; i.e., the constitution of Inventions 1, 2, 11, and 12 according to the different features.

C Defendant's allegation

(A) "Infiltration, invasion"

Defendant argues that the term "infiltration, invasion" includes the case of "infiltrate" and the case of "invasion", and a person skilled in the art would not recognize "invasion", which is a process of metastasis to penetrate a basement membrane from A1 with only the former description (infiltrating). Thus consideration will be given as below.

a As for the terminology,

It is recognized that "infiltrate, invade" means growth while destroying an adjacent tissue, and the boundary is ambiguous (A42, 45). It cannot be seen from the descriptions of A11, B6 to B8, and B23-1 and -2 that "infiltrate" is distinguished from "invade" with a criterion of whether or not it penetrates a basement membrane.

Indeed, it is recognized that the following descriptions of A39 and A40 may understand the infiltration in relation to the basement membrane.

1 (Trial Decision's note: 1 in a circle) "pathology and pathological cytology" (A39 [1995]): "Tumor stage is represented by spread of the tumor. ... Tumor stage of malignant tumor is divided into early stage, advanced stage, and end stage. ... Carcinoma in situ is a cancer localized to an epithelial layer. It does not penetrate a basement membrane. ... Non-infiltrating cartinoma is a symptom similar to carcinoma in situ, but used for breast cancer, etc. Cancer is localized to only an iter or within lobules, and does not infiltrate the surrounding supporting connective tissue (interstice). Early infiltrating cartinoma is a cancer with a shallow infiltration. Advanced cancer is a cancer in a stage where a tumor infiltrates interstice to spread over a large area (infiltrating cartinoma), in which metastasis can frequently be seen, and is difficult to heal." (page 56, lines 11 to 21)

2 (Trial Decision's note: 2 in a circle) "General theory of modern pathology" (A40 [1979]) "c: carcinoma in situ. Epithelium has been replaced with a cancerized cell, but the infiltration penetrating a basement membrane is not found.

d: invasive carcinoma. The infiltration of cancer to a deep part penetrating a basement membrane was observed." (Explanation of page 338, FIG. IX/10)

On the contrary, however, the following descriptions of A42 and A54 express even an invasive carcinoma, which means an advanced cancer through the destruction of a basement membrane, as "infiltrative".

1 (Trial Decision's note: 1 in a circle) "Illustrated Pathology" (A42 [1987])

"... includes growing in an infiltrative manner. ... In a manner that malignant tumors grow, ... in the case of infiltrative growth, it usually involves the destruction of surrounding tissues." (page 89)

2 (Trial Decision's note: 2 in a circle) "Latest Medical Dictionary" (A54 [1992])

"infiltrative growth": "One characteristic to distinguish malignant tumor from benign tumor. A benign tumor has a pattern of growth of expansive and definite boundary of tumor, whereas a malignant tumor grows by the infiltration into the surrounding and distant metastasis, and thus has a somewhat indefinite boundary." (page 714)

"infiltrative cancer": "it refers to a level of progression in terms of the morphology of cancer. It refers to one where a cancer cell destroys a basement membrane and infiltrates and grow into subepithelial tissue or another adjacent organ. The term corresponding to intraepithelial cancer or non-invasive cancer." (page 714)

Further, A55 defines "invasion" as "The infiltration of adjacent tissues by a

disease process, usually cancer".

As seen above, there is no ground sufficient to accept the Defendant's argument to the effect that "infiltrate" and "invasion" are distinguished from each other with a criterion of whether or not a basement membrane is penetrated.

b Regarding the progression of cancer,

As aforementioned, it was supposed that malignant tumor progresses in a living body as in the order of 1 (Trial Decision's note: 1 in a circle) tumor growth, 2 (Trial Decision's note: 2 in a circle) infiltration to adjacent tissue, and 3 (Trial Decision's note: 3 in a circle) the metastasis to other tissue via blood vessels and lymph channels; however, it depends on the kind of cancer as to whether or not a basement membrane is penetrated; however, it is a distinction by tumor stage (A39, 40, 41). It is hard to find from each piece of evidence that a tumor in a stage where a basement membrane is not penetrated ceases its growth and infiltration to other tissues at the basement membrane without exception, despite the passage of time. Further, it was supposed that the progression of human tumor in a nude mouse in which a human tumor was implanted might proceed similarly.

c "Infiltrate"

As seen above, a person skilled in the art would not instantly recognize from the term "infiltrate" that the malignant tumor did not penetrate a basement membrane, nor would recognize that the malignant tumor expressed as "infiltrate" would not cause metastasis.

d "Infiltrating" of A1 invention

As in the above A(A), A1 discloses that the nipple rudiment and adjacent portions of the fat pad up to the site of the inguinal lymph node (i.e. mammary gland including mammary duct and the surrounding mammary fat pad) were surgically excised in the fourth mammary fat pads, and three to four weeks later, when a nude mouse became six to eight week old, a defect was created in the excised fourth mammary fat pads (cleared fat pad; CFP), and implanted herein the tissue transplants obtained from a biopsy specimen of human breast tissue diagnosed as "infiltrating ductal carcinoma", and two months later, it showed the tumor to be healthy and beginning to infiltrate the fat pad, and the basic appearance of the mouse CFP was essentially the same as that of the original human biopsy specimen, having ducts lined with multiple layers of abnormal epithelium, strands of infiltrating tumor cells, and abundant fibrous stroma.

e Summary

The infiltration of tissue transplants used in A1 into a fat pad also means "infiltrate", which is a typical nature of a malignant tumor. Thus it can be said that a person skilled in the art is likely to recognize the cause as metastasis via blood vessels and lymph channels if a range of infiltration spreads.

The Defendant's allegation described above is not acceptable.

(B) "Orthotopic implantation"

Defendant argues that the A1 invention does not implement orthotopic

implantation, and thus a consideration is given hereinafter.

a Regarding the implantation method of the A1 invention,

According to the description of the above item A(A), the A1 invention is set forth as below: On the premise of the findings that human breast tissue subcutaneously implanted in a nude mouse is grown only limitedly, the nipple rudiment and adjacent portions of the fat pad up to the site of the inguinal lymph node (i.e. mammary gland including the mammary duct and the surrounding mammary fat pad) were surgically excised from the inguinal mammary fat pads of a female nude mouse to obtain CFP (cleared mammary fat pads), and the tissue transplants of human breast tissue diagnosed as infiltrating ductal carcinoma (invasive ductal carcinoma) were introduced into a defect formed in the aforesaid CFP, which resulted in the infiltration from the implanted human breast tissue to a fatty pad.

