IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

BAYER PHARMA AG, BAYER INTELLECTUAL PROPERTY GMBH, and BAYER HEALTHCARE PHARMACEUTICALS, INC.,	:	
Plaintiffs,	:	
v.	:	Civil Action No. 12-1726-LPS
	:	**FILED UNDER SEAL**
WATSON LABORATORIES, INC.,	:	
Defendant.	:	

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MEMORANDUM OPINION

July 18, 2016
Wilmington, Delaware

STARK, U.S. District Judge:

Bayer Pharma AG, Bayer Intellectual Property GmbH, and Bayer Healthcare Pharmaceuticals Inc. (collectively, "Bayer" or "Plaintiffs") allege that Watson Laboratories, Inc. ("Watson" or "Defendant") infringes United States Patent No. 8,071,577 ("the '577 patent" or "the patent-in-suit"). (D.I. 1) The '577 patent relates to a multiphasic regimen and method for oral contraception containing estradiol valerate ("EV") and dienogest ("DNG"). (D.I. 1-1) EV and DNG are the active ingredients of Bayer's Natazia® product. (D.I. 1 ¶ 17)

In September 2014, the Court construed the disputed terms of the patents-in-suit.[1] (D.I. 99, 111) The Court then held a four-day bench trial in December 2014. (*See* D.I. 125, 126, 127, 128) ("Tr.") After several extensions, the parties completed post-trial briefing on July 2, 2015. (D.I. 136, 138, 141) In connection with the briefing, the parties submitted proposed findings of fact (D.I. 135, 137, 139), as well as a Stipulation of Uncontested Facts ("SUF") (D.I. 142).

Pursuant to Federal Rule of Civil Procedure 52(a), and after having considered the entire record in this case and the applicable law, the Court concludes that: (1) Defendant has stipulated that its proposed products infringe claims 1-3 of the '577 patent; (2) Defendant has failed to prove by clear and convincing evidence that claims 1-3 of the '577 patent are invalid for obviousness-type double patenting; and (3) Defendant has failed to prove by clear and convincing evidence that claims 1-3 of the '577 patent are invalid for obviousness. The Court's findings of fact and conclusions of law are set forth in detail below.[2]

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[1]Neither party objected to the Report and Recommendations regarding Claim Construction prepared by Magistrate Judge Burke.

[2]At the conclusion of trial, the parties proposed a stipulation by which post-trial briefing would have been completed by April 3, 2015. (*See* D.I. 120) Thereafter, on February 17, March 2, and

FINDINGS OF FACT

This section contains the Court's findings of fact ("FF") on disputes raised by the parties during trial, as well as the facts stipulated to by the parties. Certain findings of fact are also provided in connection with the Court's conclusions of law.

A. The Parties

1. Plaintiff Bayer Pharma AG ("Bayer Pharma"), formerly known as Bayer Schering AG, is a corporation organized and existing under the laws of the Federal Republic of Germany, having a principal place of business at Müllerstrasse 178, 13353 Berlin, Germany. (SUF ¶ 1)

2. Plaintiff Bayer HealthCare Pharmaceuticals Inc. ("Bayer HealthCare"), formerly known as Berlex, Inc., is a corporation organized and existing under the laws of the State of Delaware, having a principal place of business at 100 Bayer Boulevard, Whippany, New Jersey, 07981 USA. (*Id.* ¶ 2)

3. Plaintiff Bayer Intellectual Property GmbH ("Bayer IP") is a corporation organized and existing under the laws of the Federal Republic of Germany, with a place of business at Alfred-Nobel-Strasse 10, 40789 Monheim, Germany. (*Id.* ¶ 3)

4. Defendant Watson Laboratories, Inc. is a corporation organized and existing under the laws of the State of Nevada, having a principal place of business at 132 Business Center Drive, Corona, California 92880 USA. (*Id.* ¶ 4)

April 2, 2015, the parties stipulated to extensions, such that the first of their briefs was not filed until May 15, 2015 and briefing was not completed until July 1, 2015. (*See, e.g.*, D.I. 129, 131, 132) On September 11, 2015, the Court held a teleconference to assess the time sensitivity of the case. (*See* D.I. 146) Among other things, the parties advised the Court that there is no automatic 30-month stay of United States Food and Drug Administration ("FDA") approval of Watson's proposed generic product. (*See id.* at 3) On May 13, 2016, Bayer advised the Court that on May 6, 2016 Watson had received FDA approval for its generic version of Natazia®. (D.I. 151)

B. The Menstrual Cycle and Combined Oral Contraceptives

5. The menstrual cycle is the biological process where, over the course of a month, a woman produces a follicle that then ovulates. Ovulation occurs when a dominant follicle develops, ruptures, and releases an egg. (DDX108; Simon Tr. at 101-02)[3] If a woman does not become pregnant during that month, she will menstruate and begin the cycle again. (Barnhart Tr. at 367-68)

6. The initial phase of the menstrual cycle is called the proliferative phase, during which the endometrial lining of the uterus thickens under the dominant influence of estrogen. After ovulation, progesterone levels increase. Progesterone is anti-proliferative and acts to stop the endometrium from further thickening and, if no pregnancy occurs, initiates the sloughing of the uterine lining and bleeding that characterizes menstruation. (Barnhart Tr. at 368-69; Simon Tr. at 102)

7. The menstrual cycle changes considerably in the presence of a combined oral contraceptive ("COC"). A COC is a drug that combines an estrogen hormone with a synthetic progesterone, or progestin, hormone (also known as a gestagen or gestogen) to provide a contraceptive effect. (Simon Tr. at 99-100) In a COC, the estrogen component is primarily responsible for providing cycle control, while the progestin hormone suppresses the growth of follicles, preventing ovulation, and thereby providing contraception. (Simon Tr. at 100-04; Barnhart Tr. at 372)

8. The hormone levels associated with a natural menstrual cycle are considerably

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[3]Citations to the trial transcript (which can be found at D.I. 125, 126, 127, 128) are in the form of: ("[Witness last name] Tr. at [page]").

lower, almost flat-lined, when a woman is taking a COC. The endometrial lining of the uterus when a woman is taking a COC is also considerably different from the natural menstrual cycle. In the initial proliferative phase of the menstrual cycle of a woman taking a COC, there is less proliferation, and the lining of the uterus is much thinner than in the natural menstrual cycle. (Barnhart Tr. at 370-72)

9. It is necessary that a COC promote enough proliferation, however, to maintain a stable endometrial lining during the menstrual cycle, in order to avoid intracyclic bleeding. (*Id.* at 370-71) If the endometrium becomes too thin under the influence of the COC or is otherwise unstable, the result is undesirable intracyclic bleeding and inadequate cycle control. (*Id.* at 371-72)

10. At trial, both sides' experts agreed that cycle control is an important feature of a successful COC. (Simon Tr. at 100-01; Barnhart Tr. at 372) Cycle control refers to avoiding unscheduled bleeding during a contraceptive cycle. (Simon Tr. at 100-01; Barnhart Tr. at 372) Cycle control is important because unscheduled bleeding and spotting negatively affect women and their contraceptive use. (Simon Tr. at 100-01) Poor cycle control can be inconvenient, and this may lead to a failure to take all required doses, which can result in a pregnancy. (Barnhart Tr. at 372)

C. Selecting the Components and Dosages for a COC

11. Historically, the estrogen component in COCs has been nearly universally a synthetic estrogen called ethinylestradiol ("EE"). (JTX3 at 105-06; Simon Tr. at 111; Holtz Tr. at 330) In general, EE is highly effective for preserving cycle control. (Simon Tr. at 112) However, EE, at certain doses, is associated with a risk of venous thromboembolism, or blood

clotting. (*Id.* at 112-13) To minimize this side effect, over the course of decades drug manufacturers systematically reduced the dose of EE in COCs. (*Id.* at 113)

12. As an alternative to reducing EE doses, drug manufacturers attempted to replace the EE component with natural estrogens, such as estradiol valerate ("EV"). (*Id.* at 114)

13. EE behaves differently than EV with respect to cycle control. (Simon Tr. at 242) The differences between EE and EV with respect to cycle control resulted in 30-40 years of failures caused by poor cycle control in efforts to develop a COC with natural estrogen. (Barnhart Tr. at 420)

14. Prior art references disclosed COCs using daily doses of EE in the amounts of 3, 2, and 1 mg, including embodiments using daily doses of 3-2-1 mg on different days of a single cycle. (JTX14 at 3:16-53; DTX74 at 3-4; JTX68 at 3; JTX3 at 108; JTX2 at 460)

15. A progestin's effect of inhibiting follicular development and ovulation depends on the dose in which it is given, such that ovarian suppression increases with increasing absolute doses of progestin. (JTX4 at 277 ("[T]he ovulation inhibitory effects of dienogest are directly related to the dose received."); JTX20 at 2 (Endrikat declaration submitted in prosecution of '577 patent, stating "it was commonly known to one of ordinary skill in the art that higher progestin doses provide higher ovarian suppression with increasing absolute doses"); Barnhart Tr. at 479-80 (discussing dose-response relationship around anti-ovulatory dose); Simon Tr. at 105-06, 146-47 (discussing JTX215 at depo. tr. p. 59))

16. One progestin that had been commonly used in prior art COCs is dienogest, or "DNG". (JTX3 at 8; Simon Tr. at 119) DNG had been used safely since 1995 in a prior art COC, Valette®, with a daily dose of 2 mg. (JTX173 at 534)

17. The prior art includes a dose-ranging study by Dr. Claudia Moore, aimed at determining the minimum dosage of DNG alone required for consistent ovulation inhibition. (JTX4) Moore determined that 1.0 mg of DNG "reliably inhibited ovulation." (*Id.* at 277) Moore's study was art of record before the Examiner during the prosecution of the '577 Patent. (JTX1; JTX265 at 20, 131)

18. Persons of ordinary skill in the art ("POSA") understand that a COC will sometimes utilize the minimum single-agent ovulation inhibition dose of a progestin and double it as a maximum daily dose for the COC. This typical "rule of thumb" applicable to COCs accounts for the facts that a pill must be dosed in a one-size-fits-all manner and that patients are known to sometimes miss pills. (Simon Tr. at 126-30; Barnhart Tr. at 458-59 (discussing estimates of 30% of women missing at least one pill in a cycle)) POSAs would generally understand this potential two-times the minimum ovulation inhibition dose to be a ceiling for potential COCs. (Barnhart Tr. at 420-21) POSAs would also understand that COCs can have progestin dosing below the minimum single-agent dose. (*Id.* at 312, 428, 430-31)

19. Another guiding principle in COC development has been the trend to lower hormone doses. (Barnhart Tr. at 398) Over the past 40 years, the doses of estrogen and progestin used in COCs have gradually declined. (JTX136 at 185; JTX173 at 518; Barnhart Tr. at 399; Simon Tr. at 171) This development trend is also part of the FDA's labeling guidance to pharmaceutical companies. (JTX133 at 47; JTX134 at 4; Barnhart Tr. at 400-01; Allen Tr. at 583)

20. The historical trend towards lowering hormone doses over time would have taugh a POSA that it would be appropriate to use less than 2 mg of DNG in a COC. (Barnhart Tr. at

421-22)

21. COCs are typically monophasic, meaning "the amount of each particular hormone in each day of use is the same," but there are also biphasic, triphasic, and a few multiphasic contraceptive regimens in which the amount of each hormone differs at different phases of a cycle. (Simon Tr. at 96)

D. Assessing the Effectiveness of COCs

22. In 1993, a prior-art article by Hoogland described a method to evaluate the effectiveness of contraceptives by assessing residual ovarian activity. (JTX214; Simon Tr. at 107-10) The method utilizes ultrasound to assess follicular growth in women taking a contraceptive progestin. (Simon Tr. at 107)

23. Hoogland describes a six-point scale to characterize residual ovarian activity, ranging from no ovarian activity (at the low end) to an ovulation (at the high end). (JTX214 at 585; Simon Tr. at 107-08) A score of three on a scale starting with zero (or four on a scale starting with one (this latter scale indicated in parentheses going forward)) is an active follicular-like structure ("FLS"), which is greater than 13 millimeters in size and begins to produce estradiol. (Simon Tr. at 108; Barnhart Tr. at 511) A score of four (or five) is a luteinized unruptured follicle ("LUF"), which indicates further activity where the follicle produces progesterone and estradiol. (Simon Tr. at 108) Active FLSs and LUFs represent residual ovarian activity. (JTX214 at 585; JTX12 at 109; Simon Tr. at 142-43; Barnhart Tr. at 513-14) A score of five (or six) is ovulation. (JTX214 at 585)

24. The rationale for Hoogland's method of characterizing ovarian activity into six categories was an observation that "[t]he trend towards changing the composition of the

contraceptive pill in order to decrease side effects might lead to increased ovarian activity. This may decrease reliability." (*Id.* at 583) Hoogland taught "that the degree of residual ovarian activity under oral contraceptives should be regarded as the best possible parameter of medicine dependent efficacy," and that "follicular growth and ovulation are significant parameters to define pill reliability." (*Id.* at 587 (emphasis omitted); Simon Tr. at 111)

25. Other than being labels assigned to categories, the numbers in the Hoogland scale have no meaning. (Simon Tr. at 230-32) That is, there is no mathematical relationship between a 3 and a 4, for example, on the Hoogland scale. (Barnhart Tr. at 373) Moreover, each menstrual cycle is characterized by one and only one Hoogland score; it is not as if every month a cycle passes through lower number stages on the way to higher number stages. (*Id.* at 373-76)

26. While contraceptive efficacy must ultimately be determined by a large Phase III clinical trial, a common method for determining the potential efficacy of a COC is a smaller Phase II ovulation inhibition study, typically involving 10-30 women. (Allen Tr. at 564-65) Ovulation inhibition studies measure the degree of ovarian suppression. (*Id.* at 562-64; Barnhart Tr. at 373-77)

27. Another measure of contraceptive effectiveness is called the "Pearl Index." (Simon Tr. at 173; Allen Tr. at 566) A Pearl Index is a calculation of the number of pregnancies per 100 woman years based on data from a Phase III clinical trial. (Simon Tr. at 173; Allen Tr. at 567) COCs on the market at the time of the invention of the patent-in-suit had Pearl Index values of 2.92 or less. (Allen Tr. at 568-69)

28. The principal end point being measured in any study of contraceptive efficacy is ovulation. (Barnhart Tr. at 379-80)

E. Bayer's Natazia®

29. Bayer is the holder of New Drug Application ("NDA") No. 22-252, which relates to an oral contraceptive regimen known by and sold in the United States under the trademark Natazia®. (SUF ¶¶ 5, 8)

30. On May 6, 2010, the FDA approved the marketing of the product described in NDA No. 22-252 for the prevention of pregnancy in women who choose to use an oral contraceptive. (*Id.* ¶ 6)

31. On March 14, 2012, the FDA further approved the marketing of the product described in NDA No. 22-252 for the treatment of heavy menstrual bleeding ("HMB") in women without organic pathology who choose to use an oral contraceptive as their method of contraception. (*Id.* ¶ 7)

32. Natazia® is a multiphasic COC that uses EV as the estrogen component and DNG as the progestin component. (JTX1; Simon Tr. at 97-98) The Natazia® regimen involves daily doses of EV of 0, 1, 2, and 3 mg, depending on the phase of the cycle, and daily doses of DNG of 0, 2, and 3 mg, again depending on the phase of the cycle. (JTX1; Zelano Tr. at 278)

33. Prior to the discovery of Natazia®, all prior art describing specific examples of DNG-containing COC regimens recommended a daily dose of 2 mg or less, including the Moore article, the Hoffmann articles, the Dittgen patents and applications, and the Gast patent. (All of this prior art is addressed in greater detail below.)

