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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte SUSANNA A. SAAKIAN

Appeal 2019-005346
Application 15/919,361
Technology Center 1600

Before DONALD E. ADAMS, ERIC B. GRIMES, and RICHARD M. LEBOVITZ, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL

Pursuant to 35 U.S.C. § 134(a), Appellant[1] appeals[2] from Examiner's decision to reject claims 1–4 and 6–8.[3] We have jurisdiction under 35 U.S.C. § 6(b). We AFFIRM-IN-PART.

[1] We use the word "Appellant" to refer to "applicant" as defined in 37 C.F.R. § 1.42. Appellant identifies the real party in interest as "ASE Pharmaceuticals, LLC" (Appellant's April 10, 2019 Appeal Brief (Appeal Br.) 3).

[2] Appellant states that "[t]his [A]ppeal is related to Appeal 2014-008576, [Application 13/140,259,] the [D]ecision of which affirmed the rejections . . . on appeal" was entered July 20, 2016(Appeal Br. 4).

[3] Examiner finds Appellant's pending claim 5 "allowable if rewritten in independent form including all of the limitations of the base claim and any

STATEMENT OF THE CASE

Appellant's disclosure relates "to the fields of organic chemistry, drug development, pharmacology, and medicine. More particularly, the invention relates to modulating human physiology by administration of one or more [2.2.2] bicyclic derivatives" (Spec.[4] 3). Appellant's only independent claim, claim 1, is reproduced below:

> 1. A method for reducing the number or strength of seizures in a human subject suffering from epilepsy, the method comprising the step of orally administering to the subject 50-1200 mg of the bicyclo-[2.2.2]-octane-2-carboxylate salt per day at least until the number or strength of seizures in a human subject is reduced.

(Appeal Br. 12.)

Grounds of rejection before this Panel for review:

Claims 1–3 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian.[5]

Claim 4 stands rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Hanshermann.[6]

Claim 6 stands rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Ledford.[7]

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intervening claims" (Examiner's November 27, 2018 Final Office Action (Final Act.) 19).

[4] Appellant's March 13, 2018 Specification.

[5] Saakian et al., WO 99/23056, published Mar. 14, 1999, as machine translated.

[6] Hanshermann et al., US 2005/0202088 A1, published Sept. 15, 2005.

[7] Heidi Ledford, *Epilepsy drug may help alcoholics*, available at http://www.nature.com/news/2008/080528/full/news.2008.859.html, published May 28, 2008.

Claim 7 stands rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Rao.[8]

Claim 8 stands rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Zoons.[9]

Claims 1–4 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Kalimullina[10] and Saakian.

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 1. Saakian discloses

> that derivatives of bicyclo [2.2.2] octane-2-carboxylic acid, in particular its alkali metal and alkaline-earth metals possess anticonvulsant activity in the absence of any side effects and may be useful for the prevention and [treatment of] epilepsy due to their efficient and selective effect on convulsive response in mammals regardless of the sex of animals.

(Saakian 2[11]; *see id.* (Saakian "provides a method of arresting a convulsive state, which comprises administering to the animal an effective amount of a

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[8] Marie Luise Rao et al., *Serum Amino Acids, Liver Status, and Antiepileptic Drug Therapy in Epilepsy*, 33 Epilepsia 347–354 (1993).
[9] E. Zoons et al., *Seizures in adults with bacterial meningitis*, 70 Neurology 2109–2115 (2008).
[10] L.B. Kalimullina et al., *The piriform cortex and cortical nucleus of the amygdala in epileptogenesis: The role of the rostro-caudal gradient*," 31 USPEKHI FIZIOLOGICHESKIKH NAUK 63–74 (2000), as translated in PTO 122278.
[11] Saakian is not paginated. Therefore, all reference to a page number of this machine translation refers to a page number as if the document was paginated consecutively beginning with the first page.

bicyclo [2.2.2] octane-2-carboxylic acid"); *id.* at 5 (Saakian discloses that the "Na-salt of said acid – Sakritsin – was more preferred for use as an anticonvulsant compared to known drugs such as phenobarbital, phenytoin and konvuleks"); *see generally* Ans.[12] 4–5.)

