12/01/97	3056829	Trinordiol
12/01/97	3058001-4	Triphasil-28
6/18/01	3741376-8	Nordette-21
7/17/04	4412805-1	Nordette-21
2/2/06	4902505-3	Nordette-21
2/28/03	4065974-X	
11/30/99	3416111-3	Triphasil-28
6/30/00	3	
12/29/00	3640160-3	Triphasil-21
1/25/01	3656040-3	Mirena
3/26/01	3700957-8	Levlite
6/18/01	3741376-8	Nordette-21
8/21/01	3781552-1	Mirena
9/20/01	3796431-3	Alesse-28
8/09/02	3961641-9	Levlite-21
8/15/02	3964208-1	Triquilar
2/20/03	4061279-1	Mirena
3/05/03	4071425-1	Microgynon
11/03/03	4226802-2	Tridiol-28
12/02/03	4245542-7	Mirena
5/21/04	4363772-0	Nordette-21
6/17/04	4382494-3	Mirena
9/27/04	4462728-7	Levlen
2/28/05	4596309-1	
4/04/05	4628502-3	Trinordiol
6/03/05	4686111-4	Alesse-28
7/29/05	4734121-0	Seasonale
8/10/05	4743529-9	Levora-28
3/22/06	4954000-3	Mirena
4/10/06	4975478-5	Mirena
7/20/06	5060812-0	Seasonale
8/17/06	5086087-4	Trinodiol
8/30/06	5095100-X	Plan b
7/21/06	5058172-4	Trinovum
11/21/06	5161338-6	Mirena
4/25/07	5314285-0	Seasonale
5/29/07	5337347-0	Mirena
7/23/07	5399025-1	Seasonale
11/12/99	3396782-0	Nordette

Levonorgestrel

(FDA - more cases are being recorded)

10/5/2001	3810911-3	Uterine rupture	Mirena	22
1/7/2002	3849708-7	Uterine rupture	Mirena	26
1/7/2002	3849709-9	Uterine rupture	Mirena	
1/7/2002	3849711-7	Uterine rupture	Mirena	
4/2/2002	3896625-2	Uterine rupture	Mirena	22
4/2/2002	3896630-6	Uterine rupture	Mirena	27
4/2/2002	3896633-1	Uterine rupture	Mirena	37
4/2/2002	3896635-5	Uterine rupture	Mirena	34
7/5/2002	3988713-7	Uterine rupture	Mirena	
10/7/2002	4011784-9	Uterine rupture	Mirena	32
10/7/2002	4011785-0	Uterine rupture	Mirena	35
10/7/2002	4011786-2	Uterine rupture	Mirena	40
10/7/2002	4011789-8	Uterine rupture	Mirena	
10/7/2002	4011790-4	Uterine rupture	Mirena	
10/7/2002	4011792-8	Uterine rupture	Mirena	
10/7/2002	4011845-4	Uterine rupture	Mirena	
10/7/2002	4011846-6	Uterine rupture	Mirena	24
10/7/2002	4114540-6	Uterine rupture	Mirena	
10/7/2002	4011850-8	Uterine rupture	Mirena	
10/7/2002	4011851-X	Uterine rupture	Mirena	
10/7/2002	4011853-3	Uterine rupture	Mirena	
10/7/2002	4011855-7	Uterine rupture	Mirena	
5/20/2003	4114540-6	Uterine rupture	Mirena	25
5/28/2003	4119350-1	Uterine rupture	Mirena	
11/29/1997	3002759-7	Blindness	Trigoa	25
11/26/1997	3002759-7	Renal Artery-Blindness	Trigoa	
2/4/1998	3040177-6	Cerebrovascular-Blind	Nordette-28	29
2/25/1998	3036909-3	Cerebrovascular-Blind	Nordette-28	28
4/21/1998	3065844-X	Blindness	Norplant	18
8/17/2001	378037-2	Blindness	Alesse-28	21
9/9/2002	3974077-1	Blindness	Mirena	40
7/1/2003	4140637-0	Blindness	Microgyno	48
11/3/2003	4226800-9	Blindness	Mirena	22
1/23/2004	4303313-7	Blindness	Mirena	46
3/5/2004	4318867-4	Blindness	Alesse-28	51
4/20/2004	4345337-X	Blindness	Alesse-28	
11/12/2004	4503181-4	Blindness	Nordette-28	17
12/2/2004	4519404-1	Blindness	Levonova	32
12/30/2004	4544258-7	Blindness	Microval	42
2/23/2005	4594822-4	Blindness	Mirena	42
3/21/2005	4616743-0	Blindness	Mirena	
4/7/2005	4631509-3	Blindness		42
6/14/2005	4692274-7	Blindness	Microval	42
5/16/2005	4664826-1	Blindness	Mirena	
6/28/2005	4704285-3	Blindness	Mirena	27
7/8/2005	4711193-0	Blindness	Mirena	27
8/24/2005	47534662-4	Blindness	Trinordiol	37
8/29/2005	4757247-4	Blindness	Trinordiol	37
10/20/2005	4807821-1	Blindness	Trinordiol	35
10/20/2005	4808026-0	Blindness		35
2/3/2006	4905825-1	Blindness	Mirena	

Levonorgestrel

2/28/2006	4930117-4	Blindness	Mirena	40
3/8/2006	4941330-4	Blindness	Mirena	38
3/16/2000	4950874-0	Blindness	Mirena	42
3/29/2006	4961617-9	Renal Artery-Blindness		
4/12/2006	4977413-2	Blindness	Mini-ovral-21	25
4/25/2006	4988256-8	Blindness	Mini-ovral-21	25
6/28/2006	5043057-X	Blindness	Mirena	
10/30/2006	5143233-1	Disability-Blind	Neogentrol	22
11/21/2006	5162086-9	Blindness	Neogentrol	22
7/27/2007	5399461-3	Blindness	Mirena	23

10/5/2001	3810911-3	Uterine rupture	Mirena	22
1/7/2002	3849708-7	Uterine rupture	Mirena	26
1/7/2002	3849709-9	Uterine rupture	Mirena	
1/7/2002	3849711-7	Uterine rupture	Mirena	
4/2/2002	3896625-2	Uterine rupture	Mirena	22
4/2/2002	3896630-6	Uterine rupture	Mirena	27
4/2/2002	3896633-1	Uterine rupture	Mirena	37
4/2/2002	3896635-5	Uterine rupture	Mirena	34
7/5/2002	3988713-7	Uterine rupture	Mirena	
10/7/2002	4011784-9	Uterine rupture	Mirena	32
10/7/2002	4011785-0	Uterine rupture	Mirena	35
10/7/2002	4011786-2	Uterine rupture	Mirena	40
10/7/2002	4011789-8	Uterine rupture	Mirena	
10/7/2002	4011790-4	Uterine rupture	Mirena	
10/7/2002	4011792-8	Uterine rupture	Mirena	
10/7/2002	4011845-4	Uterine rupture	Mirena	
10/7/2002	4011846-6	Uterine rupture	Mirena	24
10/7/2002	4114540-6	Uterine rupture	Mirena	
10/7/2002	4011850-8	Uterine rupture	Mirena	
10/7/2002	4011851-X	Uterine rupture	Mirena	
10/7/2002	4011853-3	Uterine rupture	Mirena	
10/7/2002	4011855-7	Uterine rupture	Mirena	
5/20/2003	4114540-6	Uterine rupture	Mirena	25
5/28/2003	4119350-1	Uterine rupture	Mirena	
11/29/1997	3002759-7	Blindness	Trigoa	25
11/26/1997	3002759-7	Renal Artery-Blindness	Trigoa	
2/4/1998	3040177-6	Cerebrovascular-Blind	Nordette-28	29
2/25/1998	3036909-3	Cerebrovascular-Blind	Nordette-28	28
4/21/1998	3065844-X	Blindness	Norplant	18
8/17/2001	378037-2	Blindness	Alesse-28	21
9/9/2002	3974077-1	Blindness	Mirena	40
7/1/2003	4140637-0	Blindness	Microgyno	48
11/3/2003	4226800-9	Blindness	Mirena	22
1/23/2004	4303313-7	Blindness	Mirena	46
3/5/2004	4318867-4	Blindness	Alesse-28	51
4/20/2004	4345337-X	Blindness	Alesse-28	
11/12/2004	4503181-4	Blindness	Nordette-28	17
12/2/2004	4519404-1	Blindness	Levonova	32
12/30/2004	4544258-7	Blindness	Microval	42
2/23/2005	4594822-4	Blindness	Mirena	42
3/21/2005	4616743-0	Blindness	Mirena	
4/7/2005	4631509-3	Blindness		42
6/14/2005	4692274-7	Blindness	Microval	42
5/16/2005	4664826-1	Blindness	Mirena	
6/28/2005	4704285-3	Blindness	Mirena	27
7/8/2005	4711193-0	Blindness	Mirena	27
8/24/2005	47534662-4	Blindness	Trinordiol	37
8/29/2005	4757247-4	Blindness	Trinordiol	37
10/20/2005	4807821-1	Blindness	Trinordiol	35
10/20/2005	4808026-0	Blindness		35
2/3/2006	4905825-1	Blindness	Mirena	

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2/28/2006	4930117-4	Blindness	Mirena	40
3/8/2006	4941330-4	Blindness	Mirena	38
3/16/2000	4950874-0	Blindness	Mirena	42
3/29/2006	4961617-9	Renal Artery-Blindness		
4/12/2006	4977413-2	Blindness	Mini-ovral-21	25
4/25/2006	4988256-8	Blindness	Mini-ovral-21	25
6/28/2006	5043057-X	Blindness	Mirena	
10/30/2006	5143233-1	Disability-Blind	Neogentrol	22
11/21/2006	5162086-9	Blindness	Neogentrol	22
7/27/2007	5399461-3	Blindness	Mirena	23

12/1/1997	3058004-X	Triphasil-28	Pulmonary Embolism	
12/17/1997	3011767-1	Tri Levlen	Pulmonary Embolism	21
1/27/1998	3092371-6	Alesse	Pulmonary Embolism	38
2/6/1998	3110645-7	Norplant	Ectopic	18
2/6/1998	3110645-7	Norplant	Ectopic	26
2/6/1998	3119326-7	Norplant	Ectopic	19
2/6/1998	3119794-0	Norplant	Ectopic	30
2/6/1998	3120219-X	Norplant	Ectopic	34
2/6/1998	3120230-9	Norplant	Ectopic	33
2/6/1998	3122909-1	Norplant	Ectopic	26
2/6/1998	3122913-3	Norplant	Ectopic	21
2/6/1998	3122916-9	Norplant	Ectopic	27
2/6/1998	3122921-2	Norplant	Ectopic	37
2/6/1998	3122920-0	Norplant	Ectopic	27
2/6/1998	3122923-6	Norplant	Ectopic	
2/6/1998	3123983-9	Norplant	Ectopic	34
2/24/1998	3120340-6	Norplant	Ectopic	26
3/6/1998	3043939-4	Norplant	Ectopic	35
6/19/1998	3096813-1	Norplant	Ectopic	
7/3/1998	3112441-3	Norplant	Ectopic	
7/8/1998	3103241-9	Norplant	Ectopic	19
8/12/1998	3116969-1	Norplant	Ectopic	37
8/21/1998	3120149-3	Norplant	Ectopic	37
10/15/1998	3143524-X	Norplant	Ectopic	29
4/23/1999	3245978-7	Norplant	Ectopic	26
4/29/1999	3250006-3	Norplant	Ectopic	19
5/13/1999	3261246-1	Norplant	Ectopic	23
6/8/1999	3278037-8		Ectopic	
6/14/1999	3282670-7	Norplant	Ectopic	19
6/23/1999	3289826-8			23
6/30/1999	3295104-3	Norplant	Ectopic	39
3/19/2003	4078643-7	Mirena	Ectopic	
3/19/2003	4079085-0	Levonell-2	Ectopic	22
3/26/2003	4084226-5		Ectopic	35
4/7/2003	4102614-5	Mirena	Ectopic	22
4/7/2003	4102617-0		Ectopic	23
4/7/2003	4102621-2	Mirena	Ectopic	
4/7/2003	4102637-6	Mirena	Ectopic	
4/18/2003	4098438-8	Levonell-2	Ectopic	39
4/21/2003	4099584-5		Ectopic	35
5/23/2003	4116850-5	Postinor-2	Ectopic	34
5/23/2003	4116880-3	Postinor-2	Ectopic	19
5/23/2003	4116881-5	Postinor-2	Ectopic	34
5/23/2003	4116892-X	Postinor-2	Ectopic	20
5/23/2003	4116893-1	Levonell-2	Ectopic	18
5/29/2003	4120381-6	Levonell-2	Ectopic	15
5/29/2003	4120452-4	Levonell-2	Ectopic	15
7/8/2003	4145069-7	Mirena	Ectopic	31
7/16/2003	4150560-9	Levonell-2	Ectopic	35
8/19/2003	4174717-0	Mirena	Ectopic	38
8/28/2003	4181339-4	similar Plan b	Ectopic	

