NOTE: This order is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: HARITHA SAMARANAYAKE, JERE PIKKARAINEN, ANN-MARIE MAATTA, SEPPO YLA-HERTTUALA,
Appellants

2020-1158

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 13/877,246.

ON PETITION FOR PANEL REHEARING

Before DYK, O'MALLEY, and REYNA, *Circuit Judges*.

PER CURIAM.

O R D E R

Appellants Ann-Marie Maatta, Jere Pikkarainen, Haritha Samaranayake and Seppo Yla-Herttuala filed a petition for panel rehearing.

Upon consideration thereof,

IT IS ORDERED THAT:

The petition for panel rehearing is denied.

The mandate of the court will issue on October 26, 2020.

FOR THE COURT

September 30, 2020	/s/ Peter R. Marksteiner
Date	Peter R. Marksteiner
	Clerk of Court

NOTE: This order is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: HARITHA SAMARANAYAKE, JERE PIKKARAINEN, ANN-MARIE MAATTA, SEPPO YLA-HERTTUALA,
Appellants

2020-1158

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 13/877,246.

ON MOTION

Before DYK, O'MALLEY, and REYNA, *Circuit Judges*.

PER CURIAM.

O R D E R

Appellants move for the court to strike pages 62-151 (SAppx6-44 and SAppx56-106) from Director Iancu's supplemental appendix in ECF No. 18, or, in the alternative, for leave to introduce new evidence to rebut the information presented on the pages in question. The Director responds in opposition, and Appellants reply.

Upon consideration thereof,

IT IS ORDERED THAT:

The motion is denied.

FOR THE COURT

September 2, 2020
Date

/s/ Peter R. Marksteiner
Peter R. Marksteiner
Clerk of Court

NOTE: This disposition is nonprecedential.

United States Court of Appeals for the Federal Circuit

IN RE: HARITHA SAMARANAYAKE, JERE PIKKARAINEN, ANN-MARIE MAATTA, SEPPO YLA-HERTTUALA,
Appellants

2020-1158

Appeal from the United States Patent and Trademark Office, Patent Trial and Appeal Board in No. 13/877,246.

JUDGMENT

J. MARK POHL, Pharmaceutical Patent Attorneys, LLC, Morristown, NJ, argued for appellants.

AMY J. NELSON, Office of the Solicitor, United States Patent and Trademark Office, Alexandria, VA, argued for appellee Andrei Iancu. Also represented by MARY L. KELLY, THOMAS W. KRAUSE.

THIS CAUSE having been heard and considered, it is

ORDERED and ADJUDGED:

PER CURIAM (DYK, O'MALLEY, and REYNA, *Circuit Judges*).

AFFIRMED. See Fed. Cir. R. 36.

ENTERED BY ORDER OF THE COURT

September 2, 2020	/s/ Peter R. Marksteiner
Date	Peter R. Marksteiner
	Clerk of Court

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte HARITHA SAMARANAYAKE,
JERE PIKKARAINEN, ANN-MARIE MAATTA,
SEPPO YLA-HERTTUALA[1]

Appeal 2018-001996
Application 13/877,246
Technology Center 1600

Before RICHARD M. LEBOVITZ, JEFFREY N. FREDMAN, and DAVID COTTA, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

REQUEST FOR REHEARING

This is a request for rehearing under 37 C.F.R. 41.79 ("Req. Reh'g") of the Decision on Appeal entered May 30, 2019 ("Dec. App.").

Appellants argue that three erroneous factual findings were made in the Decision on Appeal. Req. Reh'g 1. We have considered Appellants' arguments, but we are not persuaded to change the outcome of the Decision. Each of three arguments made by Appellants are discussed below.

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[1] The Appeal Brief ("Appeal Br." entered July 27, 2016) lists Trizell Limited as the Real Party in Interest. Appeal Br. 1.

Is Hegi (2008) of record?

Appellants contend that Hegi (*J. Clin. Oncol.* 26: 4189–4199, 2008) ("Hegi (2008)") is not of record. Req. Reh'g 1.

Hegi (2008) was cited in the Answer, but not in the Final Office Action, as part of a new ground of rejection.[2] Ans. 14, 19. The Examiner stated that Hegi (2008) was cited in an Information Disclosure statement ("IDS"). Ans. 14, 19. The Decision on Appeal agreed that Hegi was of record because it was cited in an IDS. Dec. App. 18. However, as pointed out by Appellants, the "Hegi" publication listed in the IDS is not the same Hegi (2008) publication cited in the Answer. Req. Reh'g 1. Thus, the statement that Hegi (2008) was listed on the IDS is an error.

Nonetheless, we do not agree with Appellants that Hegi (2008) is not of record. Hegi (2008) was made of record in the Examiner's Answer because the Examiner provided a full citation to it. Even if the publication was not listed by the Examiner on a disclosure form, this deficiency does not mean it is not "of record." The Manual of Patent Examining Procedures ("MPEP") (Ninth Edition, Last Revised January 2018) explains the purpose of listing a publication on a disclosure form:

> MPEP 707.05(a) Copies of Cited References
> . . .
> To assist in providing copies of, or access to, references, the examiner should:
> (A) Type the citation of the references on form PTO-892, "Notice of References Cited" using OACS;

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[2] Appellants had the option to reopen prosecution in response to the new ground, but did not do so and addressed the Hegi (2008) reference in the Reply Brief (*see* Reply Br. 12).

> (B) Include in the eRed Folder all of the references cited by the examiner which are to be furnished to the applicant.

The MPEP does not indicate that the failure to list a publication on form PTO-892 establishes that a publication is "not of record" as stated by Appellants. Rather, the purpose is to assist in providing a copy or access to the publication. The Answer provided Appellants with the complete citation to Hegi (2008) in the Answer and thus Hegi (2008) is recorded in the examination record. Appellants did not provide legal basis for the assertion Hegi (2008) is not of record, that they lacked access to the reference, or that they were prejudiced in any way.

Antibody detection in the '855 patent

In the Decision on Appeal, Appellants' statement that "certain cancer therapies should not be given to immunocompetent patients" was addressed. Dec. App. 9. In addressing this argument, the declaration by Mr. Seppo Yla-Herttuala describing results reported in U.S. Pat. 6,579,855 ("the '855 patent") was discussed. Mr. Yla-Herttuala is a co-inventor of the '855 patent and also a co-inventor of the application involved in this appeal.

