

# The BIRTH of a NEW MARKET

WOMEN WANT  
MORE THAN JUST  
BIRTH CONTROL.

They are  
looking for  
additional  
benefits  
from  
contraceptives

TO MEET  
THEIR  
INDIVIDUAL  
NEEDS.



# New Choices in Contraceptives

A wide choice of contraceptive products has been introduced to the market in recent years, representing innovative new products and options in birth control. Experts agree that during the next five to 10 years, there are further opportunities for companies to provide women with more individualized options.

## THE FUTURE IS About Choice

As researchers continuously study ways to improve contraception products, industry experts say the future contraceptive market will be all about choice.

"Choices will expand beyond the reference point of the pill," says Nicholas J. Hart, senior director of contraceptives for Organon USA.

Modern contraceptive methods have a short history and are dominated by oral products, which came to the market in 1960. Since then, there have been important developments, and recently a wide choice of contraceptive options has been introduced to the market. These include implants, hormone-releasing vaginal rings, monthly injections, weekly transdermal patches, a pill that limits menstruation to four periods a year, and a new intrauterine device (IUD) that provides contraception for years and limits menstruation.

According to researchers at Kalorama Information, there is also an array of new oral contraceptives (OCs) with different dosages and combinations of hormones designed to limit the side effects of earlier versions, such as excessive bleeding, acne, and weight gain. There is also a wide variety of over-the-counter products, such as condoms for men and women, diaphragms, cervical caps and sponges, and spermicides.

The Contraceptive Report, which was sponsored by the Dannemiller Memorial Educational Foundation and a grant from Wyeth, in 2000 found the top methods of contraception in the United States were oral contraceptives, female sterilization, condoms, and vasectomies. These four accounted for about 85% of U.S. contraceptive practices.



Nicholas Hart Organon USA



Marjorie Miller

Wyeth Pharmaceuticals

**We recognize that there is a constellation of issues that surround women of reproductive age; OUR ULTIMATE GOAL IS TO ADDRESS THEIR UNMET NEEDS.**

CONTRACEPTIVE CHOICES WILL EXPAND AND **women will have options beyond the reference point of the pill.**

According to Kalorama research, the hormonal contraceptive market was expected to reach \$2.93 billion in 2005 in the United States alone. In 2004, oral formulations and injectable contraceptives held 83% of the market share in the United States, while the contraceptive patch had about 15% of the market, and devices had a 2% market share. The world hormonal contraceptive market is expected to increase at an annual growth rate of 8% to reach \$7.89 billion in 2008.

Researchers from a variety of leading pharmaceutical manufacturing companies, such as Barr Laboratories, Berlex Inc., Conceptus Inc., Ferring Pharmaceuticals, Organon, Ortho-McNeil Pharmaceutical, Pfizer, Serono, Wat-

son, and Wyeth are pursuing new formulations and delivery systems to provide an even wider choice of contraceptives for women.

