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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ARKADY RUBIN [1]

Appeal 2018-000302
Application 14/017,524
Technology Center 1600

Before FRANCISCO C. PRATS, JAMES A. WORTH, and JOHN E. SCHNEIDER, *Administrative Patent Judges*.

SCHNEIDER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[2] under 35 U.S.C. § 134 from the Examiner's rejection of claims to an intravaginal drug delivery device which have been rejected as anticipated and as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellant identifies the real party in interest as ARSTAT, Inc. Br. 3.
[2] We have considered and herein refer to the Specification of Sept. 4, 2013 ("Spec."); Final Office Action of June 22, 2016 ("Final Act."); Appeal Brief of Mar. 15, 2017 ("Br."); and Examiner's Answer of July 13, 2017 ("Ans.").

STATEMENT OF THE CASE

"Uterine fibroids are common. They include fibromyomas, myomas, fibromas, leiomyomata, etc. and are classified into submucosal, intramural, and subserosal fibroids." Spec. 1. "Uterine fibroids may be associated with a number of symptoms, including heavy menstrual bleeding (sometimes accompanied by anemia), menstrual pain, pelvic or abdominal pressure, pain during intercourse and obstructive symptoms, including increased frequency of urination (due to diminished bladder capacity) and constipation.[] Fibroids may also cause infertility." *Id.* The Specification describes

> a method for effectively reducing the size of uterine fibroids or the uterus and/or improving fibroid-related symptoms without the undesirable side effects of oral medications by providing for intravaginal delivery of a selective progesterone receptor modulator (SPRM), anti-progestin, or anti-progestational agent at doses which are significantly lower than oral doses known in the art.

Id. at 5.

Claims 15–17, 20, and 26 are on appeal.[3] Claim 1 is the sole independent claim on appeal and reads as follows:

> 15. An intravaginal drug delivery device comprising:
> a drug delivery device; and
> a therapeutically effective amount of an active agent,
> wherein the drug delivery device is configured to deliver the active agent directly to uterine fibroids, wherein further the drug delivery device delivers a daily dose of the active agent

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[3] Claims 1–14, 18, 21, 22, 24, 25, and 27 are pending in the application but have been withdrawn from consideration as directed to non-elected species. Final Act. 3. Appellant elected examination of the remaining claims with mifepristone as the active agent, a vaginal ring as the delivery device and where the active agent is mixed throughout the vaginal ring. *Id.* at 2.

> which does not exceed 500 mcg, wherein the active agent is mifepristone.

The claims stand rejected as follows[4]:

Claims 15–17 have been rejected under 35 U.S.C. § 102(b) as anticipated by Chen.[5]

Claims 15–17 and 20 have been rejected under 35 U.S.C. § 102(b) or § 103(a) and anticipated by or as unpatentable over Chen.

Claim 26 has been rejected under 35 U.S.C. § 103(a) as unpatentable over Chen.

FIRST ANTICIPATION REJECTION – CLAIMS 15–17

The issue with respect to this rejection is whether a preponderance of the evidence supports the Examiner's conclusion that claims 15–17 are anticipated by Chen.

The Examiner finds that Chen, in paragraph 84, discloses a vaginal ring which comprise Mifepristone. Final Act. 5. The Examiner finds that the release rate for the ring as shown in Figure 3, reproduced below, is less than 500 μg per day. *Id.*

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[4] Claim 20 was also rejected under 35 U.S.C. § 112, first paragraph for failure to comply with the written description requirement. Final Act. 34. This rejection was withdrawn by the Examiner. Ans. 2.

[5] Chen et al., US 2005/0197651 A1, published Sept. 8, 2005 ("Chen").