34. Natazia® is the first "natural" estrogen COC marketed in the United States. (JTX265 at 1313-14; Holtz Tr. at 330; Barnhart Tr. at 434)

35. Natazia® was launched in Europe under the name "Qlaira®" in May 2009 and in

the United States in July 2010. (Holtz Tr. at 329)

F. The Patent-in-Suit: U.S. Patent No. 8,071,577

36. The patent-in-suit is the '577 patent. (JTX1) Jan Endrikat and Bernd Düsterberg are identified as inventors on the '577 patent, which was filed on April 15, 2005 and claims priority to a German patent filing on April 20, 2004. (SUF ¶ 9) The '577 patent was issued December 6, 2011. (*Id.*) Bayer IP is the current owner of the '577 patent. (*Id.*)

37. The '577 patent is directed to multiphasic regimens for oral contraception involving the estrogen EV, the progestin DNG, and placebo. (JTX1) The '577 patent has two examples and three claims. (*Id.* at cols. 3-4) Each claim relates to a particular contraceptive regimen, as presented in the table below:

Table 1. '577 Patent/Natazia® Regimen

Phase	Days	Dose Elements
Phase 1	2 daily doses	3 mg EV
Phase 2, group 1	5 daily doses	2 mg EV and 2 mg DNG
Phase 2, group 2	17 daily doses	2 mg EV and 3 mg DNG
Phase 3	2 daily doses	1 mg EV
Phase 4	2 daily doses	Placebo

38. As displayed in Table 1 above, the claimed regimen has three basic components. First, the claims involve a particular phasic pattern – that the Court will refer to as the "2-5-17-2-2" dosing pattern – which represents the calendar days EV, DNG, and placebo are to be given. Second, the claims require daily doses of EV at 3 mg in the first phase, 2 mg in the second phase, and 1 mg in the third phase. Third, the claims require daily doses of DNG at 2 mg

during Phase 2, group 1 and 3 mg during Phase 2, group 2. (*Id.*; Simon Tr. at 121)

39. Natazia® is a commercial embodiment of the claims of the '577 patent. (JTX1; Zelano Tr. at 278)

40. The '577 patent, which expires on May 13, 2026, is listed in the entry for Natazia® in the FDA's "Approved Drug Products with Therapeutic Equivalence Evaluations" ("Orange Book"). (SUF ¶ 10) Previously, Bayer had listed U.S. Patent No. 6,133,251 ("the '251 patent") and U.S. Patent No. 6,884,793 ("the '793 patent") in the FDA's Orange Book as protecting Natazia®, until 2011 when it disclaimed all interest in these patents. (DTX 42 at 4-11; DTX43; DTX44; Matthey Tr. at 316-17, 320-21)

G. Bayer's Prior Patents Covering Natazia®

41. The '577 patent is the third patent that Bayer has owned that covers the Natazia® regimen. (*Id.*; JTX14; JTX19; JTX1)

42. Bayer's corporate representative witness, Anthony Zelano, the attorney who prosecuted the '577 patent, testified about the prosecution of all three patents. (*See generally* Zelano Tr. at 278-313)

1. The '251 patent and its prosecution

43. On October 25, 1996, Bayer's subsidiary, Jenapharm, filed U.S. Patent Application No. 08/738,314 ("the '314 application"), naming Michael Dittgen and others as inventors ("the Dittgen group"). (DTX69; Zelano Tr. at 280) The '314 application issued as the '251 patent on October 17, 2000. (JTX14) The '251 patent involves a "Combination Compound for Contraception Based on Natural Estrogen." (*Id.*)

44. The '251 patent describes and claims a genus of multiphasic regimens effective

for oral contraception. (*Id.* at 1) The scope of the regimens claimed in the '251 patent is as follows:

Table 2. '251 Patent Regimen

Phase	Days	Dose Elements
Phase 1	**2**-4 daily doses	Natural estrogen compound
Phase 2, group 1	3-**5** daily doses	Natural estrogen compound and synthetic or natural gestogen
Phase 2, group 2	13-**17** daily doses	Natural estrogen compound and synthetic or natural gestogen (more gestogen than in Phase 1)
Phase 3	**2**-4 daily doses	Natural estrogen compound (less than in Phase 1)
Phase 4	**2**-4 daily doses	Placebo

(*Id.* at 6:31-64 (emphasis added); Simon Tr. at 115-16) As shown above in bold, the '251 patent's claimed range of days includes the 2-5-17-2-2 daily dosing regimen of the '577 patent.

45. The '251 patent specification describes that increasing the DNG dose by 1.5 to 3 times in Phase 2, group 2 – in comparison to Phase 2, group 1 – is advantageous for use in the multiphasic regimens described and claimed in the patent. (JTX14 at 3:34-43 ("Advantageously the gestogen content of the individual portions of the second group amounts to 1.5 to 3 times the gestogen content of the individual portions of the first group."); *id.* at 6:65-7:2 (claiming such

dosing); Simon Tr. at 154)

46. The '251 patent contains five examples utilizing natural estrogens in a multiphasic regimen having positive results for cycle control. (JTX14 at 4:28-6:7) Example 1 of the '251 patent specification describes the 3-2-1 mg dosing pattern of EV (in conjunction with the progestin desogestrel), and teaches that it offered good cycle control. (*Id.* at 4:28-30 ("The improvement of the cyclic bleeding behavior in women is also proven."); *id.* at 4:46-50; Simon Tr. at 116) Example 5 of the '251 patent specification describes the use of 1 mg DNG and 2 mg DNG given in Phases 2 and 3, respectively, of a five-phase regimen. (JTX14 at 5:53-61; JTX5 at 3)

47. To overcome an overbreadth rejection under 35 U.S.C. § 112, Jenapharm told the Patent Office that "the amount of experimentation to obtain exemplary compositions based on amended claim 8 and methods of administration according to claim 12 is reasonably limited." (DTX71 at 10; DTX 72; Zelano Tr. at 283-84) Natazia® was such an "exemplary composition" and a member of the claimed genus. (Zelano Tr. at 281-84)

48. To overcome an obviousness rejection to amended claim 8, Jenapharm submitted a declaration from Michael Dittgen and others, dated April 10, 2000. (JTX5; DTX74) This declaration, which published in the prior art as part of the file history of the '251 patent, describes an additional regimen, apart from the patent's five examples, that falls within the scope of the '251 patent's claims (the "Dittgen Regimen"). (*Id.*) The Dittgen Regimen involves the 3-2-1 mg EV dosing pattern, 1 mg and 2 mg DNG, and placebo in a 3-4-16-2-3 multiphasic regimen:

Table 3. Dittgen Regimen

Phase	Days	Dose Elements
Phase 1	3 daily doses	3 mg EV
Phase 2, group 1	4 daily doses	2 mg EV and 1 mg DNG
Phase 2, group 2	16 daily doses	2 mg EV and 2 mg DNG
Phase 3	2 daily doses	1 mg EV
Phase 4	3 daily doses	Placebo

49. The results of a phase II ovulation inhibition study of the Dittgen Regimen were reported in a Declaration ("Dittgen Declaration") to the United States Patent and Trademark Office ("PTO") that is part of the prior art. (JTX5 at 6; DTX74 at 6; Simon Tr. at 117) The Dittgen Declaration reports Hoogland results for a group of 21 women following the Dittgen Regimen. (JTX5) The results showed that none of the 21 women participating in the study ovulated. (JTX5 at 6; DTX74 at 6) However, 9 out of the 21 women (43%) showed active FLSs or LUFs in at least one of the three cycles tested. (*Id.*; Simon Tr. at 138-39)

50. The '251 patent was set to expire in 2016 (Matthey Tr. at 317); however, Bayer disclaimed all interest in the patent on March 4, 2011 (DTX44; Matthey Tr. at 321).

51. Bayer owned the '251 patent prior to acquiring the '577 patent. (Matthey Tr. at 279)

2. The '793 patent and its prosecution

52. On September 12, 2001, Bayer's subsidiary, Jenapharm, filed U.S. Patent Application 09/950,915 ("the '915 application"), naming the same Dittgen group from the '251 patent as the inventors. (JTX228) The '915 application claimed priority to the '314 application

and shared the same written description as the '314 application. (*Id.*)

53. The '915 application published on August 8, 2002. (DTX81; Zelano Tr. at 291-92) At the time of the application's publication in 2002, the application and its file history became open to the public. (Zelano Tr. at 292) Following that publication, all subsequent documents filed with the PTO during prosecution of the '915 patent would also be public. (*Id.* at 291-92)

54. On December 18, 2003 – several months before the April 2004 priority date of the '577 patent – Jenapharm filed an Amendment cancelling all previously pending claims in the '915 application and substituting application claim 15 ("New Claim 15") as the sole prosecution claim. (JTX68) The Amendment was available online through the PTO's Patent Application Information Retrieval ("PAIR") system for accessing published file histories, on or about the time it was filed. (Zelano Tr. at 293)

55. In New Claim 15, Jenapharm specifically claimed a multiphasic 2-5-17-2-2 pattern of EV, DNG, and placebo consistent with, though broader than, that used in Natazia®. (JTX68; DTX82; Zelano Tr. at 294-99) The regimen of New Claim 15 is presented in the table below:

Table 4. New Claim 15 Regimen

Phase	Days	Dose Elements
Phase 1	2 daily doses	Effective amount of EV
Phase 2, group 1	5 daily doses	Combination of EV and DNG
Phase 2, group 2	17 daily doses	EV and DNG, with more DNG than in group 1
Phase 3	2 daily doses	Effective amount of EV, lower than in Phase 1
Phase 4	2 daily doses	Placebo

(JTX68; Simon Tr. at 153)

56. In presenting New Claim 15 to the PTO, Jenapharm stated it was "very similar" to the Dittgen Regimen, and further that "[t]he showing in the previously filed [Dittgen] Declaration proves that the claimed contraceptive preparation of new claim 15 has unexpectedly improved properties in comparison to the closest prior art." (JTX68 at 6) The regimen described in New Claim 15 was different, however, from the Dittgen Regimen: the "length of the first and additional stages differs by one day in the case of claim 15 from the example in the Declaration." (*Id.*) Jenapharm did not, at that time, present the PTO with any claim that covered the 3-4-16-2-3 Dittgen Regimen. (*Id.* at 1-3)

57. In fact, by the time that Jenapharm presented New Claim 15 in December 2003, it had, more than two years earlier, prematurely terminated a Phase III clinical trial of the Dittgen Regimen. (JTX20 at 3 ("[T]his Phase III study had to be prematurely terminated due to a Pearl Index of 4.3 (48 pregnancies in 12,125 cycles); cycle control was also unsatisfactory compared to

current commercial 20μg EE preparations."), 34 ("Because of the unexpectedly high number of pregnancies registered, the study was prematurely terminated (Letter of termination to the Investigators on 22 Jan 2001; last patient out on 15 Sep 2001)")) Jenapharm, however, did not disclose this "shocking" failure to the PTO when presenting New Claim 15. (JTX68; Allen Tr. at 592-93) Rather, it presented the Dittgen Regimen as a basis for allowing New Claim 15. (JTX68)

58. On August 19, 2004, after the claimed April 2004 priority date for the '577 patent but before the '577 patent issued, Jenapharm amended New Claim 15 to "further distinguish it from the cited prior art" (DTX78 at 176), by specifying that the DNG dosage be increased 1.5 to 3 times in Phase 2, group 2 as compared to Phase 2, group 1 (*id.* at 174).

59. On April 26, 2005, the '915 application issued as the '793 patent. (JTX19) The amended New Claim 15 of the '915 application issued as claim 1 of the '793 patent. (*Id.*)

60. As shown below, the only difference between New Claim 15 and issued claim 1 of the '793 patent is that the latter contains the additional, narrowing requirement that the DNG dose be 1.5 to 3 times higher in Phase 2, group 2 than in Phase 2, group 1. (*Compare* JTX68 at 3 *with* JTX19 at 6:50-7:13; Simon Tr. at 153)

Table 5. '793 Patent Claim 1 Regimen

Phase	Days	Dose Elements
Phase 1	2 daily doses	Effective amount of EV
Phase 2, group 1	5 daily doses	Combination of EV and DNG
Phase 2, group 2	17 daily doses	EV and DNG, with 1.5 to 3X more DNG than in group 1
Phase 3	2 daily doses	Effective amount of EV, lower than in Phase 1
Phase 4	2 daily doses	Placebo

61. The '793 patent was set to expire on October 25, 2016. (DTX43; Zelano Tr. at 290) However, Bayer disclaimed all interest in the patent on March 4, 2011. (Matthey Tr. at 321)

62. Bayer owned the '793 patent prior to acquiring the '577 patent. (*Id.* at 318-19; Zelano Tr. at 279, 310)

H. Prosecution History of the '729 Application and the '577 Patent

63. Shortly after Bayer presented New Claim 15 in the prosecution leading to the '793 patent, Bayer filed two patent applications disclosing an example containing the 2-5-17-2-2 regimen and the precise dosages used in Natazia®, but claiming two different inventive entities were responsible for the invention. (DTX86 at 18; JTX265 at 13; Zelano Tr. at 301-02)

64. Bayer filed the first application, U.S. Patent Application 10/891,729 ("the '729 application"), on July 15, 2004, attributing the Natazia® example to the same Dittgen group identified as inventors of the '251 and '793 patents. (DTX86 at 4, 18) Amended claim 8 of the

'729 application differs from the '577 patent only in that it provides for DNG doses of 2-3 mg and 3-4 mg instead of the precise amounts found in Natazia® of 2 mg and 3 mg. (*Compare* DTX93 at 3 *with* JTX1 at 4:16-28) Because the co-inventorship of the '729 application and the '793 patent was clear in the '729 application, the PTO rejected claims that were "specific to Natazia®" for double patenting over claims 1-5 of the '793 patent. (DTX94 at 9; Zelano Tr. at 306-09) Bayer overcame that double patenting rejection by terminally disclaiming its application to the '793 patent's 2016 expiration, before abandoning that application altogether by failure to pay the filing fee. (DTX95 at 4; Zelano Tr. at 308-09)

65. In the second application, U.S. Application No. 11/578,771 ("the '771 application"), which led to the '577 patent-in-suit, Bayer identified different inventors – Jan Endrikat and Bernd Düsterberg – as being responsible for the Natazia® example. (JTX265 at 13; JTX1) Because Endrikat and Duesterberg were not identified as inventors in the '793 patent, there was no co-***inventorship***. (*Compare* JTX19 *with* JTX1) The co-***ownership*** of the '771 application and the '793 patent was not obvious on the face of the '771 application, because the '793 patent issued in the name of Bayer's subsidiary, Jenapharm, while Bayer filed the '771 application in its own name. (*Id.*) However, by the time that the '771 application was being substantively prosecuted in 2009, Bayer owned the '793 patent and had listed it in the FDA's Orange Book. (DTX43; Matthey Tr. at 318)

66. The same Examiner, San-Ming Hui, examined the applications leading to the '793 patent and the '577 patent, but a different Examiner, Samira Jean-Louis, examined the '729 application. (*Compare* JTX1 *and* JTX19 *with* JTX265 at 1622)

67. On November 12, 2009, Bayer filed – in the '314 patent application (which had

issued as the '251 patent), the '915 patent application (which had issued as the '793 patent), the '729 application (which had not issued), and the '771 application (which had not yet issued as the '577 patent) – a Revocation of Power of Attorney and Appointment of New Attorney, identifying Bayer as the assignee of these patent applications. (JTX265 at 259-60; DTX78 at 203-04)

68. On January 27, 2010, during the prosecution of the '577 patent, Bayer filed an Identification of Related Applications listing eleven patent applications – including the '314 application (and the resulting '251 patent), the '915 application (and the resulting '793 patent), and the '729 application (indicating it was "now allowed and to be abandoned") – as related to the '577 patent. (JTX265 at 315-16)

69. Mr. Zelano, the prosecuting attorney, testified that he did not recall having apprised the "Examiner that the '793 patent was owned by Bayer at the time of the '577 prosecution," but "the Patent Office, of course, has databases indicating current ownership." (Zelano Tr. at 311) Moreover, that there was co-ownership of the '771 application and the '793 patent was discernable from the record before the PTO because the '251 patent, the '793 patent, and the '915 application (including New Claim 15) were "cited references" on the face of the '771 application considered by the Examiner. (JTX1; JTX265 at 2215-19; Barnhart Tr. at 223-24) Additionally, there is no evidence in the record that Bayer falsely denied joint ownership or affirmatively misled the PTO about ownership.