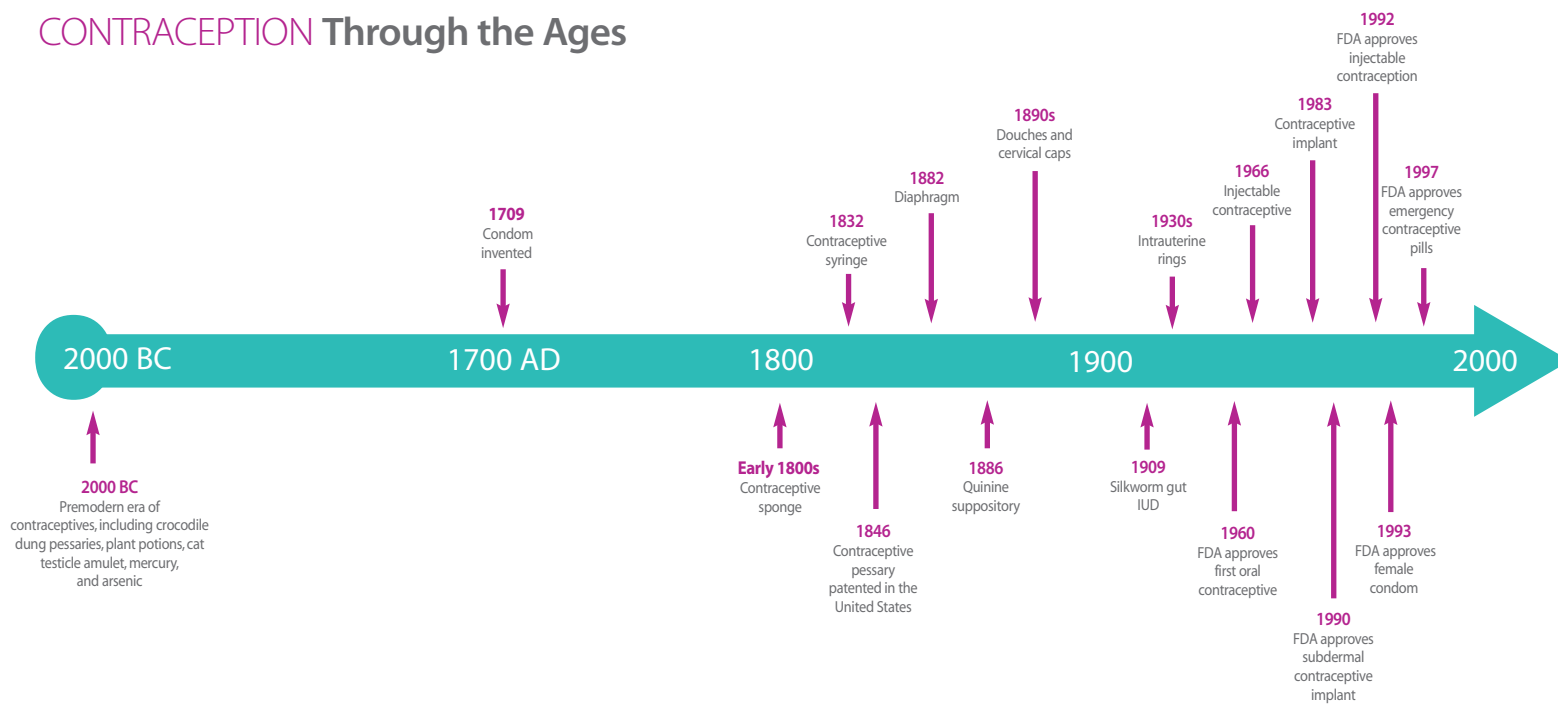
Among the newer delivery systems is Ortho-McNeil's combined hormonal patch, Ortho Evra, which has been available since 2001.

Ortho Evra quickly gained market share, particularly in the United States. According to Kalorama marketing analysts, sales exceeded \$400 million in 2004 and accounted for 15% of the hormonal market.

Another choice in the hormonal contraceptive market is Organon's NuvaRing. Market analysis by Kalorama had 2004 worldwide sales at \$107 million. The product has experienced stronger growth in Europe than the United States, according to industry analysts.

NuvaRing is a once-a-month contraceptive device that is left in place for three weeks. It delivers 15 micrograms of estrogen and 120 micrograms of etonogestrel per day over three consecutive weeks. After three weeks,

## CONTRACEPTION Through the Ages



the user removes and discards the ring. During the following ring-free week, menstrual bleeding will occur. After the ring-free week the women will insert a new ring for the next cycle.

“The NuvaRing is a unique device that is 99% effective, when used as directed,” Mr. Hart says. “It provides women with a once-a-month option.”

Despite many advances in the marketplace, one challenge that sets contraception products apart from other types of medications is that they are extremely personal, and there is a high degree of sensitivity surrounding them, says Marjorie C. Miller, assistant VP and global business manager, contraception, for women’s healthcare at Wyeth Pharmaceuticals.

“At Wyeth Women’s Health Institute, researchers work closely with internal teams, the medical community, and patients to ensure that they investigate areas of need, such as the issue of unplanned pregnancies, endometriosis, and polycystic ovarian syndrome,” she says.

The hurdles that must be overcome in marketing a contraceptive involve more than demonstrating safety and efficacy, Mr. Hart says.

“The benchmark is 99% efficacy,” he says. “Contraception is a competitive therapeutic area. Organon continues to research innovative contraception options to provide women with convenient birth control they don’t have to think about every day.”

Minimizing side effects is another benefit that companies have been focusing on in the last decade or so. Research has been on reduc-

ing the amount of estrogen to the lowest effective dose while balancing it with an adequate progestational agent that minimizes side effects.

“The trends in contraception are now centered on extended-cycles, lower-dose pills, and increased consumer awareness,” says David M. Plourd, M.D., assistant professor of ob/gyn at the Naval Medical Center San Diego.

Dr. Plourd’s insights are supported by the fact that several companies are launching new and improved products.

For example, Barr Laboratories has launched Seasonale and is waiting for approval from the FDA for Seasonique. Seasonale is an extended-cycle oral contraceptive that has been available since 2003. It is a combined hormone pill that is taken for 84 consecutive days followed by seven days of placebo.