In connection with a method for preparing CFP, Evidence A No. 1 cites "SLEMMER GL: Interactions of separate types of cells during normal and neoplastic mammary gland growth. J Invest Dermatol 63:27-47, 1974" (B15-1). B15-1 cites "K. B. DeOme, L. J. Faulkin, JR., Howard A. Bern, AND Phyllis B. Blair: Development of mammary tumors from hyperplastic alveolar nodules transplanted into gland-free mammary fat pads of female C3H mice. Cancer Res195919:515" (B16-1) (B15-2). B16-1 (Translation relies on B16-2; obvious errors have been corrected) includes the following description of CFP preparation. According to this, the A1 invention is not the implanted one as opposed to the Defendant's allegation, but it is recognized that the blood flow of capillary and lymph flow in CFP of A1 invention are not blocked (the same can apply in view of the fact that the infiltration may not occur unless nutrients necessary for growth and infiltration of the tumor are supplied via blood flow). "a nipple region, thick veins in a ventral side of lymph node and a portion between the fourth and fifth mammary fat pads were respectively cauterized. ... The remaining parts of the mammary fat pads retained blood circulation; however, there was no tissue of a host (mouse). In this state, the mouse was prepared to accept implantation, or implanted at a later date subsequent to the suture of a skin flap. ... Their studies demonstrate that a fourth fat pad usually has three separate blood-supplying channels, and surgery described herein does not prevent the blood flow of the remaining mammary fat pad." (Evidence B No. 16-1, page 516, right upper column, line 5 to page, right bottom column, line 3)

Further, there is no evidence to show the recognition in the business field that it did not correspond to orthotopic implantation in the absence of mammary gland in the excised fourth mammary fat pads (CFP) of nude mouse. In addition, it is a well-known fact that breast is widely spread on the ventral surface from the chest region to the inguinal region.

Further, A1 also discloses that the conventional cause of failure is the subcutaneous implantation of human breast tissue, whereas the implantation method of the A1 invention provides the possibility of providing data for the growth and the behavior of human breast tissue.

Therefore, a person skilled in the art who read the description of A1 would recognize that the A1 invention is not intended for a simple implantation and growth of tumor tissues, but an experiment in which a human breast cancer tissue was directly implanted in the corresponding breast organ of a nude mouse in place of the method of

subcutaneous implantation for the purpose of investigating the progression of malignant tumor that progresses in the order of growth, infiltration, and metastasis.

b Regarding "orthotopic implantation" of the Invention,

The specification discloses that "an implant or graft transferred to a position formerly occupied by tissue of the same kind ... the grafting of human neoplastic tumor tissue from a human organ into the corresponding organ of an immunodeficient laboratory animal" with respect to orthotopic implantation (page 4, lines 11 to 13).

Specifically, it discloses that orthotopic implantation is implemented by forming an opening or a defect in each corresponding organ of the recipient animal and disposing therein a human neoplastic tissue from such as liver, pancreas, and lung, and suturing.

Further, it discloses that tissue implantation from human breast cancer "is implemented by surgically forming a pocket on a chest of a recipient female animal." (page 5, lines 19 to 20). Thus it is implemented by simply forming a pocket "on a chest", not directly embedding into a mammary duct or a lobule of a recipient female animal. The term "on a chest" used herein is construed as meaning the whole breast organ of the recipient female animal.

Therefore, it is recognized that at least in the case of implantation of human breast cancer tissue, the Invention is to form an opening or a defect, etc. "on a chest"; i.e., anywhere in a "breast organ", which was "a position previously occupied by" breast cancer, and dispose the human breast cancer tissue.

c Summary

In view of the above items a and b, the Invention and the A1 invention differ from each other in that the A1 invention removes a mammary gland and the surroundings of a nude mouse, which differs from a specific implantation method of human breast cancer tissue described in the specification. The excised fourth mammary fat pads (CFP) of A1 are a site corresponding to "on a chest" (breast organ), which was previously occupied by a human breast cancer tissue, and thus it is obviously included into the one "implanted into a corresponding organ" of the Invention.

The Defendant's allegation described above is not acceptable.

D Summary

As described above, the judggement of the trial decision of the different feature between Inventions 1, 2, 11, and 12 and the A1 invention made an error.

Therefore, at least the Reason for rescission 5-3 has a point with respect to each of the above Inventions.

No. 6 Conclusion

As seen above, the Reason for rescission 5-3 has a point, and this conclusion is likely to affect the determination of the inventive step of Inventions 3 to 10, and 13 to 19 on the basis of the A1 invention.

Accordingly, the trial decision shall be rescinded as a whole, and the court sentences as in the formal adjudication." (Court decision, page 30, line 7 to page 48, line 23)

Further, the above court decision binds the collegial body for the Patent invalidation trial case under the provision of Article 33(1) of the Administrative Case Litigation Act.

(2) Inventions 1, 2, 11, 12

Invention 1 restricts "implantation" to "orthotopic implantation", and "neoplastic tissue" to "human neoplastic tissue" with respect to the invention according to Claim 1 before the Correction that has determined in the above court decision. The above court decision determined on the basis of the finding that the A1 invention was an invention where human breast cancer tissue was orthotopically implanted in a breast organ of a nude mouse.

Consequently, the determination of Invention 1 is based on the same Finding and legal determination necessary for introducing the formal adjudication of the above court decision. Therefore, as per the above court decision, Invention 1 was easily conceivable by a person skilled in the art on the basis of then A1 invention and the inventions described in A3 and A4.

Further, the same can also apply to Inventions 2, 11, and 12.

(3) Inventions 3 to 10, 13 to 19

Inventions 3 and 13 specify a human neoplastic tissue as any tumor tissue obtained from human liver, kidney, stomach, pancreas, colon, breast, prostate, lung, or testis.

Inventions 4 and 14 specify a human neoplastic tissue as a human tumor renal tissue obtained from human kidney.

Inventions 6 and 16 specify a human neoplastic tissue as a human neoplastic stomach tissue obtained from human stomach.

Inventions 8 and 18 specify a human neoplastic tissue as being obtained from human colon.

Invention 9 specifies a human neoplastic tissue as being obtained from a female human breast.

Further, Inventions 5, 7, 8, 15, 17, and 18 respectively include the transplantation of a neoplastic tissue obtained from a human organ implanted into the corresponding organ of an animal.

Here, as the previous trial decision found, the A1 invention is
"a nude mouse, wherein the #4 inguinal mammary fat pads of germfree female nude mice 20-25 days of age were cleared of host epithelium by surgical extirpation of the nipple rudiment and adjacent portions of the fat pad up to the site of the inguinal lymph node, and wherein a human breast tissue diagnosed as infiltrating ductal carcinoma is implanted into said cleared portion, and wherein sections of the fat pad 2 months after transplantation showed the tumor to be healthy and beginning to infiltrate the fat pad" in which a human breast cancer tissue is transplanted into a mouse breast (breast region).