Levonorgestrel

8/13/2007 5412700-5	Mirena	Ectopic	37
8/14/2007 5414340-0	Mirena	Ectopic	
8/14/2007 5414344-8	Mirena	Ectopic	35
2/2/2002 3873965-4	Mirena	Ectopic	
2/28/2002 3877342-1	Levonell-2	Ectopic	20
4/2/2002 3896625-2	Mirena	Ectopic	
4/2/2002 3896628-8	Mirena	Ectopic	30
4/2/2002 3896630-6	Mirena	Ectopic	27
4/2/2002 3896633-1	Mirena	Ectopic	27
4/2/2002 3896635-5	Mirena	Ectopic	34
4/4/2002 3896143-1	Postinor-2	Ectopic	34
5/2/2002 3911763-3	Mirena	Ectopic	34
8/20/2002 3965210-6	Mirena	Ectopic	32
8/21/2002 3966451-4	Mirena	Ectopic	32
10/7/2002 4011787-4	Mirena	Ectopic	
12/24/2002 4035344-9	Mirena	Ectopic	23
12/24/2002 4035347-4	Mirena	Ectopic	33
5/31/2001 3731599-6	Levonell-2	Ectopic	19
11/27/2001 3831699-6	Levonell-2	Ectopic	19
11/27/2001 3831700-X	Levonell-2	Ectopic	19
11/30/2001 3833289-8	Levonell-2	Ectopic	20
2/28/2001 3877342-1	Levonell-2	Ectopic	20
9/11/2001 3974444-6	Levonell-2	Ectopic	29
9/11/2002 3974465-3	Levonell-2	Ectopic	38
3/7/2003 4072621-X	Levonell-2	Ectopic	28
3/7/2003 4072625-7	Levonell-2	Ectopic	26
3/19/2003 4079085-0	Levonell-2	Ectopic	32
4/8/2003 4098438-8	Levonell-2	Ectopic	39
5/23/2003 4116893-1	Levonell-2	Ectopic-cystectomy	18
5/29/2003 4120452-4	Levonell-2	Ectopic	15
7/6/2003 4150460-9	Levonell-2	Ectopic	35
2/12/2004 4295472-X	Levonell-2	Ectopic	22
11/27/2001 3831699-6	Postinor-2	Ectopic	19
11/29/2001 3844159-3	Postinor-2	Ectopic	34
4/4/2002 3896143-1	Postinor-2	Ectopic	26
9/11/2002 3974488-4	Postinor-2	Ectopic	26
10/9/2002 3991046-6	Postinor-2	Ectopic	26
5/23/2003 4116850-5	Postinor-2	Ectopic	34
5/23/2003 4116881-5	Postinor-2	Ectopic	34
5/23/2003 4116892-X	Postinor-2	Ectopic	20
4/20/2004 4345050-9	Plan b	Ectopic	35
3/2/2001 3688557-X	Plan b	Ectopic	35
4/20/2004 4345056-X	Plan b	Ectopic	26
4/13/2005 4635478-1	Nordette-21	Ectopic	34
7/13/2000 3538271-6	Plan b	Ectopic	
8/4/2000 3542945-0	Plan b	Ectopic	27
1/2/2001 3640939-8	Plan b	Ectopic	34
8/28/2003 4182227-X	similar Plan b	Ectopic	
9/29/2003 4201989-6	similar Plan b	Ectopic	26
4/9/2001 3701868-4	Plan b	Ectopic	
5/31/2001 3731596-0	Plan b	Ectopic	
8/8/2003 4181339-4	similar Plan b	Ectopic	
9/2/2005 4764187-3	Plan b	Ectopic	28
5/10/2006 4999818-6	Plan b	Ectopic	27

NORTH CAROLINA DEPARTMENT OF HEALTH AND HUMAN SERVICES
N. C. VITAL RECORDS

CERTIFICATE OF DEATH

Registration District No. 06045 Local No. 200600 3714

DECEDENT

DECEDENT'S NAME (First, Middle, Last)			SEX	DATE OF DEATH (Month, Day, Year)
1. NIKITA	D	SMOUTHERSON	2. F	3. August 10, 2006

SOCIAL SECURITY NUMBER	AGE—Last Birthday (Years)	UNDER 1 YEAR: Months / Days	UNDER 1 DAY: Hours / Minutes	DATE OF BIRTH (Month, Day, Year)	BIRTHPLACE (City and State or Foreign Country)
4. 581-94-5037	5. 30	5b.	5c.	6. May 24, 1976	7. Washinton DC

WAS DECEDENT EVER IN U.S. ARMED FORCES? (Yes or No)	8a. PLACE OF DEATH (Check only one)
8. No	HOSPITAL: ☐ Inpatient ☒ ER/Outpatient ☐ DOA OTHER: ☐ Nursing Home ☐ Residence ☐ Other (Specify)

FACILITY NAME (If not institution, give street and number)	CITY, TOWN, OR LOCATION OF DEATH	INSIDE CITY LIMITS? (Yes or No)	COUNTY OF DEATH
9b. CMC -UNIVERSITY	9c. Charlotte	9d. Yes	9e. Mecklenburg Co.

MARITAL STATUS—Married, Never Married, Widowed, Divorced (Specify)	SURVIVING SPOUSE (If wife, give maiden name)	DECEDENT'S USUAL OCCUPATION (Give kind of work done during most of working life. Do not use retired.)	KIND OF BUSINESS/INDUSTRY
10. Divorced	11.	12a. Park Entertainer	12b. Amusement Park

RESIDENCE—STATE	COUNTY	CITY, TOWN, OR LOCATION	STREET AND NUMBER
13a. NC	13b. Mecklenburg	13c. Charlotte	13d. 6630 Pinta Court

INSIDE CITY LIMITS? (Yes or No)	ZIP CODE	Was Decedent of Hispanic Origin? (Specify Yes or No. If yes, specify Cuban, Mexican, Puerto Rican, etc.)	RACE—American Indian, Black, White, Etc. (Specify)	DECEDENT'S EDUCATION (Specify only highest grade completed) Elementary/Secondary (0-12) College (13-17+)
13e. Yes	13f. 28227	14. ☐ Yes ☒ No (Specify)	15. Blk	16. 17+

PARENTS

FATHER'S NAME (First, Middle, Last)	MOTHER'S NAME (First, Middle, Maiden Surname)
17. Klevin Stouffer	18. Sheila Moody

INFORMANT

INFORMANT'S NAME (Type/Print)	MAILING ADDRESS (Street or Rural Route Number, City or Town, State, Zip Code)	DATE AMENDED
19a. Sheila Moody	19b. 753 Chris Dr, Mooresville, NC 28082	19c.

CAUSE OF DEATH

Part I. Enter the diseases, injuries, or complications that caused the death. Do not enter the mode of dying, such as cardiac or respiratory arrest, shock or heart failure. If appropriate, enter tobacco, alcohol, or drug use. List only one cause on each line. (PRINT or TYPE)

		Approximate Interval Between Onset and Death
IMMEDIATE CAUSE (Final disease or condition resulting in death)	a. Pulmonary Emboli — DUE TO (OR AS A CONSEQUENCE OF):	
Sequentially list conditions if any, leading to immediate cause. Enter UNDERLYING CAUSE (Disease or injury that initiated events resulting in death) LAST.	b. Oral Contraceptive Use — DUE TO (OR AS A CONSEQUENCE OF):	
20a.	c. — DUE TO (OR AS A CONSEQUENCE OF):	
	d.	

Part II. Other significant conditions contributing to death but not resulting in the underlying cause given in Part I, such as tobacco, alcohol, or drug use; diabetes, etc.

20b.

AUTOPSY? (Yes or No)	If yes, were findings considered in determining cause of death?	Was case referred to Medical Examiner? (Yes or No)	TIME OF DEATH
21a.	21b.	21c.	22. M.

NOTICE: STATE LAW REQUIRES THAT ALL DEATHS DUE TO TRAUMA, ACCIDENT, HOMICIDE, SUICIDE, OR UNDER SUSPICIOUS, UNUSUAL OR UNNATURAL CIRCUMSTANCES BE REPORTED TO, AND CERTIFIED BY A MEDICAL EXAMINER-ON A MEDICAL EXAMINER'S CERTIFICATE OF DEATH. ANY DEATH FALLING INTO THESE CATEGORIES IS WITHIN THE MEDICAL EXAMINER'S JURISDICTION REGARDLESS OF THE LENGTH OF SURVIVAL FOLLOWING THE UNDERLYING INJURY.

CERTIFIER

SIGNATURE AND TITLE OF CERTIFIER	DATE SIGNED (Month, Day, Year)
23a.	23b. 08/28/2006

NAME AND ADDRESS OF PERSON WHO COMPLETED CAUSE OF DEATH (ITEM 20) (Type or Print)

24. C Dutton r.D. P.O. Box 560727 Charlotte, NC 28256

DISPOSITION

METHOD OF DISPOSITION	PLACE OF DISPOSITION (Name of cemetery, crematory, or other place)	LOCATION — City or Town, State, Zip Code
X ☐ Burial ☐ Cremation ☐ Removal 25a. ☐ Donation ☐ Other	25b. Rutherford Park Cemetery	25c. Concord, NC

NAME AND ADDRESS OF FUNERAL HOME	NAME OF FUNERAL DIRECTOR	LICENSE NUMBER
26a. Bryant Lytle Young/Mooresville, NC	26b. W. H. Bryant	26c. 1890

REGISTRAR'S SIGNATURE	DATE FILED (Month, Day, Year)	NAME OF EMBALMER	LICENSE NUMBER
27. Earl Nunez Mabry MD VR	28. AUG 30 2006	29d. W. H. Bryant	29e. 1079

DHHS 1872 (Revised 3/03 Review 3/08) VITAL RECORDS

UNOFFICIAL

over

Contentions Rise over the "Morning after Pill"

KEENE – The Keene Planned Parenthood office was one of seven Northern New England Planned Parenthood facilities in New Hampshire that gave away free Plan B emergency contraception on Wednesday December 6. Three Free EC signs were displayed at the Planned Parenthood office at 8 Middle St. in Keene. Protesters against Planned Parenthood gathered outside the office to demonstrate their concerns regarding the safety the Plan B pill.

Wednesday evening, the Respect Life Committee sponsored a discussion about the dangers of birth control pills and emergency contraception at the Clairvaux Center in downtown Keene. The event was well attended and the audience included students from Keene State College. The discussion featured two guest speakers, Ebony Moody from Washington D.C., and Dr. Jonathan Abel, a board certified family medicine doctor from Massachusetts.

Ms. Moody spoke concerning the August 2006 death of her sister, Niki Moody, from a pulmonary embolism, which was directly attributed to the oral contraceptive Lo Ovral. Niki Moody was a college graduate and a young mother, who had only begun using the oral contraceptive three weeks prior to her death. A FDA Freedom of Information Report Selected for Ethinyl and Lo Ovral details 34,980 adverse cases reported to the FDA since 1997. This FDA report covers only oral contraceptives, such as Lo Ovral, which contain the hormone Ethinyl estradiol.

Following Ms. Moody's heartbreaking story, Dr. Abel gave a talk called, "What Happened to Plan A?" He gave an introduction to oral contraceptives and spoke about the health risks associated with oral contraceptives and the emergency contraception Plan B. Dr. Abel stressed that oral contraceptives are not necessary in family planning, since safe alternatives exist. In addition, Dr. Abel pointed out that emergency contraception can cause a chemical abortion, which many women taking Plan B may not know. Dr. Abel's informative presentation led into an animated question and answer period.

Jack Laurent, a former New Hampshire state representative, presented additional information regarding a parental abortion notification bill, which passed the N.H. state legislature and was signed into law by former Governor Craig Benson. The bill has been challenged by Planned Parenthood as unconstitutional and Mr. Laurent states that the bill will most likely be repealed. Mr. Laurent also discussed an emergency contraception bill, Senate Bill 30, which was passed into state law in June 2005. This law makes New Hampshire a "pharmaceutical collaborative" state (with eight other states) and allows a nurse or pharmacist to dispense emergency contraception with no age restrictions for minors. According to www.GO2EC.org, approximately 200 pharmacists in N.H. have received training to initiate prescriptions for emergency contraception. Emergency contraception is covered by Medicaid, HMOs, and Title X. Title X provides federal money to the state for funding school programs. This state law effectively means that even young children may get emergency contraception over the counter.

WYETH

RECEIVED AT DRUG SAFETY SURVEILLANCE
01-DEC-1997-2084

ME
ICAL PRO

ST. DAVIDS, PA. 19087

Page

Individual Safety Report
3056829-8-00

3/93
03N

FDA Use Only

A. Patient Information

1. Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
[redacted] In confidence	19 YR / Unknown	[X] female [ ] male	lbs / or / kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [X] death [redacted] (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [X] other: serious

3. Date of event (mo/day/yr): 04 / 10 / 97

4. Date of this report (mo/day/yr): 06 / 25 / 97

5. Describe event or problem

The patient, who took Trinordiol (equivalent to Triphasil), experienced diarrhea, vomiting and headache for two days prior to lapsing into a coma. An MRI revealed CEREBRAL THROMBOPHLEBITIS; the patient subsequently died. No autopsy.

8. Relevant tests/laboratory data, including dates

DATE	TEST	RESULT
Unknown	MRI	Cerebral thrombophlebitis

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

None provided

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 TRINORDIOL (0.05MG LNG/0.03MG E.E., 0.075 LNG/0.04MG E.E., 0.125MG LNG/0.03MG E.E.)
#2

2. Dose, frequency & route used
#1 1 TABLET ONCE DAILY ORAL
#2

3. Therapy dates (if unknown, give duration)
#1 1 YEAR
#2

4. Diagnosis for use (indication)
#1 Unknown
#2

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
See following page

G. All manufacturers

1. Contact office - name/address (& MFG site for devices)
WYETH-AYERST LABORATORIES
170 RADNOR CHESTER ROAD
ST. DAVIDS, PA. 19087

KAREL F. BERNADY, PH.D.

2. Phone number
(610) 902-3760

3. Report source (check all that apply)
- [X] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 06 / 24 / 97

5. (A)NDA # 19-192
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day
- [ ] 10-day
- [X] initial
- [ ] 15-day
- [X] periodic
- [ ] follow-up #

8. Adverse event term(s)
CEREBRAL THROMBOSIS
VOMITING
DIARRHEA
HEADACHE

9. Mfr. report number
8-97176-003N

E. Initial reporter

1. Name, address & phone #
[redacted]

[redacted]

FRANCE

4

2. Health professional? [X] yes [ ] no

3. Occupation
N/A

4. Initial reporter also sent report to FDA
[ ] yes [X] no [ ] unk

DATE SENT TO FDA: NOV 25 1997
19970380

Submission of a report does not constitute an admission that

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

SPASMINE 3 tablets daily ORAL (02 / 18 / 97 to 04 / 12 / 97)
ZOVIRAX 800 mg QID ORAL (04 / 00 / 96 to 04 / 00 / 97)

WYETH AYERST

MEDWATC

WYETH-AYERST LABORATORIES — THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

170 ST. RECEIVED AT DRUG SAFETY SURVEILLANCE

01-DEC-1997-5265

Individual Safety Report

3058001-4-00

FDA Use Only

A. Patient Information

1. Patient identifier	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
[redacted] In confidence	23 YR [redacted]	[X] female [ ] male	129 lbs or kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [X] death — Unknown (mo/day/yr)
- [ ] life-threatening
- [X] hospitalization - initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
04 / 14 / 97	04 / 28 / 97

5. Describe event or problem

The patient, with Down's Syndrome, presented to the ER unresponsive with CPR in progress. Her color was dusty-blue, petechia were present on face, skin cool and she had orange-red emesis coming from her mouth. Suctioning and intubation were attempted; intubation was unsuccessful and the patient subsequently died. The provisional autopsy report revealed an ACUTE PULMONARY EMBOLUS.