The company received an approvable letter from the FDA in August 2005 for Seasonique, which has the same dosing and 84-day regimen, but the seven placebos are replaced with pills containing unopposed estrogen.

A new drug application also is pending for Seasonale Lo, which contains lower doses of levonorgestrel and ethinyl estradiol.

Wyeth has filed global registrations (United States, Canada, and Europe) for a low-dose combination of levonorgestrel/ethinyl estradiol to be taken 365 days a year. It also is being developed for the treatment of premenstrual dysphoric disorder.

Dr. Plourd believes that some areas of research that may bring forth useful products in the near future are those that combine contraceptives with bactericides that protect

against sexually transmitted diseases, as well as male contraceptives.

There are a few topical bactericides or microbicides that look promising based on market analysis by Kalorama. Two such products are Pro 2000 and Ushercell.

Indevus Pharmaceuticals Inc. is conducting Phase III trials with its microbicide, Pro 2000. Some attributes of this product are its activity against chlamydia, herpes, gonorrhea, and HIV. It also is compatible with latex condoms, has potential contraceptive activity, and is nonabsorbable.

Ushercell is a cellulose sulfate vaginal gel that is being developed by Polydex Pharmaceuticals Ltd. and the Program for Topical Prevention of Conception and Disease (TOP-CAD). This product is also in Phase III trials for use as a contraceptive and for the prevention of HIV and other sexually transmitted diseases.

Male hormonal contraception research has existed for some time, yet methods to date have produced side effects. Some promising areas of study are a long-acting testosterone and a small, reversible plug implanted into the vas deferens tube that blocks the flow of sperm yet is easily removed and completely reversible.

One area that Ms. Miller at Wyeth believes has future potential is menstrual management. Many products, which approach this area in different ways, will provide women with new options to address their periods. Wyeth had its NDA for Lybrel accepted for review by the FDA last summer. It is a low-dose combination contraceptive that is taken once a day, 365 days a year.

Real Doctors • Real Patients •

# Real Life



In the real world, there is so much you can learn.

## *Dimensional HealthCare— the Late-phase Specialists*

**Dimensional HealthCare, Inc (DHC)** offers unmatched expertise in conducting late-phase clinical trials (IIIb and IV) that yield a *real-world view* of therapeutic clinical strategies. We enable our clients to better realize scientific objectives and clinically relevant findings through trial design and execution, while meeting marketing objectives for the dissemination of real-world trial results utilizing proven channels and methods.

The team at **DHC** will work with your clinical and medical affairs team to create solutions to your research challenges:

- Phase IIIb/IV Study Design & Implementation
- Community-based Trials
- Specialized Investigator Training
- Patient Identification and Recruitment
- Clinical Experience Programs



**Real World Results™**  
dhcare.com

Adam Serody  
VP, Clinical Solutions  
aserody@dhcare.com

Lauren Gaffney  
Senior VP, Trial Launch Services  
lgaffney@dhcare.com

Robert Pallay, MD  
President, Clinical Trial Services  
rpallay@dhcare.com

Call or e-mail us to find out more about how we can generate *Real World Results™* for you: 1-877-DHC-FIRST



Dr. David Plourd Naval Medical Center San Diego

THERE IS A TREND TOWARD EXTENDED-CYCLE CONTRACEPTION. **There is also increased awareness and more implementation of emergency contraception requests.**

“Now women choosing a combined OC will have the option of not having their period,” Ms. Miller says.

**THE Market**

According to Dr. Plourd, there are other niches that need to be addressed since half of the women with unplanned pregnancies were using some form of contraception.

In a 2004 report, the Alan Guttmacher Institute stated that providing contraceptives to 500 million women in the developing world prevented 187 million unintended pregnancies. Despite the widespread availability of contraceptives in the United States, it’s projected that at least half of all pregnancies are unintended, according to the Institute.

Kalorama reports that about 60 million women in the United States are in their child-bearing years (15 to 44); and 64% of these women use a method of contraception. The report found that 31% do not use contraception because of infertility, currently pregnant, postpartum or desiring pregnancy, have never had intercourse, or are not sexually active.