FF 2. Saakian discloses dosage forms designed for a single dose, including orally administrable tablets, capsules or powders, "comprising an effective amount of a salt of bicyclo [2.2.2] octane-2-carboxylic acid" (Saakian 2; *see id.* (Saakian discloses that its dosage forms, i.e. compositions, are formulated "to produce the desired therapeutic effect"); *id.* (Saakian discloses "[p]harmaceutical compositions in the form of tablets or capsules containing from 50 to 100 mg of active ingredient"); *see generally* Ans. 5).

FF 3. Saakian discloses that "[t]he term 'effective amount' means an amount of compound required to relieve convulsive state or any of its symptoms, conducted by a pharmaceutical composition comprising a compound" within the scope of Saakian's disclosure (Saakian 2; *see id.* at 2–3 (Saakian discloses that "[a]n effective amount is generally determined by the physician in each case and depends on the severity of the disease, age and weight of the recipient and route of administration"); *see generally* Ans. 5).

FF 4. Saakian discloses that "[t]he term 'relief of convulsive state' . . . includes prevention, containment, lessening the severity of a disease or a symptom or its consequences" (Saakian 2; *see generally* Ans. 5).

[12] Examiner's May 3, 2019 Answer.

FF 5. Examiner finds that Saakian does not disclose sustained or delayed release tablets and relies on Hanshermann to make up for this deficiency in the Saakian (Ans. 6–7 (citing Hanshermann's claims 1, 7, 8, 14, 15, and 21)).

FF 6. Examiner finds that although Saakian suggests administering a bicyclo-[2.2.2]-octane-2-carboxylate salt "generally to all human subjects with epilepsy, the reference do[es] not explicitly . . . [disclose administration to,] human subjects suffer[ing] from ethanol addiction" and relies on Ledford's disclosure that the "epilepsy drug (e.g. gabapentin) may help alcoholics; a drug used to treat epilepsy could also ease cravings in alcoholics" (Ans. 7 (citing Ledford 1); *see* Ledford 1 (Ledford discloses that "[p]reliminary small clinical trials have suggested that gabapentin[, a drug approved for treatment of epileptic seizures and for some conditions that cause chronic pain,] could . . . be useful in the treatment of drug addiction")).

FF 7. Ledford discloses that

> Gabapentin is structurally similar to a neurotransmitter called γ-aminobutyric acid, or GABA, which can slow communication between neurons in the brain. Although the drug does not function in precisely the same way as GABA, it can prevent the chaotic electrical activity in the brain that triggers a seizure.
>
> Alcohol affects the GABA system by mimicking GABA's activity in the brain, which contributes to alcohol's sedative effect. But chronic drinking can lead to tolerance: a condition in which more and more alcohol is required to produce the same GABA response. Without an increasing supply of alcohol, alcoholics can begin to feel agitated.
>
> There has been a lot of interest in whether epilepsy drugs might also be useful for treating alcoholism . . . . The drugs could

> help an alcoholic during the early stages of abstinence, until normal GABA tolerance has been restored.

(Ledford 1–2.)

FF 8. Examiner finds that Saakian does not disclose the treatment of humans having an "elevated level of liver function markers" and relies on Rao to make up for this deficiency (Ans. 8 (citing Rao, Abstract and Table 3)).

FF 9. Rao discloses that "[s]timulation of hepatic enzymes by [antiepileptic drugs (AEDs)] administered in therapeutic dosages has been observed to vary with respect to the different AEDs" (Rao 347).

FF 10. Rao discloses a study of "serum [amino acid (AA)] profiles and liver enzymes in 73 epileptic patients and 90 healthy subjects," and found that "[s]eventy-two percent of the AED-treated patients and 33% of the unmedicated patients showed an increase in one or several serum liver enzymes [alanine aminotransferase (ALT), aspartate amino transferase (AST), and/or γ-glutamyl transferase (γ-GT)]; particularly γ-GT" (Rao, Abstract (alteration original)).