6. Relevant tests/laboratory data, including dates

(Cont.)

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

Down's Syndrome; hypothyroidism; used Depo-Provera in the past (q 3 months from [redacted] to [redacted]) with weight gain ~101 lb. [redacted] to 125 lb. [redacted]. No previous history of T. Upjohn has been notified of this adverse event.

DATE SENT TO FDA [illegible] 28

Submission of a report does not constitute an admission that

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 TRIPHASIL-28 TABLETS
#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1 1 TABLET ONCE DAILY ORAL	#1 08 / 08 / 96 to 04 / 14 / 97
#2	#2

4. Diagnosis for use (indication)
#1 REGULATE MENSES/DYSMENORRHEA
#2

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [X] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
See following page

G. All manufacturers

1. Contact office - name/address (& MFG site for devices)

WYETH-AYERST LABORATORIES
170 RADNOR CHESTER ROAD
ST. DAVIDS, PA. 19087

KAREL F. BERNADY, PH.D.

2. Phone number
(610). 902-3760

3. Report source (check all that apply)
- [ ] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr)
04 / 24 / 97

5. (A) NDA # 19-190
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day
- [ ] 10-day
- [X] initial
- [ ] 15-day
- [X] periodic
- [ ] follow-up #

8. Adverse event term(s)
PULMONARY EMBOLUS

9. Mfr. report number
8-97118-249N

DEC 01 1997

E. Initial reporter

1. Name, address & phone #
[redacted]

00006

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
[X] ... [ ] ...	Pharmacist	[ ] ... [X] ...

WYETH AYERST

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Approved by the FDA on 11/10/93

WYETH-AYERST LABORATORIES
170 ST.

RECEIVED AT DRUG SAFETY SURVEILLANCE
01-DEC-1997-5266

Mfr report # 8-97118-249N

UF/Dist report #

FDA Use Only

Box B.6 - Relevant Tests/Laboratory Data, including dates (Continuation)

DATE	TEST	RESULT
[redacted]	Provisional autopsy report	Coiled thrombus in main pulmonary artery occluding both right and left pulmonary arteries with partial organization of thrombus in secondary branch of left pulmonary artery; peripheral wedge infarct of lower left lung lobe

Box C.10 - Concomitant medical products and therapy dates (exclude treatment of event) (Continuation)

LEVOTHYROXINE 0.075 mg
IRON SUPPLEMENT

Individual Safety Report
3058001-4-00

DEC 0 1 1997

3741376-8-00-01

ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month /)	2a. AGE UNITS	3. SEX	4–6. EXPERIENCE (Day / Month / Year)
[redacted]	Denmark	[redacted] / [redacted] / [redacted]	33Yr	F	20 / APR / 2001

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM

Information was received on 14-JUN-2001 from the Health Authority via Schering AG Germany concerning a 33-year-old female patient who had taken therapy with Microgynon (0.15mg levonorgestrel/0.03mg ethinyl estradiol) (equivalent to Nordette) for an unspecified indication. Therapy began in 1997 and ended on 20-APR-2001. Medical history was not provided. The dose regimen was 1 tablet daily. It is unknown if the patient was taking concomitant therapy. The patient experienced pulmonary embolism (pulmonary embolism) on [redacted] and was hospitalized. Her treatment was unspecified. The patient died on [redacted].

8–12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

None Provided.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 MICROGYNON (0.15MG LEVONORGESTREL/0.03MG ETHINYL ESTRADIOL, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG? [ ] YES [X] NO [ ] N/A

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINSTRATION
#1 1 Tablet 1x per 1 Day	#1 Oral

17. INDICATION(S) FOR USE

#1

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)	19. THERAPY DURATION
#1 00-UNK-1997 / 20-Apr-2001	#1 3 Yr

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

UNK

RECEIVED
JUN 18 2001
CDR/CDSH

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

OTHER REFERENCE NUMBERS:

Regulatory Authority (HP) (via Schering AG) 01/01922-CDS

DSS
JUN 19 2001

Local Marketing No	24b. MFR CONTROL NO.
NDA 18-668	HQ2066414JUN2001.

24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
14-Jun-2001	[ ] STUDY [ ] CONSUMER [ ] LITERATURE [X] REGULATORY AUTHORITY [X] HEALTH PROFESSIONAL [ ] LICENSE

Date of this report	25a. REPORT TYPE
15-Jun-2001	[X] INITIAL [ ] FOLLOWUP

JUN 15 2001
DATE SENT TO FDA

Individual Safety Report

4412805-1-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

or use by user-facilities, utors and manufacturers for MANDATORY reporting
King Pharmaceuticals, Inc.

Relays International, Inc.
FDA Facsimile Approval: 30-JUN-1998

Mfr report # K200400695
UF/Dist report #
FDA Use Only

A. Patient Information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] In confidence	16 Years or Date of birth: [redacted]	☒ female ☐ male	154.3 lbs or 70.0 kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem(e.g., defects/malfunction)

2. Outcomes attributed to adverse event (check all that apply)

☒ death [redacted]
☐ life-threatening
☐ hospitalization - initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☐ other:

3. Date of event	4. Date of this report
03/31/2004	07/26/2004

5. Describe event or problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any seperated by commas)

Pulmonary infarction[Pulmonary infarction]
Pulmonary embolism[Pulmonary embolism]
Pulmonary edema[Pulmonary oedema NOS]
Small pericardial effusion[Pericardial effusion]

Case Description:
This report was received by King Pharmaceuticals, Inc. on 10MAY2004 via fax from Berlex Laboratories. A regulatory authority reported that a 16 year-old female patient received oral levonorgestrel/ethinyl estradiol 1 tablet daily started 13JAN2004 for oral contraception. There were no concomitant medications. Past medical history was significant for smoking three cigarettes/day, being overweight with a body mass index of 27.7, a rupture of the lateral collateral ligament of the left ankle on 06NOV2001, closed fracture of the right fifth metatarsal, tonsillitis diagnosed on 25NOV2003 and treated with penicillin, and a recurrence of tonsillitis symptoms on
continued in additional info section...

6. Relevant tests/laboratory data, including dates
#1 [redacted] Blood pressure 120/70 mmHg
#2 [redacted] Blood tests Normal
#3 [redacted] Respiratory rate 20
#4 [redacted] Pulse rate 76
#5 [redacted] Blood pressure 119/57 mmHg
#6 [redacted] Oxygen saturation measurement on air 100 %
continued in additional info section...

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 [redacted] to UNK Historical Condition, (continued)
#2 [redacted] to UNK Historical Condition, (continued)
#3 [redacted] to Ongoing Historical Condition, (continued)
#4 UNK, Current Condition, Smoker (3 per day)
#5 UNK, Current Condition, Overweight (continued)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1. NORDETTE -21(LEVONORGEST (continued)
#2.

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1. 1 tablet, qd, Oral	#1. 01/13/2004 to 03/31/2004
#2.	#2.

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1. Oral contraception	#1. ☐ yes ☒ no ☐ doesn't apply
#2.	#2. ☐ yes ☐ no ☐ doesn't apply

6. Lot# (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1. UNK	#1. UNK	#1. ☐ yes ☐ no ☒ doesn't apply
#2.	#2.	#2. ☐ yes ☐ no ☐ doesn't apply

9. NDC# - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
NI

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
King Pharmaceuticals, Inc.

501 Fifth Street
Bristol, TN 37620 UNITED STATES

2. Phone number 9196537005

3. Report source (check all that apply)
☒ foreign GBR
☐ study
☐ literature
☐ consumer
☒ health professional
☐ user facility
☐ company representative
☐ distributor
☒ other: Manufacturer

4. Date received by manufacturer 07/14/2004

5. (A)NDA # 18-668
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ periodic
☐ initial ☒ follow-up # 1

8. Adverse event term(s)
Pulmonary infarction, Pulmonary embolism, Chest pain, Dyspnoea, Cough, Granuloma NOS, Pulmonary oedema NOS,
continued in additional info section...

9. Mfr. report number
K200400695

E. Initial reporter

1. Name & address
phone # [redacted]
[redacted] UNITED STATES

2. Health professional ?	3. Occupation	4. Initial reporter also sent report to FDA
☒ yes ☐ no	Other Manufacturer	☐ yes ☐ no ☒ unk

FDA
3500A - Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

26-Jul-2004 13:14

JUL 27 2004

JUL 28 2004

Additional Information

B5. EVENT DESCRIPTION (cont.)

13JAN2004. The patient's mother reported that her daughter experienced right sided pain on 27MAR2004. She denied having fallen or knocked it. The patient took two unspecified pain killers and went to bed. The next day she reported feeling better but that it still hurt slightly. On [redacted], she returned from school due to pain. That evening the patient reported feeling better. The mother was unable to make an appointment with her general practitioner and took the patient to the emergency department on [redacted]. On the way to the emergency department, the mother reported that the patient experienced difficulty breathing and that it hurt to cough. The patient presented to the emergency department with a six day history of right-sided chest pain, which was dull with sharp exacerbations, and associated non-productive cough. She denied any history of trauma, expectorating blood, fever, or shortness of breath. An examination did not reveal any abnormalities. The right chest wall was mildly tender along the fourth, fifth, and sixth ribs with no associated swelling or skin changes noted. Her pulse was 76, blood pressure 119/57 mmHg, respiratory rate 20, and her oxygen saturation was 100% on room air. There was equal expansion of both lung fields and good air entry bilaterally. An electrocardiogram was performed and nothing abnormal was detected. The patient was diagnosed with a soft tissue injury to the rib. She was discharged on diclofenac and paracetamol and advised to follow-up with her general practitioner if the pain persisted. Levonorgestrel/ethinyl estradiol was discontinued. During the subsequent week, the patient continued to experience pain and difficulty breathing. On [redacted], the patient complained to her mother of feeling unwell and later that evening she vomited. On [redacted], she was observed sleeping at 9 am and 1:30 pm by her parents. At 5:30 pm, the mother was unable to awaken her daughter and observed that she was pale and did not appear to be breathing. The patient died on [redacted]. A post mortem examination revealed a large thrombotic pulmonary embolus mainly affecting the right pulmonary artery and the right pulmonary tree. There were also smaller amounts of thrombotic emboli present in the left lung. There was a wedge shaped pulmonary infarct in the right lower lobe overlying the area of hemorrhage on the right parietal pleura. There was also bilateral pulmonary edema and a small pericardial effusion. There was no evidence of pneumonia or lung tumors. Paracetamol was within the therapeutic range at 4 mg/l and does not support acute paracetamol overdose as a cause of death. There was no obvious evidence of liver toxicity that might have followed a previous overdose. No other drugs were detected in the blood. The pathologist commented that the pulmonary infarct in the right lung was not acute and probably occurred one to two weeks previously, secondary to a small embolus, and was likely to have been the cause of the chest pain. The large pulmonary embolus was very recent. The pathologist stated that the right calf was slightly larger at 40 cm diameter than the left calf at 38 cm diameter and may well have been the source of the pulmonary embolus. The cause of death was 1) thrombotic pulmonary embolus and 2) pulmonary infarct. The coroner concluded that the death was due to natural causes.

Follow-up information was received by King Pharmaceuticals, Inc. on 14JUL2004 via fax from Berlex Laboratories. Additional events, event details, past medical history, medical records, laboratory and diagnostic test results, and post mortem examination results were provided. The date and cause of death were updated.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
7	[redacted]	Electrocardiogram	Nothing abnormal detected	
8	[redacted]	Post mortem Summary of pathological findings were: 1. Large thrombotic pulmonary embolus 2. Peripheral pulmonary infarction right lung 3. Right pleural granulation tissue reaction with inflammation 4. Pulmonary edema 5. Small pericardial effusion		
9	[redacted]	Paracetamol level No other drugs were detected in the blood.	4 mg/l	6 2

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	[redacted] UNK	Historical Condition Ligament injury NOS	Left ankle injury: rupture of lateral collateral ligament.

JUL 2 7 2004

DCS

JUL 2 8 2004

2	[redacted]	Historical Condition	Right closed fracture metatarsal 5th
	UNK	Foot fracture	
3	[redacted]	Historical Condition	Sore throat with swollen red tonsils. Occasional dizziness and fever and feeling tired. No nodes. Treated with penicillin, sore throat symptom ongoing 3/52. Recurrence of symptoms noted on 13JAN2004
	Ongoing	Tonsillitis	
5	UNK	Current Condition	Body mass Index = 27.7 (70 kg, 159 cm)
		Overweight	

C1. Name (cont.)
Suspect Medication #1: NORDETTE -21(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet

G8. ADVERSE EVENT TERMS (cont.)
Pericardial effusion

4363772-0-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

user-facilities, manufacturers for RY reporting
King Pharmaceuticals, Inc.

Reisys International, Inc.
FDA Facsimile Approval: 31-JUN-1999

Mfr report # K200400695
IR/Dist report #
FDA Use Only

A. Patient Information

1. Patient Identifier: UNK — In confidence
2. Age at time of event: 16 Years — or Date of birth: UNK
3. Sex: ☒ female ☐ male
4. Weight: UNK lbs — or UNK kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem(e.g., defects/malfunction)

2. Outcomes attributed to adverse event (check all that apply)
- ☒ death [redacted]
- ☐ life-threatening
- ☐ hospitalization - initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other:

3. Date of event: 03/31/2004
4. Date of this report: 05/18/2004

5. Describe event or problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any seperated by commas)
Pulmonary embolism[Pulmonary embolism]

Case Description:
This report was received by King Pharmaceuticals, Inc. on 10MAY2004 via fax from Berlex Laboratories. A regulatory authority reported that a 16 year-old female patient received oral levonorgestrel/ethinyl estradiol 1 tablet daily started 13JAN2004 for oral contraception. There were no concomitant medications or significant past medical history. On [redacted], after the initiation of levonorgestrel/ethinyl estradiol therapy, the patient experienced a pulmonary embolism and died. There was no post mortem examination performed. The probable cause of death was listed as pulmonary embolism.

6. Relevant tests/laboratory data, including dates
None

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
NI

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1. NORDETTE -21(LEVONORGEST (continued)
#2.