**KEY EVENTS IN THE Development of Oral Contraceptives**

- 1950 Katherine McCormick and Margaret Sanger collaborate to promote development of a physiological contraceptive for women; Ms. McCormick agrees to fund the work of Gregory Pincus
- 1951 Carl Djerassi applies for a patent for norethindrone
- 1953 Frank Colton applies for a patent for norethynodrel
- 1954 Gregory Pincus and John Rock first administer synthetic progestins to women
- 1956 Celso-Ramon Garcia and Edris Rice-Wray conduct first large clinical trials in Puerto Rico
- 1957 Trials are expanded to sites in Haiti, Mexico, and the United States; FDA approves norethindrone and norethynodrel for treatment of gynecologic disorders
- 1959 Searle applies for FDA indication for contraception
- 1960 FDA grants contraception indication; Enovid becomes the first approved oral contraceptive

Source: The Contraceptive Report, 2000. Sponsored by the Dannemiller Memorial Educational Foundation through a grant from Wyeth.



Don Atkinson Berlex Inc.

**DURING THE NEXT FIVE TO 10 YEARS, we will look to provide women with more individualized contraceptive options.**

ket share; Ortho-McNeil had a 22% market share; Organon had 12% of the market; and Wyeth had 10%.

According to Don Atkinson, general manager and VP of female healthcare for Berlex, one of the reasons the company has a strong presence is that it manufactures and markets innovative contraceptive products designed to meet women’s individual needs.

Berlex’s top-selling contraceptive is Yasmin. According to Kalorama, in 2004, Yasmin eclipsed former top-seller, Ortho-McNeil’s Ortho Tri-Cyclen, which lost its patent protection in 2003.

Yasmin, approved for U.S. marketing in May 2001, contains 30 micrograms of ethinyl estradiol and 3 milligrams of a new progestin, drospirenone. Drospirenone is a progesterone that is similar to the progesterone naturally created by a woman’s body, and it counteracts the water retention, weight gain, and breast tenderness issues caused by the estrogen contained in the medication. It also blocks androgen receptors in the skin and therefore is marketed as improving acne.

Schering AG received U.S. regulatory approval in March 2006 for its new low-dose, monophasic oral contraceptive Yaz (3 mg drospirenone/20 mcg ethinyl estradiol). Yaz is the first pill with the innovative progestin drospirenone and a low dose of ethinyl estradiol in a new dosing regimen of 24 days of active hormone pills and four days of placebo. Oral contraceptives typically have a regimen of 21 days of active pills and seven days of placebo.

Berlex, a U.S. subsidiary of Schering, will launch the product in the United States in April 2006.

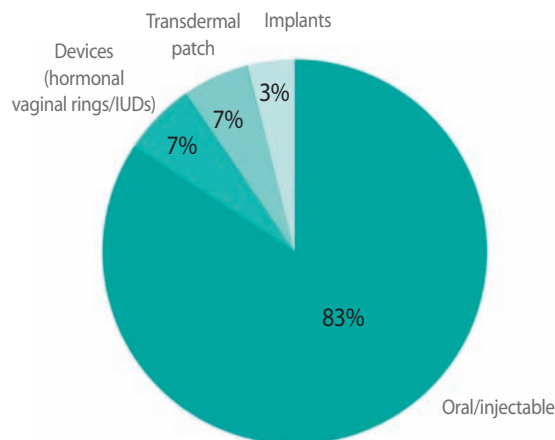


**This breakthrough medical product will make it to market in record time.** It was tested in 30 countries with thousands of subjects with no paper case report forms. Investigators and coordinators entered data quickly using a secure, simple user interface and robust edit checks were performed instantaneously. Monitors and data managers leveraged real-time access to listings, metrics and aggregate reports, and ultimately cleaner study data led to faster and better decision-making at a lower cost. **Hope it's not your competitor's...**



## HORMONAL CONTRACEPTION PRODUCTS

### 2004 World Market Share by Type



Source: Kalorama Information, New York. For more information, visit [kaloramainformation.com](http://kaloramainformation.com).

## THE WORLD MARKET FOR Hormonal Contraceptives 2000-2005

YEAR	REVENUE (\$ IN MILLIONS)	% GROWTH
2000	\$4,238	—
2001	4,575	8%
2002	4,940	8%
2003	5,337	8%
2004	5,754	8%
2005	6,231	8.1%

Source: Kalorama Information, New York. For more information, visit [kaloramainformation.com](http://kaloramainformation.com).

## WORLD HORMONAL CONTRACEPTIVE 2004 Market Share by Company

COMPANY	MARKET SHARE	REVENUE (\$ IN MILLIONS)
Berlex	34%	\$1,974
Ortho-McNeil	22%	1,258
Organon	12%	682
Wyeth	10%	592
Barr Labs	7%	404
Watson	6%	336
Pfizer	5%	280
Others*	4%	230
<b>TOTAL</b>	<b>100%</b>	<b>\$5,764</b>

\* Others include: Andrx, FEI Women's Health, King Pharmaceuticals, Proasco Laboratories, Warner Chilcott, and Teva.