70. During prosecution of the '577 patent, Bayer told the Examiner:

> Both the original and allowed claims of the '729 are drawn to essentially the same invention as the instant application. The persons who signed the declaration in the '729 (Michael Dittgen . . .) are not the same as the inventors of the instant application. It is the current inventors, Endrikat and Düsterberg, who are the true inventors of the claimed subject matter in the instant application.

(JTX265 at 313-14)

71. On July 14, 2011, Bayer confirmed:

> As noted in . . . Applicants' response of January 27, 2010, an inventive entity different from that of this application previously filed a U.S. application (10/891,729 . . .) claiming the same subject matter as this application. This was a result of a mistake on the part of the other inventive entity. . . . The examiner is referred to the file history of the mentioned '729 application since the claims of the latter were allowed. The office actions and responses filed in '729 are being filed herewith for the examiner's convenience. However, because of the mentioned mistake in the filing of such application by its inventors, the issue fee was never paid. Nevertheless, the examiner may be interested in the nature of the proceedings which led to the allowance in the '729 application. These included the publication of the application and filing of a terminal disclaimer over the US '793 patent of record to render moot an obviousness-type double patenting rejection. Because the current claims are not obvious over the claims of the US '793 patent, or its parent US '251 patent, no terminal disclaimer is necessary.

(*Id.* at 1533-34)

72. During the prosecution of the '577 patent, the Examiner rejected the claims multiple times in light of the Dittgen Regimen, which combined 3 mg, 2 mg, and 1 mg EV doses with 1 mg and 2 mg DNG doses in a 3-4-16-2-3 daily dosing pattern. (*Id.* at 246-54 (7/27/2009 Office Action), 896-903 (4/27/2010 Office Action), 1221-25 (12/08/2010 Office Action)) Following the submission of three declarations from Jan Endrikat (JTX20 at 2-3 (explaining why arriving at Natazia® was not a matter of "routine optimization" of Dittgen Regimen and noting Dittgen Regimen's Phase III contraceptive efficacy failure and "unsatisfactory" cycle control); JTX265 at 1523 (correcting misstatement from first declaration); *id.* at 2172 (correcting misstatement from second declaration)), and additional remarks regarding the evidence of the Dittgen Regimen's failure, along with argument that "only hindsight leads a skilled worker to

select Example 5 of the Dittgen EP '388 [the Dittgen Regimen] as a starting point" (*id.* at 1309-12), the Examiner allowed the claims because of "the unexpected effectiveness of the herein claimed specific contraception regimen" (*id.* at 2194-96).

73. Rather than expiring in 2016 – as did the '251 and '793 patents before Bayer disclaimed all interest in them, and as the '729 application would have done had Bayer not abandoned it after terminally disclaiming it to the '793 patent – the '577 patent issued with a term extending until 2026. (DTX43; DTX95 at 4; Zelano Tr. at 308-09, 322)

74. The list of "cited references" on the face of the '577 patent includes, among other things, the '251 patent, the '793 patent, the Schmidt-Gollwitzer patent, the Kullman patent, the Dittgen Declaration, the Hoffman article, the Moore articles, and the Gräser article. (JTX1 at 1-4)

I. Scope and Teachings of the Prior Art

75. Claim 1 of the '793 patent, discussed above, is not in the prior art. The prior art of record on which Watson relies is summarized below.

1. Dittgen Materials

76. As noted above, the Dittgen Declaration reports Hoogland results for a group of 21 women following the Dittgen Regimen (with 1 mg and 2 mg DNG doses). The results showed that, while none of the 21 women ovulated, 9 of them (43%) showed active FLSs or LUFs in each of the three cycles tested. (JTX5 at 6; Simon Tr. at 138-39)

77. Dr. Allen testified "that the developmental studies of the Dittgen Regimen [including the Hoffman articles, discussed below] would have provided the FDA with more than sufficient information to take that product into Phase III clinical trials." (Allen Tr. at 545-46)

78. However, Watson's expert, Dr. Simon, analogized the Hoogland results reported in the Dittgen Declaration to those found in a paper by Lüdicke and others, which published in the prior art in 2001. The Lüdicke authors used the Hoogland scoring system to compare and evaluate two contraceptive regimens, each containing different doses of the progestin gestodene. (JTX217; Simon Tr. at 140) The regimen containing a lower dose of progestin showed one ovulation and several active FLSs and LUFs, thus showing insufficient ovarian suppression. (Simon Tr. 140-42; JTX217 at 245)

79. While the Hoogland scores for the Dittgen Regimen were broadly similar to the results for the regimen Lüdicke determined to have insufficient ovarian suppression (Simon Tr. at 142), the presence of one ovulation in the Lüdicke regimen compared to no ovulations observed in those following the Dittgen Regimen is a material difference relevant to whether or not to pursue further development (Barnhart Tr. at 404-09). Dr. Barnhart testified credibly and persuasively that a POSA would not consider the failure of the Lüdicke regimen to be comparable to the success of the 1 mg/2 mg DNG regimen of Dittgen because there was an ovulation with Lüdicke, and none with the Dittgen Regimen. (*Id.*) As Dr. Barnhart noted, the presence of an ovulation with Lüdicke in an ovulation inhibition study is a failure, and makes the regimen not worth pursuing further. (*Id.*) Statistically, the presence of a single ovulation tells a POSA that the possible range of actual ovulation could be as high as 20-25% (while zero ovulations means the actual ovulation rate is less than approximately 15%, which would be comparable to existing successful contraceptives). (*Id.* at 407-10)

2. Hoffman Articles

80. Dr. Herbert Hoffmann and others published two articles ("the Hoffmann

Articles"), in 1998 and 1999, that tested a series of COCs utilizing Moore's recommended maximum dose of 2 mg DNG in combination with EV, in an effort to find an effective natural estrogen COC. (JTX2; JTX3) The Hoffmann Articles, which are prior art, were authored by the same Dittgen group responsible for the '251 and '793 patents. (*Compare* JTX2 *and* JTX3 *with* JTX14 *and* JTX19)

81. Hoffmann experimented with a biphasic regimen of 2 mg of EV with 2 mg of DNG and a triphasic regimen of 2 mg, 4 mg, and 2 mg of EV with 2 mg of DNG. (JTX2 at 460; JTX3 at 108) Hoffman found that "[w]hereas both combinations were capable of completely inhibiting the ovulation, the resulting bleeding pattern was not acceptable by the women." (JTX2 at 460; JTX3 at 108)

82. After presenting these failures, the Hoffman Articles reported the results of a pilot study of the Dittgen Regimen in 100 women over six menstrual cycles, with a total of 573 cycles ultimately documented. (JTX2 at 461; JTX3 at 109) Zero pregnancies occurred across the 573 cycles, and there was sufficient cycle control. (*Id.*) Hoffman referred to the 1 mg dose of DNG used as "borderline" and said that the 1 mg and 2 mg DNG doses were "regarded as effective for contraception." (*Id.*) Hoffmann concluded that the pilot study results justified starting a Phase III trial of the Dittgen Regimen. (JTX3 at 110)

83. Hoffman found that the cycle control of the Dittgen Regimen "might be acceptable" to women. (*Id.* at 109; JTX2 at 461) He explained that the descending 3-2-1 EV dosing pattern was expected to be responsible for the increased cycle stability of the Dittgen Regimen over the other two regimens that were tested. (JTX3 at 108; *see also* JTX2 at 460)

3. Bayer's '722 Patent ("Schmidt-Gollwitzer") and Kullman Patent Application

84. U.S. Patent No. 6,312,722 ("the '722 patent"), Bayer's Schmidt-Gollwitzer patent, which issued in November 2001, is prior art. (JTX210) The Schmidt-Gollwitzer patent described COCs including EV and DNG: "Preferably, in the present invention the oestrogen of the first hormone component is contained in each daily unit dose in a dose of . . . from 1.0 to 4.0 mg of 17ß-oestradiol valerate and the gestagen is contained in each daily unit dose in a dose of from 1.0 to 3.0 mg of dienogest . . . ." (*Id.* at 6:35-40; Simon Tr. at 133; Barnhart Tr. 471)

85. The Schmidt-Gollwitzer patent taught that "[t]he daily dosage amount of [the progestin] component corresponds at least to the threshold dose considered necessary for the [progestin] in question to inhibit ovulation." (JTX210 at 1:52-55)

86. Bayer's Kullmann patent application, WO 02/22110 A2, which was published on March 21, 2002, is prior art. (JTX205) It described "estradiol (as a representative of natural estrogen) 0.25 to 4 mg inclusive" and "dienogest 1 to 3 mg inclusive." (*Id.* at 4; Barnhart Tr. at 472-73)

4. Oettel and Moore Articles

87. An article by Oettel and others, published in 1995, concluded that "the ovulation-inhibiting dose [of DNG] in cyclic women amounts to about 1mg/day." (JTX173 at 529 table VII) Oettel, which is prior art, compared the cycle control of a very low dose of DNG (0.225 mg, below the ovulation inhibition dose) with a 2.0 mg dose of DNG, where both doses were given with 0.05 mg EE (i.e., the synthetic estrogen ethinylestradiol). (*Id.* at 529-30) Whereas the low DNG dose resulted in "bad cycle control and poor ovulation inhibition," with 71.2% bleeding disturbances and two pregnancies, "[e]levating the dienogest dose to 2 mg/day resulted in better

cycle control without pregnancies." (*Id.* at 530; *see also* Barnhart Tr. at 464)

88. Oettel also set forth ovulation inhibition data for 0.5 mg, 1 mg, 1.5 mg, and 2 mg doses of DNG. (JTX173 at 529 table VII)

89. A prior art article by Moore and others, published in 1999, described a dose-ranging study of DNG to determine its minimum ovulation inhibitory dose. (JTX4) The authors tested DNG at increments of 0.5 mg, 1 mg, 1.5 mg, and 2 mg, and found that "[d]ienogest 1.0 mg is the minimal daily dose needed to inhibit ovulation in healthy individuals with normal ovulatory cycles." (JTX4 at Abstract; *id.* at 276 (describing 1 mg dose as "the threshold dose" for ovulation inhibition)) However, because "[o]ral contraceptives usually contain double the determined ovulation inhibitory dose of the progestin," Moore "recommended" using "dienogest 2.0 mg." (*Id.* at 277; *see also* Simon Tr. at 130 (explaining that, as typical rule of thumb, person having ordinary skill in art would dose progestin in COC at double the dose of progestin that has been shown to inhibit ovulation))

90. Moore explained that "the ovulation inhibitory effects of dienogest are directly related to the dose received." (JTX4 at 277) Moore further reported that "dienogest was well tolerated" up to 2 mg. (*Id.*) In the tested doses of DNG from 0.5 mg to 2 mg, "dienogest alone improved menstrual complaints and shortened the duration of progestin withdrawal bleeding in a dose-dependent manner." (*Id.*)

5. Valette® and other prior art products

91. Consistent with the teachings of Moore and Oettel, a prior-art product known as Valette® was marketed in Europe, containing 2 mg DNG in conjunction with 0.03 mg EE. (JTX173 at 534 ("Dienogest in combination with ethinyl estradiol (2 mg dienogest and 0.03 mg

ethinyl estradiol/day over 21 days) has been on the market in Germany as an oral contraceptive since March 1995."); Simon Tr. at 136-37)

92. Only four marketed drugs (and their generic equivalents where available) – Natazia®, Valette®, Climodien® (a hormone replacement therapy), and Visanne® (a treatment for pelvic pain associated with endometriosis) – contain DNG, and only two of those are COCs: Natazia® and Valette®. (Holtz Tr. at 333) Other than Natazia®, every other drug containing DNG has a maximum daily dose of 2 mg. (Simon Tr. at 192; Holtz Tr. at 335-36)

6. Gast application

93. The Gast application, WO98/04268, specifies a range of 0.25 mg to 4 mg daily DNG doses for use with EE. (JTX201 at 8; *see also* Simon Tr. at 269) The preferred regimens described in the Gast application's examples have a daily dose of 500 µg (i.e., 0.5 mg) to 1 mg DNG per day. (JTX201 at 10; Simon Tr. at 186-87)

94. The Gast application, which is prior art, does not disclose any clinical data. (Simon Tr. at 269-70)

7. Gräser article

95. A prior art article by Gräser, published in 2000, studied the ratio of atrophic to proliferative endometrial material in post-menopausal women to determine the optimal DNG dose for producing an atrophic endometrium and a favorable bleeding profile. (JTX225) Gräser compared combinations of 2 mg EV with DNG doses of 0.5 mg, 1 mg, 2 mg, 3 mg, and 4 mg for use in continuous-combined hormone replacement therapy. (*Id.*)

96. Gräser found that "the two lowest dosages of dienogest evaluated in this study (0.5 and 1.0 mg) are unsuitable for use in a continuous-combined therapy for the treatment of

postmenopausal women." (*Id.* at 259) The 2, 3, and 4 mg doses were suitable with this population for this purpose. (*Id.*)

97. Gräser further concluded that the "most favourable bleeding profile was seen in the 3.0 mg dienogest group." (JTX225 at Abstract)

98. Relying in part on Gräser, Watson's Dr. Simon opined that the prior art taught that 2 mg and 3 mg doses of DNG were well tolerated without any dose dependent side effects. (Simon Tr. at 147) Dr. Simon explained Gräser's conclusion that there was "no dose-dependency in terms of adverse events," and that 2 mg and 3 mg DNG "are the optimal doses for combination with 2.0 mg oestradiol valerate for continuous-combined hormone replacement therapy." (Simon Tr. at 148-49)

99. Bayer's Dr. Allen testified that the Gräser article's conclusions cannot be applied to pre-menopausal women – i.e., those women who can become pregnant and who may choose to use a COC – because they are a different patient population. (Allen Tr. at 607-09)

8. Endrikat article

100. In a 2003 article in the prior art, Endrikat – a co-inventor on the '577 patent – published a meta-analysis of clinical trials, assessing the correlation between higher degrees of ovarian suppression and cycle control. (JTX12; Simon Tr. at 144) For purposes of his publication, Endrikat considered the first three Hoogland categories "as indicative of sufficient ovarian suppression." (JTX12 at 109)

101. Based on his analysis, Endrikat concluded that "higher ovarian suppression measured by the Hoogland Score is correlated with improved cycle control." (*Id.* at 112) He further concluded that contraceptive "formulations with higher ovarian suppression are expected

to provide less intermenstrual bleeding." (*Id.*)

102. Consistent with his publication, Endrikat, told the PTO in a declaration: "According to the knowledge at the filing date, a person of ordinary skill in the art would consider the absolute amount of 4 mg of dienogest in Regimen 2C clinically tolerable in young women, as the examiner alleges." (JTX20 at 5; Simon Tr. at 147-48)

J. Estrogen Dominance

103. Bayer's expert, Dr. Barnhart, testified credibly and persuasively that "estrogen dominance" was an important concept in the prior art, and, accordingly, at the date of the '577 patent's invention a POSA would have believed that an effective COC had to be estrogen dominant. He explained that estrogen dominance refers to the competition between the proliferative effect of estrogen in a COC– which increases the uterine lining's thickness – and the antiproliferative effect of progestins in a COC – which stops the proliferation of the uterine lining. (Barnhart Tr. at 410)

104. An estrogen dominant pill has sufficient estrogen relative to progestin to promote proliferation of the uterine lining. (*Id.*) Estrogen dominance is important during the proliferative phase (of the endometrius) of a cycle – that is, the first seven to nine days or so of a cycle – when the daily dose of EV should exceed the daily dose of DNG. (*Id.* at 414-15)

105. Dr. Barnhart identified support for the estrogen dominance theory in the Hoffman Articles discussing the pilot study of the Dittgen Regimen (*id.* at 499-501), which states:

> Bearing in mind that sequential preparations are known to improve cycle stability in women complaining of bleeding irregularities, our efforts were directed at designing a sequential 28-day regime. ***To ensure estrogen dominance in the first cycle phase, i.e., the stage at which the endometrial proliferation is promoted under estrogen influence***, 17ß-estradiol valerate was given on days 1-25

> of the menstrual cycle at doses stepped from 3 mg to 1 mg. Basically, the shortening of the hormone-free interval to only 3 cycle days and the prolongation of the estrogen phase at the end of the progestin phase were expected to increase the cycle stability of the ethinylestradiol-free combination considerably.