2. Dose, frequency & route used
#1. 1 tablet, qd, Oral
#2.

3. Therapy dates (if unknown, give duration)
#1. 01/13/2004 to 03/31/2004
#2.

4. Diagnosis for use (indication)
#1. Oral contraception
#2.

5. Event abated after use stopped or dose reduced
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

6. Lot# (if known)
#1. UNK
#2.

7. Exp. date (if known)
#1. UNK
#2.

8. Event reappeared after reintroduction
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

9. NDC# - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
NI

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
King Pharmaceuticals, Inc.
501 Fifth Street
Bristol, TN 37620 UNITED STATES

2. Phone number: 9196537005

3. Report source (check all that apply)
- ☒ foreign GBR
- ☐ study
- ☐ literature
- ☐ consumer
- ☒ health professional
- ☐ user facility
- ☐ company representative
- ☐ distributor
- ☒ other: Manufacturer

4. Date received by manufacturer: 05/10/2004

5. (A)NDA # 18-668
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
- ☐ 5-day ☒ 15-day
- ☐ 10-day ☐ periodic
- ☒ initial ☐ follow-up #

8. Adverse event term(s)
Pulmonary embolism

9. Mfr. report number
K200400695

E. Initial reporter

1. Name & address [redacted] phone # [redacted]
[redacted] UNITED STATES

DSS
MAY 21 2004

2. Health professional ?
☒ yes ☐ no

3. Occupation
Other Manufacturer

4. Initial reporter also sent report to FDA
☐ yes ☐ no ☒ unk

FDA
3500A - Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

18-May-2004 13:10

MAY 19 2004

King Pharmaceuticals, Inc.

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service - Food and Drug Administration

Mfr report #

K200400695

UF/Diet report #

FDA Use Only

Additional Information

C1. Name (cont.)
Suspect Medication #1: NORDETTE -21(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet

DSS

MAY 2 1 2004

MAY 1 9 2004

4902505-3-00-01

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

or use by user-facilities, , distributors and manufacturers for MANDATORY reporting

Rolays International, Inc., FDA Facsimile Approved: 11-JUN-1999

Mfr Report # 006392

Page 1 of 2

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event: / or Date of Birth:	3. Sex	4. Weight
UNK In confidence	UNK UNK	☒ Female ☐ Male	UNK lbs or UNK kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

☒ Death UNK (mo/day/yr)
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Disability
☐ Congenital Anomaly
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Other:

3. Date of Event (mo/day/year): UNK

4. Date of This Report (mo/day/year): 02/01/2006

5. Describe Event or Problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Severe neutropenia[Neutropenia]
Anemia[Anaemia]
Leukopenia[Leukopenia]

Case Description:
Information regarding an adverse event associated with Nordette was derived from scientific literature. The article, A Trial of Contraceptive Methods in Women with Systemic Lupus Erythematosus, was obtained from The New England Journal of Medicine. It discussed findings from a single blind clinical trial involving 162 women with systemic lupus erythematosus, who were randomly assigned to combined oral contraceptives, a progestin-only pill, or a copper intrauterine device (IUD). The combined oral contraceptive regimen consisted of 30 µg of ethinyl estradiol plus 150 µg of levonorgestrel (Nordette). The progestin-only pill contained 30 µg of levonorgestrel (Microlut, Schering Mexicana). The continued in additional Info section...

6. Relevant Tests/Laboratory Data, Including Dates
#1 Anemia, Leukopenia 500 (neutrophils 55%)

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 UNK, Historical Memo, History of drug related leukopenia (Azathioprine)

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)
#1. Nordette 21 Day(LEVONORGE (continued)
#2. AMOXICILLIN(AMOXICILLIN) (continued)

2. Dose, Frequency & Route Used	3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. UNK, UNK, Oral	#1. duration 183 days
#2. 1.5 g, qd, Oral	#2. UNK

4. Diagnosis for Use (Indication)	5. Event Abated After Use Stopped or Dose Reduced?
#1. UNK	#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. Upper respiratory (continued)	#2. ☐ Yes ☐ No ☒ Doesn't Apply

6. Lot # (if known)	7. Exp. Date (if known)	8. Event Reappeared After Reintroduction?
#1. UNK	#1. UNK	#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. UNK	#2. UNK	#2. ☐ Yes ☐ No ☒ Doesn't Apply

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
NI

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Barr Laboratories

400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677-7668 UNITED STATES

2. Phone Number: 2019303302

3. Report Source (Check all that apply)
☐ Foreign
☐ Study
☒ Literature
☐ Consumer
☒ Health Professional
☐ User Facility
☐ Company Representative
☐ Distributor
☐ Other:

4. Date Received by Manufacturer (mo/day/yr): 01/26/2006

5. (A)NDA # 18-668
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ Periodic
☐ Initial ☒ Follow-up #1

8. Adverse Event Term(s)
Neutropenia, Anaemia, Leukopenia

9. Manufacturer Report Number
006392

E. INITIAL REPORTER

1. Name and Address
[redacted]
Phone # UNK

2. Health Professional?	3. Occupation	4. Initial Reporter Also Sent Report to FDA
☒ Yes ☐ No	Physician	☐ Yes ☐ No ☒ Unk

FDA

3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

DSS

FEB 0 3 2006

01-Feb-2006 11:50

Additional Information

B5. EVENT DESCRIPTION (cont.)

IUD was TCu 380A copper device (Ortho Pharmaceuticals).

The objective of the study was to investigate whether there were clinically significant differences in systemic lupus erythematosus activity, as measured by the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), in women taking combined oral contraceptives in comparison with those using a progestin-only pill or IUD.

Findings of the study revealed that there were no significant differences among the groups during the trial in global or maximum disease activity, incidence or probability of flares, or medication use.

One patient, receiving combined oral contraceptives (Nordette), died during the trial; her death was ascribed to amoxicillin-related severe neutropenia.

Additional information was received on 01/26/2006.

The author reported that the duration of Nordette therapy was six months. Amoxicillin 1.5 grams/day was prescribed for an upper respiratory tract infection. On an unknown date, lab work indicated anemia, leukopenia 500 (neutrophils 55%). In addition, it was reported that the patient had a history of drug related leukopenia (azathioprine).

MedWatch Case Comment:
Submission of this 15-day report does not constitute an admission that the reported event is an unlabeled event.

C1. Name (cont.)
Suspect Medication #1: Nordette 21 Day(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet
Suspect Medication #2: AMOXICILLIN(AMOXICILLIN)

C4. Diagnosis for use (cont.)
#2: Upper respiratory tract infection

G3. Report source literature description

Journal: The New England Journal of Medicine
Author: Sanchez-Guerrero, J, Uribe AG, Jimenez-Santana L, Mestanza-Peralta M, Lara-Reyes P, Seuc AH, Cravioto MD
Title: A trial of contraceptive methods in women with systemic lupus ergthematosus
Volume: 353 Year: 2005 Pages: 2539-2549

Individual Safety Report

4065974-X-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

VOLUNTARY reporting
alth professionals of adverse
nts and product problems

CDER

Page 1 of 1

Form Approved: OMB No. 0910-0291 Expires: 12/31/94
See OMB statement on reverse

FDA Use Only H Pad

Triage unit sequence # 187724

A. Patient information

1. Patient identifier [redacted] In confidence
2. Age at time of event: 40 or Date of birth:
3. Sex: ☒ female ☐ male
4. Weight: 153 lbs or ____ kgs

B. Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event (check all that apply)
   - ☐ death ____ (mo/day/yr)
   - ☐ life-threatening
   - ☒ hospitalization – initial or prolonged
   - ☐ disability
   - ☐ congenital anomaly
   - ☐ required intervention to prevent permanent impairment/damage
   - ☐ other:
3. Date of event (mo/day/yr): 2-20-03
4. Date of this report (mo/day/yr): 2-21-03
5. Describe event or problem

Pulmonary Embolus – patient had been on Ortho Novum 150 for an unspecified time period, & was recently D'd to Nordette 21 day – presented with PE on 2-20-03

6. Relevant tests/laboratory data, including dates

DSS
FEB 28 2003

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

ø smoking
ø alcohol

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
   - #1 Nordette 21 day
   - #2 Ortho Novum 150 28 day
2. Dose, frequency & route used
   - #1 1 po QD
   - #2 1 po QD
3. Therapy dates (if unknown, give duration) from/to (or best estimate)
   - #1 [redacted] 2 weeks
   - #2 unknown
4. Diagnosis for use (indication)
   - #1 menorrheagia
   - #2 menorrhegia
5. Event abated after use stopped or dose reduced
   - #1 ☒ yes ☐ no ☐ doesn't apply
   - #2 ☐ yes ☐ no ☐ doesn't apply
6. Lot # (if known)
   - #1 N/A
   - #2
7. Exp. date (if known)
   - #1 N/A
   - #2
8. Event reappeared after reintroduction
   - #1 ☐ yes ☐ no ☒ doesn't apply
   - #2 ☐ yes ☐ no ☐ doesn't apply
9. NDC # (for product problems only)
10. Concomitant medical products and therapy dates (exclude treatment of event)

D. Suspect medical device

1. Brand name
2. Type of device
3. Manufacturer name & address
4. Operator of device
   - ☐ health professional
   - ☐ lay user/patient
   - ☐ other:
5. Expiration date (mo/day/yr)
6. RECEIVED
   - model #
   - catalog # FEB 28 2003
   - serial # MEDWATCH CTU
   - lot #
   - other #
7. If implanted, give date (mo/day/yr)
8. If explanted, give date (mo/day/yr)
9. Device available for evaluation? (Do not send to FDA)
   ☐ yes ☐ no ☐ returned to manufacturer on ____ (mo/day/yr)
10. Concomitant medical products and therapy dates (exclude treatment of event)

E. Reporter (see confidentiality section on back)

1. Name, address & phone #
   [redacted] PharmD
2. Health professional? ☒ yes ☐ no
3. Occupation: PharmD
4. Also reported to
   - ☐ manufacturer
   - ☐ user facility
   - ☐ distributor
5. If you do NOT want your identity disclosed to the manufacturer, place an " X " in this box. ☐

FDA

Mail to: MEDWATCH, 5600 Fishers Lane, Rockville, MD 20852-9787 or FAX to: 1-800-FDA-0178

FDA Form 3500 (6/93)

Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

WYETH-AYERST
BOX 8299
PHILADELPHIA,

3416111-3-00-01

MEDWATCH

ORTING PROGRAM

Approved by the FDA on 09/24/1999

Mfr report # 8-99180-072A

UF/Dist report #

FDA Use Only

A. Patient Information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
UNK	or UNK	[X] female	UNK lbs
in confidence	Date of Birth:	[ ] male	or kgs

B. Adverse event or product problem

1. [X] Adverse event [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [X] death (mo/day/yr)
- [ ] life-threatening
- [ ] hospitalization–initial or prolonged
- [ ] recovered
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (mo/day/yr)	4. Date of this report (mo/day/yr)
UNK	11/23/1999

5. Describe event or problem

STROKE. Information has been received from an attorney, regarding an unidentified female patient (age unspecified) who had been prescribed Triphasil-28 therapy (dates unspecified). Medical history included long-term heavy bleeding with her menses resulting in persistent iron deficiency anemia. Concomitant drug therapy was not provided. The patient was given a pack of pills in the physician's office, and over the next 12 days the patient took 4 tablets. The interval at which the patient took the tablets is unknown. Twelve days after receiving Tripasil-28 therapy the patient suffered a stroke and died. No further information was provided.

6. Relevant tests/laboratory data, including dates

None Provided.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

OTHER MEDICAL HISTORY:
Long-term heavy bleeding with her menses and persistent iron deficiency anemia.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 TRIPHASIL-28

#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1 1 Tablet 1x per 1 Day, Oral	#1 12 Day
#2	#2

4. Diagnosis for use (indication)

#1 UNK

#2

5. Event abated after use stopped or dose reduced

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp date (if known)
#1	#1
#2	#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [X] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # – for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

G. All manufacturers

1. Contact office – name/address

WYETH LABS (RA)
170 Radnor Chester
St. Davids, PA 19087

Karel F. Bernady, Ph.D.

NOV 3 0 1999

2. Phone number: 6109023760

3. Report source (check all that apply)

- [ ] foreign
- [ ] study
- [ ] literature
- [X] consumer
- [ ] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (mo/day/yr): 06/22/1999

5. (A)NDA 19-190
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report

- [ ] 5-day [ ] 15-day
- [ ] 10-day [X] periodic
- [X] initial [ ] follow-up #

8. Adverse event term(s)

Cerebrovascular accident NOS

9. Mfr. report number: 8-99180-072A

H. Initial reporter

1. Name & address [redacted] phone # [redacted]

2. Health professional? [ ] yes [X] no

3. Occupation

4. Initial reporter also sent report to FDA [ ] yes [ ] no [X] unk

FDA Form 3500A (facsimile)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

Individual Safety Report

3648168-3-00-01

ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE (Day / Month / Year)
	France		38Yr	F	

7. DESCRIBE EXPERIENCE(S)

THROMBOTIC THROMBOCYTOPENIC PURPURA

Information was received on 08-DEC-2000, from a Literature abstract (Zenut, et al. Fatal thrombocytopenic purpura: Role of oral contraceptives? Therapie 2000; 55: Abstract; 42b) concerning a 38 Yr old female patient who had taken therapy with TRINORDIOL (0.05MG LEVONORGESTREL/0.03MG ETHINYL ESTRADIOL/0.075MG LEVONORGESTREL/0.04MG ETHINYL ESTRADIOL/0.125MG LEVONORGESTREL/0.03MG ETHINYL ESTRADIOL) (equivalent to Triphasil) for an 18 month duration (therapy dates and indication were unspecified). Her medication history included prior use of the oral contraceptive Adepal (levonorgestrel and ethinyl estradiol). Concomitant therapy included occasional use of TYLENOL (PARACETAMOL). The patient was casually noted to have severe thrombocytopenia (10 giga/L). Some time following the initial diagnosis, the patient was hospitalized. On admission, a clinical examination revealed purpura, large ecchymoses, cephalalgia and eyeground minor bleeding. A cranial

(cont'd)

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [X] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

See following page.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 TRINORDIOL (0.05MG LNG/0.03MG EE/0.075MG LNG/0.04MG EE/0.125MG LNG/0.03MG EE, TABLET)

15. DAILY DOSE(S)

#1

16. ROUTE(S) OF ADMINSTRATION

#1 Unknown

17. INDICATION(S) FOR USE

#1

18. THERAPY DATES (FROM/TO)

#1 Unknown

19. THERAPY DURATION

#1 Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?