It was stated in the Decision on Appeal:

> The declaration [describing the results in U.S. Pat. 6,579,855] does not say patients were "only" treated "if" antivirus antibody was below the detectable level as asserted by Appellants. Instead, Mr. Yla-Herrtuala [Yla-Herttuala] states that antibody was not measured before gene transfer because it would have been below detection levels. The apparent reason for this is because the patients had not yet been exposed to the viral vector and had not yet developed an immune reaction it.

Dec. App. 10.

Appellants state the Decision erred in finding that antibody was not measured in the '855 patent before gene transfer. Req. Reh'g 3. We agree this is an error, but the error does not change our conclusion that patients having a normal immune response were treated in the cited prior art publication. Dec. App. 9. The reasoning set forth in the Decision on Appeal is unchanged.

We clarify that the '855 patent states that antibodies were measured before *and* after gene therapy. '855 patent, col. 4: 9–10, 53–54. However, Mr. Yla-Herttuala makes the following statement in his declaration:

> The patent does not disclose the measure of anti-virus antibodies measured before gene transfer.
>
> This is because as measured before gene transfer, anti-virus antibody was below detectable limits for all patients.

Yla-Herttuala ¶ 3.

Thus, antibody was measured, but not reported in the '855 patent before gene transfer because it was "below detectable limits."

Does Ulasov teach a transgene?

Claim 1 recites a step of "administering to said human patient a viral gene therapy vector having a transgene." As explained in the Decision on Appeal, the Examiner found that Ulasov describes introducing the E1A gene into a viral vector and driving its expression with a survivin promoter, which the Examiner determined met the claimed requirement of a "transgene." As explained in the Decision:

> Ulasov discloses "CRAd-Survivin-pk7 (CRAd-S-pk7), a novel oncolytic adenoviral vector that utilises the survivin promoter to drive E1A expression and binds to heparan sulphate proteoglycans expressed on malignant glioma." Ulasov 1155.

> The E1A gene, normally present in the virus, was not the copy that was used in Ulasov's experiment. Instead, Ulasov teaches that "the survivin-controlled E1 expression cassette was placed in the native E1 region of the Ad genome to avoid nonspecific viral replication." *Id.* For this reason, we do not agree with Appellants that reading the term "transgene" on the E1 expression cassette would "read" the limitation out of the claim, allegedly because all the viral DNA would be considered a transgene. Reply Br. 3. Rather, the Examiner correctly found that the E1A expression cassette is a "transgene" because it was introduced into the adenovirus and is not native to it. The E1A expression cassette is an E1 gene operably connected to the non-native survivin promoter.

Dec. App. 7–8.

Appellants contend that the Examiner erred in finding that Ulasov describes a "transgene," and that such finding was made only after prosecution had been closed ("She raised it only *after* she had closed the record to the introduction of rebuttal evidence."). Req. Reh'g 3–4. Appellants also state that the Board invited Appellants to provide rebuttal evidence, and "[i]n response to the Board's kind invitation to do so, however, Appellant here provides the rebuttal evidence you request: a *Declaration* (July 2019) from Professor Yla-Herttuala explaining how the voluminous evidence of record contradicts the Examiner's incorrect interpretation of the term 'transgene.'" Req. Reh'g 4.

While the Examiner did not raise the transgene issue with respect to Ulasov until the Answer, Appellants had the opportunity to reopen prosecution (Ans. 33) and introduce new evidence at that time. Appellants chose not to reopen prosecution, but instead filed a Reply Brief. The Declaration was not provided at this time. The Decision on Appeal did not subsequently "invite" Appellants to provide rebuttal evidence. New

evidence is not permitted in a Request for Rehearing "except as permitted by paragraphs (a)(2) through (a)(4) of" 37 C.F.R § 41.52(a). Appellants did not establish that such conditions were met, and thus the new Declaration is not permitted and has not been considered.

The term "transgene" does not appear in the Specification as originally filed. In the Appeal Brief, Appellants identified page 1, line 6 of the Specification as providing support for the term. Appeal Br. 1. The complete sentence spanning line 6 of the Specification is reproduced below:

> Herpes simplex virus type 1, thymidine kinase (HSV-tk) gene therapy is based on the prodrug activating enzyme that converts a non-toxic compounds such as ganciclovir, (GCV) into a toxic metabolite.

Spec. 1:6–8. This disclosure does not elucidate the meaning of "transgene."

In the Reply Brief, Appellants defined a "transgene" as "foreign genetic material." Reply Br. 2. Appellants further state that the transgene must code for a polypeptide. Req. Reh'g 4. Appellants also argue that the E1 gene is native to adenovirus and therefore not a foreign gene. *Id.* at 3.

The E1A gene utilized in Ulasov codes for a protein and is not the same copy that is present in the vector, but instead was introduced into the vector. Ulasov 1155. The E1A gene is therefore "foreign" to the adenoviral genome present in the vector because it is not the "native" copy present in the adenoviral genome. Accordingly, we decline to change our determination that Ulasov describes a transgene consistent with the broadest reasonable interpretation of that term as it would have been understood by an ordinary artisan. "[D]uring patent prosecution when claims can be amended, ambiguities should be recognized, scope and breadth of language

explored, and clarification imposed." *In re Zletz*, 893 F.2d 319, 321 (Fed. Cir. 1989).

REHEARING DENIED

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte HARITHA SAMARANAYAKE,
JERE PIKKARAINEN, ANN-MARIE MAATTA,
SEPPO YLA-HERTTUALA[1]

Appeal 2018-001996
Application 13/877,246
Technology Center 1600

Before RICHARD M. LEBOVITZ, JEFFREY N. FREDMAN, and DAVID COTTA, and *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

The rejected claims in this appeal are directed to a viral gene therapy vector for treating cancer. The Examiner rejected the claims under 35 U.S.C. § 103 as obvious and 35 U.S.C. § 102 as anticipated. Pursuant to 35 U.S.C. § 134, Appellants appeal the Examiner's determination that the claims are unpatentable. We have jurisdiction for the appeal under 35 U.S.C. § 6(b). The Examiner's decision is affirmed-in-part.

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[1] The Appeal Brief ("Appeal Br." entered July 27, 2016) lists Trizell Limited as the Real Party in Interest. Appeal Br. 1.