(JTX3 at 108 (emphasis added); JTX2 at 460)

106. Hoffmann's development of an estrogen dominant regimen with EV and DNG appeared to solve the cycle control problem that had caused the failure of every other prior effort to develop a natural estrogen COC. (Barnhart Tr. at 411)

107. Hoffmann and his colleagues, including Dittgen, wrote similarly in the Dittgen patents and applications, stating:

> In the combination preparation according to the invention ***the estrogen-gestogen balance is shifted largely in favor of the estrogen ingredient and in a predetermined stage the gestogen is completely eliminated from the daily dosage***. Furthermore this regimen allows an extremely high estrogen daily dosage (more than 4 mg estradiol equivalents/day).

(*E.g.*, JTX19 at 4:8-13) (emphasis added)

108. Dr. Barnhart testified that a POSA would understand Hoffmann's teachings about the significance of estrogen dominance and its importance to the cycle control success of the 1 mg/2 mg DNG regimen. (Barnhart Tr. at 411, 417) Dr. Barnhart went on to testify that a POSA would recognize that making the change from 1 mg/2 mg of DNG to higher doses of DNG (such as Natazia®'s 2 mg/3 mg doses) would significantly reduce and eliminate the key estrogen dominance during the early proliferative phase. (Barnhart Tr. at 417-18) He further testified that a POSA would not believe that Natazia® was reasonably likely to succeed in maintaining sufficient cycle control because of its lack of estrogen dominance. (*Id.*)

109. As further support for his opinion that a POSA would have believed estrogen

dominance was necessary for an effective COC, Dr. Barnhart pointed to the Gräser 2000 paper. (*Id.* at 529-30) Dr. Gräser's article on the treatment of menopause with EV and DNG describes the countervailing proliferative and antiproliferative influences of EV and DNG, respectively, at different doses. (JTX225) Although Bayer's Dr. Allen testified that Gräser is irrelevant to contraception because it deals with hormone replacement therapy ("HRT") (Allen Tr. at 607-09), it does show specific pharmacological interactions of EV and DNG at different doses, and the concepts of estrogen or progestin being "dominant" as measured (at least in part) by their relative weight amounts in a daily dose (Barnhart Tr. at 529).

110. Gräser found that, in combination with 2 mg EV:

> The prevalence of proliferative material and atrophic endometrium indicated that the two lowest dosages of dienogest evaluated in this study (0.5 and 1.0 mg) are unsuitable for use in a continuous-combined therapy for the treatment of postmenopausal women. The ratio of atrophic to proliferative material was 0.7 and 1.0, respectively, in the 0.5 and 1.0 mg dosage groups demonstrating a lack of clinical efficacy at these dosages. Conversely, the 3.0 and 4.0 mg doses of dienogest are both suitable with atrophic:proliferative material ratios of 5.0 and 6.0, respectively. The 2.0 mg dienogest dose is also appropriate for use in continuous-combined HRT. The atrophic:proliferative ratio was 2.0 in this group, however, the high prevalence of nonassessable and unavailable biopsies in this group meant that this ratio was based on data from only 6 patients rather than 10-14 patients in the other dosage groups.

(JTX225 at 259)

111. Applying Gräser's findings to this case (to the extent relevant) is complicated by the fact that Gräser reports results in the form of DNG:EV ratios, the opposite of the EV:DNG ratios the parties and the Court have used here. (Relatedly, Gräser reports the atrophic:proliferative ratio – i.e., breaking down:building up ratio – whereas the Court is

discussing its analysis in the form of proliferative:atrophic ratios, consistent with the course of a menstrual cycle, which is characterized by the building up and later breaking down of the endometrius.) "Translating" Gräser's results to the EV:DNG ratio used throughout this Opinion shows the following:

Table 6. Translating Gräser

Amt. EV	Amt. DNG	Atrophic: Proliferative Ratio	Proliferative: Atrophic Ratio	HRT Suitable?	Dom-in-ant?	EV:DNG Ratio
2 mg	.5 mg	0.7 [0.7/1]	1.43 [1/0.7]	NO	Estr.	4:1
2 mg	1 mg	1.0 [1/1]	1.0 [1/1]	NO	Estr.	2:1
2 mg	2 mg	2.0 [2/1]	0.5 [½]	YES	Prog.	1:1
2 mg	3 mg	5.0 [5/1]	0.2 [1/5]	YES	Prog.	2:3
2 mg	4 mg	6.0 [6/1]	0.17 [1/6]	YES	Prog.	1:2

112. As Dr. Barnhart admitted, the Hoffmann paper does not compare the weights of EV and DNG; nor does it calculate ratios between them. (Barnhart Tr. at 492) Neither the Dittgen patent specification nor the claims of the '251 or '793 Dittgen patents recites ratios of EV:DNG either. (JTX 14; JTX19)

113. The '577 patent is silent on whether estrogen or progestin are dominant in its examples or claims. (JTX1)

114. However, a person of skill in the art could "do the math" and calculate the ratios of estrogen and progestin, based on daily dose weights, even if those ratios are not expressly disclosed in a reference. (*See* Barnhart Tr. at 493, 501-02, 527)

115. None of Endrikat's three declarations discusses estrogen "dominance" in the first

phase of a cycle (or at any other point). (*See* JTX20 ("First Endrikat Declaration") at 1-7; JTX265 ("Second Endrikat Declaration") at 1523; *id.* at 2172 ("Third Endrikat Declaration")) The First Endrikat Declaration does discuss the putative importance of ratios of estrogen:progestin, but does not identify the important part of the regimen for calculating ratios as the first phase; rather, the First Endrikat Declaration indicates that the important point is the second phase, the days in the middle of the regimen – i.e., days 8 to 23 of Dittgen. (JTX20 at 6, 10-16) In the Second Endrikat Declaration, Endrikat corrected his assertion about the importance of a particular ratio in the second phase to the decision to further investigate a particular regimen. (JTX265 ('577 File History) at 1523) The Third Endrikat Declaration says nothing about ratios at all. (*Id.* at 2172)

116. Watson's Dr. Simon acknowledged that it is the estrogen component of the COC that acts to provide cycle control. (Simon Tr. at 112) He further admitted that early efforts to develop a natural estrogen COC failed because of failures of cycle control. (Simon Tr. at 242)

117. The Natazia® regimen – which is the regimen of the asserted claims of the '577 patent – is not as estrogen dominant in the proliferative phase of the menstrual cycle as the Dittgen Regimen. (Barnhart Tr. at 417) Compared to the Dittgen Regimen (1 mg/2 mg DNG), the Natazia® regimen: (i) shortens the initial EV-only stage from three days to two days; (ii) doubles the DNG dose (from 1 mg to 2 mg) during the subsequent, longer, first group of Phase 2, resulting in five days of an equal 2:2 mg EV:DNG ratio compared with Dittgen's four days of 2:1 mg EV:DNG ratio in that same stage; and (iii) lengthens the second group of Phase 2 (to 17 days), a stage in which Natazia® doses DNG at 50% greater weight than EV, for a 2:3 mg EV:DNG ratio, compared to Dittgen's 16 days of equal 2:2 mg EV:DNG.

118. Other illustrations that the Natazia® regimen is not as estrogen dominant as the Dittgen Regimen include: (i) during each of the first seven days of a cycle with the Dittgen Regimen, a woman takes more EV than DNG, whereas with Natazia® a woman takes more EV than DNG for only the first two of the first seven days; (ii) during the first seven days of a cycle with the Dittgen Regimen, a woman takes 17 mg of EV and 4 mg of DNG, whereas with Natazia® a woman takes 16 mg of EV and 10 mg of DNG during the first seven days of a cycle; (iii) over an entire cycle on the Dittgen Regimen, the total amount of EV:DNG is 51:36 mg, whereas over an entire cycle on the Natazia® regimen the total amount of EV:DNG is 52:61 mg; and (iv) while a woman on the Dittgen Regimen never takes a greater amount of DNG than the amount of EV she is taking on the same day, with the Natazia® regimen a woman takes a greater amount of DNG than EV on 17 out of 28 days of a cycle.

119. Neither Dr. Simon nor any other Watson witness provided any persuasive testimony or evidence in rebuttal to Dr. Barnhart's opinions on the issue of estrogen dominance, its significance to the success of the 1 mg/2 mg DNG regimen described in the Hoffmann Articles, the lack of estrogen dominance in Natazia® relative to the 1 mg/2 mg DNG regimen, or how a person of ordinary skill in April 2004 would find no reasonable expectation of success for the Natazia® regimen based on its lack of estrogen dominance.

K. Long-Felt But Unmet Need

120. Bayer established that Natazia® fulfilled a long-felt unmet need for an oral contraceptive with natural estrogen, given that previous attempts had failed due to unacceptable bleeding problems. (*See generally* Barnhart Tr. at 420)

121. Persons of ordinary skill have been trying since the 1970's to develop a natural

estrogen COC. (*Id.* at 434)

122. Natazia® was launched in Europe under the name "Qlaira®" in May 2009 and in the United States in July 2010. (Holtz Tr. at 329) Natazia® was the first, and remains the only, natural estrogen COC in the United States. Natazia® was also the first natural estrogen COC approved anywhere in the world for use in all healthy women. (JTX265 at 1313-14; Holtz Tr. at 330; Barnhart Tr. at 434)

1. Early Failures of Others

123. Early regimens using natural estrogen suffered from poor cycle control. (JTX2 at 460; JTX3 at 108; JTX169 at 619; JTX174 at 471; JTX176 at 458; JTX177 at 543; JTX178 at 9; Simon Tr. at 114-15; Barnhart Tr. at 436-37)

124. For instance, in 1979, Serup reported efforts to substitute natural estrogen (in the form of estradiol and estriol) for synthetic estrogen in COCs, based on a view that "natural oestrogens may be safer." (JTX174 at 471) Although the natural estrogen COC provided adequate contraceptive efficacy, Serup reported that because of the "high frequency of bleeding irregularities the natural oestrogen pill we investigated is not acceptable for general use." (JTX174 at 471)

125. In 1980, Koetsawang similarly reported that a natural estrogen pill was of "high efficacy" but that the "high incidence of menstrual problems associated with the combination of 'natural' estrogens and norethisterone acetate make it much less suitable for general use in family planning programmes than combinations containing synthetic estrogens." (JTX176 at 458)

126. In 1987, Schubert tested a natural estrogen pill utilizing estradiol cyclo-octyl acetate with a progestin and found that, consistent with past experiments, "follicular hormonal

activity and ovulation was inhibited by this combination," yet "[b]leeding control was, however unacceptable in all volunteers." (JTX177 at 543)

127. In 1993, Wenzl tried to develop a natural estrogen pill utilizing micronized estradiol together with the progestin desogestrel, but found that despite providing "complete ovulation inhibition," the "bleeding pattern does not show an acceptable profile." (JTX169 at 616) Wenzl hypothesized: "This most probably is due to the progestogen dominance of the combination." (JTX169 at 619; *see also* Barnhart Tr. at 411-12)

2. Failure of the Dittgen Regimen

128. As recommended by Hoffmann, the Dittgen Regimen was tested in a Phase III clinical study (known as AZ94). (JTX6) AZ94 was a large scale Phase III clinical trial enrolling approximately 1,800 women for a planned 20-cycle study. (*Id.* at 2; Allen Tr. at 578)

129. The AZ94 study was stopped after only 14 cycles because of an unexpectedly high number of pregnancies. (JTX6 at 2-3) It resulted in an adjusted "Pearl Index" of 4.3 (reflecting the number of pregnancies per hundred woman-years not due to subject failures) and an unadjusted Pearl Index of 5.3 (including subject failures). (*Id.* at 2-3; Allen Tr. at 567, 578-79, 597)

130. Bayer's regulatory expert, Dr. Allen, called the results a "shocking" failure. (Allen Tr. at 578, 592-93) Based on the Phase II clinical study results found with the Dittgen Regimen – reported, for instance, in the Hoffman Articles and the Dittgen Declaration (JTX3 at 110; JTX5; JTX19 at 5:20-52, 6:1-27; *see also* Barnhart Tr. at 386-87) – the FDA would have expected a Pearl Index for the Dittgen Regimen of less than 2 (Allen Tr. at 579).

131. Even though it occurred years before the priority date of the '577 patent, the

failure of AZ94 was known only to Bayer and was not known in the prior art. (Simon Tr. at 164)

3. Failure of the "Modified Dittgen Regimen"

132. The Modified Dittgen Regimen is a 2-5-17-2-2 regimen of EV, DNG, and placebo that uses the 3-2-1 mg EV dosing pattern and 1 mg/2 mg doses of DNG. (JTX11 at 220 Fig. 1) As an extension of the original Dittgen Regimen, the Modified Dittgen Regimen added one day of the phase with 2 mg EV and 1 mg DNG (at Day 3, in place of one day of unopposed 3 mg EV in the Dittgen Regimen), and added one day of the phase with 2 mg EV and 2 mg DNG (at Day 24, extending the end of cycle by one day). (JTX11 at 220 Fig. 1)

133. The Modified Dittgen Regimen was tested in a Phase II ovulation inhibition study initiated after the failure of AZ94. (JTX15; Allen Tr. at 580-81) This study enrolled 192 women, with 96 women per study arm. (JTX15 at 3)

134. An Endrikat 2008 article, which is not prior art, describes a Phase II ovulation inhibition study of the Modified Dittgen Regimen. (JTX11) The study used new parameters Bayer set "to be on the safe side" after the failure of the Dittgen Regimen. (*Id.* at 223; Allen Tr. at 580-83, 614) Bayer decided to "consider a Hoogland score of 5 (LUF) to be as critical as a Hoogland score of 6 (ovulation), since the transition from a persisting FLS into a ruptured FLS might happen easily in subsequent cycles," and "[a]n ovulation rate of <5%" would be required "in an effort to be 'on the safe side' before initiating a Phase III clinical trial program." (JTX11 at 223)

135. The ovulation inhibition data showed an ovulation rate of approximately 5-6% for the Modified Dittgen Regimen. (Allen Tr. at 581) The Phase II ovulation inhibition study results were outside of Bayer's "safe side" criteria. (JTX11 at 223) (showing ovulation/LUF rate of

6.38%)

136. Dr. Simon testified that a person of ordinary skill would have expected that the extension of the 1 mg/2 mg DNG daily dose by an additional day in the Modified Dittgen Regimen would have improved ovarian suppression. (Simon Tr. at 244)

137. Dr. Allen testified that without the shocking failure of the 1mg/2mg DNG doses of the Dittgen Regimen in the Phase III clinical study AZ94, the Modified Dittgen Regimen would have been acceptable to take to Phase III trials, without concern, based on its Phase 2 ovulation inhibition results. But with the failure of AZ94, the Modified Dittgen Regimen's ovulation inhibition results were deemed a failure and not an acceptable candidate to take into Phase III trials. (Allen Tr. at 581-82, 614)

L. Watson's ANDA No. 202349

138. Watson submitted to the FDA ANDA No. 202349 under the provisions of 21 U.S.C. § 355(j), seeking approval to engage in the commercial manufacture, use, offer for sale, sale, and/or importation of a generic version of Bayer's Natazia® tablets. (SUF ¶ 11)

139. Watson has amended its ANDA to include a certification under 21 U.S.C. § 355(j)(2)(A)(vii)(IV) asserting that, in its opinion, the '577 patent is invalid, unenforceable, or will not be infringed by the manufacture, use, offer for sale, sale, and/or importation of Watson's ANDA product. (*Id.* ¶ 12)

M. Infringement

140. The parties have stipulated that the filing of Watson's ANDA No. 202349 constitutes an act of infringement of claims 1 through 3 of the '577 patent pursuant to 35 U.S.C. § 271(e)(2). (*Id.* ¶ 13)

