

Clearblue®

Advanced Digital Ovulation Test

Typically identifies
4 or more fertile days¹



Professional Series
Ovulation



About Clearblue®

Clearblue® is the world's #1 selling brand in home pregnancy and fertility tests.^a Consumers trust the Clearblue® brand because it delivers the accurate information they want. The Clearblue® product range is built on a strong foundation of peer-reviewed science and consumer understanding. Clearblue® is supported by over 30 years of expertise, quality, and innovation in consumer diagnostics.

If you are a healthcare professional and wish to contact a member of the Clearblue® support team about any product in the Clearblue® range, please send an email to [**spdproductsupport@spdspark.com**](mailto:spdproductsupport@spdspark.com)

Ovulation

Clearblue® Advanced Digital Ovulation Test

Typically identifies 4 or more fertile days¹



Today's busy lifestyle means women often wish to actively plan their family and expect pregnancy to happen quickly. The Clearblue® Advanced Digital Ovulation Test helps women become pregnant faster in a natural way^b by assisting them to time intercourse appropriately within their fertile window.

The only ovulation test to identify a wider fertile window than luteinizing hormone (LH)-only ovulation tests

The Clearblue® Advanced Digital Ovulation Test is the first and only ovulation test that accurately identifies a wider fertile window than LH-only ovulation tests. It tracks changing levels of LH, a key fertility hormone, and estrone-3-glucuronide (E3G),^c a principal urinary metabolite of estradiol. The Clearblue® Advanced Digital Ovulation Test incorporates the latest fertility monitoring technology, which is more than 99% accurate at detecting the LH surge.² The device accurately adapts to a woman's personal menstrual cycle to typically identify 4 or more fertile days; this is more than any other ovulation test, thus providing women with greater opportunities to become pregnant naturally.¹

How does the Clearblue® Advanced Digital Ovulation Test work?

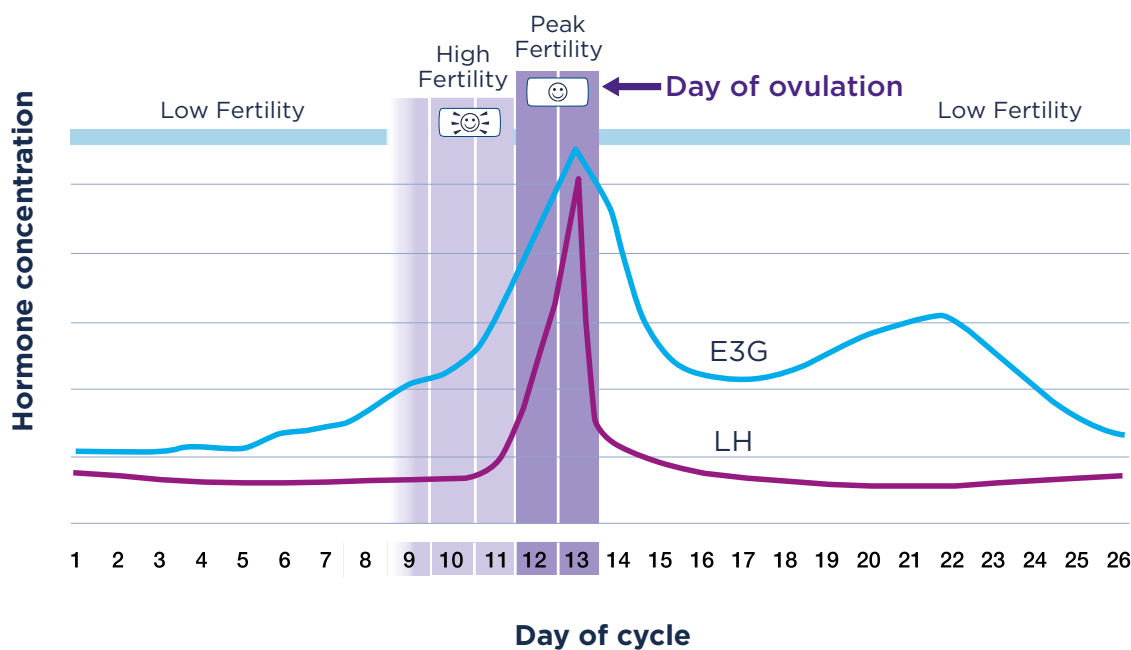
The Clearblue® Advanced Digital Ovulation Test consists of disposable test sticks and a test holder. The test holder reads the test sticks to identify changes in hormone levels by detecting urinary LH and E3G.^{3,4}