STATEMENT OF THE CASE

This appeal is related to Appeal No. 2017-003624 of Application 13/858,393. A decision was entered Nov. 13, 2017. The application was abandoned on May 3, 2018.

The Examiner withdrew all of the rejections set forth in the Final Office Action, and set forth 12 new grounds of rejection in the Examiner's Answer. The new grounds of rejection are as follows:

1. Claim 41 under pre-AIA 35 U.S.C. § 102(b) as anticipated by Ulasov et al. (*Combination of adenoviral virotherapy and temozolomide chemotherapy eradicates malignant glioma through autophagic and apoptotic cell death in vivo,* Br. J. Cancer, 100(7): 1154–1164, 2009, (IDS)) ("Ulasov"). Ans. 2.

2. Claims 1, 9, 14, 15, 27, 28, 31, and 33 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov and Balmaceda et al. (*Multi-Institutional Phase II Study of Temozolomide Administered Twice Daily in the Treatment of Recurrent High-Grade Gliomas,* Am. Cancer Soc'y, 112(5): 1139–46, 2008 (IDS)) ("Balmaceda"). Ans. 4.

3. Claims 1–8, 41, and 42 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, King et al. (*High-Capacity Adenovirus Vector-Mediated Anti-Glioma Gene Therapy in the Presence of Systemic Antiadenovirus Immunity*, J. of Virology, 82(9): 4680–4684, 2008, (IDS)) ("King"), and Rainov et al. (*Temozolomide enhances herpes simplex virus thymidine kinase/ganciclovir therapy of malignant glioma,* Cancer Gene Therapy, Vol. 8(9), 662–668, 2001 (IDS)) ("Rainov"). Ans. 6.

4. Claims 1 and 10–12 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, and Chiocca et al. (*A Phase I Open-Label,*

Dose-Escalation Trial of Injection with an E1B-Atteniated Adenovirus, ONYX-015, into the Peritumoral Region of Recurrent Malignant Gliomas, in the Adjuvant Setting, Mol. Ther., 10(5): 958- 966, 2004) ("Chiocca (2004)"). Ans. 9.

5. Claims 1 and 13 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, and Stupp et al. (*Radiotherapy plus Concomitant and Adjuvant Temozolomide for Glioblastoma,* N. Engl. J. Med., 352*:* 987-996, 2005 (IDS)) ("Stupp"). Ans. 10–11.

6. Claim 1 and 16 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, and Brandes et al. (*First-Line Chemotherapy With Cisplatin Plus Fractionated Temozolomide in Recurrent Gliblastoma Multiforme: A Phase II Study of the Gruppo Italiano Cooperativo di Neuro-Oncologia,* J. Clin. Oncol. 22(9):1598-604, 2004) ("Brandes"). Ans. 12.

7. Claims 1 and 17 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, and Yu (WO 2008/008767 A2, published Jan. 17, 2008). Ans. 13.

8. Claims 1 and 18 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, and Hegi et al. (*Correlation of O^6-Methylguanine Methyltransferase (MGMT) Promoter Methylation With Clinical Outcomes in Glioblastoma and Clinical Strategies to Modulate MGMT Activity*, J. Clin. Oncol. 26:4189-4199, 2008 (IDS)) ("Hegi (2008)"). Ans. 14.

9. Claims 19 and 20 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of "Preliminary Cerepro (R) Phase III Results Meet Primary Endpoint-Operable Primary Malignant Glioma" (2008) (http://www.medicalnewstoday.com/articles/116938.php);

http://www.virtualtrials.com /news3.cfmitem=4320&showtext=y ("Medical News Today") and Immonen et al. (*AdvHSV-tk Gene Therapy with Intravenous Ganciclovir Improves Survival in Human Malignant Glioma: A Randomised, Controlled Study*, Mol. Ther. 10: 967-972, 2004 (IDS)) ("Immonen"). Ans. 15–16.

10. Claims 19, 20, and 21–26 under pre-AIA 35 U.S.C. § 103(a) as obvious in view Medical News Today, Immonen, Balmaceda, and Hegi (2008). Ans. 17.

11. Claims 27, 29–32, and 35–40 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, Immonen, and Rainov. Ans. 20.

12. Claims 27 and 34 under pre-AIA 35 U.S.C. § 103(a) as obvious in view of Ulasov, Balmaceda, Immonen, and Stupp. Ans. 23.

REJECTION 1. ANTICIPATION BY ULASOV

The Examiner rejected claim 41 as anticipated by Ulasov. Claim 41 is reproduced below:

> 41. A kit comprising a viral vector and temozolomide, said viral vector and said temozolomide present in an amount effective to treat brain cancer in a human patient.
>
> The Examiner found that Ulasov describes:
>
> a combination of a conditionally replicative adenoviruses (CRAds) vector expressing the gene E1A under transcriptional control of the survivin promoter (CRAd-S-pk7) and temozolomide (TMZ), a cytotoxic agent, in amounts effective to treat malignant glioma (p 1154-1161; (p 1156, 2nd column) in amount effective to treat human gliomas (p 1164, 1st column under discussion).

Ans. 3.

The "conditionally replicative adenoviruses (CRAds) vector", which is "CRAd-S-pk7," corresponds to the claimed "viral vector." Ulasov evaluated the efficacy of CRAd-S-pk7 and temozolomide (TMZ) *in vivo* in a mouse to which a human glioma cell line U87MC had been subcutaneously administered. Ulasov 1159. Ulasov discloses that a "dose of 10 mg kg^{-1} body weight was used, which corresponded to a dose of 25 mg kg^{-1} m^{-2} in humans." Ulasov 1155 (1st col.). Appellants argue that this dosage is not "in an amount effective to treat brain cancer in a human patient" as recited in claim 41. As evidence of this, Appellants cite Balmaceda which discloses dosages of TMZ used to treat patients with high grade glioma. Balmaceda discloses:

> An initial oral dose of 200 mg/m^2 of temozolomide was followed by 9 consecutive doses of 90 mg/m^2 every 12 hours. Treatment cycles were repeated every 28 days. Doses were escalated to 100 mg/m^2 twice daily in the absence of unacceptable toxicity or were reduced if unacceptable toxicity occurred.

Balmaceda 1139 (Abstract).