N. Expert Witnesses

141. Dr. James Simon testified at trial as an expert witness in reproductive endocrinology, gynecology, and contraception, on behalf of Watson. (Simon Tr. at 95-96) Dr. Simon is a clinical professor of obstetrics and gynecology at George Washington University, formerly a clinical professor at Georgetown University, and has been a practicing physician for 30 years. (*Id.* at 88, 90, 92; DTX122) After graduating from medical school, he completed a post-doctoral fellowship in reproductive endocrinology and infertility. (Simon Tr. at 88, 92) He has authored hundreds of papers and abstracts in the field of reproductive endocrinology. (*Id.* at 94-95) Dr. Simon has acted as principal investigator in approximately 300 clinical trials involving women's health care products and reproductive endocrinology, including about a dozen involving contraceptives. (*Id.* at 90-91)

142. Dr. Kurt Barnhart testified as an expert witness in contraception, obstetrics, gynecology, and reproductive endrocrinology, on behalf of Bayer. (Barnhart Tr. at 365) Dr. Barnhart is a professor of obstetrics, gynecology, and epidemiology at the University of Pennsylvania, and the Vice Chair for the Department of Obstetrics and Gynecology for Clinical Research at the same institution. He has a medical degree as well as a Master of Science in Clinical Epidemiology. (*Id.* at 358-60) Dr. Barnhart has approximately 300 publications and has been involved in approximately 80 clinical trials in the field of obstetrics and gynecology. (*Id.* at 361-63)

143. Dr. Susan Allen testified as an expert witness on the FDA's regulatory guidance and requirements for the development and approval of a combined hormonal contraceptive, on behalf of Bayer. (Allen Tr. at 560) Dr. Allen has a medical degree and a Master's Degree in

Public Health; she is board certified in Preventative Medicine and Public Health. (*Id.* at 547-48) Dr. Allen practiced medicine for five years and worked for the FDA for approximately eight years. (*Id.* at 548-49) At the FDA, Dr. Allen worked in the Division of Reproductive and Urologic Drug products (the division responsible for reviewing and approving COCs), ultimately running the unit as Medical Team Leader. She also worked as the Associate Director of Scientific and Medical Affairs in the Office of Compliance. (*Id.* at 549-50)

144. The Court found each of the witnesses who testified – expert as well as fact witnesses – to be credible.

O. Person Having Ordinary Skill in the Art

145. Dr. Simon explained that the POSA to whom the '577 patent is directed would be a medical doctor who specializes in obstetrics, gynecology, and reproductive endocrinology, having experience in "clinical development and prescribing hormonal contraceptives." (Simon Tr. at 151-53) Bayer's expert, Dr. Barnhart, agreed that a POSA would have at least these qualifications. (Barnhart Tr. at 366-67) The Court finds that Dr. Simon has appropriately characterized the POSA.

146. A POSA would understand that, in order to be marketed, oral contraceptives must be efficacious in a large and varied patient population, and that it is necessary to dose a progestin in a way that takes into account individual variability and imperfect user compliance. (Simon Tr. 104-05; Barnhart Tr. at 458-59)

147. A POSA would understand that a guiding principle in COC development was the desire to use the lowest effective doses of any hormone to avoid adverse side effects. (Barnhart

Tr. at 398; Simon Tr. at 171)[4]

148. However, a person having ordinary skill in the art would not have thought there were significant safety concerns associated with DNG or other progestins. (Simon Tr. at 113-14 ("[T]here were large studies on progestin only oral contraceptives which did not show risks of blood clotting or the downstream sequelae heart attacks, et cetera."); *id.* at 147-48; Allen Tr. at 604 ("[Based on] information that was publicly available prior to April of 2004 . . . I don't recall there being any significant safety concerns with dienogest, correct"); JTX20 at 5 (First Endrikat Declaration during prosecution of '577 patent: "According to the knowledge at the filing date, a person of ordinary skill in the art would consider the absolute amount of 4 mg of dienogest in Regimen 2C clinically tolerable in young women, as the examiner alleges."); Barnhart Tr. at 479 (agreeing that prior art did not suggest that DNG doses over 2 mg are dangerous or ineffective))

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[4]For example, a prior art article by Spona published in 1987 explained:

> The aim of this research work was to develop new contraceptives which contained the lowest possible dose of estrogen and progestagen. This is in accordance with a recommendation which was issued by the World Health Organization as early as 1978 with the objective in mind to keep side effects on the parameters of the hemostatic system and of metabolic functions as low as possible.

(JTX136 at 185 (citing JTX133 (World Health Organization report)); *see also* JTX173 at 518 (Oettel 1995 article stating: "[T]he aims of subsequent research [include:] to find the lowest combined total dose of each steroid to inhibit ovulation and to prevent bleeding pattern irregularities in the hope of reducing the possibility of major complications . . . ."); JTX134 at 4 (FDA labeling guidance: "For any particular estrogen/progestin combination, the recommended dosage regimen is that which contains the least amount of estrogen and progestin that is compatible with a low pregnancy rate and the medical needs of the individual patient."))

LEGAL STANDARDS

I. Presumption of Validity

An issued patent is presumed to be valid. *See* 35 U.S.C. § 282. Therefore, to invalidate a patent, a party must carry its burden of proof by "clear and convincing evidence." *See Otsuka Pharm. Co., Ltd. v. Sandoz, Inc.*, 678 F.3d 1280, 1289-90 (Fed. Cir. 2012) (obviousness-type double patenting); *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 994 (Fed. Cir. 2009) (obviousness). Clear and convincing evidence is evidence that "proves in the mind of the trier of fact an abiding conviction that the truth of [the] factual contentions [is] highly probable." *Intel Corp. v. ITC*, 946 F.2d 821, 830 (Fed. Cir. 1991) (internal quotation marks omitted; first modification in original). A defendant's burden to prove invalidity is "especially difficult when the prior art [on which it relies] was before the PTO examiner during prosecution of the application." *Hewlett-Packard Co. v. Bausch & Lamb Inc.*, 909 F.2d 1464, 1467 (Fed. Cir. 1990).

II. Obviousness Type Double Patenting

Under the doctrine of obviousness-type double patenting, a party is prohibited "from obtaining an extension of the right to exclude through claims in a later patent that are not patentably distinct from claims in a commonly owned earlier patent." *Eli Lilly & Co. v. Barr Labs., Inc.*, 251 F.3d 955, 967 (Fed. Cir. 2001). "[T]he fundamental reason for [this] rule is to prevent unjustified timewise extension of the right to exclude granted by a patent no matter how the extension is brought about." *Id.* at 968 (internal citation and quotation marks omitted). The doctrine thus "ensures that the public gets the benefit of the invention after the original period of monopoly expires," *Abbvie Inc. v. Mathilda & Terence Kennedy Inst. Rheumatology Trust*, 764

F.3d 1366, 1373 (Fed. Cir. 2014), and also "prevent[s] multiple infringement suits by different assignees asserting essentially the same patented invention," *In re Hubbell*, 709 F.3d 1140, 1145 (Fed. Cir. 2013).

The double patenting inquiry consists of two steps. "First, the court construes the claim[s] in the earlier patent and the claim[s] in the later patent and determines the differences. Second, the court determines whether those differences render the claims patentably distinct." *Abbvie*, 764 F.3d at 1374 (internal citation and quotation marks omitted); *see also Eli Lilly & Co. v. Teva Parenteral Med., Inc.*, 689 F.3d 1368, 1377 (Fed. Cir. 2012) (applying two-step analysis). At step two, to be "patentably distinct" and valid a claim must not be obvious over or anticipated by an earlier claim by the same inventor. *Abbvie*, 764 F.3d at 1374. "The focus of the obviousness-type double patenting doctrine thus rests on preventing a patentee from claiming an obvious variant of what it has previously ***claimed***, not what it has previously ***disclosed***." *Eli Lilly v. Teva*, 689 F.3d at 1379 (emphasis in original).

Whether or not a patent is invalid due to double patenting is a question of law. *See In re Hubbell*, 709 F.3d at 1145.

III. Obviousness

A patent may not issue "if the differences between the claimed invention and the prior art are such that the claimed invention as a whole would have been obvious before the effective filing date of the claimed invention to a person having ordinary skill in the art to which the claimed invention pertains." 35 U.S.C. § 103(a). Obviousness is a question of law based on underlying factual findings concerning: (1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the art; and

(4) objective considerations of nonobviousness. *See Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

To prove that a patent is obvious, a party must demonstrate "that a skilled artisan would have had reason to combine the teaching of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so." *In re Cyclobenzaprine*, 676 F.3d 1063, 1069 (Fed. Cir. 2012) (internal citation and quotation marks omitted); *see also Amgen, Inc. v. F. Hoffman-La Roche Ltd.*, 580 F.3d 1340, 1362 (Fed. Cir. 2009) ("An obviousness determination requires that a skilled artisan would have perceived a reasonable expectation of success in making the invention in light of the prior art."). While an analysis of any teaching, suggestion, or motivation to combine known elements is useful to an obviousness analysis, the overall obviousness inquiry must be expansive and flexible. *See KSR Int'l Co. v. Teleflex, Inc.*, 550 U.S. 398, 415, 419 (2007).

The use of hindsight is not permitted when determining whether a claim would have been obvious to one having ordinary skill in the art. *See id.* at 421 (cautioning against "the distortion caused by hindsight bias" and obviousness "arguments reliant upon *ex post* reasoning"). To protect against the improper use of hindsight when assessing obviousness, the Court is required to consider objective (or "secondary") considerations of non-obviousness, such as commercial success, failure of others, unexpected results, and long-felt but unmet need. *See, e.g., Leo Pharm. Prods., Ltd. v. Rea*, 726 F.3d 1346, 1358 (Fed. Cir. 2013). Secondary considerations "may often be the most probative and cogent evidence in the record" relating to obviousness. *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 1538 (Fed. Cir. 1983).

DISCUSSION

Watson contends that the '577 patent is invalid due to obviousness type double patenting as well as obviousness. The starting point for the double patenting analysis is claim 1 of the '793 patent, while the starting point for the obviousness analysis is New Claim 15. (*See* D.I. 138 (Watson's Post-Trial Reply Brief) ("RB") at 6) As noted above, for both obviousness type double patenting and obviousness, the burden is on Watson to prove invalidity by clear and convincing evidence. *See Otsuka*, 678 F.3d at 1289-90; *Procter & Gamble Co.*, 566 F.3d at 994. As explained below, the Court concludes that Watson has failed to meet its burden.

I. The Double Patenting and Obviousness Analyses Will Be Undertaken Separately

Bayer argues that, in the circumstances presented here, the obviousness type double patenting ("OTDP" or "double patenting") analysis and the obviousness analysis collapse into a single inquiry. Bayer contends this is so because "[t]he statutory prior art for § 103 [obviousness] in this case includes the '793 Patent's Prosecution History (called the '915 Application) and its 'New Claim 15,' as well as the '793 Patent's parent, the '251 Patent, all three of which share the same specification . . . [, and] therefore encompasses all of the teachings of Claim 1 of the '793 patent." (D.I. 141 (Bayer's Post-Trial Answering Brief) ("AB") at 4) As Bayer observes, the parties agree that "[t]he only difference between New Claim 15 [the primary statutory prior art reference for obviousness] and Claim 1 of the '793 Patent [the basis for OTDP] is that the latter has a limitation requiring that the second DNG dose must be 1.5-3x the first dose," although this dosing requirement is also found in the '793 patent's specification, which

refers to it as "advantageous." (AB at 4 n.2; RB at 7 n.3)[5]

By contrast, Watson urges the Court to undertake separate OTDP and obviousness analyses, for several reasons. First, the starting point for the OTDP analysis here – claim 1 of the '793 patent – is not found in the prior art. (RB at 3) Second, while all of the prior art on which Watson bases its obviousness analysis was before the PTO Examiner, claim 1 of the '793 patent was not before the Examiner, suggesting it should be easier for Watson to prevail on double patenting. *See Hewlett-Packard Co. v. Bausch & Lomb Inc.*, 909 F.2d 1464, 1467 (Fed. Cir. 1990) (explaining that defendant's "burden is especially difficult when the prior art was before the PTO Examiner during prosecution of the application"), claim 1 of the '793 patent was not before the Examiner, suggesting it should be easier for Watson to prevail on double patenting. Finally, Watson contends that while in an obviousness context the Court must consider whether a POSA might have been motivated to modify aspects of a prior art reference that are common as between the prior art and the patent-in-suit, an OTDP analysis is limited to consideration of the

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[5]None of the cases cited by Bayer stand for the proposition that obviousness and OTDP collapse into a single inquiry when the prior art encompasses the teachings of the double patenting reference yet that double patenting reference itself is not prior art. *See, e.g.*, *Ex parte Yokogawa*, 1999 WL 33220561, at *2 (B.P.A.I. Feb. 11, 1999) ("[I]n the case before us, the underlying U.S. Patent 5,478,936 constitutes prior art . . . ."); *Eli Lilly & Co. v. Zenith Goldline Pharm., Inc.*, 364 F. Supp. 2d 820, 910-11 (S.D. Ind. 2005), *aff'd*, 471 F.3d 1369 (Fed. Cir. 2006) ("Where the reference patent is prior art, as in this case, the analysis for obviousness-type double patenting and obviousness under § 103 certainly begin the same way."); *see also Sun Pharmaceutical Industries, Ltd. v. Eli Lily & Co.*, 625 F.3d 719, 721 (Fed. Cir. 2010) (Newman, J., dissenting from denial of reh'g *en banc*) ("A double patenting analysis occurs only when the earlier patent is not prior art against the later patent."). *In re Ornitz*, 376 F.2d 330, 334 (C.C.P.A. 1967), merely explains that "[w]here it is possible to conduct the broader inquiry permitted by sections 102(e) and 103 because the references are 'prior art,' it does not make sense to resort to the narrower inquiry which underlies a 'double patenting' rejection." From this it does not follow that an OTDP analysis is always narrower than an obviousness analysis, particularly where (as here) the OTDP reference patent is not prior art.

differences between the reference patent and the patent-in-suit. Here, then, according to Watson, the Court must assume that everything in common between claim 1 of the '793 patent and the claims of the '577 patent are fixed and that a POSA would not consider modifying any of those commonalities. *See generally Eli Lilly v. Teva*, 689 F.3d at 1377 (finding no error in district court consideration of compounds as a whole and whether one of skill would be motivated to modify compound in reference patent).

Because the Court concludes that Watson has failed to meet its burden even if the OTDP analysis should proceed in the manner proposed by Watson, the Court need not decide if the law compels the separate analysis being undertaken here. The Court merely assumes, *arguendo*, that separate analyses are required. *See generally Otsuka*, 678 F.3d at 1297 ("Otsuka contends that there is no difference between obviousness under § 103 and obviousness-type double patenting. That is not entirely correct. . . . Important differences remain . . . . [For example,] [t]he patent principally underlying the double patenting rejection need not be prior art.") (internal citations omitted).

II. The Claims of the '577 Patent Are Not Invalid for Double Patenting

Watson's double patenting position is based on a comparison between the asserted claims of the '577 patent and claim 1 of the '793 patent. Watson contends that the asserted claims of the '577 patent are invalid as obvious over claim 1 of the '793 patent. According to Watson, the asserted claims are prima facie obvious because the whole regimen of EV and DNG in the '577 patent was already claimed in the '793 patent, and the specific doses of EV and DNG came straight out of the prior art ranges taught to be effective. Watson further contends that Bayer cannot overcome prima facie obviousness through secondary considerations.

As already noted, the double patenting analysis consists of two steps. "First, the court construes the claim[s] in the earlier patent and the claim[s] in the later patent and determines the differences. Second, the court determines whether those differences render the claims patentably distinct." *Abbvie*, 764 F.3d at 1374 (internal citation and quotation marks omitted). The Court now undertakes these two steps.

A. Differences between '793 patent claim 1 and '577 patent claims

The first step in the double patenting analysis is to determine the differences between the claims of the patent-in-suit, the '577 patent, and the claim of the earlier patent, which here is claim 1 of the '793 patent. In assessing those differences, the Court will apply the claim constructions it adopted earlier in this case.