The fertile window

Changes in hormone levels control the fertile window

The menstrual cycle is controlled by the anterior pituitary gonadotropins (follicle-stimulating hormone and LH) and the gonadal sex hormones (estrogen and progesterone).⁵ Changing plasma hormone levels throughout the menstrual cycle control ovum development and ovulation.⁶

Figure One: Schematic of typical hormone levels found in urine throughout the menstrual cycle^{5,6}



E3G

The concentration of E3G in urine gradually increases from the start of the cycle, and usually reaches its peak around 24 hours prior to ovulation (range 0-48 hours – see Figure One).^{7,8} A sustained increase in E3G in urine can be used to identify the onset of the fertile window.⁷⁻¹¹

LH

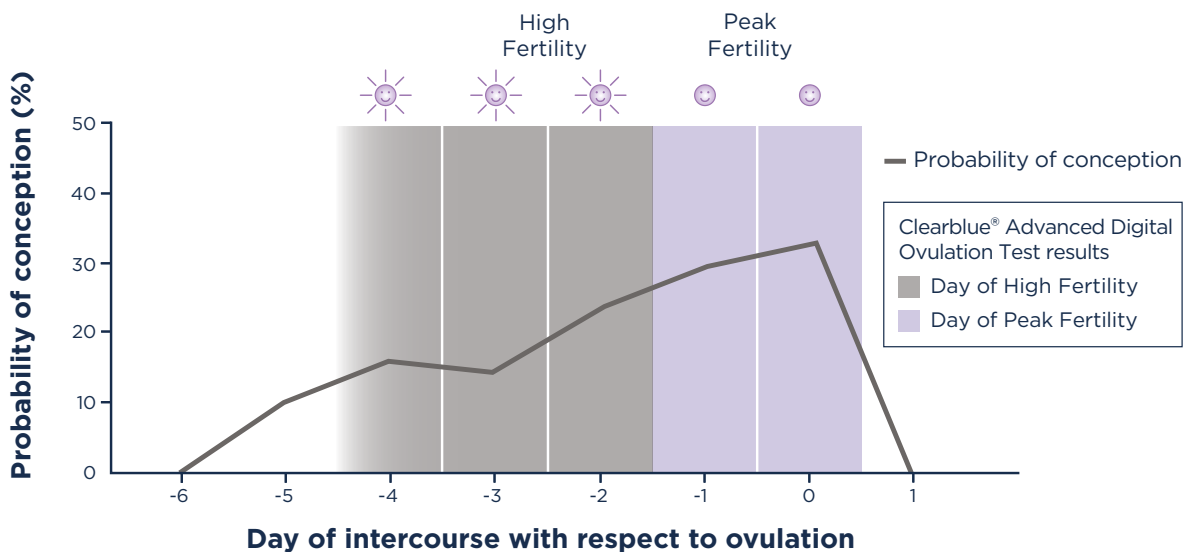
The level of LH surges immediately prior to ovulation, making LH an ideal ovulation marker.^{7,8,10} Ovulation typically occurs within 24-36 hours of the LH surge.^{6,7} Following the LH surge, it becomes increasingly difficult for sperm to penetrate the cervical mucus.¹² This is due to a fall in the level of estradiol and a rise in progesterone. The fertile window closes shortly after ovulation.

The chance of conception increases in the days preceding ovulation

The duration of the fertile window is determined by both the viability of sperm in the days preceding ovulation and the lifespan of the ovum; it is generally accepted that sperm can survive for up to 5 days in sperm-supportive cervical mucus, while ova typically survive for 12–24 hours after ovulation.^{13,14}

Several studies have examined the length of the fertile window. For example, Wilcox AJ, *et al.* (1995) analyzed the menstrual cycle in 221 women and found the fertile window was 6 days long, ranging from 5 days prior to the estimated day of ovulation (EDO) to the EDO itself. Results showed that for every cycle in which conception occurred, there was intercourse at least once in this 6-day period. Conversely, where no intercourse occurred during this period, pregnancy did not result (Figure Two).¹⁵

Figure Two: Probability of conception with respect to day of ovulation. Data from 129 ovulatory cycles in which a single act of intercourse led to pregnancy were used to calculate the probability of conception, and data from the statistical model applied to the 625 ovulatory cycles examined in this study. Adapted from Wilcox AJ, *et al* (1995)¹⁵