Source: Kalorama Information, New York. For more information, visit [kaloramainformation.com](http://kaloramainformation.com).

According to Schering, the Yaz approval is an important milestone for the company and significantly adds to the blockbuster potential of its Yasmin product family.

"We have also conducted research on its effectiveness on the symptoms of premenstrual dysphoric disorder, a severe form of PMS," Mr. Atkinson says.

In late January 2006, the company received an approvable letter from the FDA for the pre-

menstrual dysphoric disorder (PMDD) indication. Berlex continues to work with the FDA to seek approval for this indication.

While IUDs have decreased in popularity in the United States during the last 30 years because of reports of serious adverse effects from older devices, provider and patient misconceptions, and provider fear of litigation, newer, safer devices may have increased the popularity of this contraceptive again. The top-selling IUD in 2004 was Berlex's Mirena, which delivers 20 micrograms of levonorgestrel each day and is approved for use for five years. According to Kalorama, sales of Mirena have increased about 20% annually since 2002.

"Mirena not only provides women with a long-term contraceptive option, but it may also result in lighter periods," Mr. Atkinson says.

Injectable contraceptives have been available for about 30 years. One such version is Pfizer's Depo-Provera, a progestin-only product that is injected once every three months. One drawback of the progestin-only product is that there are data showing that long-term use of this product may result in loss of bone density that is not completely reversible. This issue, as well as the fact that it is now available as a generic from Teva, will significantly impact Pfizer's market share.

Berlex markets a two-month injectable progestin, Noristerat, but it is not available in the United States. Since 2000, a combined hormonal injection, Lunelle, has been available from Pfizer. This too is a once-a-month injection, but the bone-density issue is eliminated because the product is counter-balanced with an estrogen component.

No area of the contraceptive market has generated as much press of late as the issue of emergency contraception (EC). Both daily birth control pills and IUDs can be used as emergency contraceptives after unprotected sex or a contraceptive failure; but contraceptive pills are by far the most commonly used method of emergency contraception. Emergency contraceptive pills are specific concentrated doses of ordinary oral contraceptives. If taken within 72 hours of contraceptive failure or unprotected sex, EC can reduce the risk of pregnancy by up to 89%. If taken within the first 24 hours, EC can reduce the risk of pregnancy up to 95%.

Analysis conducted by the Alan Guttmacher Institute estimates that 51,000 abortions were prevented by EC use in 2000, and that increased use of EC accounted for up to 43% of the total decline in abortion rates between 1994 and 2000.

Often EC is confused with mifepristone, the generic name for a drug formerly known as RU-486, which is an early option for non-surgical abortion.

Mifepristone was approved for use in the United States in 2000 and is trademarked for sale as Mifeprex by Danco Laboratories LLC.

But unlike mifepristone, which is approved in the United States for pregnancy termination, emergency contraceptive pills work like regular birth control pills to prevent pregnancy before a pregnancy is established. ♦

PharmaVOICE welcomes comments about this article. E-mail us at [feedback@pharmavoiced.com](mailto:feedback@pharmavoiced.com).

## Experts on this topic

**DON ATKINSON**, General Manager and VP of Female Healthcare, Berlex Inc., Wayne, N.J.; Berlex is a specialty pharmaceutical company and the U.S. affiliate of Schering AG Germany. For more information, visit [berlex.com](http://berlex.com).

**NICHOLAS J. HART**, Senior Director, Contraceptives, Organon USA, Roseland, N.J.; Organon, the human healthcare business of Akzo Nobel, creates, manufactures, and markets prescription medicines that improve the health and quality of human life. For more information, visit [organon-usa.com](http://organon-usa.com).

**MARJORIE C. MILLER**, Assistant VP and Global Business Manager, Contraception, Women's Healthcare, Wyeth Pharmaceuticals, Madison, N.J.; Wyeth is one of the world's largest research-driven pharmaceutical and healthcare products companies. For more information, visit [wyeth.com](http://wyeth.com).

**DAVID M. PLOURD, M.D.**, Assistant Professor, Ob/Gyn, the Naval Medical Center San Diego, San Diego; NMCS D is the largest medical center in the armed forces comprised of more than 6,000 healthcare professionals. For more information, visit [www-nmcsd.med.navy.mil](http://www-nmcsd.med.navy.mil).