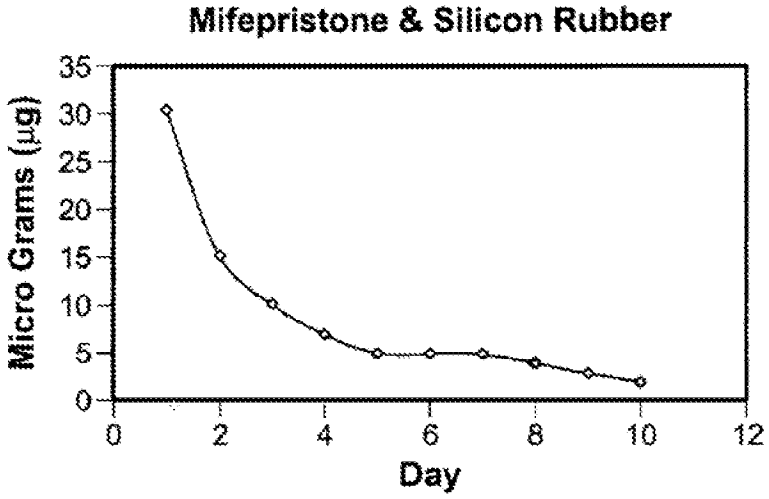

FIG. 3

Figure 3 of Chen shows the release rate of a prior art vaginal ring containing Mifepristone.

The Examiner finds that the limitation "configured to deliver the active agent directly to uterine fibroids" is a characteristic of a vaginal ring containing Mifepristone citing *In re Best*, 562 F.2d 1252 (CCPA 1977),and *In re Fitzgerald,* 619 F.2d 67 (CCPA 1980). Final Act. 6.
Appellant does not present any arguments on appeal with respect to this rejection. *See* Br. 8; Ans. 2–3. Therefore, we affirm the rejection with respect to claims 15–17, and 20. 37 C.F.R. § 41.37(c)(1)(iv).

SECOND ANTICIPATION REJECTION – CLAIMS 15–17 AND 20

Issue

The issue with respect to this rejection is whether a preponderance of the evidence supports the Examiner's conclusion that claims 15–17 and 20 are anticipated by Chen. Alternatively, the issue is whether a preponderance

of the evidence supports the Examiner's conclusion that the subject matter of claims 15–17 and 20 would have been obvious over Chen.

The Examiner finds that Chen discloses the preparation of vaginal rings with an active agent mixed throughout. Final Act. 18. The Examiner finds that in the discussion of Application 3, Chen discloses a vaginal ring containing Mifepristone. *Id.* The Examiner finds that Chen discloses that a vaginal ring of Chen containing Mifepristone was used to treat a woman with uterine myoma (fibroids). Final Act. 19. The Examiner fids that Chen discloses that the use of the ring was clinically effective. *Id.* The Examiner finds that Figure 4 of Chen, reproduced below, teaches that the ring of Application 3 had a maximum weekly release rate of 1200 µg during the first week, which equates to an average daily release rate of 170 µg. *Id.* at 19–20.

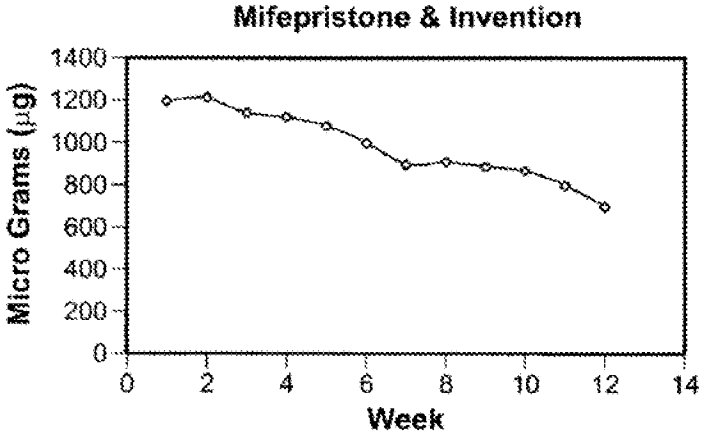

FIG. 4

Figure 4 of Chen shows the weekly release rate of a vaginal ring containing Milfepristone.

Alternatively, the Examiner finds that Chen discloses that based on the disclosure in Clinical Trial I of Chen, the vaginal ring used would have a daily release rate of 400 mcg at the end of the last week on the trial. Final

Act. 21. In reaching this finding the Examiner assumes that the release rate disclosed in Figure 4 is actually a daily release rate and that the release rate on day 1 was 1200 μg. *Id.*

Principles of Law

> [T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant.
>
> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

In re Oetiker, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

"Anticipation requires that all of the claim elements and their limitations are shown in a single prior art reference." *In re Skvorecz*, 580 F.3d 1262, 1266 (Fed. Cir. 2009).