Further, as per the above court decision, a person skilled in the art could have easily conceived of applying the findings of A3 and A4 with respect to hepatoma to the above A1 invention regarding breast cancer to achieve an animal model for metastasis

of human tumor. Thus, it is recognized that a person skilled in the art could have easily conceived of preparing an animal model for metastasis of human tumor for tumor tissues other than breast cancer.

Therefore, Inventions 3 to 10 and 13 to 19 were also easily conceivable by a person skilled in the art on the basis of the A1 invention and the inventions described in A3 and A4.

3 Other Reasons for Invalidation

As discussed in the above item "2 Reasons for invalidation 5 -1 [violation of Article 29(2) of the Patent Act (Inventive step)]", at least the inventive step of Reason for Invalidation 5-1 has a point, and the remaining Reasons for Invalidation are considered in the following:

(1) Reason for invalidation 1 [Violation of Article 29(1), main paragraph of the Patent Act (Incomplete Invention)]

A Description of the specification

The specification has the following descriptions of Examples relating to metastasis.

"Example III

Specimens of human tissue removed from a human colon and pathologically diagnosed as colon carcinoma were prepared to size by the teasing procedure described earlier. Five athymic nude mice, age four (4) to six (6) weeks were selected as the animal recipients for the implants. In preparation for surgery, the mice were anesthetized with ether.

Each anesthetized mouse was incised to provide access to the colon. A pocket of cavity was surgically formed in the seromuscular layer with care exercised not to enter the lumen. A selected tumor mass of approximately 0.5 x 0.2 cm was inserted into the pocket, which was then closed with a suture.

Four of the five mice which underwent this implant surgery have survived for three to four months and appear to be in good health. Approximately one month following tissue implantation, the mice were surgically opened and the tumors were observed to have taken. None of the tumors appeared not to have metastasized to other organs at this time." (The specification, page 8, line 21 to page 9, line 3)

B Matter to be recognized from Example III

(A) Implanted neoplastic tissue

The tissue to be implanted in Example III is a lump of tissue in view of "preparing specimens of human tissue" "removed from a human colon" and "pathologically diagnosed as colon carcinoma to size by the teasing procedure described earlier". It corresponds to "neoplastic tissue obtained from a human organ other than brain" of Inventions 1 to 10 and "neoplastic tissue obtained from a human organ other than brain" of Inventions 11 to 19.

(B) Implantation into a corresponding organ

In "a pocket of cavity" "surgically formed in the seromuscular layer" of colon of non-human animal model of athymic mouse, there is inserted "a tumor mass" "of

approximately 0.5 x 0.2 cm" diagnosed as colon carcinoma. As seen above, a colon cancer tissue was implanted in the colon of a thymic mouse in Example III. Thus the implantation was made corresponding to "the corresponding organ of said animal" of Inventions 1 to 10.

Further, the implantation corresponding to "the corresponding organ of the immunodeficient animal" of Inventions 11 to 19 was performed.

(C) Metastasis

In Example III, it discloses that "Four of the five mice which underwent this implant surgery have survived for three to four months" and "Approximately one month following tissue implantation, the mice were surgically opened and the tumors were observed to have taken." In view of this, one out of five died at any time point; however, the tumors have obviously taken for at least four of the five mice.

Further, one month later, while the mice were surgically opened to confirm the engraftment, an observation was delivered on the metastasis to the other organ as follows: "None of the tumors appeared not to have metastasized to other organs at this time."

This sentence is a double negation, and when summarizing the negation, it is construed as meaning "the tumors appeared to have metastasized to other organs."

Here, you may note an indefinite expression of "appeared"; however, in view of the following description:

(i) The specification describes the matters specifying Inventions 1 to 19 as "non-human animal model for the metastasis of human tumor tissue";

(ii) For background of the Invention, the specification refers to a conventional problem that "In these models, tumors that took often grew to a great extent at the site of implant and rarely metastasized, even if the original tumor had been highly metastatic in the donor. Accordingly, the subcutaneous nude mouse human tumor model, although better than the previously described rodent model, still had a substantial drawback; i.e., the subcutaneous transplant lacked the ability to metastasize." (the specification, page 3, lines 19 to 23); and

(iii) The patent invention solves such a problem, and there is a description that "In accordance with the primary aspect of the present invention, a novel animal model for human neoplastic disease is provided having neoplastic tissue obtained from a human organ implanted into the corresponding organ of the animal and having sufficient immunodeficiency to allow the implanted tissue to grow and metastasize." (The specification, page 4, lines 1 to 4),

it is obvious that it aimed to prepare a non-human animal model with an ability sufficient to metastasize, for which Example III was a confirmatory experiment.

Further, Example III

(iv) was obviously conducted by a person who had a skill in surgery and an ability to confirm the effects of the patent invention, as evident from the fact that "Four of the five mice which underwent this implant surgery have survived for three to four months".

(v) The observation of "none of the tumors appeared not to have metastasized to other organs at this time" was made simultaneously with the observation of "Approximately one month following tissue implantation, the mice were surgically opened and the tumors were observed to have taken". Thus it is inferred that the observation was made by sight.

(vi) At least four of the five mice are subjected to a surgical incision one month after the tissue implantation, and the observation was made to the effect that "none of the tumors appeared not to have metastasized to other organs at this time" at the time, as evident from the fact that "Four of the five mice which underwent this implant surgery have survived for three to four months".

In view of the description of "none of", evidence of appearing to have metastasized to other organs was obtained from at least four of five mice, the same evidence was obtained in a plurality of mice.

Further, it can be seen from the description of "four of the five mice which underwent this implant surgery have survived for three to four months" that any mouse served for "surgical incision of mouse about one month after tissue implantation" was sutured, and "four of the five mice achieved survival for three to four months".

As described in the above "(v)", the observation of Example III was made by visual inspection, and a strict inspection such as tissue testing was not conducted, which might lead to the observation such as "appeared"; however, as described in the following Publications A and B, before the priority date of the Patent it was usual practice to confirm the metastasis by visual inspection. Thus it cannot be said that the observation of Example III was uncertain because it was made by visual inspection. In addition, a person skilled in surgery with an ability to confirm the effects of the patent invention delivered an observation that
"None of the tumors appeared not to have metastasized to other organs at this time", which could be seen as a metastasis, in at least four of five mice. In view that it is unusual that the same evidence was observed incidentally and simultaneously in four mice, it is natural to believe that there was a metastasis derived from implanted neoplastic tissue. It cannot be said that the occurrence of metastasis has not been confirmed.