Adaptive algorithm that measures each cycle's unique hormone profile

Each menstrual cycle is unique, and the Clearblue® Advanced Digital Ovulation Test uses an algorithm that adapts to each individual cycle to give personalized results:

- Trend analysis is applied to the E3G measurements to identify the first day of the sustained rise in E3G above baseline, on which the device begins to display a flashing 😊 indicating a 'High Fertility' result
- The device also sets a personalized LH threshold level for each woman by measuring changes in hormone levels from baseline, as many women naturally have low levels of LH in their urine
- A static 😊 indicating a 'Peak Fertility' result is displayed when the personal LH threshold is reached

The importance of timing intercourse

Conception is most likely to occur when intercourse takes place on the day before or day of ovulation,¹⁶ but it has a possibility of occurring throughout the fertile window. Conception has been proposed to occur more quickly with fertility-focused intercourse,¹⁶⁻¹⁸ and intercourse across the fertile period is more likely to lead to pregnancy than intercourse during Peak Fertility alone.¹⁹

There are two main reasons why couples may incorrectly time intercourse.²⁰ First, couples may be unaware of the most appropriate time in their cycle to try to conceive. Second, the assumption that the fertile window usually occurs between days 10-17 of the menstrual cycle is often incorrect.^{15,21,22} This is because, although women with a normal menstrual cycle have a mean cycle length of 27-28 days, the range both within and between individuals is considerably wider.²³ In a study of 850 women who were seeking to conceive, the actual cycle length ranged from 17 to 53 days.²⁴ Interestingly, although 34% of women thought that they had a 28-day cycle, only 14% were shown in this study to have a cycle of this length. In a population of 101 women considered to have normal menstrual cycles, the range in cycle length was recorded as 13-51 days.²⁵ In another study of over 130 women, 46% were found to have an individual cycle range of 7 days or more.²⁶ Most of this variability is attributable to the follicular phase of the cycle.^{25,27}

A study of women trying to conceive examined how accurately they predict their day of ovulation and found that only 12.7% correctly estimated their ovulation day.²⁸ This study demonstrates the importance of a prospective method of identifying the fertile window, rather than relying on menstrual cycle characteristics.

Stress and digital ovulation tests

A study has demonstrated that the use of digital ovulation tests neither increases nor decreases the levels of stress in users, and importantly digital ovulation test use may shorten the time to conception.²⁹ The study also found that the use of digital ovulation tests provided additional benefits, including an increased understanding of the menstrual cycle, reassurance, and confidence in focusing intercourse at the correct time in the cycle.³⁰

Can apps be used to accurately predict ovulation?

Many women turn to apps to help them identify their fertile days. However, many apps indicate day of ovulation and fertile days using cycle length information alone, without accounting for cycle length variability. Furthermore, few apps publish the algorithm used to determine fertile days.

Examination of 108 English language iOS apps found only 19% of free apps are accurate. In this study, simulation assumed ovulation 13–15 days before the start of the next cycle.³¹ A further study of 33 Android and iOS apps using a simulated 28-day cycle found only 9% accurately predicted the fertile window.³²

How to use the test

A woman needs to test every day from her calculated start date, using her first urine sample after the longest sleep of the day. The user should consult the table below (Table One), found on the in-pack instruction leaflet, to calculate when she should start testing. If a woman does not know her cycle length, she should wait at least one menstrual cycle and note the length. Women with variable cycle lengths should use their shortest cycle in the last 6 months to calculate when to start testing. Testing can be performed in-stream or on a collected sample.

Table One: Table to indicate which day to start testing

Length of your cycle (days)	21 or less	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41 or more
Note the day your period starts as day 1. Start testing on the day shown under your cycle length	5	6	6	6	7	7	7	8	9	10	11	12	13	14	15	16	17	18	19	20	20 days before you expect your next period

The Clearblue® Advanced Digital Ovulation Test is available in a pack containing a test holder and 10 or 20 test sticks. If a woman has not detected days of both High and Peak Fertility using the test sticks in her first pack, she can continue testing in that cycle using the same test holder and test sticks from a new pack.

Once she has started testing, she should only test once a day until the flashing 😊 indicating 'High Fertility' is displayed. When High Fertility is indicated, she may test more than once a day if desired, but it is important that she does not urinate for 4 hours before testing.

What the results mean

After 5 minutes, the holder automatically reads and interprets the test result and delivers a digital indication of the woman's fertility status:

Low Fertility



It is unlikely, but not impossible, that intercourse at this time will result in pregnancy. The woman should test again the following day. This result will be displayed for 8 minutes.