FF 11. Rao "observed a significant increase in serum concentrations of glutamine and glycine and decreased levels of taurine, threonine, serine, valine, methionine, isoleucine, leucine, phenylalanine, histidine, tryptophan, and arginine in AED-treated patients but not in unmedicated patients," and concludes that "[t]hese results show that the changes in the serum AA profiles of epileptic patients treated with AEDs occur in patients with alteration of serum liver enzymes; whether this implies a causal relation is still uncertain" (Rao, Abstract).

FF 12. Rao discloses that

> Nine of [its] patients who were AED-free for ≥4 weeks had an AA profile which was not different from that of healthy subjects. On the other hand, 3 of the 9 patients not receiving AEDs and 74% of the patients receiving AEDs had increases in one or more of the serum liver enzyme levels, i.e., mostly increases (induction) in γ-GT. Thus, the AED-induced hepatic changes may have been involved in the AA alteration in epilepsy.

(Rao 353.)

FF 13. Examiner finds that Saakian does not disclose the treatment of humans having "elevated erythrocyte sedimentation" and relies on Zoons to make up for this deficiency (Ans. 9 (citing Zoons, Abstract; 2111: col. 2, ll. 10–11; Tables 2–3; and 2112: col. 2, para. 2)).

FF 14. Zoons discloses an evaluation of "the occurrence and prognostic relevance of seizures in adults with community-acquired bacterial meningitis" (Zoons, Abstract).

FF 15. Zoons discloses that "[p]atients with in-hospital seizures were more likely to have . . .[, *inter alia*,] higher median erythrocyte sedimentation rate . . . than patients without in-hospital seizures" and that antiepileptic medications were administered to treat seizures (Zoons, Abstract, *see also id.* at 2111 (Zoons discloses that "[p]atients with in-hospital seizures were more likely to have . . . higher median erythrocyte sedimentation rate (ESR)"); *id.* at 2112 ("[a]ntiepileptic medication was administered in 98 of 111 evaluated episodes (85%) with seizures")).

FF 16. Kalimullina discloses

> The amygdaloid complex (AC) of the brain is a nuclearpaleocortical component of the encephalon inasmuch as its composition includes, in addition to typical nuclei, formations whose cytoarchitectonic properties are of the

> paleocortical or transitional kind (Figure 1). This applies primarily to the cortical nucleus of AC, whose seizure susceptibility was investigated in . . . [Kalimullina's] study.

(Kalimullina 3.)

FF 17. Kalimullina discloses that "[e]lectrical kindling of AC in rats is being successfully used to screen new anticonvulsant drugs, and in the present study it was used to investigate Sacricin" (Kalimullina 16; *see* Ans. 17).

FF 18. Kalimullina discloses

> A single 200 mg/kg dose of Sacricin was administered intraabdominally following the formation of a partial kindling. The drug was injected 30 minutes prior to the stimulation because pharmacokinetic studies have shown that during that period its concentration in the blood plasma reaches a maximum. To detect trace effects, the daily electrostimulation séances were continued in the following days.

(Kalimullina 17; *see* Ans. 17.)

FF 19. Kalimullina discloses that "in every rat study, Sacricin was found to reduce the representation of epileptiform activity, both that arising spontaneously and that relating to LPT evoked by stimulation" (Kalimullina 19; *see id.* at 20 (Kalimullina discloses that "[t]he anticonvulsant effect of Sacricin manifested itself in a decline in the severity of seizures"); *id.* at 22 (Kalimullina discloses that "[t]he administration of Sacricin resulted in a statistically significant decrease in the number of 2nd stage seizures and completely blocked the more severe stages (3rd–5th)"); *see also* Ans. 17–18).