The evidence supports Appellants' argument that the dosages of TMZ administered in Ulasov are different from those said by Balmaceda to be effective in human patients. Specifically, the dosage of TMZ in Ulasov is listed as 25 mg *per kg, per meter squared*, while Balmaceda's are expressed on a patient basis of 200, 100, and 90 mg *per meter squared* per patient. The Examiner did not explain how the doses in Ulasov used to treat a human glioma xenograft in mice would be effective to treat brain cancer in a human patient. The Examiner has the burden of establishing that the dosages used in Ulasov were the same or in the same range as those disclosed in Balmaceda and would be effective and absent "unacceptable toxicity"

(Balmaceda 1139 (Abstract)) to treat brain cancer in a human patient as required by the claim. Because this burden was not met, the anticipation rejection of claim 41 is reversed.

REJECTION 2. OBVIOUSNESS BASED ON ULASOV AND BALMACEDA

The Examiner rejected claims 1, 9, 14, 15, 27, 28, 31, and 33 as obvious based on Ulasov and Balmaceda.

Claims 1, 9, 14, 15, 31, and 33

Claim 1, which is representative of the rejected claims, is reproduced below:

> 1. A method of treating cancer in a human patient, said method comprising:
> - diagnosing a cancer in a human patient,
> - administering to said human patient a viral gene therapy vector having a transgene, and
> - within about 30 days of said administration of said viral gene therapy vector, administering to said human patient a cytotoxic agent other than gancylovir [*sic*, ganciclovir; this error is repeated throughout the claims].

The Examiner found that Ulasov describes administering a conditionally replicative adenoviruses (CRAds) vector expressing the gene E1A under transcriptional control of the survivin promoter (CRAd-S-pk7) and temozolomide (TMZ), a cytotoxic agent. Ans. 3, 4. The Examiner found that CRAd-S-pk7 is "a viral gene therapy vector having a transgene" as recited in claim 1, where the E1A gene under control of the survivin is the claimed transgene.

The Examiner recognized that "Ulasov does not per se teach administration into a human or an immunocompetent human patient" as

required by the claims, but found that Balmaceda teaches administering TMZ to human patients with brain cancer. Ans. 5. The Examiner stated it would have been obvious to one of ordinary skill in the art to combine the teaching of Ulasov and Balmaceda to administer adenovirus vector and TMZ, a "cytotoxic agent" as required by the claims, to a human subject as disclosed by Balmaceda, to treat malignant glioma, with reasonable expectation of success. Ans. 6. The Examiner found that the skilled worker would have been "motivated to do so to receive the expected benefit of combination therapy in [a] human patient." *Id.*

Appellants argue that Ulasov does not describe a transgene. Reply Br. 2. Appellants argue that the gene determined by the Examiner to be a transgene is the viral gene E1, which is native to adenovirus, and therefore is not a "'trans' (foreign) gene." Reply Br. 3. Appellants contend that it could be argued that "viral DNA is by definition foreign to the infected cell, so *all* viral DNA is transgene, including Ulasov's E1," but that "interpretation. . . would render the term 'transgene' redundant to the term 'virus' . . . [and] would read out of the claim an entire phrase: 'viral gene therapy vector having a transgene' would simply mean 'virus.'" *Id.*

We are persuaded that the viral E1 gene used by Ulasov is a "transgene" as determined by the Examiner.

Ulasov discloses "CRAd-Survivin-pk7 (CRAd-S-pk7), a novel oncolytic adenoviral vector that utilises the survivin promoter to drive E1A expression and binds to heparan sulphate proteoglycans expressed on malignant glioma." Ulasov 1155. The E1A gene, normally present in the virus, was not the copy that was used in Ulasov's experiment. Instead, Ulasov teaches that "the survivin-controlled El expression cassette was

placed in the native El region of the Ad genome to avoid nonspecific viral replication." *Id.* For this reason, we do not agree with Appellants that reading the term "transgene" on the E1 expression cassette would "read" the limitation out of the claim, allegedly because all the viral DNA would be considered a transgene. Reply Br. 3. Rather, the Examiner correctly found that the E1A expression cassette is a "transgene" because it was introduced into the adenovirus and is not native to it. The E1A expression cassette is an E1 gene operably connected to the non-native survivin promoter.

Appellants also argue that claim 1 requires a viral gene therapy vector having a transgene and that neither Ulasov nor Balmaceda describe such a vector. Reply Br. 2. Appellants state that "Ulasov teaches adenovirus. In contrast, a 'vector' is a virus/plasmid etc. which delivers foreign genetic material *(e.g.,* a transgene) for expression in a host cell." *Id.*

This argument is not persuasive. First, Appellants have not provided objective evidence of their definition of a "vector" with, e.g., a definition in a scientific publication or expert testimony. Second, as explained above, Ulasov teaches a "transgene" expression cassette in its adenovirus. Thus, even under Appellants' definition, Ulasov describes the claimed viral vector because it delivers a transgene to a host cell.

For the foregoing reasons and those of the Examiner, the obviousness rejection of claim 1, and of claims 9, 14, 15, 31, and 33, which were not argued separately, is affirmed. 37 C.F.R. § 41.37(c)(1)(iv).

Claim 27

Independent claim 27 is similar to claim 1, but requires administering the viral gene therapy vector and cytotoxic agent to "an immunocompetent human patient." The term "immunocompetent" does not appear in the Specification nor is it defined by Appellants. We interpret it to mean a patient with a normal immune system typically found in a healthy human that produces a normal immune response.

Appellants contend that Balmaceda fails to teach "immune competent patients", but do not identify any teaching in Balmaceda that suggests that the patient population treated in Balmaceda is immunocompromised or lacking a normal immune response. Reply Br. 4–5. Absent such a suggestion, we interpret Balmaceda as disclosing the treatment of patients having normal immune response.

Appellants argue that certain cancer therapies should not be given to immunocompetent patients, citing a declaration by one of the inventors Sepp Yla-Herrtuala (dated June 2, 2014) which Appellants assert teaches: "screened human cancer patients, and then treated the patient only if 'anti-virus antibody was below detectable limit.'" Reply Br. 4.