- [ ] YES [ ] NO [X] N/A

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

- [ ] YES [ ] NO [X] N/A

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

TYLENOL (PARACETAMOL), Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

UNK

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

Local Marketing No.: NDA 19-192

24b. MFR CONTROL NO.: HQ4722412DEC2000

24c. DATE RECEIVED BY MANUFACTURER: 20-Dec-2000

24d. REPORT SOURCE

- [ ] STUDY
- [ ] CONSUMER
- [X] LITERATURE
- [ ] REGULATORY AUTHORITY
- [ ] HEALTH PROFESSIONAL
- [ ] LICENSE

DEC 28 2000
DATE SENT TO FDA

25a. REPORT TYPE

- [ ] INITIAL
- [X] FOLLOWUP

CENTER FOR DRUG RESEARCH AND EVALUATION RECD DEC 29 2000

DSS JAN 02 2001

DEC 29 2000

Individual Safety Report

3648168-3-00-02

IIES

ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: HQ4722412DEC2000

Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

densitometry was performed and was normal. Laboratory testing revealed hemolytic anemia, the presence of schizocytes, persistent thrombopenia (without coagulation disorders) and acute renal failure. In addition, infectious etiologies and collagen disease were ruled out. The patient was diagnosed with thrombotic thrombocytopenic purpura (Thrombotic thrombocytopenic purpura). Despite intensive treatment which included fresh frozen plasma, plasma exchange and platelet infusions, the patient died on day twelve of the hospitalization. An autopsy revealed diffuse capillary thrombi involving most organs and confirmed diagnosis of thrombotic microangiopathy. A copy of the literature abstract is attached.
CANCELED: This case is canceled as it is a duplicate of 8-99182-003A.

Box # 13 - RELEVANT TESTS/LABORATORY DATA (Continuation)

Test Name	*Date*	*Result*	*Normal Range*
Laboratory test abnormal NOS		Autopsy showed diffuse capillary thrombi involving most organs and confirmed diagnosis of thrombotic microangiopathy.	-
Platelet count decreased		10 giga L	-

DSS

JAN 0 2 2001

DEC 2 9 2000

<13>
Unique Identifier
203439
Title
Fatal thrombotic thrombocytopenic purpura: Role of oral contraceptives?
Author
Zenut M. Lamaison D. Merle P. Souweine B. Caillaud D
Institution
Centre Regional de Pharmacovigilance, BP: 38 - 68001
Source
Therapie 55(3):413, Abstr: 42b, 2000 May-Jun
Meeting Data
4th Annual Congress of French Society of Pharmacology, Rouen, 10-12 Apr 2000
Abstract
A severe thrombopenia (10 giga/l) was casually discovered in a 38 year-old woman. She has been for few years on oral contraceptives ADEPAL(R) (levonorgestrel and ethinylestradiol) then TRINORDIOL(R) (levonorgestrel and ethinylestradiol) for 18 months and occasionally acetaminophen. On admission, she presented with purpura and large ecchymoses, cephalalgia and eyeground minor bleeding otherwise clinical examination and cranial tomodensitometry were normal. Additional investigation showed hemolytic anemia and the presence of schizocytes, persistent thrombopenia (without coagulation disorders) and acute renal failure, leading to the diagnosis of thrombotic thrombocytopenic purpura (TTP). Diagnostic of infectious etiologies and collagen disease was ruled out. Despite intense treatment combining fresh frozen plasma, plasma exchange, and platelet infusion the patient died on hospital day 12. Autopsy showed diffuse capillaries thrombi involving the most organs and confirmed the diagnosis of thrombotic microangiopathy. Due to the lack of other etiologies, the responsibility of TRINORDIOL(R) (C1S2) was raised. Nine cases of thrombocytopenia were reported in women treated by levonorgestrel implant, three of whom were hospitalized and treated for TTP, one another died (WYSOWSKI DK and GREEN L., 1995). Another case of TTP has been mentioned in a 16 old girl on low dose oral progestatives (CAILLARD S., 1998).

Individual Safety Report

3656040-3-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Page 1 of 2

Facsimile FDA Form 3500A
Printed by
BERLEX Laboratories
Wayne, NJ

Approved by FDA, Oct. 15th, 1990

Mfr report # 00/01147-GBD

UF/Dist report #

FDA Use Only

A. Patient information

1. Patient initials	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
[redacted] In confidence	34 years	[x] female [ ] male	____ lbs or 70 kgs

B. Adverse event or product problem

1. [x] Adverse event and/or [ ] Product problem e.g., (defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [x] death [redacted] (dd Mon yyyy)
- [x] life-threatening
- [x] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other: _____

3. Date of event (dd Mon yyyy)	4. Date of this report (dd Mon yyyy)
10 Apr 2000	24 Jan 2001

5. Describe event or problem

The initial and four(4) follow-up reports for this case involving Mirena have been submitted to IND 22,697. The initial case was submitted on 24 Jul 00 (serial no. 056); follow-up #1 on 23 Aug 00 (serial no. 061); follow-up #2 on 15 Sep 00 (serial no. 068); follow-up #3 on 24 Oct 00 (serial no. 081); and follow-up #4 on 03 Jan 01 (serial no. 092).

Based on additional information received post-approval, this case was determined to be reportable to the Mirena NDA (21-225).

Physician's report via sales rep on 20 Jul 00 and phone call on 21 Jul 00:

34 year-old patient who was on Mirena since Aug 99 collapsed in bathroom. Resusitation without success. Pt died. Autopsy was not performed. No risk factors. Physician is not informed about further details. However, although he does not see any causal relationship to Mirena, he will send a written report.

Suppl. (16 Aug 00):
<continued>

6. Relevant tests/laboratory data, including dates

None reported

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunctions, etc.)

Patient has asthma in history, multipara (2 children), allergy to penicillin. No clotting disorder in known.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1 MIRENA (levonorgestrel)

#2

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 <continued>	#1 238 days
#2	#2

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1 Contraception	#1 [ ] yes [ ] no [x] doesn't apply
#2	#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp. date (if known)
#1 Unknown	#1
#2	#2

8. Event reappeared after reintroduction

#1 [ ] yes [ ] no [x] doesn't apply

#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

Unknown

G. All manufacturers

1. Contact office - name/address & mfring site for devices

Berlex Laboratories, Inc.
300 Fairfield Road
Wayne, NJ 07470
USA

2. Phone number: (888)237-5394

3. Report source (check all that apply)

- [x] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [x] health professional
- [ ] user facility
- [x] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (dd Mon yyyy): 20 Jul 2000

5. similar to: (A)NDA # 21-225; IND # ____; PLA # ____; pre-1938 [ ] yes; OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)

- [ ] 5-day
- [x] 15-day
- [ ] 10-day
- [ ] periodic
- [x] initial
- [ ] follow-up # ____

8. Adverse event term(s)

EMB PULM
THROMBOPHLEB DEEP
CONVULS
HEART ARREST

9. Mfr. report number: 00/01147-GBD

E. Reporter

1. Name, address & phone #

[redacted]

DSS

JAN 26 2001

Country of origin: Germany

2. Health professional?	3. Occupation	4. Initial reporter also sent report to FDA
[x] yes [ ] no	Physician	[ ] yes [x] no [ ] unk

JAN 25 2001

FDA Form 3500A (6/93)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor manufacturer or product caused or contributed to the event.

Individual Safety Report

3656040-3-00-02

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

Facsimile FDA Form 3500A
Printed by
BERLEX Laboratories
Wayne, NJ

Approved by FDA, Oct. 15th, 199

Mfr report # 00/01147-GBD

UF/Dist report #

FDA Use Only

Continuing Page

B.5. Describe event or problem

Gynecologist's written report:
Patient suffered from cardiac arrest in [redacted]. Patient died.
No further information obtainable.

Suppl. (11 Sep 00):
Phone call with the reporting physician: There is no evidence for extrauterine pregnancy and abdominal bleeding in this patient. The patient probably died due to a cardiac event. Unfortunately no autopsy was done.

Suppl. (18 Oct 00):
Phone call with reporting physician. Physician spoke to patient's sister who told him that patient's mother was with the patient when the event occurred. It was said that pt developed "convulsions". There were no signs of an ectopic pregnancy.

Suppl. (20 Dec 00):
Report from the emergency physician and written report from the hospital (department of internal medicine). Emergency physician was called on [redacted] When emergency physician arrived husband had already perfomed CPR for 15 minutes because of apnea/ difficult breathing. An intubation and a defibrillation (due to ventricular fibrillation) were performed. Patient received 1 ampoule of adrenalin via tube and 6 ampoules adrenalin i.v.. Red scum was discharged out of the tubus. No spontaneous breathing could be observed. For a short time pain reaction was still present. A buffering was performed with sodium bicarbonate and 50 mg Dopamine were applied i.v. Only little cardiac reaction to continued CPR with deformed ventricular complex. Due to dilated pupils, no RR and no cardiac rhythm CPR was stopped.
Patients husband refused an autopsy.
Husband said that an attack of asthma is unlikely. As the patient was already dead when she was admitted to the hospital no lab data or other investigations were done.
Diagnosis: suspected fulminant pulmonary embolism due to thrombosis of pelvic vein.

Suppl. (16 Jan 01):
Phone call with gynecologist to get further information.
No clotting disorder is known in this patient and in patient's sister.

Suppl. (17 Jan 01):
Phone call with internist to get further information. Deep vein thrombosis as well as pulmonary embolism are only tentative diagnoses, unconfirmed by any investigations, based solely on the clinical symptoms.

Further information will be requested.

C. Suspect medication #1

C.2. Dose, frequency & route used

0.02 mg intra-uterine IUS

DSS

JAN 2 6 2001

JAN 2 5 2001

Individual Safety Report

3700957-8-00-01

Facsimile FDA Form 3500A
Printed by
BERLEX Laboratories
Wayne, NJ

Approved by FDA, Oct 15th, 199

Mfr report # 01/00393-GBD

UF/Dist report #

FDA Use Only

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

A. Patient information

1. Patient initials	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
— In confidence	45 years / Unknown	[x] female [ ] male	____ lbs or ____ kgs

B. Adverse event or product problem

1. [x] Adverse event and/or [ ] Product problem e.g., (defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [x] death 2001 (dd Mon yyyy)
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (dd Mon yyyy): 2001

4. Date of this report (dd Mon yyyy): 6 Apr 2001

5. Describe event or problem

Gynecologist's report:

Pt has been taking Miranova for approximately five years. Pt had a history of hypertension prior to intake of Miranova. Pt could not work for three weeks in Jan 01 due to cardiovascular problems. Gynecologist saw the pt in [redacted] for the last time and examination was unremarkable. At this time blood pressure was 150/ 90 mm Hg (the same value as it was the years before). Pt did not have a varicosis. Some days ago pt died suddenly while teaching in school. Physician did not arrange for an autopsy, but pt's relatives did. At time of event pt was still under Miranova.

Pathologist's report to gynecologist: Autopsy results are not clear yet. Pt had a hypertrophy of the right heart. No embolism and no cerebral infarction could be found. Pathologist told the reporting gynecologist that an intoxication might be possible. Neither gynecologist nor pathologist see a causal relationship between exitus and Miranova in this pt.

<continued>

6. Relevant tests/laboratory data, including dates

Diagnostic Investigation: Autopsy was performed: No embolism, no cerebral infarction, pt had hypertrophy of the right heart. Intoxication might be possible.
Suppl. ([redacted]): Autopsy result: acute heart failure rt because of heart valve hypertrophy which was not known.

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunctions, etc.)

Pt had a history of hypertension prior to intake of Miranova.

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 MIRANOVA (levonorgestrel, ethinylestradiol)
#2

2. Dose, frequency & route used
#1 1 coated tablet p.o.
#2

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 1996 - approx. 5 years
#2

4. Diagnosis for use (indication)
#1 Unknown
#2

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [ ] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1 Unknown
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [ ] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
Unknown

G. All manufacturers

1. Contact office - name/address & mfring site for devices
Berlex Laboratories, Inc.
300 Fairfield Road
Wayne, NJ 07470
USA

2. Phone number: (888)237-5394

3. Report source (check all that apply)
- [x] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [x] health professional
- [ ] user facility
- [x] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (dd Mon yyyy): 26 Mar 2001

5. similar to:
(A)NDA # 20-860
IND # ____
PLA # ____
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day
- [x] 15-day
- [ ] 10-day
- [ ] periodic
- [ ] initial
- [x] follow-up # 1

8. Adverse event term(s)
HEART FAIL RIGHT

9. Mfr. report number
01/00393-GBD

APR 09 2001

E. Reporter

1. Name, address & phone #
[redacted]
Country of origin: Germany

2. Health professional?
[x] yes [ ] no

3. Occupation
Physician

4. Initial reporter also sent report to FDA
[ ] yes [ ] no [x] unk

FDA
FDA Form 3500A (6/93)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor manufacturer or product caused or contributed to the event.

Facsimile FDA Form 3500A
Printed by
BERLEX Laboratories
Wayne, NJ

Approved by FDA, Oct. 15 h, 1993

Mfr report #	01/00393-GBD
IUF/Dist report #	
	FDA Use Only

Continuing Page

B.5. Describe event or problem

Suppl. (26 Mar 01): Phone call with gynecologist who reports autopsy result which was given orally (written report not available). Autopsy result: acute heart failure rt because of heart valve hypertrophy which was not known. No relationship with Miranova.

Case closed.

APR 0 9 2001

3741376-8-00-01

ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month /)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE (Day / Month / Year)
[redacted]	Denmark	[redacted] / [redacted] / [redacted]	33Yr	F	20 / APR / 2001

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM

Information was received on 14-JUN-2001 from the Health Authority via Schering AG Germany concerning a 33-year-old female patient who had taken therapy with Microgynon (0.15mg levonorgestrel/0.03mg ethinyl estradiol) (equivalent to Nordette) for an unspecified indication. Therapy began in 1997 and ended on 20-APR-2001. Medical history was not provided. The dose regimen was 1 tablet daily. It is unknown if the patient was taking concomitant therapy. The patient experienced pulmonary embolism (pulmonary embolism) on [redacted] and was hospitalized. Her treatment was unspecified. The patient died on [redacted]

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

None Provided.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 MICROGYNON (0.15MG LEVONORGESTREL/0.03MG ETHINYL ESTRADIOL, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG?