High Fertility



A rise in E3G has been detected. Intercourse today could lead to pregnancy, but the woman must also test again the following day. This result will be displayed for 8 minutes.

Peak Fertility



The LH surge has been detected. Intercourse in the next 48 hours provides the highest chance of conception. The 'Peak Fertility' icon will be displayed continuously for 48 hours and there is no need to test again during this cycle.

Every woman's cycles are unique and their hormone profiles differ. Therefore, the number of fertile days seen with the Clearblue® Advanced Digital Ovulation Test is personal to each woman. The percentage of women with 0-4, 5-9, or 10+ days of High Fertility before Peak Fertility in a study of 87 women is detailed in Table Two.³³

Table Two: Percentage of women with 0-4, 5-9, or 10+ days of High Fertility before Peak Fertility, as indicated by the Clearblue® Advanced Digital Ovulation Test

Number of days of High Fertility before Peak Fertility	Percentage of women
0-4	66%
5-9	25%
10+	1%

In 8% of women, no days of Peak Fertility were detected after days of High Fertility.

Advantages of the Clearblue® Advanced Digital Ovulation Test

Identification of additional fertile days provides couples with more flexibility to plan intercourse around their busy lifestyles

Most home ovulation tests only detect 1-2 fertile days, through identification of the LH surge, which limits the opportunity for couples to plan intercourse before ovulation occurs. The Clearblue® Advanced Digital Ovulation Test typically identifies more fertile days than other ovulation tests to help women get pregnant sooner.^b The Clearblue® Advanced Digital Ovulation Test is suitable for women with all cycle lengths.

Measures urinary intact LH

Levels of urinary intact LH have been shown to peak approximately 0.5 days prior to ovulation; however, total LH levels have been shown to peak approximately 1 day later, which can fall after ovulation has occurred.^{7,8} The Clearblue® Advanced Digital Ovulation Test measures the intact form of LH to ensure accurate prediction of ovulation.

Digital format for unmistakably clear results

Women have been shown to read ovulation tests with a digital display more accurately than non-digital tests (tests with results in the form of colored lines). In one study exploring how volunteers interpreted the results of a digital ovulation test versus three non-digital tests, over 97% of volunteers correctly read the result of the digital ovulation test compared with 84%, 73%, and 64% for the three non-digital ovulation tests.^d Ninety-seven percent of the volunteers also preferred the digital ovulation test.³⁴

More accurate than other commonly used methods

The Clearblue® Advanced Digital Ovulation Test is over 99% accurate at predicting the LH surge. In comparison, the accuracy of predicting the LH surge to within 1 day is reported to vary between 57–70% for the basal body temperature (BBT) method, and 48–76% for the cervical mucus evaluation method.³⁵

- **Calendar method** – calendar calculations are unreliable for the purpose of timing intercourse to conceive because women's cycles are known to vary from cycle to cycle and the day of ovulation itself is therefore variable^{25,27,36}
- **BBT** – the BBT method is not ideal for timing intercourse because the rise in temperature cannot be detected until after ovulation has occurred.¹¹ Furthermore, most studies examining the BBT method have concluded that it can be unreliable due to inaccurate interpretation of temperature curves, either through patient error or confounding factors (alcohol intake, timing of temperature reading, or certain medications)^{35,37}
- **Observation of cervical secretions** – monitoring of cervical mucus can provide prospective information, but it requires a level of training, is less accurate than monitoring the LH surge, and may not be acceptable to all women³⁵

Limitations

- Users should always read the manufacturer's instructions for any medication they are taking before conducting a test
- Certain medical conditions and medications can adversely affect the performance of the Clearblue® Advanced Digital Ovulation Test. Women who have menopausal symptoms, polycystic ovarian syndrome, impaired liver or kidney function, are pregnant, or have recently been pregnant (even if not carried to full term) may get misleading results. Similarly, misleading results may be obtained by women taking antibiotics containing tetracyclines, hormonal treatments (e.g. hormonal contraception or hormone replacement therapy), fertility treatments containing human chorionic gonadotropin or LH, or any treatment that might affect their cycle. Women who are affected by these medical conditions or are taking these medications are advised to wait until they have had at least two natural menstrual cycles in a row (each lasting 21-42 days), before using the Clearblue® Advanced Digital Ovulation Test
- Women who are undergoing fertility treatments (e.g. clomifene citrate or letrozole) may receive misleading 'High Fertility' results with the Clearblue® Advanced Digital Ovulation Test; 'Peak Fertility' results should be unaffected
- The Clearblue® Advanced Digital Ovulation Test should not be used as a method of contraception