We find that Appellants' interpretation of what Mr. Yla-Herrtuala stated in the declaration is not supported by his actual statement. Mr. Yla-Herrtuala stated:

> 2. The patent at col. 4, lines 9-10 says, "Anti-virus antibodies were measured before and two weeks after the gene transfer."
>
> 3. The patent at Table 1, 9th column ("Virus ab") provides the measure of antivirus antibodies measured two weeks after the gene transfer. The patent does not disclose the measure of anti-virus antibodies measured before gene transfer. This is because

> as measured before gene transfer, anti-virus antibody was below detectable limit for all patients.

The declaration does not say patients were "only" treated "if" antivirus antibody was below the detectable level as asserted by Appellants. Instead, Mr. Yla-Herrtuala states that antibody was not measured before gene transfer because it would have been below detection levels. The apparent reason for this is because the patients had not yet been exposed to the viral vector and had not yet developed an immune reaction it. Accordingly, we do not agree that the statements in the declaration support Appellants' argument that Balmaceda does not treat immunocompetent patients as required by claim 27.

For the foregoing reasons, the obviousness rejection of claim 27 is affirmed.

Claim 28

Claim 28 depends from claim 27, and further recites: "wherein said viral gene therapy vector is administered in an amount of about 3×10^3 cfu."

The Examiner found that Ulasov discloses "a dose of 3×10^9 vp per mouse injected (one or two injections)" and that it would have been "obvious to an ordinary skill in the art to convert . . . a dose of 3×10^9 vp to cfu and thus, a dose of 3×10^9 vp overlap[s] with the claimed cfu range." Ans. 5. The Examiner also found that it would be routine optimization to discover the optimal dose of virus because it is "design effective variable." *Id.*

The Examiner did not meet the burden of establishing that the claimed dosage would have been *prima facie* obvious to one of ordinary skill in the art. The Examiner states that it would be obvious to convert that "vp" units

to "cfu" and that the converted doses "overlap" with the claimed amounts, but provided no explanation of how the conversion was made, nor did the Examiner provide the calculations upon which the assertion was made. Consequently, the rejection of claim 28 is reversed.

REJECTION 3. OBVIOUSNESS BASED ON ULASOV, BALMACEDA, KING, & RAINOV

Claims 2, 3, 8, and 42

Claim 2, which depends from claim 1, further recites that the transgene codes for thymidine kinase. Claim 3 depends from claim 2 and further recites administering ganciclovir ("GCV") to the human patient. Claim 8 depends from claim 1 and further recites that the administration of the cytotoxic agent other than ganciclovir lasts for up to 50 days. Claim 42, which depends from claim 41, further recites that the viral vector comprises thymidine.[2] Thus, the claims require the vector/GCV combination and a

[2] Claim 2, 3, and 42 further narrow the claim to a specific type of viral vector that comprises the thymidine kinase gene. The mechanism in which TK viral vectors kill cells is different from the viral vector described in Ulasov. The TK vectors use ganciclovir (GCV) to make a toxic compound that kills tumor cells, while Ulasov uses a conditionally replicative adenovirus that preferentially replicates in and kills tumor cells. Ulasov 1154. For this reason, we do not consider the teaching in Ulasov regarding the success of its viral vector in combination with TMZ to be specifically pertinent to the narrower claims utilizing a different viral vector which kills cells by a different mechanism.

cytotoxic agent (recited in claim 1). The Examiner identified the teaching of TMZ in the prior art as the claimed cytotoxic agent.

The Examiner found that King describes gene therapy for treating glioblastoma multiforme (GBM) comprising administering an adenovirus carrying the thymidine kinase gene. Ans. 6. The Examiner found that King administered ganciclovir (Ans. 7), which was known at the time of invention to be converted by the enzyme thymidine kinase to a toxic substance that kills dividing cells (Ans. 16). The Examiner found it obvious to use King's vector in Ulasov to treat human patients because King discloses it as a high capacity vector which "induces tumor regression and long-term survival in an intracranial glioma model." Ans. 7. The Examiner further found that Rainov describes administering the adenoviral vector HSV-TK (HSV is human simplex virus; TK is thymidine kinase), GCV, and TMZ ("cytotoxic agent"), meeting the corresponding limitations of the claims.

Appellants argue that while Rainov reported *in vitro* synergy of the combination of vector/GCV and TMZ when applied to cell lines, Rainov did not report synergy in the *in vivo* model. Reply Br. 6–8. For this reason, Appellants argue "Rainov teaches a reasonable expectation of failure, not success, in the claimed *in vivo* method." Reply Br. 8. Appellants further argue that because TMZ is cytotoxic, and because Rainov describes no added benefit to adding to TMZ to the vector/GCV treatment, one of ordinary skill in the art would not have had reason to use the combination of the vector/HCV and TMZ to treat human patients. Reply Br. 9. In other words, Appellants argue that there would be no reason to administer a TMZ and vector/GCV combination to a patient as required by the rejected claims.

Glaser et al.[3], another publication cited during prosecution, describes using a HSV-TK vector in combination with TMZ in cell lines and also found a lack of synergy: "TK/GCV therapy does not kill glioma cells in synergy with cancer chemotherapy drugs, including lomustine, temozolomide [TMZ] and topotecan." Glaser 469 (abstract).

We are not persuaded by this evidence that the Examiner erred in rejecting the claims as obvious.

Rainov tested TMZ treatment on nude mice which had been subcutaneously injected with the U87MG (U87) human malignant glioma cell line and which were expressing HSV-tk (herpes simplex virus comprising the thymidine kinase (tk) gene) or, alternatively, with cells not expressing the tk gene as a control. Rainov 663–664. While it does not appear that Rainov describes synergy in the animal model using nude mice, Rainov still suggested that the combination merited further investigation and had clinical implications, such as reducing toxicity and decreasing the impact of acquired drug resistance. Rainov teaches:

> [T]he feasibility of a clinical study combining both *HSV-tk/*GCV gene therapy and oral TMZ at doses equal or slightly higher than the currently recommended may be predicted. Besides the synergistic cytotoxic effect, another advantage of combining *HSV- tk/* GCV gene therapy with TMZ would be the fact that this combination of drugs may reduce toxicity toward the host as indicated by the DRI (Table 1) and may decrease the impact of possible acquired drug resistance of the tumor cells.
>
> Summarizing our data, the demonstration of synergy between *HSV- tk/* GCV gene therapy and chemotherapy with

[3] T. Glaser et al., *Death receptor-independent cytochrome c release and caspase activation mediate thymidine kinase plus ganciclovir-mediated cytotoxicity in LN-18 and LN-229 human malignant glioma cells,* Gene Therapy, 8:469–476 (2001).