Claim 1 of the '577 patent claims a "multiphase product for contraception," while claim 2 claims an identical "multiphase ***oral*** contraception product" (emphasis added), each comprising:

> a first phase of 2 daily [oral] dosage units, each comprising 3 mg of estradiol valerate,
>
> a second phase of 2 groups of daily [oral] dosage units, a first group comprising 5 daily [oral] dosage units, each of which comprises 2 mg of estradiol valerate and 2 mg of dienogest, and a second group comprising 17 daily [oral] dosage units, each of which comprises 2 mg of estradiol valerate and 3 mg of dienogest;
>
> a third phase of 2 . . .[6][oral] daily dosage units, each comprising 1 mg of estradiol valerate, and
>
> a fourth phase of 2 daily [oral] dosage units, each comprising a pharmaceutically acceptable placebo.

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[6]Claim 1 appears to contain a typographical error, as it redundantly states "a third phase of ***2 two*** daily dosage units" (emphasis added). The Court does not believe this error has any impact on the analysis.

(JTX1 at 4:16-41) Claim 3 of the '577 patent claims the identical regimen, restating it in terms of a "method of oral contraception comprising orally administering to a woman" the various "oral dosage unit[s]" containing the same amounts of EV and DNG, during the same days and phases, as specified in the regimen of claims 1 and 2. (*Id.* at 4:42-53)[7]

The Court has construed "multiphase product" to mean "product composed of multiple sets of dosage units;" "multiphase oral contraception product" to mean "a contraception product composed of multiple sets of oral dosage units;" and "phase" to mean "a set of dosage units." (D.I. 99; D.I. 111) "Daily dosage units" and "daily oral dosage units" are afforded their plain and ordinary meaning. The Court further concluded that claims 1 and 2 "describe only the physical composition of the claimed drug products." (D.I. 99 at 13-14 n.8)

Claim 1 of the '793 patent claims:

> A combination preparation for contraception comprising
>
> a first stage consisting of two daily dosage portions, each consisting of an effective amount of estradiol valerate;
>
> a second stage consisting of a first group and a second group of daily dosage portions of a combination of said estradiol valerate and dionogest;
>
> a third stage consisting of two daily dosage portions, each consisting of an effective amount of said estradiol valerate, wherein said effective amount of said estradiol valerate in each of said two daily dosage portions in said third stage is the same, but smaller than said effective amount of said estradiol valerate in each of said two daily dosage portions in said first stage; and
>
> an additional stage consisting of two daily dosage portions, each consisting of a pharmaceutically acceptable placebo;

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[7]Neither Bayer nor Watson contends there is any material difference among claims 1, 2, and 3 of the '577 patent for purposes of the Court's analysis.

> wherein said first group of said daily dosage portions of said second stage consists of five of said daily dosage portions of said combination and wherein said second group of said daily dosage portions of said second stage consists of seventeen of said daily dosage portions of said combination; and
>
> wherein respective amounts of said estradiol valerate in each of said daily dosage portions of said second stage are equal and respective amounts of said dienogest in said daily dosage portions of said second group of said second stage are equal to 1.5 to 3 times corresponding amounts of said dienogest in said daily dosage portions of said first group of said second stage.

(JTX19 at 6:50 - 7:13)

Plainly, much is the same between the claims of the '577 patent and claim 1 of the '793 patent. Both claim multiphase oral contraception products. The daily dosing pattern is the same – 2:5:17:2:2. Both use as their principal ingredients EV, DNG, and a placebo. Both also generally claim the same combinations of these ingredients: 2 days of just EV, 5 days of EV and DNG, 17 more days of EV and DNG, 2 days of just EV, and finally 2 days of placebo. (*See* Simon Tr. at 124; Barnhart Tr. at 447 (agreeing that multiphasic regimen in '577 patent is "exact same" as in '793 patent)) It is undisputed that the Natazia® regimen falls within the scope of both the '577 patent's claims and claim 1 of the '793 patent. (Barnhart Tr. at 451)

Yet, there are also differences between the claims. Whereas the claims of the '577 patent identify a precise recipe of specific dosages, claim 1 of the '793 patent far more broadly claims an unspecified genus of multiple dosages. *See Abbvie*, 764 F.3d at 1379 ("It is well-settled that a narrow species can be non-obvious and patent eligible despite a patent on its genus.").[8] The

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[8]Bayer complains that "Watson improperly focuses on just the dienogest doses of the asserted claims while excluding consideration of any features the claims have in common with cherry-picked features from the prior art . . . ." (AB at 8) Citing *Teva Parenteral Meds., Inc.*, 689 F.3d at 1377, in which the Federal Circuit stated that in a double patenting analysis "the claims must

differences are depicted in the table below:

Table 7. Differences Between '577 Claims and '793 Claim 1

Phase ('577 and '793 Patents)	Days ('577 and '793 Patents)	Dose Elements of '577 Patent Claims	Dose Elements of '793 Patent Claim 1
Phase 1	2 daily doses	3 mg EV	Effective amount of EV
Phase 2, group 1	5 daily doses	2 mg EV and 2 mg DNG	Combination of EV and DNG
Phase 2, group 2	17 daily doses	2 mg EV and 3 mg DNG	Combination of EV and DNG, with EV in same amount as Phase 2, group 1 and with DNG 1.5 to 3 times more than in Phase 2, group 1
Phase 3	2 daily doses	1 mg EV	Effective amount of EV, lower than in Phase 1
Phase 4	2 daily doses	Placebo	Placebo

The differences between the claims all relate to the breadth of EV and DNG doses they cover. Claim 1 of the '793 patent recites the use of a daily "effective dose" of EV, where the "effective dose" of EV is less in Phase 3 than in Phase 1 and the amount of EV in Phase 2 relative to the amounts of EV in Phases 1 and 3 is completely unspecified. Claim 1 of the '793

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be considered as a whole," Bayer insists it is improper to assume that a POSA would keep constant everything that the '577 patent claims and claim 1 of the '793 patent have in common. The Court has already assumed, *arguendo*, that separate OTDP and obviousness analyses are necessary, and that in connection with the OTDP analysis the commonalities between the reference patent and the patent-in-suit are to be held constant. In connection with the OTDP analysis, the Court is considering the claims as a whole and identifies all of the differences between them.

patent also recites a formula for selecting DNG doses, where the dose increases 1.5 to 3 times from the first to the second group of Phase 2. (JTX19 at claim 1; Simon Tr. at 124-25) The '577 patent claims particular doses of EV and DNG: descending doses of EV (3-2-1 mg) from Phase 1 to Phase 3, and ascending doses of DNG (2-3 mg) in the two groups of Phase 2. (JTX1 at claims 1-3) It is undisputed that the EV doses recited in the claims of the '577 patent are "effective" within the meaning of the '793 patent and that the DNG dosages of the '577 patent claims "fit" the formula set forth in the '793 patent. (Barnhart Tr. at 454-55)

The differences between the claims can be summarized as follows:

- while Phase 1 of the '577 patent requires two daily doses of 3 mg EV, Phase 1 of the '793 patent requires two daily doses of an unspecified "effective amount" of EV;

- while Phase 2, group 1 of the '577 patent requires five daily doses of 2 mg EV and 2 mg DNG, Phase 2, group 1 of the '793 patent requires five daily doses of an unspecified "combination" of EV and DNG;

- while Phase 2, group 2 of the '577 patent requires seventeen daily doses of 2 mg EV and 3 mg DNG, Phase 2, group 2 of the '793 patent requires 17 daily doses of unspecified amounts of EV and DNG, where the only limits on selection of doses are that: (i) EV is the same unspecified amount as in Phase 2, group 1, and (ii) DNG is 1.5 to 3 times more than the unspecified amount in Phase 2, group 1; and

- while Phase 3 of the '577 patent requires 2 daily doses of 1 mg EV, Phase 3 of the '793 patent requires 2 daily doses of an unspecified "effective amount" of EV, where the only limit on selection of dose is that the amount of EV be "smaller than" the unspecified "effective amount" of Phase 1.

B. The differences render the claims patentably distinct

OTDP "prohibit[s] a party from obtaining an extension of the right to exclude through

claims in a later patent that are not patentably distinct from claims in a commonly owned earlier patent." *Barr Labs., Inc.*, 251 F.3d at 967. Thus, in the second step of the analysis the Court must determine if the differences between the claims identified just above are patentably distinct.

In the Court's view, the differences between the claims of the '577 patent and claim 1 of the '793 patent render the respective claims patentably distinct. Although all five of the differences are of the same general type – differences between unspecified dosages in the '793 patent and specified dosages in the '577 patent – they are, in combination, patentably distinct differences. The Court explains the reasons supporting its conclusion below.

1. A POSA would have believed estrogen dominance would be needed for an effective COC

In March 2004, a POSA using the '793 patent's claim 1 as her starting point, and "locking in" all of the features that are common to that claim and to the claims of the '577 patent, would have believed that the estrogen component of a COC should "dominate" the progestin component of the COC during the proliferative phase of a cycle. (*See, e.g.*, Findings of Fact ("FF") ¶ 102) This is Dr. Barnhart's theory of "estrogen dominance." (*Id.*) The estrogen dominance theory posits that the proliferative effect of estrogen must dominate the anti-proliferative effect of gestogen during the first seven or so days of a cycle, in order for a COC to provide good cycle control.[9] (FF ¶ 103)

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[9]Watson argues in its Reply Brief: "Nothing in the claims requires 'cycle control.' Watson bore no burden of showing a reasonable expectation in proving an unclaimed effect." (RB at 13) It is unclear on what basis Watson makes this argument. To the extent it relies on the Court's claim construction opinion – which stated "the claims themselves describe only the physical composition of the claimed drug products, a structurally complete invention" (D.I. 99 at 13-14 n.8; D.I. 111) – Watson's contention is unavailing. The parties did not ask the Court to determine, during claim construction or otherwise, whether cycle control is a limitation of the claims. At claim construction, in particular, no extrinsic evidence was presented on this point.

Bayer relies on the Hoffman Articles' description of why the Dittgen Regimen's sequentially descending EV doses were expected to improve cycle control as compared to other regimens in which EV was held constant at 2 mg or stepped from 2 mg to 4 mg and back to 2 mg:

> Bearing in mind that sequential preparations are known to improve cycle stability in women complaining of bleeding irregularities, our efforts were directed at designing a sequential 28-day regime. ***To ensure estrogen dominance in the first cycle phase, i.e., the stage at which the endometrial proliferation is promoted under estrogen influence, 17ß-estradiol valerate was given on days 1-25 of the menstrual cycle at doses stepped from 3 mg to 1 mg.*** Basically, the shortening of the hormone-free interval to only 3 cycle days and ***the prolongation of the estrogen phase at the end of the progestin phase*** were expected to increase the cycle stability of the ethinylestradiol-free combination considerably.

(FF ¶ 104) (citing JTX3 at 108; JTX2 at 460 (emphasis added)) As Dr. Barnhart testified, Hoffman – that is, the Dittgen group – "is telling us the reason that this natural estrogen pill worked when others had failed was because it was estrogen dominant." (Barnhart Tr. at 441) Dr. Simon did not testify to the contrary.[10] Bayer also points to the '915 application's explanation that "the estrogen-gestogen balance is shifted largely in favor of the estrogen ingredient." (JTX19 at 4:9-10)

While the Court rejects Waston's contention that Dr. Barnhart's theory of estrogen

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By contrast, at trial, there was a great deal of ***undisputed*** testimony that a successful COC requires both contraceptive effect and good cycle control. (*See, e.g.*, FF ¶ 10) The claims of the '577 patent claim a COC, and a COC requires both of these features. A POSA, thus, would understand the claims to require effective cycle control. The Court has never been asked to make a contrary finding and has not done so.

[10]The Court is unpersuaded by Watson's contention that Hoffman's reference to "estrogen dominance" refers to the phasic method of administration of estrogen compared to prior-art regimens.

dominance is "factually baseless" and "manufactured" (D.I. 134 (Watson Post-Trial Opening Brief) ("OB") at 24), the theory is not entirely invulnerable to criticism. At least once Dr. Barnhart appeared to contradict himself. (*Compare* Barnhart Tr. at 527 (testifying that one could infer from Hoffman that "ratio of 1 to 1, 2 to 2 milligrams [i.e., equal daily weights of EV and DNG] was not progestin dominant") *with id.* at 416 ("The equal doses, the progestin dose is actually outweighing the estrogen effect [i.e., equal daily weights of EV and DNG is progestin dominant]. Actually, if you have a higher dose of dienogest compared to estrogen, it's even more deeply progestin dominant . . . ."), 530 (testifying that Gräser suggests "[a]t two-to-two [i.e., equal daily weights of EV and DNG] it's progestin dominant")) Even then, however, Dr. Barnhart consistently explained that any ratio in which the weight amount of EV is greater than the weight amount of DNG is estrogen dominant. (*Id.* at 530 (discussing Gräser, in which applicable ratios are DNG:EV, and explaining that "[a]nything under a two-to-two milligram or one-to-one ratio is estrogen dominant," meaning that when weight amount of DNG is less than weight amount of EV the resulting combination is estrogen dominant))

Also, it is true that Bayer does not point to a great amount of prior art to support Dr. Barnhart's opinion. Moreover, the Gräser article – which Dr. Barnhart cited on redirect as an example of prior art supporting his theory of estrogen dominance (*see id.* at 529) – is not entirely consistent with Dr. Barnhart's theory of estrogen dominance. One of the Gräser article's conclusions was that the ratio of atrophic (progestin-influenced) to proliferative (estrogen-influenced) endometrial material was one-to-one (neutral) for 1 mg DNG with 2 mg EV (***not*** estrogen dominant, as Dr. Barnhart concluded), and two-to-one (i.e., not just marginally progestin dominant or neutral, but progestin dominant by a factor of two) for 2 mg DNG with 2

mg EV – although the article provided the caveat that the latter ratio was "based on data from only 6 patients rather than 10-14 patients in the other dosage groups." (JTX225 at 259)

Watson does not, however, point to these arguable inconsistencies in Dr. Barnhart's testimony or the conclusion noted just above in Gräser. This may be because Gräser concerns a different population (post-menopausal women) and a different goal (hormone replacement) than the patent-in-suit and the '793 patent, which are directed to development of a natural estrogen COC for women who can get pregnant. (*See, e.g.*, Barnhart Tr. at 529-30 ("The idea in hormone replacement therapy is you want to have the progestin dominant, to stop a process that's called estrogen over growth or hypoplasia, which may lead to cancer. So a minimum dose of progestin you want to use is the dose that counteracts the effect of estrogen . . . .")).[11] Additionally, Gräser is expressly addressing the concept of estrogen and progestin dominance in the context of post-menopausal withdrawal bleeding, which at least supports a finding that issues of estrogen-dominance and progestin-dominance were topics of interest to those who were studying cycle control.

There are other reasons the Court finds that Gräser is, overall, more supportive of Bayer's position than Watson's. Even in the different population Gräser was studying, the study's results clearly showed that the greater amount of DNG a woman is given relative to a fixed amount of EV, the greater the atrophic effect on the uterus, and therefore the greater amount of bleeding observed. (*See, e.g.*, JTX225 at 256 & Table 2) ("The frequency of uterine bleeding was lowest

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[11]Other distinctions between Gräser and the claims of the '577 patent are also readily apparent. For example, Gräser did not test a multiphasic regimen, but instead five different "fixed combination treatment" regimens; that is, each subject of the Gräser study was given a fixed amount of DNG and EV each day she participated in the study. (*See* JTX225 at 253)

in the 0.5 and highest in the 4.0 mg/day dienogest group (Fig. 1).") These findings are consistent with the "estrogen dominance" theory which posits that the estrogen must dominate progestin in order for there to be good cycle control. Gräser generally found that the less estrogen dominant a regimen is, the greater the incidence of uterine bleeding.[12]

Ultimately, given that estrogen dominance turns out ***not*** to be necessary for good cycle control in a natural estrogen COC (at least as a POSA would have understood it in March 2004),[13] the amount of evidence Bayer was able to muster in support of this theory is adequate to persuade the Court that a POSA would have believed in Dr. Barnhart's theory of estrogen dominance at the pertinent time. In reaching this conclusion, the Court again emphasizes that Watson produced no evidence that Dr. Barnhart's theory of estrogen dominance had been ***rejected*** in the prior art.