FF 20. Kalimullina discloses that

> a 200 mg/kg dose of Sacricin is effective in blocking PTZ-induced seizures, as is phenobarbital, but when the dose of Sacricin is doubled to 400 mg/kg then its anticonvulsant effects are superior to those of phenobarbital (administered in doses of

> 15 and 30 mg/kg). The behavioral changes observed in the present study in rats following a single injection of Sacricin were not of a dominant or pathological nature.

(Kalimullina 26–27; *see* Ans. 18.)

FF 21. Examiner finds that Kalimullina "does not explicitly teach the oral administration in a human subject or the dosage amount of bicyclo-[2.2.2]-octane-2-carboxylate salt as claimed [by Appellant]" and relies on Saakian to make up for this deficiency in Kalimullina (Ans. 11; *see* FF 1–4).

FF 22. Examiner finds that "the pharmaceutical forms, e.g., sustained release, immediate release are all deemed obvious since they represent conventional formulations and modes of administration and are all within the knowledge of the skilled pharmacologist" (Ans. 12).

ANALYSIS

The rejection over Saakian:

The method of Appellant's claim 1, reproduced above, comprises the step of orally administering, to a human subject suffering from epilepsy, 50–1200 mg of bicyclo-[2.2.2]-octane-2-carboxylate salt per day at least until the number or strength of seizures in a human subject is reduced (*see* Appeal Br. 12).

Saakian discloses the oral administration, to a mammal, which includes a human, suffering from epilepsy, of a single dose of 50 to 100 mg of bicyclo-[2.2.2]-octane-2-carboxylate salt to provide relief of a convulsive state, which includes "lessening the severity of a disease or a symptom or its consequences" (*see* FF 1–4). In this regard, Saakian further discloses the administration of an "effective amount" of bicyclo-[2.2.2]-octane-2-carboxylate salt to treat epilepsy in a mammal, which includes a human (*see id.*). Saakian discloses that the "effective amount is generally determined by

the physician in each case and depends on the severity of the disease, age and weight of the recipient and route of administration," wherein the "effective amount" is defined as "an amount of compound required to relieve convulsive state or any of its symptoms, conducted by a pharmaceutical composition comprising a compound" within the scope of Saakian's disclosure, i.e., a bicyclo-[2.2.2]-octane-2-carboxylate salt, such as the sodium salt–Sakritsin (*see id.*). "[W]here[, as here,] the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456 (CCPA 1955).

For the foregoing reasons, we find no error in Examiner's conclusion that, at the time Appellant's invention was made, it would have been prima facie obvious, in view of Saakian, to reduce the number or strength of seizures in a mammal, which includes a human subject, suffering from epilepsy by orally administering to the subject 50-1200 mg of the bicyclo-[2.2.2]-octane-2-carboxylate salt per day at least until the number or strength of seizures in the human subject is reduced (*see* Ans. 2–6).

For the foregoing reasons, we are not persuaded by Appellant's contention that "[t]here is no clear guidance and direction[, in Saakian,] to select orally administering 50-1200 mg of the bicycle-[2.2.2]-octane-2-carboxylate salt per day to a human subject with epilepsy at least until the number or strength of seizures in a human subject is reduced" (Appeal Br. 8; *see id.* at 6–7 (Appellant admits that "Saakian teaches the bicyclo-[2.2.2]-octane-2-carboxylate salt as recited in [Appellant's] claim 1").

A reference disclosure is not limited only to its preferred embodiments, but is available for all that it discloses and suggests to one of

ordinary skill in the art. *In re Lamberti*, 545 F.2d 747, 750 (CCPA 1976); *see also In re Susi*, 440 F.2d 442, 446 n.3 (CCPA 1971) (Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or non-preferred embodiments). Therefore, we are not persuaded by Appellant's contention that Saakian does not provide an enabling disclosure of Appellant's claimed invention, because Saakian does not disclose human clinical studies (*see* Appeal Br. 6–7).