> TMZ suggests a possible enhanced therapeutic concept for future studies in human malignant glioma. Despite many still unknown variables, the present results were clearly defined in a glioma cell culture system and confirmed in animal experiments, and therefore justify further investigation.

Rainov 667.

Thus, the lack of synergy in the animal model did not dissuade Rainov from suggesting the feasibility of the therapeutic combination of vector/GCV and TMZ for future studies, particularly given its clinical advantages ("may reduce toxicity toward the host as indicated by the DRI (Table 1) and may decrease the impact of possible acquired drug resistance of the tumor cells").

Appellants also state that they previously argued that "Rainov teaches away from combining Wick's temozolomide with King's ganciclovir *in vivo*." Reply Br. 9. Appellants argue that in response to the argument, the Examiner withdrew the rejections. *Id.* at 10. Appellants state that the Examiner "has already conceded that combining Wick's temozolomide with King's ganciclovir would eliminate efficacy and risk fatal toxicity." *Id.*

It is true that the Examiner withdrew the rejections based on Wick, but the Examiner did not explain the reason. Appellants had argued in the Appeal Brief:

> Temozolomide damage is repaired MGMT, while ganciclovir damage is repaired by hMLH1. Thus, were one to simply combine temozolomide and ganciclovir, one would need to administer a dose of temozolomide large enough to deplete MGMT (i.e., a full dose) and a dose of ganciclovir large enough to deplete hMLH1 (i.e., a full dose).
>
> The minimally-effective dose of either drug, however, is large enough to risk fatal hemotoxicity. Thus, Wick explains why two full doses of two different cytotoxics would be fatal.

Appeal Br. 21.

Appellants did not identify where Wick explained that *two different cytotoxic agents would be fatal*. Wick describes a "new" regiment for the administration of TMZ to reduce its toxicity. Wick 69–70. We have not been directed to disclosure in Wick about additional treatment with HCV-tk/GCV. Appellants' argument is therefore not substantiated by the evidence we have been directed to review.

In sum, Rainov expressly teaches that the combination of an HCV-tk/GCV and TMZ has clinical relevance, and "may reduce toxicity toward the host as indicated by the DRI (Table 1) and may decrease the impact of possible acquired drug resistance of the tumor cells." Rainov 667. Thus, even though there was a lack of synergy in an animal model as described in Rainov and Glaser, there was still reason to use the combination in humans with a reasonable expectation of success, and, thus it would have been obvious to have done so.

In view of the explicit suggestion in Rainov, we affirm the rejections of claims 2, 3, and 42.

Claim 8 was not argued separately and therefore it is affirmed for the reason set forth by the Examiner.

Claim 41

Claim 41 is directed to a "kit comprising a viral vector and temozolomide, said viral vector and said temozolomide present in an amount effective to treat brain cancer in a human patient." Ulasov describes the vector ("CRAd-S-pk7") and TMZ, but not the amount of TMZ effective to treat a brain cancer in a human patient. However, such amount is described

in Balmaceda. Ans. 5. Ulasov teaches "that pretreatment with TMZ followed by CRAd-S-pk7 (combination therapy) leads to an enhanced cytotoxic effect in all cell lines tested." Ulasov 1158 ("The additive effect observed by TMZ and CRad-S-p7 is mediated by autophagy in vitro"). Ulasov further teach:

> Consistent with the finding of an additive cytotoxic effect of TMZ and CRAd-S-pk7 *in vitro* experiments, this treatment combination led to an improved survival in mice bearing i.c. human glioma xenografts.
>
> . . .
>
> The therapeutic effects of TMZ and CRAd-S-pk7 on i.c. glioma xenografts are additive and lead to a significant increase in survival.

Ulasov 1160.

Ulasov also provides a reason to have used this combination in a human patient: "The improved therapy exhibited by the TMZ and CRAd-S-pk7 cocktail adds to the rationale for testing CRAd-S-pk7 in the clinical scenario." Ulasov 1163. Determination of the amount of vector to use to treat the brain cancer would have been routine for one of ordinary skill in the art, who would have experience in treating cancer with drugs, based on the teachings in Balmaceda,. Appellants did not provide evidence to the contrary.

Accordingly, for the foregoing reasons and those of the Examiner, the rejection of claim 41 as obvious is affirmed.

Claims 4–7

Claim 4 depends from claim 3, and further recites "said administration of said cytotoxic agent begins no earlier than 2 days after said administration of said gancyclovir begins." The Examiner found that "differences in

experimental parameters such as in this case temporal administration of ganciclovir and TMZ will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such parameter is critical." Ans. 7–8.

Appellants responded to the rejection by citing evidence from the Specification that the recited time period of two days is critical. The Specification teaches:

> It was also found that the administration protocol of these components [GCV and a cytotoxic agent such as TMZ] is key to the surprising technical effect observed in the invention, i.e. the synergy. The inventors have found that the upregulation of the MMR pathway by vector/prodrug gene therapy takes approximately 2 days, and lasts for a maximum of 7 days after stopping prodrug therapy. Therefore, in order to see synergy it is necessary to begin administering the cytotoxic agent no later than 7 days after finishing prodrug therapy.

Spec. 2:9–15.

Because Appellants provided rebuttal evidence, and the Examiner did not identify a defect in the evidence, the rejection of claim 4, and claims 5–7 which depend from it, are reversed.

REJECTIONS 4–8

Appellants argue that "Ulasov combined with Balmaceda fails to teach the trans gene [and] the vector of claim 1." Reply Br. 11. Appellants state that the "Examiner tries to rehabilitate this by further combining Ulasov and Balmaceda with Chiocca (2004), Stupp, Brandes, Yu or Hegi [2008]." *Id.* Appellants argue "[n]one of these newly-cited references, however, teaches transgene nor vector." *Id.*

This argument is not persuasive because the Examiner relied upon Ulasov for describing a viral vector with a transgene. The Examiner cited the additional publications to meet limitations recited in dependent claims. Ans. 9, 11, 12, 13, 14.