Publication A: Japanese Unexamined Patent Application Publication No. S62-294432
"To a second group of rat there was injected a 'void' liposome (i.e. not mixed with MTPChol), whereas a third group of rat was left untreated. Eighteen days after tumor cells implantation, rats of each group were killed, and the number of pulmonary metastases visible to the naked eye was counted." (page 9, the right upper column, lines 4 to 9)

Publication B: Japanese Unexamined Patent Application Publication No. S61-212590
"Effect on the Formation of Metastases of the B16 Melanoma

For the treatment of metastases of the B16 melanoma, a primary tumor was induced in female C57B1/6 mice (10 animals/group) with $2x10^5$ live B16 melanoma cells. After amputation of this tumor the B16 melanoma metastasizes into the lung, and the animals died. After tumor induction, the animals were treated intraperitoneally with 50 mg/kg of the test substance obtained as in Example 7, on days 3, 5, 7, 9, 11, and 13 before or after amputation had taken place. The number of macroscopically detectable metastases in the lung was determined on days 14, 17, 21, 25, and 28 after amputation of the primary tumor had taken place.

As is evident from Table 9, the number of pulmonary metastases of the B16 melanoma was markedly less in the treated animal groups than in the corresponding

control animals." (page 13, right bottom column, line 2 to last line)

C Allegation from both parties on the basis of the specification as of the International application

Regarding the construction of "None of the tumors appeared not to have metastasized to other organs at this time" of the specification, both parties present an argument on the basis of the description of the specification as of the international application; however, pursuant to the provision of Article 184-4(4) of the Patent Act before revision, of which the provisions then in force shall remain applicable according to revision supplement Article 7 of Heisei 6-nen Law No. 116, the matters that are not described in the translation as of the expiration of Deadline of National Phase Entry but are described in the specification or the scope of claims of the International Patent Application as of the International filing date are deemed to be not described in the specification or the scope of claims of International Patent Application as of the International filing date. Therefore, the description of the specification of the International filing date cannot be a ground for the construction of the specification.

D Consideration

(A) Construction of "a neoplastic tissue obtained from human organ" of Inventions 1 to 10 and "a neoplastic tissue from a human organ" of Inventions 11 to 19

Regarding a "neoplastic tissue obtained from human organ" as provided in Inventions 1 to 10, the definition is not present in the whole disclosure of the specification, let alone the corresponding part. Here, when it comes to the column of "Detailed Description of the Invention" of the specification, there are the following descriptions:

(The specification-1) "the human neoplastic tissue utilized herein comprises tissue from fresh surgical specimens which are pathologically diagnosed tumors occurring in, for example, human kidney, liver, stomach, pancreas, colon, breast, prostate, lung, testis, and brain. Such tumors include carcinomas as well as sarcomas, and implantation thereof as carried out herein encompasses all stages, grades, and types of tumors. Further, human neoplastic tissue used are implanted in a lump without separating individual cells. A "three-dimensional structure" of a tumor tissue may be maintained by implanting a lump of the tumor tissue. Therefore, a human tumor animal model with higher reliability may be obtained." (The specification, page 4, line 20 to 28)

(The specification-2) "the present invention relates to a non-human animal model for human neoplastic disease. More particularly, the invention relates to a non-human animal model having neoplastic tissue, obtained from a human organ, implanted into the corresponding organ of the animal." (The specification, page 2, line 23 to 25)

(The specification-3) "neoplastic tissue obtained from a human organ implanted into the corresponding organ of the animal" (the specification, page 4, lines 2 to 3)

(The specification-4) "a specimen of neoplastic tissue from a human organ" (the specification, page 4, lines 7 to 8)

(The specification-5) "implantation of human neoplastic tissue" (the specification, page 4, line 11)

(The specification-6) "Prior to implantation, the human neoplastic tissue is maintained by placing in a suitable nutrient medium, such as Eagle's minimum essential medium

containing ten percent fetal calf serum and a suitable antibiotic, such as gentamycin. The medium containing the tissue is then cooled to approximately 4C. The tissue can be maintained in this manner for approximately twenty-four hours." (The specification, page 4, line 29 to page 5, line 3)

Further, in the examples of the column of "Detailed Description of the Invention" of the specification, a neoplastic tissue obtained from a human organ has been directly implanted into the corresponding organ of the animal (the specification, page 7, line 17 and later). Further, the specification also discloses that "The placement of neoplastic tissue in an immunodeficient laboratory animal according to the present invention is carried out by means of orthotopic implantation. ... (Omitted)... In the present invention, the terminology orthotopic implantation is used to refer to the grafting of human neoplastic tumor tissue from a human organ into the corresponding organ of an immunodeficient laboratory animal." (The specification, page 4, lines 17 to 20).

All the above descriptions relate to a lump of neoplastic tissue sampled from a human organ. The passage of this to the other animal is not mentioned.

In view of these points, it is reasonable to understand that the "neoplatic tissue from a human organ" is the very same neoplastic tissue sampled from a human organ. Further, if the neoplastic tissue is this sort of thing, it can be said as a matter of course that "a three-dimensional structure of a tumor tissue may be maintained".

Further, for a similar reason, it is reasonable to understand that the "neoplatic tissue from a human organ" of Inventions 11 to 19 is the very same neoplastic tissue itself sampled from a human organ.

(B) Orthotopic implantation

The means for the use in implementing Inventions 1 to 19 is an orthotopic implantation in view of the description that "The placement of neoplastic tissue in an immunodeficient laboratory animal according to the present invention is carried out by means of orthotopic implantation. This refers to an implant or graft transferred to a position formerly occupied by tissue of the same kind. In the present invention, the terminology orthotopic implantation is used to refer to the grafting of human neoplastic tumor tissue from a human organ into the corresponding organ of an immunodeficient laboratory animal." (The specification, page 4, lines 17 to 20). The specification specifically discloses a method of orthotopic implantation from page 4, last line to page 6, line 26, and the specification describes a process of orthotopic implantation in further detail in Examples I to III from page 7, line 17 to page 9, line 3.

(C) The fact that targeted technical effects are achievable

Consideration is given as to whether the targeted technical effect might be achieved by the above orthotopic implantation described in the specification. As described in the above "3(1)B Matter to be recognized from Example III", it can be seen from Example III that there was a metastasis derived from an implanted neoplastic tissue, and thus it is obvious that the targeted technical effects were achieved.

(D) The fact that technical effects are achievable by repeated trials

As discussed in the item (vi) of the above "3(1)B(C) Metastasis", similar evidence like a metastasis was observed in at least four of five mice in Example III of the specification. This suggests that repeated trials brought the same result.

(E) As for Publication distributed after the filing date of the Patent

The publication distributed after the filing of the Patent of Evidence B No. 57-1 describes a case of direct orthotopic implantation in which a colon cancer specimen was used (Evidence B No. 57-1 to -3). Although there are several samples that do not cause metastasis (Evidence B No. 57-1 to -5), in a right side colon infiltrating mucinous adenocarcinoma of sample number 1701, as a result of conducting a direct orthotopic implantation for two mice, one died, but the remaining one had a metastasis to bowel wall (Evidence B No. 57-1 to -4). Metastasis was confirmed by subjecting the very same neoplastic tissue obtained from the sample to orthotopic implantation.