[ ] YES [X] NO [ ] N/A

15. DAILY DOSE(S)

#1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINSTRATION

#1 Oral

17. INDICATION(S) FOR USE

#1

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

[ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)

#1 00-UNK-1997 / 20-Apr-2001

19. THERAPY DURATION

#1 3 Yr

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)

UNK

RECEIVED

JUN 18 2001

CDR/CDER

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

OTHER REFERENCE NUMBERS:

Regulatory Authority (HP) (via Schering AG)
01/01322-CDS

DSS

JUN 19 2001

Local Marketing No.	24b. MFR CONTROL NO.
NDA 18-668	HQ2066414JUN2001

24c. DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
14-Jun-2001	[ ] STUDY [ ] CONSUMER [ ] LITERATURE [X] REGULATORY AUTHORITY [X] HEALTH PROFESSIONAL [ ] LICENSE

Date of this report	25a. REPORT TYPE
15-Jun-2001	[X] INITIAL [ ] FOLLOWUP

JUN 15 2001

DATE SENT TO FDA

Individual Safety Report

3781552-1-00-01

Facsimile FDA Form 3500A
Printed by
BERLEX Laboratories
Wayne, NJ

Approved by FDA, Oct. 15th, 1993

Mfr report # 01/02166-CDS

UF/Dist report #

FDA Use Only

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM Page 1 of 2

A. Patient information

1. Patient initials	2. Age at time of event: / or Date of birth:	3. Sex	4. Weight
— in confidence	40 years / Unknown	[x] female [ ] male	____ lbs or ____ kgs

B. Adverse event or product problem

1. [x] Adverse event and/or [ ] Product problem e.g., (defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [x] death [redacted] (dd Mon yyyy)
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event (dd Mon yyyy): Unknown

4. Date of this report (dd Mon yyyy): 20 Aug 2001

5. Describe event or problem

Health professional reports:

A female patient who was already surgically sterilized and presenting chronic anemia had Mirena inserted on 20 Jul 01, to reduce menstrual flow as advised by her hematologist. Mirena was inserted on the second day of her menstrual cycle. Since 21 Jul 01 the patient experienced abdominal pain, vomiting and diarrhea. Her doctor recommended Buscopan (escopolamine). On [redacted] the patient visited her physician. She was dehydrated. An ultrasonogram was performed. No abnormalities in the genital area were seen and Mirena was well positioned. Due to the dehydration the patient was hospitalized on [redacted]. The gastroenterologist diagnosed pancreatitis. The patient experienced some symptoms of pancreatitis already whilst she was travelling, before returning for Mirena insertion according to patients husband.

In the morning of [redacted] the patient died.

Outcome: died
<continued>

6. Relevant tests/laboratory data, including dates

None reported

7. Other relevant history, including preexisting medical conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunctions, etc.)

The patient suffered from chronic anemia. Before Mirena insertion the patient was surgically sterilized, had been travelling and had presented some symptoms of pancreatitis.

DSS

AUG 22 2001

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1 MIRENA (levonorgestrel)
#2

2. Dose, frequency & route used
#1 0.02 mg intrauterine
#2

3. Therapy dates (if unknown, give duration) from/to (or best estimate)
#1 20 Jul 200[illegible] - 27 Jul 2001
#2

4. Diagnosis for use (indication)
#1 reduction of menstrual flow
#2

5. Event abated after use stopped or dose reduced
#1 [ ] yes [ ] no [x] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
#1 Unknown
#2

7. Exp. date (if known)
#1
#2

8. Event reappeared after reintroduction
#1 [ ] yes [ ] no [x] doesn't apply
#2 [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
none indicated

G. All manufacturers

1. Contact office - name/address & mfring site for devices
Berlex Laboratories, Inc.
300 Fairfield Road
Wayne, NJ 07470
USA

2. Phone number: (888)237-5394

3. Report source (check all that apply)
- [x] foreign
- [ ] study
- [ ] literature
- [ ] consumer
- [x] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer (dd Mon yyyy): 7 Aug 2001

5. similar to:
(A)NDA # 21-225
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day [x] 15-day
- [ ] 10-day [ ] periodic
- [ ] Initial [x] follow-up # 1

8. Adverse event term(s)
PANCREATITIS

9. Mfr. report number: 01/02166-CDS

E. Reporter

1. Name, address & phone #
[redacted]
Country of origin: Brazil

2. Health professional? [x] yes [ ] no

3. Occupation: <continued>

4. Initial reporter also sent report to FDA: [ ] yes [x] no [ ] unk

FDA
FDA Form 3500A (6/93)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor manufacturer or product caused or contributed to the event.

AUG 2 1 2001

Continuing Page

B.5. Describe event or problem

Reporters comment: It was a coincidence that the patient presented with pancreatitis during the use of Mirena.

Suppl. (07 Aug 01): According to initial information cause of death pancreatitis. During the first day of hospitalization amylase and lipase values were measured which were normal. No further information available.

Case closed.

E.3. Occupation

Health Professional

DSS

AUG 2 2 2001

AUG 2 1 2001

Individual Safety Report
3796431-3-00-01

IN

ADVERSE EXPERIENCE REPORT

SEP [illegible] 2001

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE (Day / Month / Year)
	Canada		20Yr	F	11 / SEP / 2001

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM; Convulsions NOS; Blood pressure decreased

Information was received on 13-SEP-2001, from a healthcare professional concerning a 20-year-old female patient. The patient's concurrent history included mild obesity and mental disorder NEC. Therapy with Alesse-28 (0.1mg levonorgestrel/0.02mg ethinyl estradiol/inert) (tablet) for contraception NOS began in MAR-2001. The dose regimen was one tablet daily. Concomitant therapy included Effexor XR (venlafaxine hydrochloride), Topamax (topiramate), Flonase (fluticasone propionate), Clozaril (clozapine), Clonazepam and "Serequil". The patient experienced a seizure (convulsions NOS) on [redacted] and was taken to the hospital. The following day her blood pressure dropped (blood pressure decreased). Subsequently, the patient died on [redacted]. According to the coroner, the cause of death was a pulmonary embolism (pulmonary embolism).

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [X] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

None Provided.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 ALESSE-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

15. DAILY DOSE(S)

#1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINSTRATION

#1 Oral

17. INDICATION(S) FOR USE

#1 Contraception NOS

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)

#1 00-Mar-2001 / 00-UNK-2001

19. THERAPY DURATION

#1 Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR) (cont'd)

EFFEXOR XR (VENLAFAXINE HYDROCHLORIDE), Unknown
TOPAMAX (TOPIRAMATE), Unknown
FLONASE (FLUTICASONE PROPIONATE), Unknown
CLOZARIL (CLOZAPINE), Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

CONCURRENT CONDITIONS:
Obesity; Mental disorder NEC

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

OTHER REFERENCE NUMBERS:
Healthcare Professional (Wyeth-Canada) - 2001-486

Local Marketing No.: #1 NDA 20-683

24b. MFR CONTROL NO.: HQ599241 4SEP2001

24c. DATE RECEIVED BY MANUFACTURER: 13-Sep-2001

24d. REPORT SOURCE
- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [ ] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [ ] LICENSE

Date of this report: 19-Sep-2001

25a. REPORT TYPE
- [X] INITIAL
- [ ] FOLLOWUP

DSS
SEP 21 2001

SEP 20 2001

SEP 19 2001
DATE SENT TO FDA

WYETH-AYERST LABORATORIES

Individual Safety Report

3796431-3-00-02

Manufacturer Control Number: HQ5992414SEP2001

Box # 22 - CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Continuation)

CLONAZEPAM (CLONAZEPAM), Unknown

DSS

SEP 21 2001

SEP 20 2001

Individual Safety Report

3961641-9-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities, distributors and manufacturers for MANDATORY reporting
Berlex Laboratories

Reisys International, Inc.
FDA Facsimile Approval 30-JUN-1999

Mfr report # USA-2002-001670

UF/Dist. report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: or Date of birth:	3. Sex	4. Weight
UNK in confidence	41 Years / UNK	[X] female [ ] male	UNK lbs or UNK kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

[X] death UNK (mm/dd/yy) [ ] life-threatening [X] hospitalization - initial or prolonged [ ] disability [ ] congenital anomaly [ ] required intervention to prevent permanent impairment/damage [ ] other:

3. Date of event (mm/dd/yy)	4. Date of this report (mm/dd/yy)
UNK	08/07/2002

5. Describe event or problem

embolus in the right main pulmonary artery (fatal)[Pulmonary embolism]
inferior vena cava thrombus[Inferior vena caval obstruction]
focal nodular hyperplasia in the liver[Focal nodular hyperplasia]
uterine leiomyoma-associated thrombosis[Uterine fibroids]
antiphospholipid antibody syndrome[Antiphospholipid syndrome]
abdominal pain[Abdominal pain NOS]
nausea[Nausea]
diarrhea[Diarrhoea NOS]
diffuse abdominal tenderness on the right[Abdominal tenderness]
dysfibrinogenemia[Acquired dysfibrinogenaemia]

Case Description:
Literature:

continued in additional info section...

6. Relevant tests/laboratory data, including dates

#1 Prothrombin time 15.5s (11.5s to 15.0s)
#2 Activated partial thromboplastin time 34s (23s to 36s)
#3 International normalized ratio 1.21
#4 Hepatitis panel pending
#5 Urinalysis , Moderate Streptococcus viridans
#6 Stool (continued)
continued in additional info section...

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

#1 Historical Condition, Anaemia NOS (continued)
#2 UNK Historical Condition, (continued)
#3 UNK Historical Condition, (continued)
#4 UNK Other, (continued)
continued in additional info section...

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1. Levlite 21 or 28(LEVONORG (continued)
#2.

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1. UNK, UNK, UNK	#1. UNK
#2.	#2.

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1. UNK	#1. [ ] yes [ ] no [X] doesn't apply
#2.	#2. [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1. UNK	#1. UNK	#1. [ ] yes [ ] no [X] doesn't apply
#2.	#2.	#2. [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

TYLENOL EXTRA-STRENGTH UNK to UNK
FERROUS SULFATE (FERROUS SULFATE) UNK to UNK
continued in additional info section...

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Berlex Laboratories

6 West Belt
Wayne, NJ 07470-6806 UNITED STATES

2. Phone number
+1 8882375394

3. Report source (check all that apply)
[ ] foreign [ ] study [Y] literature [ ] consumer [Y] health professional [ ] user facility [ ] company representative [ ] distributor [ ] other:

4. Date received by manufacturer (mm/dd/yy)
07/26/2002

5. (A)NDA # NDA 20-860
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
[ ] 5-day [Y] 15-day [ ] 10-day [ ] periodic [Y] initial [ ] follow-up #

8. Adverse event term(s)
Pulmonary embolism, Inferior vena caval obstruction, Focal nodular hyperplasia, Uterine fibroids,
continued in additional info section...

9. Mfr. report number
USA-2002-001670

E. Initial reporter

1. Name & address [redacted]
[redacted] UNITED STATES

phone # UNK

AUG 0 9 2002

2. Health professional ?	3. Occupation	4. Initial reporter also sent report to FDA
[X] yes [ ] no	Professor / Faculty member	[ ] yes [ ] no [X] unk

FDA 3500A - Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

DSS

AUG 1 3 2002

07-Aug-2002 14:00:07

Additional Information

B5. EVENT DESCRIPTION (cont.)

'Vena Cava Thrombus and Fatal Pulmonary Embolus'

A 41 y.o. African-American female with a history of dysfunctional bleeding attributed to a history of uterine leiomyomas and heterozygous for Arg506Gln mutation of the Factor V gene (Factor V Leiden mutation), on Levlite for an unspecified amount of time and indication experienced abdominal pain, fullness in her lower extremities, nausea, and diarrhea for about 7 days duration.

She was admitted to the hospital (date unspecified) and physical examination was remarkable for tachycardia (heart rate =120), diffuse abdominal tenderness on the right, a palpable liver mass 1 cm below the costal margin, and +1 lower extremity swelling bilaterally. On the second day of hospitalization she experienced a sudden onset of dyspnea with a respiratory rate greater than 40, which rapidly progressed to apnea. She was intubated and progressed to asystole. Attempts to resuscitate failed, and she died.

An autopsy revealed a thrombus in the inferior vena cava and an embolus in the right main pulmonary artery, which caused the patient's sudden apnea and death. Postmortem examination of routine sections from the lung revealed both recent and remote, organized thromboembolia. The presence of older organizing thrombi may indicate an ongoing, chronic process and suggest a hereditary or acquired biochemical mechanism of long-standing duration. Further analysis of the postmortem gross examination and laboratory results yielded 6 possible explanations as a cause for the patient's thrombosis that led to her sudden death: (1) focal nodular hyperplasia in the liver; (2) uterine leiomyoma-associated thrombosis; (3) the antiphospholipid antibody syndrome; (4) dysfibrinogenemia; (5) oral contraceptive use; and (6) the Factor V Leiden mutation.