Appellant further argues that the Examiner has not made Hegi (2008) of record. Reply Br. 12. This argument is not understood because the Examiner cited Hegi in the Answer and identified it is as being listed in an Information Disclosure Statement ("IDS"). Ans. 14. This IDS was filed Aug. 4, 2015 by Appellants. Appellants thus made Hegi (2008) of record.

The obviousness rejections 4–8 of claims 1, 10–13, 16, 17, and 18 are affirmed for the reasons set forth by the Examiner

REJECTIONS 9 & 10.

OBVIOUSNESS BASED ON MEDICAL NEWS TODAY

Independent claim 19 is rejected by the Examiner based on Medical New Today and Immonen. Claim 19 is reproduced below:

> 19. A method of treating malignant glioma, said method comprising the steps of
> – Diagnosing in a human patient malignant glioma;
> – Identifying in said patient at least one malignant glioma tumor;
> – Resectioning said malignant glioma tumor to remove at least part of said malignant glioma tumor and expose tumor bed tissue;
> – Administering to said tumor bed tissue an Ad.HSV-tk adenoviral vector having a gene coding for thymidine kinase, whereby said Ad.HSV-tk adenoviral vector transfects said tumor bed tissue and said tumor bed tissue expresses said gene coding for thymidine kinase;
> – Within about 5 to about 19 days after administering said adenoviral vector to said human patient, further administering to said human patient ganciclovir;
> – Administering to said human patient temozolomide.

The Examiner found that claim 19, and dependent claim 20, are obvious based on the combination of Medical News Today and Immonen. Ans. 16–17. Appellants do not dispute the rejection. Reply Br. 13. We therefore affirm the rejection of these claims.

Claims 21 and 22

Claim 21 depends from claim 20 and further recites

> wherein said temozolomide is administered in a plurality of 28-day cycles, each cycle comprising administration of a dose of about 150 mg/m^2 per day each day for days 1 - 5 of said 28-day cycle, followed by a dose of about 0 mg/m^2 per day for days 6 - 28 of said 28-day cycle.

The Examiner cited Balmaceda to meet the dosage limitation of the claim. Ans. 18.

Appellants contend that Balmaceda does not disclose the claimed dosage limitation. We do not agree. Balmaceda describes in its introduction

that the "standard dosage [for TMZ] is 150 to 200 mg/m^2 once daily for 5 consecutive days in a 28-day treatment cycle," which meets the treatment regime recited in claim 21.

Claim 22 depends from claim 21 and further recites "wherein said plurality of 28-day cycles is preceded by period of about 42 days wherein temozolomide is administered at a dosage of about 75 mg/m^2 per day." The Examiner found it would have been obvious to have utilized a lower loading dose of TMZ to achieve optimal results and modulate drug resistance. Ans. 20. Appellants contend that the dose is not described in Balmaceda, but failed to address the obviousness of optimizing the dosage based on Balmaceda.[4] Reply Br. 14.

For the foregoing reasons and those of the Examiner, the obviousness rejection of claims 21 and 22 is affirmed.

Claim 23

Claim 23, depends from claim 20, and further recites "wherein said Ad.HSV-tk adenoviral vector and said ganciclovir are each administered in an amount effective to induce the MMR pathway." MMR is the "mismatch repair pathway." Spec. 1:19–25.

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[4] Stupp, cited in the rejection of other dependent claims, discloses that the "approved conventional schedule is a daily dose of 150 to 200 mg per square meter of body-surface area for 5 days of every 28-day cycle. Daily therapy at a dose of 75 mg per square meter for up to seven weeks is safe." Stupp 988. Thus, it appears that claims 21 and 22 are directed to known dosages of TMZ. Hegi (2008) also has a similar treatment plan with TMZ of a daily dose of 75 mg/m^2 for 6 to 7 weeks, every 10 weeks. Hegi (2008) 4194, Table 3; 4196, Table 4.

The Examiner found it obvious to activate MMR pathways based on teachings in Hegi (2008) and Balmaceda that MGMT (O6-methylguanine-DNA methyltransferase) activates MMR pathways and that "[g]iven the central role of MGMT in resistance to alkylating agents and its unique properties, MGMT is an ideal potential target for biochemical modulation of drug resistance." Ans. 19. The Examiner stated that "as evidenced by Hegi [2008], MGMT activates MMR pathways in patients treated with alkylating agents such as TMZ (abstract, whole document)." *Id.*

Appellants contend, again, that Hegi (2008) has not been made of record by the Examiner (Reply Br. 14), ignoring the fact that Appellants made the publication of record in an IDS and that the Examiner cited to this IDS in applying Hegi (2008) to the claims.

Appellants contend that the Examiner erroneously found that Hegi (2008) discloses MGMT as a potential target and that "the voluminous art of record shows that the overwhelming majority of 'potential targets' fail. Assuming Hegi [2008] says that MGMT is an ideal 'potential target,' that fails to provide us the reasonable expectation of success a *prima facie* case requires." Reply Br. 14.

This argument is not persuasive because Hegi (2008) expressly teaches that MGMT silencing is associated with better outcomes in treating glioma and thus is an established target of cancer treatment. Specifically, Hegi (2008) explains that when the methyl group from the guanine (added by the alkylating agent, such as TMZ) is not repaired by MGMT, the MMR pathway is activated.[5] Hegi (2008) 4190 (1st column). Hegi (2008) teaches

[5] The Specification also teaches that "[i]t is known that a functional MMR pathway is essential to make cells sensitive to TMZ." Spec. 1:21–23.

that "epigenetic silencing" of the *MGMT* gene by promoter methylation plays an important role in regulating MGMT expression in gliomas. *MGMT* promoter methylation is correlated with improved progression-free and overall survival in patients treated with alkylating agents. Hegi (2008) Abstract. Hegi (2008) at 4192 also discloses that "results showed that *MGMT* promoter methylation was associated with improved overall survival in patients treated with RT [radiotherapy] plus temozolomide but not in patients initially treated with RT alone." Thus, Hegi identified the MGMT pathway as a target for TMZ, providing a reason to silence it when treating glioma, and subsequently activate MMR pathways.

For the foregoing reason, the rejection of claim 23 is affirmed.

Summary

The obviousness rejection of claims 19–23 is affirmed. Claims 24–26 were not argued separately and fall with these claims. 37 C.F.R. § 41.37(c)(iv)(1).