"Attorney's argument in a brief cannot take the place of evidence." *In re Pearson*, 494 F.2d 1399, 1405 (CCPA 1974). Therefore, we are not persuaded by the unsupported assertions of Appellant's counsel concerning Saakian's disclosure (*see* Appeal Br. 6–10). In this regard, we recognize the unsupported assertion by Appellant's counsel that "Saakian's rodent models differ significantly from human epilepsy" (*id.* at 9). This assertion, however, fails to provide an evidentiary basis to establish that those of ordinary skill in this art would have considered Saakian's experimental models to be insufficient to support Saakian's disclosure.

The rejection over the combination of Saakian and Hanshermann:

Appellant's claim 4 depends from and further limits the method of Appellant's claim 1 to require that the bicyclo-[2.2.2]-octane-2-carboxylate salt is formulated for sustained or delayed release" (*see* Appeal Br. 12).

Based on the combination of Saakian and Hanshermann, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious "to formulate a sustained or delayed drug release comprising an anticonvulsant, sacricin from Hanshermann" (Ans. 7; *see* FF 1–5).

For the foregoing reasons, we found no deficiency in Saakian. Therefore, we are not persuaded by Appellant's contention that "[t]his rejection is in error for its reliance on Saakian for the reasons provided above" and "[b]ecause Hanshermann does not cure Saakian's lack of teaching or suggestion, this rejection is in error and should be reversed" (Appeal Br. 10).

The rejection over the combination of Saakian and Ledford:

The method of Appellant's claim 6 depends from and further limits the human subject of Appellant's claim 1 to a human subject that "also suffers from ethanol addiction and the bicyclo-[2.2.2]-octane-2-carboxylate salt is administered at least until the dysphoria and the number of strength of seizures in the subject is reduced" (*see* Appeal Br. 12).

Examiner recognizes that Saakian fails to disclose the administration of bicyclo-[2.2.2]-octane-2-carboxylate salt to individuals suffering from epilepsy and ethanol addiction (FF 6). Ledford discloses that "[a]lcohol affects the GABA system by mimicking GABA's activity in the brain, which contributes to alcohol's sedative effect" (FF 7). Ledford discloses gabapentin, a drug useful for the treatment of epilepsy, "is structurally similar to GABA" and "[a]lthough the drug does not function in precisely the same way as GABA, it can prevent the chaotic electrical activity in the brain that triggers a seizure" (FF 6–7). Ledford discloses that "[t]here has been a lot of interest in whether epilepsy drugs might . . . be useful for treating alcoholism" and that "[p]reliminary small clinical trials have suggested that gabapentin could be useful in the treatment of drug addiction" (FF 6–7).

In sum, Ledford discloses that gabapentin could be useful in treating drug addiction, based upon preliminary small clinical trials of a treatment that uses an antiepileptic drug that is structurally similar to the GABA neurotransmitter, which is involved in the same system that alcohol affects by mimicking GABA's activity in the brain (FF 6–7). Although Ledford suggests that there is interest in this art as to "whether epilepsy drugs might . . . be useful for treating alcoholism," Ledford, at best, suggests the exploration of a general approach that seems to be a promising field of experimentation, but gave only general guidance as to how to achieve Appellant's claimed result. Stated differently, the combination of Saakian and Ledbetter falls into *O'Farrell's* second class of impermissible "obvious to try" situations, where

> what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. [*In re O'Farrell*, 853 F.2d 894, 903 (Fed. Cir. 1988)]. . . . *KSR* affirmed the logical inverse of this statement by stating that § 103 bars patentability unless "the improvement is more than the predictable use of prior art elements according to their established functions." [*Teleflex, Inc. v. KSR Int'l Co.*, 550 U.S. 398, 417 (2007)].

In re Kubin, 561 F.3d 1351, 1359–60 (Fed. Cir. 2009).