References

1. Tiplady S, *et al.* Detection of two urinary hormones by a new home ovulation test to identify the wider fertile window: a randomised comparative laboratory study of home ovulation tests. *Human Reprod.* (2013) 28(Suppl 1): i244.
2. SPD data on file. Study found >99% agreement with AutoDELFIA reference method in 100 cycles (all cycles had LH surge >40mIU/mL).
3. World Health Organization. Temporal relationships between indices of the fertile period. *Fertil Steril.* (1983) 39: 647–654.
4. Catalan R, *et al.* Correlation between plasma estradiol and estrone-3-glucuronide in urine during the monitoring of ovarian induction therapy. *Int J Fertil.* (1989) 34: 271–275.
5. Martinez AR, *et al.* Prediction and detection of the fertile period: the markers. *Int J Fertil Menopausal Stud.* (1995) 40: 139–155.
6. Burger HG. Estradiol: The physiological basis of the fertile period. *Suppl Int J Gynecol Obstet.* (1989) 1: 5–9.
7. Johnson S, *et al.* Development of the first urinary reproductive hormone ranges referenced to independently determined ovulation day. *Clin Chem Lab Med.* (2015) 53: 1099–1108.
8. Roos J, *et al.* Monitoring the menstrual cycle: Comparison of urinary and serum reproductive hormones referenced to true ovulation. *Eur J Contracept Reprod Health Care.* (2015) 20: 438–450.
9. World Health Organization. A prospective multicentre study to develop universal immunochemical tests for predicting the fertile period in women. World Health Organization Task Force on Methods for the Determination of the Fertile Period, Special Programme of Research, Development and Research Training in Human Reproduction. *Int J Fertil.* (1985) 30: 18–30.
10. Behre HM, *et al.* Prediction of ovulation by urinary hormone measurements with the home use Clearplan Fertility Monitor: comparison with transvaginal ultrasound scans and serum hormone measurements. *Hum Reprod.* (2000) 15: 2478–2482.
11. Tanabe K, *et al.* Prediction of the potentially fertile period by urinary hormone measurements using a new home use monitor: Comparison with laboratory hormone analyses. *Hum Reprod.* (2001) 16: 1619–1624.
12. Royston JP. Basal body temperature, ovulation and the risk of conception, with special reference to the lifetimes of sperm and egg. *Biometrics.* (1982) 38: 397–406.
13. Lynch CD, *et al.* Estimation of the day-specific probabilities of conception: Current state of the knowledge and the relevance for epidemiological research. *Paediatr Perinat Epidemiol.* (2006) 20 (Suppl 1): 3–12.
14. Katz DF. Human cervical mucus: research update. *Am J Obstet Gynecol.* (1991) 165: 1984–1986.
15. Wilcox AJ, *et al.* Timing of sexual intercourse in relation to ovulation. *N Engl J Med.* (1995) 333: 1517–1521.
16. Wilcox A, *et al.* The timing of the “fertile window” in the menstrual cycle: day specific estimates from a prospective study. *BMJ.* (2000) 321: 1259–1262.
17. Hilgers T, *et al.* Cumulative pregnancy rates in patients with apparently normal fertility and fertility-focused intercourse. *J Reprod Med.* (1992) 37: 864–866.
18. Stanford J, *et al.* Timing intercourse to achieve pregnancy: Current evidence. *Obstet Gynecol.* (2002) 100: 1333–1341.
19. Barrett JC and Marshall J. The risk of conception on different days of the menstrual cycle. *Popul Stud.* (1969) 23: 455–461.
20. Louis GM, *et al.* Periconception window: advising the pregnancy planning couple. *Fertil Steril.* (2008) 89 (Suppl 2): e119–121.
21. Johnson SR, *et al.* Women's knowledge regarding ovulation and most likely time of conception. *Hum Reprod.* (2011) 26 (Suppl 1): i236.
22. Robinson JE and Ellis JE. Mistiming of intercourse as a primary cause of failure to conceive: results of a survey on use of a home-use fertility monitor. *Curr Med Res Opin.* (2007) 23: 301–306.
23. Johnson S, *et al.* Development of the first urinary reproductive hormone ranges referenced to independently determined ovulation day. *Clin Chem Lab Med.* (2015) 53: 1099–1108.
24. Johnson S, *et al.* Apps/calendar methods for trying to conceive: Can they accurately predict ovulation? (Abstract O-204). Presented at the Annual Meeting of the European Society of Human Reproduction and Embryology (ESHRE), Geneva, Switzerland, 2nd–5th July 2017.
25. Johnson SR, *et al.* Levels of urinary human chorionic gonadotrophin (hCG) following conception and variability of menstrual cycle length in a cohort of women attempting to conceive. *Curr Med Res Opin.* (2009) 25: 741–748.
26. Creinin MD, *et al.* How regular is regular? An analysis of menstrual cycle regularity. *Contraception.* (2004) 70: 289–292.
27. Lenton EA, *et al.* Normal variation in the length of the follicular phase of the menstrual cycle: Effect of chronological age. *Br J Obstet Gynecol.* (1984) 91: 681–684.
28. Zinaman M, *et al.* Accuracy of perception of ovulation day in women trying to conceive. *Curr Med Res Opin.* (2012) 28: 1–6.
29. Tiplady S, *et al.* Home ovulation tests and stress in women trying to conceive: a randomized controlled trial. *Hum Reprod.* (2013) 28: 138–151.
30. Jones G, *et al.* Women's experiences of ovulation testing: a qualitative analysis. *Reprod Health.* (2015) 12: 116.
31. Moglia ML, *et al.* Evaluation of smartphone menstrual cycle tracking applications using an adapted APPLICATIONS scoring system. *Obstet Gynecol.* (2016) 127: 1153–1160.
32. Setton R, *et al.* The accuracy of web sites and cellular phone applications in predicting the fertile window. *Obstet Gynecol.* (2016) 128: 58–63.
33. SPD data on file (2012). In a study of 87 women, 0–4 days of High Fertility were seen in 66% of women before days of Peak Fertility, 5–9 days in 25% of women and 10+ days in 1% of women. No days of Peak Fertility were detected after days of High Fertility in 8% of women.
34. Johnson SR, *et al.* Comparison of a digital ovulation test with three popular line ovulation tests to investigate user accuracy and certainty. *Expert Opin Med Diagn.* (2011) 5: 467–470.
35. Brezina PR, *et al.* At home testing: Optimizing management for the infertility physician. *Fertil Steril.* (2011) 95: 1867–1878.
36. Small CM, *et al.* Validity of self-reported menstrual cycle length. *Ann Epidemiol.* (2007) 17: 163–170.
37. Barron ML and Fehring RJ. Basal body temperature assessment: Is it useful to couples seeking pregnancy? *Am J Mat Child Nurs.* (2005) 30: 290–296.