In the Court's view, a POSA's belief in the necessity of estrogen dominance means that a POSA – even one with the '793 patent's claim 1 in hand – would not have reasonably expected the claims of the '577 patent to be successful. The Court agrees with Bayer that "the Dittgen

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[12]However, as Watson points out (*see* D.I. 138 at 27-28), Gräser reported the optimal bleeding profile was found with the 2:3 mg EV:DNG combination, a ratio that Gräser found was progestin dominant. (*See* JTX225 at 257)

[13]At trial, Watson surprised Bayer by presenting as evidence advertising materials from Bayer's website for Qlaira®, the European trade name for Natazia®. The Qlaira® materials explain that its regimen (identical to that used in Natazia®) has "[e]strogen dominance in the early part of the cycle," providing good cycle control. (DTX300 at 3; *see also id.* at 4 (touting that Qlaira® regimen is consistent with Hoffman article)) The Court overruled Bayer's objection to use of this evidence. (*See* Tr. at 627-28) While the Qlaira® materials seem to be inconsistent with Bayer's characterization of Natazia® as not being estrogen dominant, the materials are dated 2014 – ten years after the pertinent date of 2004 – by which time a POSA's understanding of estrogen dominance may well have evolved, for reasons including the success of Qlaira® and Natazia®.

group told the world that 'estrogen dominance' was a key part of their cycle control solution," and while the Dittgen regimen is estrogen dominant in the first cycle phase, the Natazia® invention is not. (AB at 3) There would, hence, "be no reasonable expectation of cycle control success" with the '577 patent regimen. (*Id.*)

The assumptions Watson identifies as underlying Bayer's estrogen dominance theory – for instance, that DNG dominates combinations of equal amounts of EV and DNG – are, it is true, not expressly stated in the prior art. But they are supported by Dr. Barnhart's opinion, a qualified expert whose testimony was persuasive and credible. Nor does the fact that the '577 patent is silent as to the "estrogen dominance" theory and as to the patent's inconsistency with it, persuade the Court that a POSA would have failed to understand that the patent is, in fact, inconsistent with estrogen dominance during the proliferative phase of a cycle.

Because it lacks estrogen dominance during the first cycle phase, a POSA in 2004 would not have expected the '577 regimen to have provided good cycle control. In hindsight, the POSA would have been wrong. As the '577 patent demonstrates, either estrogen dominance during the proliferative phase of a cycle is unnecessary, or alternatively what a POSA would have understood constituted estrogen dominance has turned out to be a mistaken understanding. Either way, the Court's finding remains: estrogen dominance would have been thought by a POSA at the time of the invention of the '577 patent to have been necessary to cycle control; a POSA would have understood that the '577 patent does not provide estrogen dominance; and, therefore, a POSA would not have been motivated to create the '577 patent regimen and would not have expected it to succeed.

2. A POSA would not have found it obvious to select the specific doses of the '577 patent

Given a POSA's belief that estrogen dominance during the proliferative phase of a cycle would be necessary for good cycle control, a POSA starting with '793 claim 1 would have expected that the unspecified "effective amounts" of EV in the daily doses of Phase 2, group 1 would need to be greater than the amounts of DNG. Because, in fact, the EV:DNG ratio in Phase 2, group 1 of the '577 patent's regimen is 2:2 mg, it would not have been obvious to move from the '793 patent's claim to the '577 patent's claims. Instead, the daily dosage differences between the respective claims are patentably distinct.

For these reasons, the Court is not persuaded that it would have been obvious to a POSA in 2004 to "plug in" the 3-2-1 mg descending pattern of EV doses in moving from the regimen of claim 1 of the '793 patent to the claims of the '577 patent. Watson is correct that the prior art set forth specific examples for dosing EV in a descending 3-2-1 mg pattern in a multiphasic regimen. Examples 1 and 5 of the '251 patent specification described that dosing pattern of EV and taught that it offered good cycle control. (FF ¶ 45) The Dittgen Regimen also used that same 3-2-1 mg pattern of descending EV. (FF ¶ 47) And the Court recognizes that both sides' experts agreed that it would have been obvious to a POSA to select the 3-2-1 mg descending pattern of EV doses for use in conjunction with the 2-5-17-2-2 dosing pattern set forth in the '793 patent's claim 1.

Still, the 3-2-1 mg descending pattern of EV doses, in combination with the ***increasing*** doses of DNG called for by claim 1 of the '793 patent, would not have been entirely obvious to a POSA in 2004. Notably, the Dittgen Patents and Applications also disclose higher daily dosages of EV, above the 3 mg EV of Natazia®. (*See* JTX19 at 4 ("Furthermore this regimen allows an

extremely high estrogen daily dosage (more than 4mg estradiol equivalents/day.")) As Bayer writes, "[p]ermitting other EV doses exponentially increases the number of options because there are three phases of EV dosing to relate to two phases of DNG dosing." (AB at 22) A POSA starting with the '793 patent, then, may very well have believed it would be necessary to ***increase*** the EV daily dose over the first seven or fourteen days of a cycle. Claim 1 of the '793 patent contains no limitation as to the relative amount of EV between Phase 1 and Phase 2.

At times (at least), Dr. Barnhart's testimony was consistent with this view, as the following testimony demonstrates:

> Q. Now, let's say though that you did contrary to what Moore and the other art teaches, that you did raise the dose of dienogest like Simon said you should. What would you do to the estradiol valerate dose in such a situation?
>
> A. Again, my opinion would be that you wouldn't raise the dose [of DNG] to higher than two [mg], but if you were [to do so], you would recognize the teaching of the estrogen dominance of Hoffman, and if you needed to go higher in progestin [e.g., DNG], then you should accommodate and go higher on the estrogen so you could maintain the same biologic ratio and maintain the estrogen dominance. You wouldn't just change the progestin.

(Barnhart Tr. at 422)

Regardless of whether the EV doses in the '577 patent are patentably distinct from the EV doses in the '793 patent claim 1, the Court concludes that the differences between the two patents' DNG doses – and the resulting EV:DNG daily dose combinations – are patentably distinct. No prior art disclosed any example of a dose of DNG higher than 2 mg for use in a COC. (FF ¶ 32) As Bayer correctly explains, neither Schmidt-Gollwitzer (JTX210) nor Kullman (JTX205) disclose regimens with DNG, although they state ranges of possible DNG doses of 1-3 mg. (AB at 20 n.6) Neither discloses the high overall cycle dosage of 61 mg DNG.

(*See id.*)[14] Gast has a lower range beginning at 250 µg (i.e., 0.25 mg) well below the range that Watson contends would be obvious to a POSA. (*See* JTX201 at 8) The Court agrees with Bayer that "Gast reconfirms what the person of skill in the art would believe – that 2 mg was the highest DNG dose that should be necessary." (AB at 20) That Gast discloses dosing regimens in 0.25 mg increments also demonstrates that a POSA would have considered a wide variety of DNG doses, not just the 1-2-3 mg Watson theorizes would be the full range of options considered.

A POSA would also have understood there was a general preference for minimizing a woman's overall dosage of estrogen and progestin. (FF ¶ 18) In the context of moving from the '793 patent to the '577 patent, this preference would have proved a challenge for a POSA. Estrogen dominance would have motivated the POSA to increase the estrogen doses, while the limitation that the DNG amount in Phase 2, group 2 was to be 1.5 to 3 times greater than the dose in Phase 2, group 1 would have motivated the POSA to increase the DNG dose. Because claim 1 of the '793 patent does not specify the amount of EV, and because a POSA in possession of the '793 patent would expect an effective COC to need to be estrogen dominant at least in the proliferative phase of a cycle, such a POSA would not have found it obvious to select EV:DNG dose ratios of 2:2 mg and 2:3 mg in Phase 2 of the regimen.[15]

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[14]The high per cycle DNG dose is also contrary to what a POSA would have expected or plannned. Natazia® involves 61 mg total DNG, as compared to 18 and 20.25mg for Gast, 36 mg for the Dittgen Regimen, and 42 mg DNG for Valette® over the course of a cycle. (Simon Tr. at 189-90; *see also generally* Barnhart Tr. at 491)

[15]Watson correctly states that its burden is not to prove that the specific doses of the claims of the '577 patent are the only doses that would have been obvious to a POSA. Watson need only prove that these doses would have been among the doses that would have been obvious. *See KSR Int'l Co.*, 550 U.S. at 420 ("One of the ways in which a patent's subject matter can be

3. A POSA would have believed that the Dittgen Regimen, with lower doses of DNG, solved the problem of a natural estrogen COC with good cycle control

An additional reason a POSA, starting with claim 1 of the '793 patent, would not have found it obvious to select the daily doses of the '577 patent claims – and, thus, another reason the differences between the daily doses of the former are patentably distinct from the latter – is that a POSA would have believed the Dittgen Regimen worked. A POSA at that time would have thought that the Dittgen Regimen – including its Phase 2, in which the EV:DNG ratio favored estrogen, and not progestin – constituted an effective COC with good cycle control. In fact, however, the Dittgen Regimen was a failure. This fact contributes to the Court's conclusion that the differences in the claims are patentably distinct.[16]

The Court agrees with Bayer that "even if Natazia® were an obvious solution to the efficacy problem the 1mg/2mg DNG Dittgen dosing suffered, the prior art did not disclose that

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proved obvious is by noting that there existed at the time of invention a known problem for which there was an obvious solution encompassed by the patent's claims."); OB at 18; *see also Galderma Laboratories, L.P. v. Tolmar*, 737 F.3d 731, 731 (Fed. Cir. 2013) ("Nothing in the statute or our case law requires [the Defendant] to prove obviousness by starting with a prior art commercial embodiment and then providing motivation to alter that commercial embodiment."). While there is evidence that a POSA starting with claim 1 of the '793 patent may have considered the specific doses of EV and DNG that ended up in the '577 patent's claims, Watson has not proven that a POSA reading the '793 patent would have "at once envisage[d]" every member of the genus. *See Abbvie*, 764 F.3d at 1379. More fundamentally, Watson has not, on the whole, presented clear and convincing evidence that the invention of the '577 patent's claims would have been obvious to a POSA reading claim 1 of the '793 patent.

[16]Although Bayer knew that the Dittgen Regimen had failed, this failure was not in the prior art. Hence, this failure would not have been known to a POSA. While the Court's OTDP analysis here requires the Court to contemplate a POSA starting with the '793 patent's claim 1 "in hand" – even though the '793 patent is not prior art to the '577 patent – the Court does not understand the OTDP analysis also to require it to vest the POSA with all the knowledge Bayer had in its possession if that knowledge was not also in the prior art.

problem." (AB at 11) "Even an obvious solution, however, does not render an invention obvious if the problem solved was previously unknown." *Novartis Pharm. Corp. v. Watson Labs, Inc.*, 611 Fed. App'x 988, 995 (Fed. Cir. 2015); *see also id.* at 996 ("Although the addition of an antioxidant would have been an obvious solution for a formulation with known oxidation problems, here Watson failed to prove that a rivastigmine formulation was known to be susceptible to oxidative degradation."); *see also Leo Pharm. Prods.*, 726 F.3d at 1353 ("[A]n invention can often be the recognition of a problem itself."); *id.* at 1354 ("The ordinary artisan would first have needed to recognize the problem, i.e., that the formulations disclosed in [the prior art] Dikstein and Serup were not storage stable. . . . Only after recognizing the existence of the problem would an artisan ***then*** turn to the prior art and attempt to develop a new formulation for storage stability."); *id.* at 1357 ("Because the problem was not known, the possible approaches to solving the problem were not known or finite, and the solution was not predictable, it would not have been obvious for a person of ordinary skill to make the claimed invention."); *Mintz v. Dietz & Watson, Inc.*, 679 F.3d 1372, 1377 (Fed. Cir. 2012) ("Often the inventive contribution lies in defining the problem in a new revelatory way.").

The data in the Dittgen Declaration, which was in the prior art, showed that the Dittgen Regimen was 100% effective in preventing ovulation. (FF ¶ 48) Hoffman, also prior art, further showed that this regimen successfully prevented pregnancy in 100 women across 573 cycles. (FF ¶ 81) That Bayer invested the money to go into Phase III trials is further strong evidence that a POSA would have believed that the Dittgen Regimen was likely to prove to be a successful

natural estrogen COC.[17]

The Court recognizes that this case does not line up entirely with those that Bayer relies on because, here, it was ***not the inventors of the '577 patent that discovered the failure*** of the Dittgen Regimen. Still, the fact that this failure was not known in the prior art supports Bayer's position and contributes to the Court's conclusion that Watson has not met its burden of clear and convincing evidence.

4. Secondary considerations of non-obviousness support Bayer

Further supporting the Court's conclusion is the evidence that Bayer presented of secondary considerations of non-obviousness. Such evidence contributes to the Court's findings that Watson has not made a clear and convincing showing of obviousness. *See In re Cyclobenzaprine Hydrochloride Extended-Release Capsule Patent Lit.*, 676 F.3d 1063, 1075-77 (Fed. Cir. 2012).

"Objective indicia can be the most probative evidence of nonobviousness in the record, and enables the court to avert the trap of hindsight." *Leo Pharm. Prods.*, 726 F.3d at 1358 (internal quotation marks omitted); *see also Mintz*, 679 F.3d at 1378 ("These objective guideposts are powerful tools for courts faced with the difficult task of avoiding subconscious reliance on hindsight. . . . These objective criteria thus help turn back the clock and place the claims in the context that led to their invention."). "For objective evidence [of secondary considerations] to be accorded substantial weight, its proponent must establish a nexus between

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[17]Watson contends that because prior art showed that doses of DNG lower than 2 mg were "associated with significant follicular growth," a POSA "would have every reason to consider the appropriateness of higher doses within the prior art's preferred and limited range." (OB at 13) The Court disagrees, given the overall highly successful results the Dittgen Regimen had experienced in the Phase II studies and the decision to take it into Phase III studies.

the evidence and the merits of the claimed invention." *In re GPAC Inc.*, 57 F.3d 1573, 1580 (Fed. Cir. 1995).

Here, Bayer proved long-standing need for a natural estrogen COC and the failure of others to arrive at the same successful result.

The '577 patent provides a solution to a long-felt but unmet need for a natural estrogen contraceptive. (*See generally* FF ¶¶ 118-35) As Bayer puts it, "researchers had spent decades attempting to create a workable natural estrogen oral contraceptive, because of the possibility that they would prove to have fewer undesirable and dangerous side effects." (AB at 28) It is undisputed that Natazia®, which embodies the claims of the '577 patent, is the first and only natural estrogen COC approved in the United States. (FF ¶ 120)

Bayer has proven that its success with the Natazia® regimen claimed by the '577 patent came only after decades of failed attempts by others to arrive at an effective natural estrogen COC. Bayer presented a great deal of evidence that years of attempts to make a natural estrogen COC failed due to inadequate cycle control. (FF ¶¶ 121-25) Although the Dittgen Regimen purported to have solved the cycle control problem, it, too, failed, due to efficacy concerns when tested in a Phase III clinical trial. (FF ¶¶ 126-29) The Modified Dittgen Regimen – which was tested by the inventors of the '577 patent alongside Natazia® – was not tested in Phase III clinical trials, because the results from its Phase II ovulation inhibition studies were just outside of new parameters Bayer set "to be on the safe side" after the failure of the Dittgen Regimen. (FF ¶¶ 130-35)

Watson argues: "Since the '793 patent already solved any long-felt need," Bayer failed to prove that '577 patent solved any long-felt need. (OB at 28) However, as Bayer observes,

"Watson cites no case law to support its view that Bayer must show a failure within the scope of Claim 1 of the '793 Patent." (AB at 29)[18]

Bayer also provided evidence that a POSA would have been dissuaded from moving from the daily doses of claim 1 of the '793 patent to those of the '577 patent's claims. This is because the prior art taught "estrogen dominance" was necessary for cycle control, yet the claimed invention would not, in 2004, have been understood to be estrogen dominant. While this evidence does not amount to the secondary consideration of "teaching away,"[19] the evidence nonetheless helps Bayer and does not at all help Watson meet its high, clear and convincing burden.