The publication distributed after the filing date of the Patent of Evidence B No. 69-1 discloses that, as a result of the orthotopic implantation of a poorly-differentiated giant cell flat epithelium tumor 2268 directly obtained from surgery in a left lung as a histologically intact tissue, the metastasis to the opposite side of lung has developed together with the metastasis to lymph node (Evidence B No. 69-1 to -2). This confirms the metastasis by the orthotopic implantation of the very same tumor tissue obtained from the sample.

The publication distributed after the filing date of the Patent of Evidence B No. 71-1 obtained a result that six of eight mice (75%) in an orthotopic implantation group had a plurality of metastatic nodulus in their lungs by use of a surgical sample (Evidence B No. 71-1 to -2) of a poorly-differentiated human breast duct cancer (Anticancer#2468). This confirms the metastasis by the orthotopic implantation of the very same tumor tissue obtained from the sample.

The publication distributed after the filing date of the Patent of Evidence B No. 72-1 obtained a result that tumors of Table 1 (Evidence B No. 72-1 to -2) were metastasized by use of a duct cancer sample (Evidence B No. 72-1-1) of a fresh chest lining obtained from sidewall chest lining of a 65-year-old white female. This confirms the metastasis by the orthotopic implantation of the very same tumor tissue obtained from the sample.

As seen above, in view that there are many reports that a metastasis was observed by the orthotopic implantation of the very same tumor tissue obtained from the sample, the observation of "None of the tumors appeared not to have metastasized to other organs at this time", which was observed in Example III of the specification strongly supports the actual metastasis. In addition, it strongly supports the ability to repetitively cause metastasis.

(F) Summary

Comprehensively taking the above matters into account, the means of the aforesaid "orthotopic implantation" of the specification is a means capable of repeated trials that can be easily implemented by a person skilled in surgery. It can be seen from the specification that an evidence like a metastasis was observed in at least four of five mice prepared by the means, and the metastasis was reproducible. It can be said that Inventions 1 to 19 are configured specifically and objectively to the extent that the technical content can bring about a targeted technical effect through repetitive

implementation by a person skilled in the art.

Therefore, it cannot be said that Inventions 1 to 19 were incomplete inventions.

(2) Reason for Invalidation 2 [Violation of Article 36(3) of the Patent Act (Violation of enablement requirement)]

It can be seen from the specification that the objective of Inventions 1 to 19 lies in the preparation of an animal model which has the ability to truly mimic the progression of neoplastic disease as it occurs in humans; i.e., an animal model for human neoplastic disease with an ability sufficient to metastasize and grow human neoplastic tissue.

Further, it can be seen from the specification that the effects of Inventions 1 to 19 lie in that a non-human animal model has been prepared and provided so as to have the ability to truly mimic the progression of neoplastic disease as it occurs in humans; i.e., a non-human animal model for metastasis with a human tumor tissue that can metastasize and grow, by maintaining a "three-dimensional structure" of a lump of an original tumor tissue without separating individual cells from a human tumor tissue obtained from a human organ other than brain and implanting (orthotopic implantation) the tissue in a corresponding organ of an immunodeficient animal (nude mouse, athymic mouse, athymic nude mouse).

In addition, the specification describes a means for specifically implementing the constituent elements of Inventions 1 to 19 as set forth below.

A Implanted neoplastic tissue

The specification specifically describes an access to "neoplastic tissue obtained from a human organ other than brain" of Inventions 1 to 19 on page 4, last line to page 5, line 8 of the specification.

B Animals with immunodeficiency

An access to "an animal with immunodeficiency" of Inventions 1 to 19 is described on page 4, lines 10 to 16 of the specification.

C Orthotopic implantation

The specification specifically describes a means for "implantation into the corresponding organ" (Orthotopic implantation) of Inventions 1 to 19 on page 5, line 9 to page 6, line 26 of the specification.

Furthermore, more specifically, the specification discloses in Example III (the specification, page 8, line 21 to page 9, line 3) that the processes of "preparing specimens of human tissue removed from a human colon and pathologically diagnosed as colon carcinoma to size by the teasing procedure described earlier"; "selecting five athymic nude mice, age four (4) to six (6) weeks as the animal recipients for the implants"; "incising a mouse to provide access to the colon"; "forming a pocket of cavity in the seromuscular layer with care exercised not to enter the lumen"; and "inserting a selected tumor mass of approximately 0.5 x 0.2 cm into the pocket which was then closed with a suture" resulted in "Four of the five mice which underwent this implant surgery have survived for three to four months and appear to be in good health. Approximately one month following tissue implantation, the mice were surgically

incised and the tumors were observed to have taken. None of the tumors appeared not to have metastasized to other organs at this time."

D Summary

Consequently, it can be said that the Detailed Description of the Invention of the specification describes the objective, the constituent elements, and the effects to the extent that allows a person skilled in the art who read the description to implement "an animal model" of Inventions 1 to 10 and "a method of generating an animal model" of Inventions 11 to 19.

(3) Reason for Invalidation 3 [Article 36(4)(i) of the Patent Act (Violation of supporting requirement)]

The means of the aforesaid "orthotopic implantation" of the specification is a means capable of repeated trials that can be easily implemented by a person skilled in surgery without relation to organs. As described in the above "3(1)D Consideration", it can be seen from the specification that metastasis was observed in at least four of five mice, and the metastasis was reproducible.

Therefore, Inventions 1 to 19 fall within a scope that allows a person skilled in the art to recognize that the problem to be solved by Inventions 1 to 19 might be solved, the problem is "to prepare an animal model for human neoplastic disease which has the ability to truly mimic the progression of neoplastic disease as it occurs in humans; i.e., an animal model for human neoplastic disease with an ability sufficient to metastasize and grow human neoplastic tissue, although an animal model without a thymus and their ability to reject foreign transplant tissue (nude mice, athymic mice, athymic nude mice) brought a better result than an animal model of rodent animal, it showed a varied take rate or frequency with which such human tumor tissue actually formed a tumor in the mouse depending on the individual donor and the tumor type, and had a substantial drawback of tumors that took growing to a great extent at the site of implant and rarely being metastasized, even if the original tumor had been highly metastatic in the donor; i.e., the subcutaneous transplant lacked the ability to metastasize".

(4) Reason for Invalidation 4 [Violation of Article 36(4)(ii) of the Patent Act (Violation of description requirement with regard to constituent elemental function of claim)]

As is discussed in the above "3(1)B Matter to be recognized from Example III", It is natural to construe that Example III of the specification showed a metastasis derived from implanted neoplastic tissue. It cannot be said that the occurrence of metastasis has not been confirmed.