Therefore, we are not persuaded by Examiner's conclusion, based on the combination of Saakian and Ledford, that at the time Appellant's invention was made, it would have been prima facie obvious to use Saakian's sacricin to treat a human subject suffering from both epilepsy and alcoholism, i.e. ethanol addiction, wherein Saakian's sacricin is administered at least until the dysphoria and the number or strength of seizures in the

subject is reduced (*see* Ans. 8; *see* FF 1–4, 6, and 7). Instead, we agree with Appellant's contention that "[n]either Saakian nor Ledford teach that bicyclo-[2.2.2]-octane-2-carboxylate salt acts the same way in alcohol craving as does gabapentin . . . [and], therefore, [the rejection] lacks the rational underpinning to support the legal conclusion of obviousness required by KSR. Accordingly, the rejection is in error and should be reversed" (Appeal Br. 10).

The rejection over the combination of Saakian and Rao:

The method of Appellant's claim 7 depends from and further limits the human subject of Appellant's claim 1 to a human subject that has an elevated liver function marker selected from the group consisting of AST, ALT, and bilirubin, and the bicyclo-[2.2.2]-octane-2-carboxylate salt is administered at least until the liver function marker and the number or strength of seizures in the subject is reduced (*see* Appeal Br. 13).

Based on the combination of Saakian and Rao, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious "to administer [Saakian's] sacricin at least until the liver function marker and the number or strength of seizures in the subjects is reduced . . . to treat the symptoms of epilepsy and provide therapeutic benefits in patients with elevated liver markers," because Rao discloses that liver enzymes such as AST and ALT liver markers may be elevated in patients with epilepsy (Ans. 8; *see* FF 1–4 and 8–12). We are not persuaded.

The method of Appellant's claim 7 requires the administration of bicyclo-[2.2.2]-octane-2-carboxylate salt at least until, *inter alia*, the liver function marker is reduced (*see* Appeal Br. 13). In contrast, Rao discloses a

study wherein "[s]eventy-two percent of the AED-treated patients [in the study] . . . showed an increase in one or several serum liver enzymes [alanine aminotransferase (ALT), aspartate amino transferase (AST), and/or γ-glutamyl transferase (γ-GT)]; particularly γ-GT" (FF 9). In addition, Rao discloses that although "[n]ine of [its] patients who were AED-free for ≥4 weeks had an AA profile which was not different from that of healthy subjects," "74% of [its] patients receiving AEDs had increases in one or more of the serum liver enzyme levels, i.e., mostly increases (induction) in γ-GT. Thus, [Rao concludes that] the AED-induced hepatic changes may have been involved in the AA alteration in epilepsy" (FF 12; *see also* FF 11).

In sum, Examiner failed to establish an evidentiary basis on this record to support a conclusion that the combination of Saakian and Rao suggests that treatment, of a patient suffering from epilepsy and an elevated liver function marker, with an anti-epileptic drug will reduce, *inter alia*, the liver function marker in the patient, as required by Appellant's claimed invention (*see* Appeal Br. 13; *cf.* FF 8–12). Therefore, we agree with Appellant's contention that "[t]his rejection is in error because it is not based on any evidence . . . suggesting that a bicyclo-[2.2.2]-octane-2-carboxylate salt would have been expected to reduce elevated liver enzymes" (Appeal Br. 11).

The rejection over the combination of Saakian and Zoons:

The method of Appellant's claim 8 depends from and further limits the human subject of Appellant's claim 1 to a human subject that has an elevated erythrocyte sedimentation rate, and the bicyclo-[2.2.2]-octane-2-

carboxylate salt is administered at least until the erythrocyte sedimentation rate and the number or strength of seizures in the subject is reduced (*see* Appeal Br. 13).

Based on the combination of Saakian and Zoons, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious "to administer [Saakian's] sacricin at least until the erythrocyte sedimentation rate and the number or strength of seizures in the subjects is reduced . . . to treat the symptoms of epilepsy and provide therapeutic benefits in such patients," because Zoons discloses that "erythrocyte sedimentation rate is elevated in patients with seizures and anti-epileptic medications are provided to treat seizures" (Ans. 9; *see* FF 1–4 and 13–15). We are not persuaded.