REJECTIONS 11 & 12. OBVIOUSNESS BASED ON ULASOV, BALMACEDA, IMMONEN, RAINOV & STUPP

The Examiner rejected claims 27, 29–32, and 35–40 based on Ulasov, Balmaceda, Immonen, and Rainov (Rejection 11). Ans. 23.

Appellants argue:

> Claim 27 requires an immune-competent human patient. In contrast, Ulasov and Rainov teach the opposite: immune-incompetent mice. Balmaceda, Immonen and Stupp similarly fail to teach immune competent patients. We cannot assume that Balmaceda, Immonen or Stupp's patients were immune competent because the art teaches to screen cancer patients and

> exclude immune-competent patients from certain treatments. *See* Yla-Herttuala, *Declaration* (02 June 2014) (made of record 18 in the instant application on April 2016).

Reply Br. 15.

We have already considered these arguments regarding claim 27 and the limitation that the patients are immunocompetent and found them to be unpersuasive. *Supra*. Appellants also argue that combination of a vector, GCV, and TMZ is not disclosed. Reply Br. 15–16. As already discussed, Rainov discloses the combination of both agents. This argument is duplicative of argument made elsewhere in the Reply Brief and Appellants provide no objective evidence to support the contentions nor do Appellants identify a defect in the Examiner's fact-finding or reasoning.

The obviousness rejection of claims 27, 29–32, and 35–40 is affirmed for the reasons set forth by Examiner. Ans. 20–23 (Rejection 11).

Appellants did not separately argue the rejection of claims 27 and 34 (Rejection 12). The obviousness rejection of claims 27 and 34 are affirmed for the reasons set forth by Examiner. Ans. 23–24.

SUMMARY

Rejection 1 of claim 41 is reversed.

Rejection 2 of claims 1, 9, 14, 15, 27, 31, and 33 is affirmed.

Rejection 2 of claim 28 is reversed.

Rejection 3 of claims 1, 2, 3, 8, 41, and 42 is affirmed.

Rejection 3 of claims 4–7 is reversed.

Rejections 4–8 of claims 1, 10–13, and 16–18 are affirmed.

Rejection 9 of claims 19 and 20 is affirmed.

Rejection 10 of claims 19, 20, and 21–26 is affirmed.

Rejection 11 of 27, 29–32, and 35–40 is affirmed.

Rejection 12 of claims 27 and 34 is affirmed.

Therefore, currently claims 4–7 and 28 are not subject to a pending rejection.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED-IN-PART

Relevant Constitutional Clause, Federal Statutes and Agency Regulations

U.S. CONSTITUTION 5TH AMENDMENT

No person shall be held to answer for a capital, or otherwise infamous crime, unless on a presentment or indictment of a Grand Jury, except in cases arising in the land or naval forces, or in the Militia, when in actual service in time of War or public danger; nor shall any person be subject for the same offence to be twice put in jeopardy of life or limb; nor shall be compelled in any criminal case to be a witness against himself, nor be deprived of life, liberty, or property, without due process of law; nor shall private property be taken for public use, without just compensation.

5 U.S.C. § 706

Scope of Review

To the extent necessary to decision and when presented, the reviewing court shall decide all relevant questions of law, interpret constitutional and statutory provisions, and determine the meaning or applicability of the terms of an agency action. The reviewing court shall- (1) compel agency action unlawfully withheld or unreasonably delayed; and (2) hold unlawful and set aside agency action, findings, and conclusions found to be-

(A) arbitrary, capricious, an abuse of discretion, or otherwise not in accordance with law;

(B) contrary to constitutional right, power, privilege, or immunity;

(C) in excess of statutory jurisdiction, authority, or limitations, or short of statutory right;

(D) without observance of procedure required by law;

(E) unsupported by substantial evidence in a case subject to sections 556 and 557 of this title or otherwise reviewed on the record of an agency hearing provided by statute; or

(F) unwarranted by the facts to the extent that the facts are subject to trial de novo by the reviewing court.

In making the foregoing determinations, the court shall review the whole record or those parts of it cited by a party, and due account shall be taken of the rule of prejudicial error.

35 U.S.C. § 141

Appeal to Court of Appeals for the Federal Circuit

(a) Examinations. An applicant who is dissatisfied with the final decision in an appeal to the Patent Trial and Appeal Board under section 134(a) may appeal the Board's decision to the United States Court of Appeals for the Federal Circuit. By filing such an appeal, the applicant waives his or her right to proceed under section 145.

35 U.S.C. § 143

Proceedings on Appeal

With respect to an appeal described in section 142, the Director shall transmit to the United States Court of Appeals for the Federal Circuit a certified

list of the documents comprising the record in the Patent and Trademark Office. The court may request that the Director forward the original or certified copies of such documents during pendency of the appeal. In an ex parte case, the Director shall submit to the court in writing the grounds for the decision of the Patent and Trademark Office, addressing all of the issues raised in the appeal.

35 U.S.C. § 144
Decision on Appeal

The Court of Appeals for the Federal Circuit shall review the decision from which an appeal is taken on the record before the Patent and Trademark Office. Upon its determination the court shall issue to the Director its mandate and opinion, which shall be entered of record in the Patent and Trademark Office and shall govern the further proceedings in the case.

37 C.F.R. § 41.30
Definitions

In addition to the definitions in § 41.2, the following definitions apply to proceedings under this subpart [appeals to the Patent Trial & Appeal Board] unless otherwise clear from the context:

* * *

> Record means the items listed in the content listing of the Image File Wrapper of the official file of the application or reexamination proceeding on appeal or the official file of the Office if other than the Image File Wrapper, excluding amendments, Evidence, and other documents that were not entered.

37 C.F.R. § 41.33(d)

Affidavits Or Other Evidence After Appeal

(1) An affidavit or other Evidence filed after the date of filing an appeal pursuant to § 41.31(a)(1) through (a)(3) and prior to the date of filing a brief pursuant to § 41.37 may be admitted if the examiner determines that the affidavit or other Evidence overcomes all rejections under appeal and that a showing of good and sufficient reasons why the affidavit or other Evidence is necessary and was not earlier presented has been made.

(2) All other affidavits or other Evidence filed after the date of filing an appeal pursuant to § 41.31(a)(1) through (a)(3) will not be admitted except as permitted by §§ 41.39(b)(1), 41.50(a)(2)(i), and 41.50(b)(1).