Hence, the Court concludes that the secondary considerations of non-obviousness support Bayer.

C. *Galderma* Does Not Compel a Finding of Invalidity

Watson analogizes this case to *Galderma Laboratories, L.P. v. Tolmar*, 737 F.3d 731, 738 (Fed. Cir. 2013), characterizing it as holding that "where the claimed invention involves selecting dosages from within a prior-art range, as here, the burden falls upon the patentee to

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[18]While the Federal Circuit has stated that an OTDP inquiry does not require consideration of objective indicia of non-obviousness, *see, e.g.*, *Procter & Gamble Co. v. Teva Pharm. USA, Inc.*, 566 F.3d 989, 999 (Fed. Cir. 2009); *Geneva Pharm., Inc. v. GlaxoSmithKline PLC*, 349 F.3d 1373, 1378 (Fed. Cir. 2003), it has more recently clarified that such evidence is to be considered when presented, *see Eli Lilly & Co. v. Teva Parenteral Medicines, Inc.*, 689 F.3d 1368, 1381 (Fed. Cir. 2012).

[19]*See Galderma*, 737 F.3d at 738-39 ("A reference does not teach away, however, if it merely expresses a general preference for an alternative invention but does not criticize, discredit, or otherwise discourage investigation into the invention claimed. . . . A teaching that a composition may be optimal or standard does not criticize, discredit, or otherwise discourage investigation into other compositions.").

produce evidence of 'unexpected results,' 'teaching away' or other 'pertinent secondary considerations' to save the claim." (OB at 3) In *Galderma*, 737 F.3d at 738, the Federal Circuit stated:

> [W]here there is a range disclosed in the prior art, and the claimed invention falls within that range, the burden of production falls upon the patentee to come forward with evidence that (1) the prior art taught away from the claimed invention; (2) there were new and unexpected results relative to the prior art; or (3) there are other pertinent secondary considerations.

Galderma may extend to cases in which "the prior art does not teach [the] particular combination of amounts [found in the asserted claims], [but] those amounts . . . fall within the ranges disclosed in a single reference." *Allergan, Inc. v. Sandoz Inc.*, 796 F.3d 1293, 1304 (Fed. Cir. 2015); *see also Avanir Pharm., Inc. v. Actavis South Atlantic LLC*, 36 F. Supp. 3d 475, 502 n.17 (D. Del. 2014) (distinguishing *Galderma* because "[t]he prior art here does not disclose (i) ranges encompassing the claimed doses of ***combination*** of DM/Q at the claimed doses or weight ratios (ii) ***for the treatment of PBA***") (emphases in original), *aff'd sub nom Avanir Pharms. Inc. v. Par Pharm. Inc.*, 612 Fed. App'x 613 (Fed. Cir. 2015).

Galderma, however, does not compel the Court to find the '577 patent's claims invalid due to double patenting (or due to obviousness, with respect to which Watson again relies on *Galderma*). As an initial matter, the Court has found "pertinent secondary considerations" – failure of others and long-felt but unmet need – as explained above. Also, *Galderma* involved an essentially "one dimensional range." (AB at 23) The invention at issue in *Galderma* was the selection of a dose of one ingredient from a previously-disclosed range of that one ingredient.[20]

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[20]The Court does not agree with Watson that "*Galderma* also involved a claim with multiple elements." (RB at 9) Watson's statement is based on *Galderma*'s discussion of the inactive

By contrast, in this case, as Bayer describes, "there are three phases of estradiol valerate dosing and two phases of dionegest dosing even if one locks in the day structure of New Claim 15 or Claim 1 of the '793 Patent. The skilled person thus has to make at least five decisions to come up with a regimen." (AB at 23) Moreover, *Galderma* did not involve a solution to a problem that was previously unknown in the prior art (i.e., the failure of the Dittgen Regimen).

Thus, the Court's conclusions are not inconsistent with *Galderma*.

D. Doubts As to the PTO's Knowledge of Common Ownership Do Not Alter the Outcome

The parties dispute whether the OTDP issue was considered by the PTO, which itself turns on the parties' dispute as to whether the PTO was aware of Bayer's common ownership of the '793 and '577 patents. Watson insists that Bayer failed to disclose its common ownership of the two patents and, had it done so, the PTO would have rejected the '577 patent due to OTDP, just as the PTO had rejected Bayer's '729 application for OTDP over the '793 patent.

As an initial matter, the resolution of the parties' disputes on these points will not alter the judgment the Court will enter in this case. Whether or not the PTO considered double patenting, this Court has considered the issue (after a trial and full post-trial briefing) and is empowered to make the decision announced in this Opinion. Watson's burden remains to show clear and convincing evidence of invalidity either way. As importantly, Watson has not asserted a claim that the '577 patent is unenforceable due to inequitable conduct committed by Bayer

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ingredients in the pharmaceutical at issue there. (*See id.* at 9-10) The analysis from the Federal Circuit on which Watson relies arises solely in the discussion of the selection of the specific dosage of adapalene, the active ingredient. *See Galderma*, 737 F.3d at 736-37 ("Notably, on appeal, the parties do not dispute the obviousness of the inactive ingredients of the formulation. Rather, the ***sole dispute*** between the parties is whether it was obvious to use a 0.3% adapalene composition for the treatment of acne.") (emphasis added).

during prosecution. Thus, even if Bayer did not disclose its common ownership of the '793 patent and the '577 patent to the PTO, this finding would not impact the result in this case.

In any event, on this issue the Court agrees with Bayer that it did disclose its common ownership during prosecution of the '577 patent – although it is possible the PTO did not recognize this disclosure. The evidence of disclosure consists of sparse references amongst a large prosecution history, although there is nothing in the record indicating that Bayer ever carefully drew the Examiner's attention to its common ownership.

The same examiner, San-Ming Hui, examined both the '793 and '577 patents. (FF ¶ 65) During the prosecution of the '793 patent, Bayer filed a Revocation of Power of Attorney and Appointment of New Attorney in which it notified the PTO and Examiner Hui that Bayer was the owner of the applications that would lead to the '793 and '577 patents. (FF ¶ 66) The same power of attorney with the same list of Bayer-owned patents was also filed with the PTO during the prosecution of the '577 Patent. (*Id.*; *see also* JTX265 at 259-60)

During the prosecution of the '577 Patent, Bayer filed an Identification of Related Applications in which it notified the PTO and Examiner Hui that the '577 patent and the '793 patent were related applications. (FF ¶ 67) In this filing, Bayer also notified the PTO and Examiner Hui that the '577 patent was a related application to the '251 patent, the '915 application, and the '729 application. (*Id.*) Additionally, in multiple remarks to the Examiner during the prosecution of the '577 patent, Bayer notified Examiner Hui that the '729 application had been filed incorrectly disclosing the same invention as the '577 Patent with a different (and mistaken) inventive entity, and provided every single office action and response from the '729 application prosecution. (FF ¶¶ 69-70) The '251 patent, the '793 patent, and the '915

application (including New Claim 15) were "cited references" on the face of the '771 application (which became the '577 patent) considered by the Examiner. (FF ¶ 68)

While the prosecuting attorney, Mr. Zelano, testified that he could not recall telling the Examiner about the common ownership of the '793 and '577 patents (*id.*), the record evidence cited above demonstrates that Bayer did disclose this fact during prosecution. By contrast, the record is entirely devoid of evidence that Bayer affirmatively misled the PTO regarding its common ownership of the '793 and '577 patents.

The Court recognizes the force of Watson's suggestion that the PTO ***should have*** rejected the '577 patent based on double patenting, just as it rejected the '577 patent based on obviousness over the Dittgen Regimen. (RB at 4) ("Given that the Examiner repeatedly rejected the '577 patent's claims under the ***different*** 3-4-16-2-3 dosing pattern of the Dittgen Regimen, the PTO surely would have issued a double patenting rejection under the '793 patent's ***identical*** 2-5-17-2-2 dosing pattern, had co-ownership been apparent.") (internal citation omitted; emphases in original) However, Watson's position ultimately rests on nothing more than speculation. Based on the evidence, the Court concludes that Bayer did disclose its common ownership to the PTO during prosecution of the '577 patent. Most importantly, the concerns Watson has raised about the adequacy of Bayer's disclosure of the common ownership do not – in light of the totality of the evidence – provide a basis to invalidate the '577 patent for obviousness type double patenting.

III. Obviousness

Watson contends that the claims of the '577 patent are invalid as obvious over New Claim 15 of the '915 application. It is undisputed that New Claim 15 is in the prior art.

Essentially all of the discussion above in the context of OTDP applies equally with respect to obviousness. The principal differences both favor Bayer: (i) because New Claim 15 was prior art and was before the PTO during its examination of the '577 patent, it is more difficult for Watson to prove obviousness than it is to prove double patenting, which was based on the '793 patent, which was not before the PTO during its examination of the '577 patent; and (ii) rather than "lock in" all the commonalities between the claims of the prior art patent (here New Claim 15) and the asserted claims of the patent-in-suit (the '577 patent), as the Court did as part of its OTDP analysis, with respect to obviousness and consideration of the prior art as a whole the Court must, instead, consider whether a POSA would have been motivated to modify even those commonalities (which, if so, would favor a finding of non-obviousness). Perhaps unsurprisingly, then, the Court concludes that Watson failed to meet its burden to show that the claims of the '577 patent are invalid as obvious.

As previously discussed, the prior art – including the '251 patent, the Dittgen Declaration, New Claim 15, and the Hoffman Articles – disclosed a combination of EV and DNG in a multiphasic regimen (including 2-5-17-2-2) as a potential option for a natural estrogen COC with good cycle control. (JTX14 at 3:16-53; DTX74 at 3-4; JTX68 at 3; JTX3 at 108; JTX2 at 460) Even so, given the Court's findings as to a POSA's understanding of "estrogen dominance," and the historical trend of lowering doses over time, a POSA would not have been motivated to combine the prior art to arrive at the 2-5-17-2-2 daily dosing regimen of 3-2-1 mg EV and 2-3 mg of DNG. A POSA would have had no reasonable expectation of success from such a combination.

As is extensively explained in connection with double patenting, a POSA would not

expect the Natazia® regimen to have adequate cycle control, as the prior art taught that estrogen dominance in the proliferative phase of the cycle was important for cycle control, and the '577 patent is not estrogen dominant in the first cycle phase due to its ratios of EV to DNG doses. Thus, the Court finds that a POSA would not have had a reasonable expectation of success with the formulation's particular ratios of EV to DNG for both contraceptive efficacy and cycle control.

Further, none of the prior art references disclose an actual ***use*** of 3 mg DNG in a COC. (*See* Simon Tr. at 189-90, 192-93, 208; Holtz Tr. at 335-36; JTX4 at 227; JTX2; JTX3 at Fig. 1; JTX14; JTX19; JUTX228; JTX265 at 110) Only the Gräser prior art tested DNG doses greater than 2 mg, but it did so in post-menopausal women, a different population.[21]

A POSA would not have been motivated to raise daily DNG doses higher than 2 mg also because the Dittgen Regimen – using 1 and 2 mg DNG – would have been expected to be an effective COC. (Barnhart Tr. at 395, 397, 421-22) The Hoffman Articles describing the results of the pilot study on the Dittgen Regimen reported zero pregnancies over a total of 573 cycles (JTX3 at 109), and the Dittgen Declaration stated that this was "a safe preparation which effectively inhibits ovulation" (JTX5 at 7). Peer-reviewed and published data, like the data in the Hoffmann Articles, would be evidence a POSA would "start with" in the "hierarchy of evidence," and real data that is not peer-reviewed, like the data in the Dittgen Declaration or in actual patent examples, would be the "next most important data." (Barnhart Tr. at 384-85) Given that "[a]nything short of an ovulation is an effective contraceptive regimen" (*id.* at 380,

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[21]The Gast application disclosed a DNG dose range of 0.25 mg to 4 mg, with examples of a preferred dosing range of 0.5 mg to 1 mg, but it did not provide any clinical data associated with these amounts. (JTX201; Simon Tr. at 269)

408), a POSA would have expected that the Dittgen Regimen was "at least as effective as those [COC regimens] already on the market" (*id.* at 392).

Lastly, as explained in the previous section, Bayer has established the secondary considerations of non-obviousness of failure of others and long-felt but unmet need.

For all of these reasons, the Court concludes that Watson has failed to meet its burden to show that the claims of the '577 patent are invalid as obvious.

IV. Suggestions of "Inequitable Conduct"

One final point merits discussion. Throughout this case, Watson has suggested that Bayer has done something untoward in its prosecution decisions. Although Watson has not contended that Bayer's '577 patent is unenforceable due to inequitable conduct, it has suggested inappropriate behavior which, the Court infers, Watson believes is pertinent to the issues the Court must decide. While none of these allegations is, in actuality, legally relevant, the Court briefly addresses them nonetheless.

Watson accuses Bayer of "attempt[ing] to extend its patent monopoly over the same oral contraceptive regimen by over a decade." (OB at 1) It emphasizes that Bayer obtained the '793 patent in 2005 and then, in 2012, obtained the '577 patent, after having disclaimed all interest in the '793 patent in 2011. Allegedly, "Bayer thereby obtained an extension of patent monopoly over the same oral contraceptive regimen that would last over 15 years if permitted to stand." (*Id.*)

Preventing unwarranted patent "extensions" is the principal purpose of the OTDP doctrine. *See Eli Lilly*, 251 F.3d at 968 ("[T]he fundamental reason for the rule is to prevent unjustified timewise extension of the right to exclude granted by a patent no matter how the

extension is brought about."). The prohibition on double patenting is implemented through the two-step process set out by the Federal Circuit. *See id.* The Court is obligated to apply that two-step OTDP legal analysis, without concern for the result or the parties' policy arguments about it. Having done so, the Court reiterates its conclusion that the challenged claims are not invalid due to double patenting.

Watson further suggests there was something nefarious in Bayer's decision to file "two mutually exclusive applications claiming two different entities were responsible for Natazia®." (OB at 4) Watson is referring to the '729 application – which listed the Dittgen group as inventors – and the '771 application – which listed Endrikat and his team as the inventors. Bayer explains that the reasons for its approach to prosecution are privileged (*see* Tr. at 730-31), and Watson does not dispute this point. The Court perceives nothing in this back-and-forth that should affect the conclusions it has drawn based on the evidence.

Finally, Watson contends that Bayer did something wrong in that "[r]ather than telling the PTO the Dittgen Regimen 'failed,' Bayer relied on its efficacy to obtain the '793 patent covering Natazia®. Having obtained that benefit, Bayer cannot justify its second, later-expiring patent on Natazia® by claiming the ***opposite*** now." (RB at 1 (internal citation omitted); *see also id.* at 6 ("Bayer's 'unknown problem' is based on its own failure to tell the PTO the 'truth.'")) The Dittgen Regimen's failure in the Phase III clinical trial had occurred by January 2001. (JTX6 at 3) In prosecuting the '793 application as late as December 2003, Bayer did not tell the PTO of the failure of the Dittgen Regimen, but instead pointed to the success of that regimen to support its argument for patentability of the '793 patent. (JTX68 at 6 ("[The] showing in the previously filed [Dittgen] Declaration proves that the claimed contraceptive preparation of new claim 15 has

unexpectedly improved properties in comparison to the closest prior art."))

The Court is not persuaded that anything improper has occurred here. Again, there is no claim of inequitable conduct. While Watson is perhaps suggesting the Court should estop Bayer from arguing that the Dittgen Regimen failed, Watson makes no effort to meet the requirements for estoppel. *See McCarron v. F.D.I.C.*, 111 F.3d 1089, 1097 (3d Cir. 1997) ("Judicial estoppel prevents a party from assuming a position inconsistent with one which it took in a prior proceeding. The purpose of judicial estoppel is to prevent a party from playing 'fast and loose' with courts by asserting contradictory positions.").

Thus, the Court concludes that Watson has failed to meet its burden with respect to double patenting and obviousness.

CONCLUSION

Watson has failed to prove by clear and convincing evidence that claims 1-3 of the '577 patent are invalid due to obviousness-type double patenting or obviousness. Judgment will be entered in favor of Bayer and against Watson.

An appropriate Order follows.