Analysis

We adopt the Examiner's findings of fact, reasoning on scope and content of the prior art, and conclusions set out in the Final Action and Answer regarding this rejection. Final Act. 17–24; Ans. 5–14. We find the Examiner has established that the claims 15, 16, and 20 are anticipated by Chen and that the subject matter of claim 17 would have been obvious over Chen. Appellant has not produced evidence showing, or persuasively argued, that the Examiner's determinations on anticipation with respect to claims 15, 16, and 20 and obviousness with respect to claims 17 are incorrect. Only those arguments made by Appellant in the Brief have been

considered in this Decision. Arguments not presented in the Brief are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015). We address Appellant's arguments below.

Appellant contends that Chen does not disclose a release rate of less than 500 µg per day. Br. 8. Appellant argues that the x-axis of the graph on Figure 4 of Chen should be read as days, not weeks. *Id.* Appellant argues that the Examiner concedes that the device referenced in Figure 4 has a daily release rate of greater than 500 µg. *Id.* Appellant also points to the graphs in Figures 5 and 6 which report data based on a daily release rate as supporting the contention that Figure 4 should be read as reporting daily release data. *Id.* Appellant contends that this interpretation is consistent in that Chen teaches that the release rate can reach as high as 1 to 10 mg per day. Br. 10. Appellant also contends that the Examiner has improperly extrapolated the data in Figure 4 in an effort to shown that the ring would eventually have a release rate of less than 500 µg. *Id.* at 9.

We have considered Appellant's arguments and find them unpersuasive. We do not agree with Appellant that Figure 4 would be interpreted as reporting daily and not weekly release data. The data reported in Figure 4 is consistent with the two Clinical Tests reported in Chen. In test 1, a vaginal ring containing Mifepristone was used by a patient from November 13, 2000 to March 20, 2001. Chen ¶ 90. Similarly, in test 2 the patient used the vaginal ring containing Mifepristone from July 2000 to October 2000. *Id.* ¶ 92. Thus, both tests lasted at least 12 weeks, the same time period reported in Figure 4.

Appellant's reliance of Figures 5 and 6 is misplaced. Those figures report the release rated for Danazol, a different active substance. Paragraph

83, cited by Appellant at page 10 of the Appeal Brief, refers to yet another active agent Raloxifene. Appellant has not pointed to any teaching in Chen which would suggest that a vaginal ring with Mifeprestone would exhibit the same release rate as the rings containing Danazol or Raloxifene.

Having concluded that Figure 4 teaches a weekly release rate rather that a daily release rate, we agree with the Examiner that the weekly rate correlates to a maximum average release rate of 170 μg. This rate is less than 500 μg recited in claim 15 and within the range of 100 to 400 μg recited in claim 20.

Appellant found that the Examiner presented an alternative argument regarding anticipation based on the assumption that Figure 4 reported a daily release rate as opposed to a weekly release rate. Appellant's remaining arguments address this alternate argument. *See* Br. 10–11. As discussed above, we find that Figure 4 teaches a weekly rate and not a daily rate. Appellant's arguments regarding the Examiner's extrapolation of a daily rate are not persuasive.

Claim 16

Claim 16 has not been separately argued and, therefore, falls with claim 15. 37 C.F.R. § 41.37(c)(1)(iv).

Claim 17

Appellant separately argues the patentability of claim 17. Claim 17 depends from claim 15 and adds the limitation that the active agent is mixed throughout the vaginal ring. Br. 29 (Claims App'x).

In addition to reiterating the arguments made with respect to claim 15, Appellant contends that the Mifepristone in the ring of Application 3 in Chen is not mixed throughout the ring. *Id.* at 12–13. Appellant contends

that Chen discloses a structure where the Mifepristone is applied as a layer on a ring and then covered with another layer of polymer. Br. 13 (citing Chen ¶¶ 61–63, Fig. 2B).