Therefore, the demandant's argument of "it is recognized that the recitation of the scope of claims of the specification on the premise that a non-human animal model of the Invention has an ability to metastasize does not recite all of the indispensable constituent features of the invention for which a patent is sought" is not reasonable.

(5) Regarding Reason for invalidation 5

A Reason for invalidation 5-1 [Violation of Article 29(1)(iii) of the Patent Act (Novelty)]

As described in the above item "2(1) Ruling in the Intellectual Property High Court", the court rules that "it cannot be said in the Invention that 'metastasize', and

'take' or 'infiltrate' are used to have a similar level of technical significance" (Court decision, page 32, lines 18 to 19),

Further, "comparing Inventions 1 to 19 with the A1 invention, they are at least different from each other in that the A1 invention cannot be said to be 'a non-human animal model for metastasis model'" (Court decision, page 32, last line to page 33, line 2),

And thus "the finding of the identical features and the different features is not erroneous, nor is the determination in the trial decision that Inventions 1 to 19 are not identical to the A1 invention on the premise of this different feature erroneous" (Court decision, page 33, lines 3 to 4).

Consequently, the determination of Inventions 1 to 3 and 10 to 13 is based on the same Finding and legal determination necessary for introducing the formal adjudication of the above court decision. Therefore, as in the above court decision, it cannot be said that Inventions 1 to 3, 10 to 13 are the inventions described in A1.

B Reason for invalidation 5-2 [Violation of Article 29(1)(iii) of the Patent Act (Novelty) or Violation of Article 29(2) of the Patent Act (Inventive step)]

(A) The invention described in A2

Evidence A No. 2 discloses that

"Abdominal wall and intraperitoneal implantation were implemented by use of human cancer of stomach and a histological search was conducted.

MATERIALS AND METHODS: Implantation into nude mouse (nu/nu--BALB/C/A/BOM, spf) by use of two cases of human cancer of the stomach. Primary tumors of stomach cancer were all well-differentiated tubular adenocarcinoma. Implanted tumors were subcutaneous passage tumors of fourth passage to sixth passage, and the others were primary tumors and subcutaneous passage tumors of second passage. Implanted tumors were cut to a size of 5x5x5 mm, and implanted into an abdominal wall muscle layer, muscle layer-peritoneum, intraperitoneal and gastric wall by a surgical procedure. Raising in a conventional condition, killed on a postoperative day 21 to 89 to discover a cancer infiltrative stage. ... (Omitted)...

Conclusion: There are already many reports of the possibility of the subcutaneous passage of human stomach cancer in a nude mouse, but systematically few comparative experiments in the abdominal cavity. Subcutaneous passage tumors do not show localized growth or infiltration trend, but tumors were found within an abdominal wall muscle layer and in a peritoneum in the form of infiltration, adhesion to the peritoneum, the growth within the pelvic cavity and gastric wall infiltration in the experimental method. The infiltration from serous surface to mucosa layer was observed particularly in a digestive tract. It seems to be of significance that an infiltrating image was obtained." (page 171, left bottom column, the item of "624", line 5 to last line).

In view of this, it can be recognized that A2 describes the following invention (hereinafter referred to as the "A2 invention"):

"A nude mouse in which tumors were found within an abdominal wall muscle layer and in a peritoneum in the form of infiltration, adhesion to the peritoneum, the growth within pelvic cavity and gastric wall infiltration, obtained by cutting up subcutaneous passage tumors of fourth passage to sixth passage of a well-differentiated tubular

adenocarcinoma of stomach cancer, primary tumors and subcutaneous passage tumors of second passage into a size of 5x5x5 mm, and implanting into an abdominal wall muscle layer, muscle layer-peritoneum, intraperitoneal and gastric wall of a nude mice (nu/nu--BALB/C/A/BOM, spf) by a surgical procedure."

(B) Comparison

Comparing Inventions 1 to 10 with the A2 invention, these inventions are at least different from each other in that the animal is an animal model "for the metastasis of human neoplastic disease" in Inventions 1 to 10, whereas it cannot be said that the A2 invention is "a non-human animal model for metastasis" because it was a nude mouse with an infiltrating tumor but the metastasis was unknown and it cannot be recognized as an animal model for the use in studies and tests for metastasis in place of the metastasis of human neoplastic disease.

Comparing Inventions 11 to 19 with the A2 invention, they are at least different from each other in that the method is "a method of generating a non-human animal model for the metastasis of human neoplastic disease" in Inventions 11 to 19, whereas it cannot be said that the A2 invention is a method of generating "a non-human animal model for metastasis" because it cannot be recognized as an animal model for the use in studies and tests for metastasis in place of the metastasis of human neoplastic disease, while a nude mouse with an infiltrating tumor was prepared.

(C) Consideration

Regarding the above different features, similarly to the A1 invention, as discussed in the above item "3(5)A Reasons for invalidation 5-1 [Violation of Article 29(1)(iii) of the Patent Act (Novelty)]", in the above item "2(1) Ruling in the Intellectual Property High Court", the court rules that "it cannot be said in the Invention that 'metastasize', and 'take' or 'infiltrate' are used to have a similar level of technical significance" (Court decision, page 32, lines 18 to 19).

Consequently, it is obvious that the A2 invention is not "a non-human animal model for the metastasis of human neoplastic disease" of Inventions 1 to 3 and 6, nor is it obvious that the A2 invention is "a method of generating a non-human animal model for the metastasis of human neoplastic disease" of Inventions 11 to 13 and 16.

Therefore, it cannot be said that Inventions 1 to 3, 6, 11 to 13, and 16 are identical to the A2 invention.

Regarding the above different features, however, for reasons similar to the reasons described in the above "2(2) Inventions 1, 2, 11, 12" and "2(3) Inventions 3 to 10, 13, 19", Inventions 1 to 19 were easily conceivable by a person skilled in the art on the basis of the A2 invention and the inventions described in A3 and A4.

C Reason for invalidation 5-3 [Violation of Article 29(2) of the Patent Act (Inventive step)]

(A) The invention described in A3

In Evidence A No. 3, it can be seen from the description of "FIG. 3 Tissue Observation (Hc-4) lung metastatic fociH-E dying" (page 32, FIG. 3) that the lung metastatic foci were observed for Hc-4.

Further, this Hc-4 is recognized as being sampled before and after chemotherapy for cirrhotic liver with hepatoma of a 45-year-old male, in view of the description that "Among them three cases have taken and become capable of serial transplantation: the samples before and after chemotherapy for cirrhotic liver with hepatoma (Hc-3,4) of a 45-year-old male, differentiated hepatoma (Hc-5) of a 70-year-old male and hepatoblastoma (Hb-1) of a three-year-old male infant, which have been subcultured to a sixth passage, a second passage, and a fourth passage, respectively."(page 31, left column, line 31 to right column, line 3).