Reporter's comment: Inferior vena cava stenosis and thrombosis have been implicated with oral contraceptive usage, which provides plausible explanation of the patient's thrombotic event. We believe that more than one of the identified risk factors contributed to the patient's hypercoaguable state. The possibility exists that the thrombus in the inferior vena cava may have been directly caused by the oral contraceptives with the remaining identified risk factors enhancing the hypercoaguable effect of the oral contraceptive.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
6		Stool		
		No ova or parasites; Clostridium difficile negative		
7		AST (SGOT)	65 U/L	42 U/L 10 U/L
8		ALT (SGPT)	138 U/L	33 U/L 7 U/L
9		Hemoglobin	8.0 g/dL	16.1 g/dL 12.0 g/dL
10		Hematocrit	28.5%	48.0% 36.0%
11		Thrombin time	100.0s	10.7s 8.9s
12		Antithrombin III	0.92 U/ml	1.29 U/ml 0.95 U/ml
13		Anti-phospholipid: IgG	2 GPL	11 GPL 0 GPL
14		Anti-phospholipid: IgM	5 MPL	13 MPL 0 MPL
15		Anti-cardiolipid: IgG	10 GPA	<25 GPA
16		Anti-cardiolipid: IgM	4 MPA	<10 MPA
17		Anti-cardiolipid: IgA	3 APA	<12 APA
18		Anti-phosphatidyserine: IgG	20 GPS	<10 GPS
19		Anti-phosphatidyserine: IgM	17 MPS	<26 MPS
20		Anti-Beta2GPI: IgG	3 SGA	9 SGA 0 SGA
21		Anti-Beta2GPI: IgM	9 SMA	26 SMA 0 SMA
22		Anti-Beta2GPI: IgA	7 SA	19 SA 0 SA
23		LAC screening (DW ratio)	No Clot	<1.5

24	Hexagonal phospholipid	No Clot	8s
25	Lp(a)	4.0 mg/dL	36.3 mg/dL 8.9 mg/dL
26	Reptilase time	12.2s	21.8s 13.6s
27	Fibrinogen	439 mg/dL	450 mg/dL 180 mg/dL
28	HPIA	0.1	0.5 0.0
29	TAT	74.9	2.5 1.3
30	D-DIMQ	7.0	0.3 0.0
31	Factor V Leiden	Arg506Gln - Heterozy	Arg506 - Homozygous
32	Factor II Leiden	G20210 - Homozygous	G20210 - Homozygous
33	Methylenetetrahydrofolate reductase	C677 - Homozygous	C677 - Homozygous

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	UNK Ongoing	Historical Condition Anaemia NOS	chronic anemia
2	UNK	Historical Condition Uterine fibroids	history of uterine leiomyomas
3	UNK	Historical Condition Dysfunctional uterine bleeding	attributed to a history of uterine leiomyomas
4	UNK	Other one full term pregnancy at 31 years of age	
5	UNK	Family History Diabetes mellitus NOS	
6	UNK	Family History Hypertension NOS	
7	UNK	Family History Coronary artery disease NOS	
8	UNK Ongoing	Factor V deficiency	patient is heterozygous for Arg506Gln mutation of the Factor V gene (Factor V Leiden mutation)

AUG 0 9 2002

DSS

AUG 1 3 2002

C1. Name (cont.)
Suspect Medication #1: Levlite 21 or 28(LEVONORGESTREL, ETHINYLESTRADIOL) Coated tablet

C10. CONCOMITANT MEDICAL PRODUCTS

COMPAZINE (PROCHLORPERAZINE EDISYLATE) UNK to UNK
TETRACYCLINE (TETRACYCLINE) UNK to UNK

G3. Report source literature description

Journal: Laboratory Medicine
Author:
Title: Vena cava thrombus and fatal pulmonary embolus
Volume: 33 Year: 2002 Pages: 553-555

G8. ADVERSE EVENT TERMS (cont.)
Antiphospholipid syndrome, Abdominal pain NOS, Peripheral swelling, Nausea, Diarrhoea NOS, Tachycardia NOS, Abdominal tenderness, Acquired dysfibrinogenaemia

3964208-1-00-01

INTERNATIONAL ADVERSE EXPERIENCE REPORT

RECEIVED
AUG 15 2002
CDR/CDER

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET (Day / Month / Year)
[redacted]	Denmark	[redacted] / [redacted] / [redacted]	30Yr	F	14 / JAN / 2002

7. DESCRIBE EXPERIENCE(S)

CEREBRAL INFARCTION; Carotid artery thrombosis; Convulsions NOS

Information was received from a regulatory authority (hp), via Schering AG, concerning a 30-year-old female patient. The patient's concurrent history included depression, and she was a heavy cigarette smoker. Family history included a disposition for cardiovascular diseases. Past medication history included Mercilon (desogestrel/ethinyl estradiol) for 4 months in 2000. Therapy with Triquilar (0.05mg levonorgestrel/0.03mg ethinyl estradiol/0.075mg levonorgestrel/0.04mg ethinyl estradiol/0.125mg levonorgestrel/0.03mg ethinyl estradiol) tablet, Triphasil and Fironetta equivalent, for bleeding disturbances began on 28-SEP-2001 and ended on 27-DEC-2001. The dose regimen was 1 tablet daily. Concomitant therapy included Cipramil (citalopram hydrobromide). On an unspecified date, cholesterol tests revealed nothing abnormal. On 14-JAN-2002, the patient experienced acute left-sided paralysis and convulsions (convulsions NOS) which progressed to complete right media

(cont'd)

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

See following page.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 TRIQUILAR (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

15. DAILY DOSE(S)

#1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINSTRATION

#1 Oral

17. INDICATION(S) FOR USE

#1 Menometrorrhagia

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)

#1 28-Sep-2001 / 27-Dec-2001

19. THERAPY DURATION

#1 91 Day

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

CIPRAMIL (CITALOPRAM HYDROBROMIDE), unknown, 01-May-2001 / UNK

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

CONCURRENT CONDITIONS:
Depression NEC; Cigarette smoker

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

OTHER REFERENCE NUMBERS:
Regulatory Authority (HP) - SAG-2002-001624

Local Marketing No.: #1 NDA 19-192

24b. MFR CONTROL NO.: HQ3635207AUG2002

24c. DATE RECEIVED BY MANUFACTURER: 07-Aug-2002

24d. REPORT SOURCE
- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [X] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [X] LICENSE

Date of this report: 14-Aug-2002

25a. REPORT TYPE
- [X] INITIAL
- [ ] FOLLOWUP

DAS
AUG 16 2002

AUG 14 2002
DATE SENT TO FDA
AUG 15 2002

3964208-1-00-02

ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: HQ3635207AUG2002

Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

infarction (cerebral infarction) with oedema and "incarceration" and a thrombotic mass in the right carotis interna (carotid artery thrombosis). The patient died on [redacted] as a result of the adverse event. Autopsy results showed a fixed big thrombotic mass in the right carotis interna, mild arteriosclerotic wall changes, a clot mass in the left carotis, and other vessels of the brain were normal.

Box # 13 - RELEVANT TESTS/LABORATORY DATA (Continuation)

Test Name	*Date*	*Result*	*Normal Range*
Blood cholesterol		normal	

DBS

AUG 16 2002

AUG 16

AUG 15 2002

Individual Safety Report

4061279-1-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

se by user-facilities,
rs and manufacturers for
DATORY reporting
erlex Laboratories

Retsys International, Inc.
FDA Facsimile Approval: 30-JUN-1999

Mfr report #: SAG-2002-007615
UF/Dist. report #:
FDA Use Only

A. Patient information

1. Patient Identifier: [redacted] in confidence
2. Age at time of event: 42 Years or Date of birth: UNK
3. Sex: [X] female [ ] male
4. Weight: UNK lbs or UNK kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)
- [X] death [redacted]
- [ ] life-threatening
- [ ] hospitalization - initial or prolonged
- [ ] disability
- [ ] congenital anomaly
- [ ] required intervention to prevent permanent impairment/damage
- [ ] other:

3. Date of event: 07/18/2002
4. Date of this report: 02/19/2003

5. Describe event or problem

fatal pulmonary embolism[Pulmonary embolism]

Case Description:
A health professional reported: A female patient had Mirena inserted in the indication contraception in 1999. She died suddenly. Exact cause unknown. Pulmonary embolism or cardiovascular accident?

Suppl. (13 Feb 2003): A 42-year-old female patient, not overweight, but a heavy smoker, had levonorgestrel (Mirena) inserted on the 24 Jul 2000, in the indication perimenopausal menorrhagia.

She died on the [redacted]. An autopsy was performed and the recorded cause of death was pulmonary embolism.

6. Relevant tests/laboratory data, including dates
NI

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 UNK, Concurrent Condition, Smoker (heavy smoker)
#2 UNK, Concurrent Condition (no overweight)

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
1. Mirena(LEVONORGESTREL) (continued)
2.

2. Dose, frequency & route used
1. 20 µg, (continued)
2.

3. Therapy dates (if unknown, give duration)
1. 07/24/2000 to 07/18/2002
2.

4. Diagnosis for use (indication)
1. Menorrhagia / contraception
2.

5. Event abated after use stopped or dose reduced
1. [ ] yes [ ] no [X] doesn't apply
2. [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)
1. UNK
2.

7. Exp. date (if known)
1. UNK
2.

8. Event reappeared after reintroduction
1. [ ] yes [ ] no [X] doesn't apply
2. [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
NI

D. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Berlex Laboratories
6 West Belt
Wayne, NJ 07470-6806 UNITED STATES

2. Phone number: +1 8882375394

3. Report source (check all that apply)
- [X] foreign ZAF
- [ ] study
- [X] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer: 02/11/2003

5. (A)NDA # NDA 21-225
IND #
PLA #
pre-1938 [ ] yes
OTC product [ ] yes

6. If IND, protocol #

7. Type of report (check all that apply)
- [ ] 5-day [X] 15-day
- [ ] 10-day [ ] periodic
- [ ] initial [X] follow-up # 1

8. Adverse event term(s)
Pulmonary embolism

9. Mfr. report number
SAG-2002-007615

E. Initial reporter

1. Name & address
Name and address withheld.
phone # Withheld

2. Health professional ?
[X] yes [ ] no

3. Occupation
Health Care Professional

4.

FDA

3500A - Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

FEB 2 0 2003

19-Feb-2003 16:06:28

Additional Information

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 μg, cont, Intra-uterine

Individual Safety Report

4071425-1-00-01

ADVERSE EXPERIENCE REPORT

RECEIVED

MAR 0 5 2003

CDR/CDER

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET (Day / Month / Year)	8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION
	United Kingdom	/ /	31Yr	F	00 / JAN / 2003	

7. DESCRIBE EXPERIENCE(S)

MYOCARDIAL INFARCTION(LLT:MYOCARDIAL INFARCTION); Thrombosis(LLT:Thrombosis); Atherosclerosis(LLT:Atherosclerosis)
[LLT = Lowest Level Term]

Information has been received from a regulatory authority (HP) concerning a 31-year-old female patient who was a cigarette smoker. The patient's concurrent illnesses included atherosclerosis and obesity. Therapy with Microgynon (0.15mg levonorgestrel/0.03mg ethinyl estradiol tablet; equivalent to Nordette) for oral contraception began on 6-JAN-2003 and ended on 13-JAN-2003. The dose regimen was 1 tablet daily. It is unknown if the patient was taking concomitant medication. The patient experienced a myocardial infarction (myocardial infarction), a 5 mm thrombosis (thrombosis), and atherosclerosis (atherosclerosis) in [redacted]. The patient was hospitalized. The following tests were performed with the following results: blood pressure at 130/71 mm Hg, body mass index of 28. The patient died
(cont'd)

13. RELEVANT TESTS/LABORATORY DATA
See following page.

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [X] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))
#1 MICROGYNON (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET)

15. DAILY DOSE(S)
#1 1 tablet daily

16. ROUTE(S) OF ADMINSTRATION
#1 Oral

17. INDICATION(S) FOR USE
#1 Oral contraception(LLT:Oral contraception)

18. THERAPY DATES (FROM/TO)
#1 06-Jan-2003 / 13-Jan-2003

19. THERAPY DURATION
#1 8 Day

20. DID REACTION ABATE AFTER STOPPING DRUG?
[ ] YES [ ] NO [X] N/A

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
[ ] YES [ ] NO [X] N/A

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)
Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)
CONCURRENT CONDITIONS:
Obesity(LLT:Obesity); Smoker(LLT:Cigarette smoker); Atherosclerosis(LLT:Atherosclerosis)

DSS

MAR 0 6 2003

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
WYETH LABS (RA)
201 King of Prussia
Sixth Floor
Radnor, PA 19087-5114

OTHER REFERENCE NUMBERS:
Regulatory Authority (HP)
Affiliate Ref Num -

Local Marketing No.
#1 NDA 18-668

24b. MFR CONTROL NO.
HQWYE651625FEB03

24c. DATE RECEIVED BY MANUFACTURER
24-Feb-2003

24d. REPORT SOURCE
- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [X] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [ ] LICENSE

MAR 0 4 2003
DATE SENT TO FDA

Date of this report
04-Mar-2003

25a. REPORT TYPE
[X] INITIAL [ ] FOLLOWUP

MAR 0 5 2003

Individual Safety Report

4071425-1-00-02

ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: HQWYE651625FEB03

Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

on [redacted] The cause of death was identified as the myocardial infarction.

Box # 13 - RELEVANT TESTS/LABORATORY DATA (Continuation)

Test Name / Date	Result	Normal Range
Blood pressure (LLT:Blood pressure)	130/71 mm Hg	-
Body mass index (LLT:Body mass index)	28	-

DSS

MAR 0 6 2003

MAR 0 5 2003

WYETH-AYERST LABORATORIES

Individual Safety Report

IN AL 4226802-2-00-01

RECEIVED
NOV 03 2003

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4&5. EXPERIENCE ONSET (Day / Month / Year)
[redacted]	Japan	[redacted]	43Yr	F	30 / AUG / 2003

7. DESCRIBE EXPERIENCE(S)

MYOCARDIAL INFARCTION(LLT:MYOCARDIAL INFARCTION); Sinus arrhythmia(LLT:Sinus arrhythmia); Electrocardiogram T wave abnormal(LLT:Electrocardiogram T wave abnormal)
[LLT = Lowest Level Term]

Follow-up information was received from a gynecolgist regarding patient details, product details, medical history, hospital course, lab results, treatment, cause of death and the addition of 2 serious adverse events. Information was received from a healthcare professional regarding a 43-year-old Asian female patient who received Tridiol (0.05mg levonorgestrel/0.03mg ethinyl estradiol/0.075mg levonorgestrel/0.04mg ethinyl estradiol/0.125mg levonorgestrel/0.03mg ethinyl estradiol tablet) therapy and experienced a myocardial infarction.
MEDICAL HISTORY:
The patient's concurrent illness includes cystitis.
(cont'd)

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [X] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA
See following page.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))
#1 TRIDIOL-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)
(cont'd)

20. DID REACTION ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINSTRATION
#1 1 tablet daily	#1 Oral

17. INDICATION(S) FOR USE
#1 Contraception NOS(LLT:Contraception)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)	19. THERAPY DURATION
#1 22-Sep-1999 / 00-Mar-2002	#1 29 Mth

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)
Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)
CONCURRENT CONDITIONS:
Occupational environmental problem NOS(LLT:Occupational environmental problem NOS)

PAST CONDITIONS:
Cystitis NOS(LLT:Cystitis)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
WYETH LABS (RA)
P.O. Box 7667
Philadelphia, PA 19101-7667

OTHER REFERENCE NUMBERS:
Affiliate Ref Num - TRs-

DSS
NOV 04 2003

Local Marketing No.	24b. MFR CONTROL NO.
#1 NDA 19-190	HQWYE582109SEP03

OCT 31 2003
DATE SENT TO FDA

24c. DATE RECEIVED BY MANUFACTURER: 24-Oct-2003

24d. REPORT SOURCE
- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [ ] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [ ] LICENSE

Date of this report: 31-Oct-2003

25a. REPORT TYPE [X] INITIAL [ ] FOLLOWUP

NOV 03 2003

Individual Safety Report

4226802-2-00-02

IN
AD ...E EXPERIENCE REPORT

Manufacturer Control Number: HQWYE582109SEP03

Box # 7 - DESCRIBE EXPERIENCE(S) : (Continuation)

PRODUCT DETAILS:
Indication for Tridiol-28 was contraception. The dose regimen was 1 tablet daily (oral) from 22-Sep-1999 to Mar-2002 and then was 1 tablet daily (oral) from 24-Apr-2002 to 30-Aug-2003. Therapy was permanently discontinued.
CONCOMITANT THERAPY:
Concomitant medications were not reported.
EVENT DETAILS:
On [redacted], the patient had an electrocardiogram which showed sinus arrhythmia (sinus arrhythmia) and T wave abnormal (electrocardiogram T wave abnormal). The patient was hospitalized and treatment included a cardiotonic drug. The patient was encouraged to transfer to another hospital on [redacted]; however, she refused. On 02-Sep-2003, the patient's condition worsened with increasing chest pain. An ambulance brought the patient back to another hospital. The patient experienced a myocardial infarction (myocardial infarction), and subsequently died on [redacted]. Of note, the patient's work enviroment consists of high temperatures and she sweats a lot. The weariness and malaise reportedly continued to put a high stress load on her heart. The physician's assessment of the relatedness between the events and Tridiol was possibly related.
TEST RESULTS:
Electrocardiogram (results: normal) was done in [redacted]. Electrocardiogram (results: sinus arrhythmia and T wave abnormal) was done on [redacted].
The cause of death was reported as myocardial infarction.