In reply the Examiner argues that the term "'throughout'" is defined to mean "'in or to every part.'" Ans. 13. The Examiner contends that application of a layer containing the active agent meets this definition in that the layer is applied to every part. *Id.*

We have considered both arguments and find that Appellant has the better position. The term at issue is not merely "throughout" but "mixed throughout." We interpret this phrase to call for a mixture of the active agent and polymer to be found throughout the structure, not in a discrete layer.

This does not end out inquiry, however. The Examiner has also rejected claim 17 as obvious over Chen. Chen teaches an embodiment wherein the active agent is dispersed throughout vaginal ring. Chen ¶ 42, Fig. 2A. As discussed in Chen, Figure 2A discloses a vaginal ring with the active agent dispersed within substantially all of the ring and a thin cover over the ring. Chen ¶ 39. One skilled in the art would use the design of Figure 2A for a vaginal ring because is a simpler design as opposed to the three layer construction used in Application 3. "It is ordinarily true that the omission of an element and its function is uninventive." *In re Perrine,* 111 F.2d 177, 178 (CCPA 1940).

While claim 17 is not anticipated by claim 17, we agree with the Examiner that the subject matter of claim 17 would have been obvious over Chen.

Claim 20

Claim 20 depends from claim 1 and narrow the range of active agent released to 100 to 400 μg a day. Br. 29 (Claims App'x). Appellant contends that Chen does not disclose a vaginal ring with a release rate within this range. *Id.* at 14.

Appellant's argument is not persuasive. As discussed above, the maximum daily release rate for the vaginal ring disclosed in Figure 4 of Chen is 170 μg, well within the range recited in claim 20. Therefore, Chen anticipates claim 20.

OBVIOUSNESS

The Examiner has rejected claims 15–17, 20, and 26 as obvious over Chen.

As discussed above, we find that claims 15, 16, and 20 are anticipated by Chen. Since Chen anticipates these claims, Chen also renders the claims obvious. "[A] disclosure that anticipates under § 102 also renders the claim invalid under § 103, for 'anticipation is the epitome of obviousness.'"

Connell v. Sears, Roebuck & Co., 722 F2d 1542, 1548 (Fed. Cir. 1983) (quoting *In re Fracalossi*, 681 F.2d 792, 794 (CCPA 1982)).

With respect to claim 17, we have addressed the issue of obviousness in our discussion above.

We now address the issue of whether a preponderance of the evidence supports the Examiner's conclusion that the subject matter of claim 26 would have been obvious over Chen.

Claim 26 depends from claim 20 and narrows the daily release rate to a range of from 250 μg to 300 μg. Br. 30 (Claims App'x).

The Examiner finds

> it would alternately have been obvious to one of ordinary skill in the art at the time of the instant invention to explore the optimal daily dosage to achieve treatment of uterine fibroids (selection of initial daily doses, between the Figure 3 and Figure 4 encompass a range to explore that includes the recited ranges of claims 15, 20 and 26, including the narrower range of claim 26, from 250-300 μg/day), while balancing minimization of side effects and reducing cost of the drug, giving daily dosages within the ranges of claims 15, 20 and 26, giving the instant elected mifepristone vaginal rings. Chen teaches the same therapeutic purpose as the instant application, treatment of uterine fibroids; therefore routine optimization for the same purpose would have arrived at the same daily dosing as a result of this optimization process.

Final Act. 23.

Principles of Law

> [T]he examiner bears the initial burden, on review of the prior art or on any other ground, of presenting a *prima facie* case of unpatentability. If that burden is met, the burden of coming forward with evidence or argument shifts to the applicant.

> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

Oetiker, 977 F.2d at 1445.

"[W]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).

"To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention." *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, 752 F.3d 967, 977 (Fed. Cir. 2014).

"Consistent with the rule that all evidence of nonobviousness must be considered when assessing patentability, the PTO must consider comparative data in the specification in determining whether the claimed invention provides unexpected results." *In re Soni*, 54 F.3d 746, 750 (Fed. Cir. 1995); *see also In re Margolis*, 785 F.2d 1029, 1031 (Fed. Cir. 1986). However, "[i]t is well settled that unexpected results must be established by factual evidence. Mere argument or conclusory statements in the specification does not suffice." *In re De Blauwe*, 736 F.2d 699, 705 (Fed. Cir. 1984); *see also In re Wood*, 582 F.2d 638, 642 (CCPA 1978) ("Mere lawyer's arguments and conclusory statements in the specification, unsupported by objective evidence, are insufficient to establish unexpected results."); *Soni*, 54 F.3d at 750.