Further, "Remarkably, a subcultured second passage rat (Trial Decision's note: it is construed as a typographical error of "subcultured second passage mouse") formed a tumor mass with a size of about 1.5 cm as a result of the implantation of a piece of tumor mass into a liver at a deep region of a right flank region (FIG. 1). The tumor mass was a massive type, which had spread across the lobes with only a left lateral lobe being left. No ascites fluid or lymph node metastasis to hepatic portal region was observed, but a spherical metastasis with a diameter of about 2 mm was observed in the right lower lobe." (page 31, right column, line 18 to page 32, right column, line 1) The implanted tumor was a second passage of hepatoma tumor (Hc-4), which was sampled from a 45-year-old male after chemotherapy for a cirrhotic liver with hepatoma, and subcultured in a mouse.

Further, in view of "The mice used were male or female nude mice" (page 31, left column, lines 19 to 20), the mouse used for implantation was a nude mouse.

Comprehensively taking the above matters into account, it can be recognized that A3 describes the following invention (hereinafter referred to as the "A3 invention"):

"A nude mouse, wherein a second passage of hepatoma (Hc-4) sampled after chemotherapy from cirrhotic liver with hepatoma of a 45-year-old male is implanted into a deep region of a right flank region of the nude mouse, and as a result of implantation of a piece of tissue into a liver, a tumor mass of about 1.5 cm forms and spherical metastasis with a diameter of about 2 mm is observed in a right lower lobe."

(B) Comparison

Comparing Inventions 1 to 19 respectively with the A3 invention, these inventions are at least different from each other in that a tumor to be implanted is "a neoplastic tissue obtained from human organ" of Inventions 1 to 10 and "a neoplastic tissue from a human organ" of Inventions 11 to 19, and as mentioned in the above "3(1)D(A) Construction of 'a neoplastic tissue obtained from human organ' of Inventions 1 to 10 and 'a neoplastic tissue from a human organ' of Inventions 11 to 19", the tumor is "a very same neoplastic tissue itself sampled from a human organ", whereas in the A3 invention, the tumor is "a second passage of hepatoma (Hc-4) sampled after chemotherapy from cirrhotic liver with hepatoma of a 45-year-old male"; i.e., a cultivated neoplastic tissue.

(C) Consideration

A3 discloses that "Human tumor implanted in a nude mouse showed almost no metastasis. This is supposed to be an animal of immunodeficiency animal a change of biological nature of implanted tumor, or a death prior to metastasis due to a few case of

long-term survival since it was not conducted under an SPF environment. One possible major factor may be that the implanted site was a hypodermal tissue." (page 33, left column, lines 11 to 16).

Further, as described in the above "2(3) Inventions 3 to 10, 13 to 19" and the above "3(5)B(A) The invention described in A2", A1 and A2 respectively disclose that the implantation of the very same neoplastic tissue sampled from a human organ causes infiltration.

Further, in the above item "2(1) Ruling in the Intellectual Property High Court", the court rules that
"it was supposed as of the priority date of the Patent that malignant tumor became advanced in a living body as in the order of [1] tumor growth, [2] infiltration to adjacent tissue, and [3] the metastasis to the other tissue via blood vessels and lymph channels (A23, 41, 43), and it is recognized that it was generally known as a matter of common general knowledge of the process of cancer progression that metastasis would occur with some level of probability (frequency) in a stage where the infiltration of tumor was observed if the spread of infiltration was wide, or the metastasis was likely to occur due to a future spread of infiltration as time passed (A39, A44 to A48)." (Court decision, page 42, lines 5 to 11).

Consequently, it can be said that there was a motivation to adopt in the A3 invention "a human breast tissue diagnosed as infiltrating ductal carcinoma" of A1 regarding infiltration or "primary tumors" of a "well-differentiated tubular adenocarcinoma of stomach cancer" of A2 in place of "a second passage of hepatoma (Hc-4)", which was a tumor to metastasize that had been subjected to serial cultivation in view of the common general knowledge as of the priority date of the Patent that the metastasis is likely to be caused as the infiltration further spreads.

Therefore, Inventions 1 to 19 were easily conceivable by a person skilled in the art on the basis of the A3 invention and the inventions described in A1 and A2.

D Reason for invalidation 5-4 [Violation of Article 29(2) of the Patent Act (Inventive step)]
(A) The invention described in A4
a Implanted human hepatoma

A4 discloses that "It was 10 mice which were subjected to the subcostal insertion of a needle into a right flank region of nude mouse to implant into a liver, but only two mice consisting of a second passage of Hc-3 and a third passage of Hc-5 achieved success. Implantation into a liver was conducted by opening the abdominal cavity for two of the sixth passage of Hc-4. Both have taken, but one has gotten wasting disease 18 days after implantation, the other 38 days after implantation, and both have died. After death, the presence of hepatoma was observed for all four mice. Further, a lung metastasis was observed in the second passage of Hc-3 implanted into a right subcostal region[27)]." (page 306, left column, lines 16 to 23).

According to (page 303, right column, line 19 to page 304, left column, line 9), the "second passage of Hc-3" in which a metastasis to lung was observed is derived

from the one "who was hospitalized in First Surgery Department of Hokkaido University and underwent laparotomy from November 1976 to May 1978" and "the implantation system is described as Hc for hepatocellular tumor, and Hb for hepatoblastoma, which are respectively numbered in the order of implantation." Therefore, it can be seen as a second passage of human hepatocellular cancer.

Further, regarding implanted human hepatoma, it discloses that "a piece of tissue with 1 to 2 mm square prepared by the aforesaid method was implanted into a liver middle lobe by use of a needle with an outer diameter of 2.5 to 1.5 mm." (page 304, left column, lines 35 to 37), "aforesaid method" used herein means that "When tumors that have undergone first passage or serial transplantation reached a certain size, the nude mouse was cardiopunctured under anesthesia with ether, followed by blood drawing, and then tumors were aseptically isolated. This tumor was immediately put into a physiological saline, and cut out into about 2 mm square" (page 304, left column, lines 24 to 27). Therefore, it can be seen that implanted human hepatoma was obtained by isolating a subcultured human hepatoma from under the skin of nude mouse, and cutting out into a piece of tissue of 1 to 2 mm square.

b Passage

On page 304, left column, lines 23 to 29, it describes "(b) Serial transplantation When tumors that have undergone first passage or serial transplantation reached a certain size, ... (Omitted)... tumors were aseptically isolated. This tumor was immediately put into a physiological saline, and cut out into about 2 mm square, and one or several pieces thereof were implanted subcutaneously into a lateral region or a dorsal region of another new nude mouse by use of a needle." In view of this, it can be seen that passage means passage by implanting a tumor under the skin of a nude mouse for passage; i.e., subcutaneous passage.

c Mouse in implantation into liver

On page 304, left column, line 34, it describes "(c) Implantation into a nude mouse liver". Thus it can be seen as a nude mouse subjected to implantation that is implanted into a liver.