Examiner recognizes that Saakian does not disclose the treatment of humans having "elevated erythrocyte sedimentation" (FF 13). Zoons discloses that "seizures in adults with community-acquired bacterial meningitis" correspond to, *inter alia*, higher median erythrocyte sedimentation rate" and that these seizures are treated with antiepileptic medication (*see* FF 13–15). Examiner does not identify, nor do we find, a disclosure in Zoons that establishes that the treatment of seizures in patients with community-acquired bacterial meningitis necessarily results in a reduced erythrocyte sedimentation rate in these patients. Thus, we agree with Appellant's contention that "[t]his rejection is in error because it is not based on any evidence . . . suggesting that a bicyclo-[2.2.2]-octane-2-carboxylate salt would have been expected to reduce elevated erythrocyte sedimentation rates" (Appeal Br. 11).

The rejection over the combination of Kalimullina and Saakian:

Based on the combination of Kalimullina and Saakian, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious to reduce the number or strength of seizures in a mammal, which includes a human subject, suffering from epilepsy by orally administering to the subject 50-1200 mg of the bicyclo-[2.2.2]-octane-2-carboxylate salt per day at least until the number or strength of seizures in the human subject is reduced, wherein "the pharmaceutical forms, e.g., sustained release, immediate release are all deemed obvious since they represent conventional formulations and modes of administration and are all within the knowledge of the skilled pharmacologist (*see* Ans. 11–12; *see* FF 1–4 and 16–22).

Claim 1:

For the reasons set forth above, with respect to the rejection of claim 1 over Saakian, we are not persuaded by Appellant's contention that

> This rejection is in error for the same reasons as the 103 rejection over only Saakian (section A above). Because this art is highly unpredictable, and neither Kalimullina nor Saakian's present any data from human subjects with epilepsy, any data concerning the efficacy of oral administration in any species, or any data from experiments with a dosage/administration protocol in any way similar to that in claim 1 in any species, the only reasonable conclusion that the skilled artisan, balancing the Wands factors in view of claims 1-3 and Kalimullina and Saakian, could arrive at that undue experimentation would have been required to arrive at the subject matter of claims 1-3.

(Appeal Br. 11.)

Claim 4:

Appellant does not address the rejection of claim 4. We do not find, and Appellant does not identify, error in Examiner's rejection of claim 4 over the combination of Kalimullina and Saakian (*see* Ans. 10–12; *see also* FF 1–4 and 16–22). Therefore, affirm the rejection of claim 4 over the combination of Kalimullina and Saakian (*see* Ans. 10–12; FF 1–4 and 16–22).

CONCLUSION

The preponderance of evidence relied upon by Examiner supports a conclusion of obviousness with respect to Appellant's claims 1–4.

The rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over Saakian is affirmed. Claims 2 and 3 are not separately argued and, therefore, fall with claim 1.

The rejection of claim 4 under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Hanshermann is affirmed.

The rejection of claims 1 and 4 under 35 U.S.C. § 103(a) as unpatentable over the combination of Kalimullina and Saakian. Claims 2 and 3 are not separately argued and, therefore, fall with claim 1.

The preponderance of evidence relied upon by Examiner fails to support a conclusion of obviousness with respect to Appellant's claims 6–8.

The rejection of claim 6 under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Ledford is reversed.

The rejection of claim 7 under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Rao is reversed.

The rejection of claim 8 under 35 U.S.C. § 103(a) as unpatentable over the combination of Saakian and Zoons is reversed.

DECISION SUMMARY

In summary:

Claims Rejected	35 U.S.C. §	Reference(s)/Basis	Affirmed	Reversed
1–3	103	Saakian	1–3	
4	103	Saakian, Hanshermann	4	
6	103	Saakian, Ledford		6
7	103	Saakian, Rao		7
8	103	Saakian, Zoons		8
1–4	103	Kalimullina, Saakian	1–4	
Overall Outcome			1–4	6–8

TIME PERIOD FOR RESPONSE

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

AFFIRMED-IN-PART