Clearblue® Advanced Digital Ovulation Test is:

Unique – the first and only ovulation test that typically identifies 4 or more fertile days¹

Accurate – the only ovulation test to accurately track two key fertility hormones^c

Adaptive – a digital ovulation test that can adapt to a woman's individual hormone levels every time she tests

Unmistakably clear – digital results displayed as a smiley face 😊 for High and Peak Fertility days

Reliable – uses innovation based on established technology

^a Based on international sales compiled using independent market research data (data on file).

^b Using the Clearblue® Advanced Digital Ovulation Test to identify a woman's most fertile days can help her become pregnant faster vs not using a method to identify fertile days.

^c E3G is recognized by the World Health Organization as a principal metabolite of estradiol that can be used to identify the onset of the fertile phase.³ The urinary levels of E3G correspond to the serum levels of estradiol.⁴

^d Although the study was conducted using the Clearblue® Digital Ovulation Test rather than the Clearblue® Advanced Digital Ovulation Test, it highlights that women find ovulation tests with a digital display easier to read than visual tests.

This material is intended for healthcare professionals only. It is for general information only with no warranties, representations or undertakings, express or implied, and does not constitute medical advice. Product images are for illustration only. Clearblue® is a registered trademark of SPD Swiss Precision Diagnostics GmbH ("SPD"). © 2018 SPD (except for any third-party content identified as such). All rights reserved.



For more information about the Clearblue® Advanced Digital Ovulation Test, please visit our websites:

www.Clearblue.com

www.swissprecisiondiagnostics.com



SPD Swiss Precision Diagnostics GmbH, 47 route de Saint-Georges, 1213 Petit Lancy, Geneva, Switzerland

Clearblue® Professional Series: HCP-0086.5