Furthermore, both the nude mouse for implantation and the nude mouse for subcutaneous passage are "male and female BALB/c nude mice (nu/nu) raised under a specific pathogen free condition in Central Institute for Experimental Animals at 5 to 7 weeks old" (page 303, the right column, lines 11 to 13). But as aforementioned, these mice are different in the purpose for implantation and implanting organ. Thus nude mice are distinguished by adding the uses of "for implantation" and "for passage" to nude mice.

d Implantation and metastasis to a liver

It can be seen from the description of page 306, left column, lines 16 to 23 that the subcostal insertion of a needle into a right flank region of a nude mouse to implant into a liver achieved success only in two of the second passage of Hc-3 and the third passage of Hc-5. Further, it can be seen that "a lung metastasis was observed in the second passage of Hc-3" as a result of "subcostal insertion of a needle into a right flank region of nude mouse to implant into a liver".

Further, in view of "subcostal insertion of a needle into a right flank region of

nude mouse to implant into a liver", it is obvious that the implantation was conducted into a liver.

In addition, on page 306, left column, lines 16 to 23, "27)" is cited as a document. Document "27)" is "Junichi UCHINO, Takehiko KUWAHARA and others: Implantation into a nude mouse of human hepatoma, Journal of Clinical and Experimental Medicine, 104:31, 1978." (page 313, right column), which corresponds to A3. As mentioned in the above "3(5)C(A) The invention described in A3", the metastasis achieved success in "a second passage of hepatoma tumor (Hc-4), which was sampled after chemotherapy from a 45-year-old male bearing a cirrhotic liver with hepatoma, and subcultured in a mouse". On the other hand, it was a "second passage of Hc-3" in A4 that caused a metastasis to lung. Further, regarding tumors that caused a metastasis to lung, there is no particular inconsistency between A3 and A4. It is recognized that a metastasis to lung was observed in a second passage of Hc-4 in A3, and a metastasis was observed in a second passage of Hc-3 in A4.

e Infiltration

On page 312, the right column, lines 14 to 15, it describes "6) Metastasis was observed in only one where an infiltrative tumor was formed in a liver, which was a lung metastasis." A4 describes a metastasis to lung for only the one where "a lung metastasis was observed in the second passage of Hc-3 implanted into a right subcostal region" (page 306, left column, lines 22 to 23). Therefore, it can be seen that a metastasis to lung was observed in "the second passage of Hc-3 implanted into a right subcostal region", and an infiltrative tumor was formed.

f Summary

Comprehensively taking the above matters into account, it can be recognized that A4 describes the following invention (hereinafter referred to as the "A4 invention"):
"A nude mouse, in which a metastasis to lung was observed and an infiltrative tumor was formed, obtained by isolating a second passage tumor of human hepatocellular tumor Hc-3 in which a human hepatocellular tumor Hc-3 has undergone subcutaneous passage in a nude mouse for passage to obtain a piece of tissue of 1 to 2 mm square, and subcostally inserting a needle into a right flank region of a nude mouse for implantation to implant into a liver."

(B) Comparison

Comparing Inventions 1 to 19 respectively with the A4 invention, these inventions are at least different from each other in that the tumor to be implanted is "a neoplastic tissue obtained from human organ" in Inventions 1 to 10 and "a neoplastic tissue from a human organ" in Inventions 11 to 19, and as mentioned in the above "3(1)D(A) Construction of 'a neoplastic tissue obtained from human organ' of Inventions 1 to 10 and 'a neoplastic tissue from a human organ' of Inventions 11 to 19", the tumor is "the very same neoplastic tissue itself sampled from a human organ", whereas in the A4 invention, the tumor is "a second passage tumor of human hepatocellular tumor Hc-3 in which a human hepatocellular tumor Hc-3 has undergone subcutaneous passage in a nude mouse for passage"; i.e., a cultivated neoplastic tissue.

(C) Consideration

The different feature is similar to the case of the above "3(5)C(C) Consideration". It can be said that there was a motivation to adopt in the A4 invention "a human breast tissue diagnosed as infiltrating ductal carcinoma" of A1 regarding infiltration or "primary tumors" of a "well-differentiated tubular adenocarcinoma of stomach cancer" of A2 in place of "a second passage tumor of human hepatocellular tumor Hc-3 in which a human hepatocellular tumor Hc-3 has undergone subcutaneous passage in a nude mouse for passage", which was a tumor to metastasize that had been subjected to serial cultivation in view of the common general knowledge as of the priority date of the Patent that the metastasis is likely to be caused as the infiltration further spreads.

Therefore, Inventions 1 to 19 were easily conceivable by a person skilled in the art on the basis of the A4 invention and the inventions described in A1 and A2.

E Reasons for invalidation 5-5 to 5-7 [Violation of Article 29(1)(iii) of the Patent Act (Novelty) or Violation of Article 29(2) of the Patent Act (Inventive step)]

As mentioned in the above "3(1)D(A) Construction of 'a neoplastic tissue obtained from human organ' of Inventions 1 to 10 and 'a neoplastic tissue from a human organ' of Inventions 11 to 19", It is reasonable to understand that the "neoplatic tissue from a human organ" of Inventions 1 to 10 is the very same neoplastic tissue sampled from a human organ, and it is also reasonable to understand that the "neoplatic tissue from a human organ" of Inventions 11 to 19 is the very same neoplastic tissue itself sampled from a human organ.

Therefore, the auxiliary request of Reason for Invalidation 5-5 to Reason for Invalidation 5-7 needs not be considered, since it is based on the premise that a "neoplatic tissue from a human organ" is construed as including ones that have undergone subcutaneous passage.

No. 7 Conclusion

As seen above, the patents according to Inventions 1 to 19 have been granted in violation of the provision of Article 29(2) of the Patent Act. Consequently, the patents correspond to the provision of Article 123(1)(ii) of the Patent Act. Therefore, the Patent should be invalidated.

Accordingly, the costs in connection with the trial shall be borne by the demandee under the provision of Article 61 of the Code of Civil Procedure which is applied mutatis mutandis in Article 169 of the Patent Act, and the trial decision shall be made as described in the Conclusion.

July 7, 2017

Chief administrative judge: NAKAJIMA, Yoko
Administrative judge: YAMAMOTO, Kyoko
Administrative judge: TAKABORI, Eiji