Analysis

We find the Examiner has established that the subject matter of claim 26 would have been obvious to one of ordinary skill in the art at the time the invention was made over Chen. Appellant has not produced evidence showing, or persuasively argued, that the Examiner's determinations on obviousness are incorrect. Only those arguments made by Appellant in the Brief have been considered in this Decision. Arguments not presented in the Brief are waived. *See* 37 C.F.R. § 41.37(c)(1)(iv) (2015). We address Appellant's arguments below.

Appellant's arguments are primarily based on the assumption that Figure 4 of Chen discloses a daily release rate of 1200 μg and not a weekly rate. *See* Br. 15–26. As discussed above, we have concluded that Figure 4 of Chen discloses a weekly release rate of 1200μg which equates to a daily release rate of 170μg.

Appellant contends that Chen teaches a release rate for Mifepristone significantly greater than 500 μg and that one skilled in the art would not be motivated to use a lower dose of Mifepristone. Br. 16–18. We are unpersuaded by this argument.

Chen teaches a daily release rate of 170 μg of Mifepristone. Chen, Fig. 4; Final Act. 20. Chen also teaches that the prior art taught a ring that had a maximum release rate of 30 μg/day. Chen, Fig. 3. Chen goes on to teach that it is an object of Chen to produce a vaginal ring that has a large enough quantity of an active agent to be medically effective over time while reducing the side effects associated with the active agent. *Id.* ¶¶ 8, 14. We agree with the Examiner that one skilled in the art would be motivated to

optimize the amount of Mifepristone to achieve maximum effectiveness with a minimum degree of side effects. Final Act. 23.

Appellant argues that the claimed invention produces surprising and unexpected results. Br. 17. Appellant contends that the present invention permits the use of lower doses of active agent that traditional oral administration. *Id.* Appellant also argues that the doses and treatment periods recited in the Specification are unexpected shorter than that recited in Chen. *Id.*

We have considered Appellant's arguments and are unpersuaded. Other than the statement in the Brief, Appellant has offered no evidence that the results achieved by the claimed invention are unexpected. In addition, Appellant has not presented any evidence showing a comparison of the claimed invention against the closet art, namely Chen. Absent actual evidence, statements in the brief and attorney arguments are insufficient to overcome a finding of obviousness.

Appellant's remaining arguments address the extrapolation by the Examiner showing that even if Figure 4 recited daily release rates, the vaginal rings would, at some point in time exhibit a release rate of less than 500μg. Br. 19–20. We find these arguments unpersuasive for the reasons stated above.

Appellant also argues that Chen teaches away from the claimed invention. *Id.* at 21. Appellant's argument is based on the assumption that Chen teaches a daily release rate of 1200μg of Milfepristone in Figure 4 and that Chen teaches maximizing the dosage of active agent. *Id.*

Again we find this argument unpersuasive as Chen does not criticize, discredit, or otherwise discourage the use of the claimed dosage range. *In re*

Fulton, 391 F.3d 1195, 1201 (Fed. Cir. 2004). In fact, as discussed above, Chen does the opposite. Figure 4 of Chen does not teach a daily release rate of greater than 500 µg but in fact teaches a lower daily amount, 170µg. Final Act. 20. This lower amount, coupled with the teaching in Chen to maximize the amount while reducing side effects would lead one skilled in the art to optimize the amount of Mifepristone to arrive at the range of Mifepristone recited in claim 26.

Conclusion

We conclude that a preponderance of the evidence supports the Examiner's conclusion that the subject matter of the claims would have been obvious over Chen.

DECISION

We affirm the first rejection of claims 15–17 and 20 under 35 U.S.C. § 102(b).

We affirm the second rejection of claims 15, 16, and 20 under 35 U.S.C. § 102(b).

We reverse the second rejection of claim 17 under 35 U.S.C. § 102(b).

We affirm the rejection of claims 15–17, 20, and 26 under 35 U.S.C. § 103(a).

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