Box # 13 - RELEVANT TESTS/LABORATORY DATA (Continuation)

Test Name	Date	Result	Normal Range
Electrocardiogram(LLT:Electrocardiogram)			
	[redacted]	normal	
	[redacted]	sinus arrhythmia and T wave abnormal	

SUSPECT DRUG(S) INFORMATION (Continuation)

14. SUSPECT DRUG(S)

1.2 TRIDIOL-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)

15. DAILY DOSE(S)

1.2 1 tablet daily

16. ROUTE OF ADMINISTRATION

1.2 Oral

18. THERAPY DATES

1.2 24-Apr-2002 / 30-Aug-2003

19. THERAPY DURATION

1.2 494 Day

DSS

NOV 0 4 2003

NOV 0 3 2003

Individual Safety Report

4245542-7-00-01

For use by user-facilities, ibutors and manufacturers for MANDATORY reporting Berlex Laboratories

Relsys International, Inc.
FDA Facsimile Approval: 30-JUN-1999

Mfr report # CO-SHR-03-017632

LIF/Dist. report #

FDA Use Only

A. Patient information

1. Patient identifier	2. Age at time of event: 40 Years or Date of birth:	3. Sex	4. Weight
[redacted] in confidence		[X] female [ ] male	143.3 lbs or 65.0 kgs

B. Adverse event or product problem

1. [X] Adverse event and/or [ ] Product problem (e.g., defects/malfunctions)

2. Outcomes attributed to adverse event (check all that apply)

- [ ] disability
- [X] death [redacted]
- [ ] congenital anomaly
- [ ] life-threatening
- [ ] required intervention to prevent permanent impairment/damage
- [X] hospitalization - initial or prolonged
- [X] other: Medically Significant

3. Date of event	4. Date of this report
11/17/2003	12/01/2003

5. Describe event or problem

fatal septic shock[Septic shock]
bilateral salpingitis[Salpingitis NOS]
myometritis[Myometritis]
leucopenia with 40% "cayados" (drop)[Leukopenia NOS]
dyspnea, increased respiratory difficulties[Dyspnoea NOS]
abdominal pain in right hypochondrium[Abdominal pain NOS]

Case Description:
A health care professional reported the occurrence of fatal septic shock in a 40 year-old female who received levonorgestrel-releasing intrauterine system (Mirena).

The patient's past medical history included no previous deliveries. No concurrent medical conditions were specified other than the patient being somewhat overweight (BMI = 27). No co-suspect medications or concomitant medications were reported.
continued in additional info section...

6. Relevant tests/laboratory data, including dates

#1 [redacted] Liver test , changes noted (unspecified)
#2 [redacted] Coagulation test (continued)
#3 [redacted] Leucocytes abnormal (continued)

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

#1 UNK, Social Circumstance, Nulli gravida
#2 [redacted] to [redacted] Past Drug Name, (continued)
#3 [redacted] to [redacted] AE Procedure, (continued)
#4 [redacted] to [redacted] AE Procedure, (continued)
continued in additional info section...

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)

#1. Mirena(LEVONORGESTREL) (continued)
#2.

2. Dose, frequency & route used	3. Therapy dates (if unknown, give duration)
#1. 20 (continued)	#1. 11/13/2003 to 11/18/2003
#2.	#2.

4. Diagnosis for use (indication)	5. Event abated after use stopped or dose reduced
#1. Menorrhagia	#1. [ ] yes [ ] no [X] doesn't apply
#2.	#2. [ ] yes [ ] no [ ] doesn't apply

6. Lot # (if known)	7. Exp. date (if known)	8. Event reappeared after reintroduction
#1. UNK	#1. UNK	#1. [ ] yes [ ] no [X] doesn't apply
#2.	#2.	#2. [ ] yes [ ] no [ ] doesn't apply

9. NDC # - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)

NONE UNK to UNK

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)

Berlex Laboratories
Harri Helajarvi, M.D.
Director, Medical Assessment
harri.helajarvi@berlex.com
Fax: +1 973 305 5315
Global Med. Safety Surveillance, 6 West Belt
Wayne, NJ 07470-6806 UNITED STATES

2. Phone number: +1 8882375394

3. Report source (check all that apply)

- [X] foreign COL
- [ ] study
- [ ] literature
- [ ] consumer
- [X] health professional
- [ ] user facility
- [ ] company representative
- [ ] distributor
- [ ] other:

4. Date received by manufacturer	5. (A)NDA # NDA 21-225
11/19/2003	IND #
6. If IND, protocol #	PLA #
	pre-1938 [ ] yes
7. Type of report (check all that apply)	OTC product [ ] yes
[ ] 5-day [X] 15-day	
[ ] 10-day [ ] periodic	
[X] initial [ ] follow-up #	

8. Adverse event term(s)

Septic shock, Salpingitis NOS, Myometritis, Leukopenia NOS, Dyspnoea NOS, Abdominal pain NOS

9. Mfr. report number: CO-SHR-03-017632

E. Initial reporter

1. Name & address: UNK

phone # UNK

2. Health professional ?	3. Occupation	4. Initial reporter also sent report to FDA
[X] yes [ ] no	Health Care Professional	[ ] yes [ ] no [X] unk

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

FDA

3500A - Facsimile

Additional Information

B5. EVENT DESCRIPTION (cont.)

On 13 Nov 2003, Mirena was inserted for menorrhagia.

Approximately 4 days following insertion, the patient was hospitalized for abdominal pain in the right hypochrondrium, with dyspnea. Abdominal CT and ultrasound ruled out biliary disease and any abdominal abscess. Twelve hours following admission, the patient experienced changes in her liver and coagulation tests (results not specified) and leucopenia with 40% "cayados" (drop) with increased respiratory difficulty. Repeat CT and abdominal ultrasound were unremarkable. A laparotomy was performed with the following finding: myometritis and bilateral salpingitis; no uterine or intestinal perforation was noted. Treatment included a hysterectomy, left salpingo-oophorectomy and right salpingectomy. Approximately six hours following procedure, the patient presented with hemodynamic impairment, septic shock and died on 18 Nov 2003.

An autopsy was performed with the recorded cause of death noted as septic shock.

Reporter's Comment:
The reporting health care professional considered that the event was possibily related to treatment with Mirena.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
2	[redacted]	Coagulation test changes noted (unspecified)		
3	[redacted]	Leucocytes abnormal leucopenia with 40% of "cayados"		

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
2	[redacted]	Past Drug Name T CU 380A	No similar reaction observed.
3		AE Procedure Computerised tomogram	Ruled out biliary disease or abdominal abscess; upon repeat no abnormal findings noted.
4		AE Procedure Ultrasound abdomen	Ruled out biliary disease or abdominal abscess; upon repeat no abnormal findings noted.
5		AE Procedure Laparotomy	Myometritis and bilateral salpingitis were noted. No uterine or intestinal perforation was seen.
6		AE Procedure Hysterectomy NOS	
7		AE Procedure Salpingo-oophorectomy unilateral	left
8		AE Procedure Salpingectomy	right
9	UNK	Concurrent Condition Overweight	Body Mass Index = 27 (65 kg, 157 cm)

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 µg/day, cont, Intra-uterine

DSS

DEC 0 2 2003

DEC 0 2 2003

Individual Safety Report

4382494-3-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

For use by user-facilities, distributors and manufacturers for MANDATORY reporting
Berlex Laboratories

Page 1 of 2

Relays International, Inc.
FDA Facsimile Approval: 30-JUN-1999

Mfr report # CH-2004-025211
UF/Dist report #
FDA Use Only

A. Patient Information

1. Patient identifier [redacted] In confidence
2. Age at time of event: 34 years or Date of birth: [redacted]
3. Sex: ☒ female ☐ male
4. Weight: 220.5 lbs or 100.0 kgs

B. Adverse event or product problem

1 ☒ Adverse event and/or ☐ Product problem(e.g., defects/malfunction)

2. Outcomes attributed to adverse event (check all that apply)
☒ death [redacted] ☐ disability
☐ life-threatening ☐ congenital anomaly
☒ hospitalization - initial or prolonged ☐ required intervention to prevent permanent impairment/damage
☐ other:

3. Date of event: 04/02/2004
4. Date of this report: 06/16/2004

5. Describe event or problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any seperated by commas)
glioblastoma (severe headache, brain edema, death)[Glioblastoma]

Case Description:
A treating physician reported on 11 May 2004 the occurrence of headache and death in a female who was prescribed levonorgestrel IUD (Mirena).

Concurrent medical conditions and concomitant medications were not reported.

The patient had Mirena inserted for contraception in [redacted].

Before Easter she complained about headache but did not want Mirena to be removed. The patient has been hospitalized, but the cause of the headache was diagnosed to be "psychological". continued in additional info section...

6. Relevant tests/laboratory data, including dates
NI

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 UNK, AE Dx procedure, Computerised tomogram abnormal (CT; suspected thalamus infarction and thrombosis basilaris.)

D53

JUN 21 2004

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

FDA

3500A - Facsimile

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1. Mirena(LEVONORGESTREL) (continued)
#2.

2. Dose, frequency & route used
#1. 20 (continued)
#2.

3. Therapy dates (if unknown, give duration)
#1. 11/--/2003, duration UNK
#2.

4. Diagnosis for use (indication)
#1. Contraception
#2.

5. Event abated after use stopped or dose reduced
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

6. Lot# (if known)
#1. UNK
#2.

7. Exp. date (if known)
#1. UNK
#2.

8. Event reappeared after reintroduction
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

9. NDC# - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
NI

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Berlex Inc.
Harri Helajarvi, M.D.
Director, Medical Assessment
harri.helajarvi@berlex.com
Fax: +1 973 305 5315
Global Med. Safety Surveillance, 6 West Belt
Wayne, NJ 07470-6806 UNITED STATES

2. Phone number: +1 8882375394

3. Report source (check all that apply)
☒ foreign CHE
☐ study
☐ literature
☐ consumer
☒ health professional
☐ user facility
☐ company representative
☐ distributor
☐ other:

4. Date received by manufacturer: 06/14/2004

5. (A)NDA # NDA 21-225
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ periodic
☐ initial ☒ follow-up # 1

8. Adverse event term(s)
Glioblastoma

9. Mfr. report number
CH-2004-025211

E. Initial reporter

1. Name & address
Name and address withheld.

phone # Withheld

2. Health professional ?
☒ yes ☐ no

3. Occupation
physician

4. Initial reporter also sent report to FDA
☐ yes ☐ no ☒ unk

JUN 17 2004

16-Jun-2004 07:57

Additional Information

B5. EVENT DESCRIPTION (cont.)

After Easter, the treating physician has seen an obituary notice in the newspaper and is now contacting the physicians in the hospital to find out more about the cause of death of this patient.

Further information has been requested.

Suppl. (14 Jun 2004): Patient's demographics added. Patient was 34 years old, patient's weight was 100 kg. Reaction onset was 2 Apr 2004. Patient has had severe headache for one week. She vomited once during the night. Afterwards pronounced brain oedema. CT findings: suspected thalamus infarction and thrombosis basilaris. Patient died on [redacted]

Report from the pathology: brain tumor / glioblastoma.

Reporter's Comment:
Suppl. (14 Jun 2004): Reporter's opinion: No causal relationship with Mirena

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 µg/day, cont, intra-uterine

DSS

JUN 2 1 2004

JUN 1 7 2004

Individual Safety Report

N 4462728-7-00-01

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

-facilities, ufacturers for ...ATORY reporting Berlex Laboratories

Page 1 of 2

Reisys International, Inc.
FDA Facsimile Approved: 30-JUN-1999

Mfr report # US-2004-028202
UF/Dist report #
FDA Use Only

A Patient Information

1. Patient identifier	2. Age at time of event:	3. Sex	4. Weight
[redacted] in confidence	24 years or Date of birth: [redacted]	☒ female ☐ male	240.0 lbs or 108.8 kgs

B Adverse event or product problem

1. ☒ Adverse event and/or ☐ Product problem(e.g., defects/malfunction)

2. Outcomes attributed to adverse event (check all that apply)

- ☒ death [redacted]
- ☐ life-threatening
- ☒ hospitalization - initial or prolonged
- ☐ disability
- ☐ congenital anomaly
- ☐ required intervention to prevent permanent impairment/damage
- ☐ other:

3. Date of event: 06/09/2004

4. Date of this report: 09/24/2004

5. Describe event or problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any seperated by commas)

blood clots in the brain (severe headache, vomiting, lethargy)[Cerebral thrombosis]
Hemorrhagic stroke[Haemorrhagic stroke]
Heart failure[Cardiac failure]

Case Description:
A nurse reported the occurrence of a fatal blood clots in the brain with a severe headache, vomiting, and lethargy in an overweight 24 year-old Caucasian female who received ethinyl estradiol/levonorgestrel (Levlen 28). The patient had no significant past medical history, reportedly had no health problems and took no concomitant medications. She was a non-smoker and had no allergies. In MAR 2004, the patient initiated Levlen 28 for contraception. Approximately 3 months later on [redacted], the patient experienced severe headache, vomiting, and lethargy. She was transported to the emergency room by the family and was subsequently hospitalized. The
continued in additional info section...

6. Relevant tests/laboratory data, including dates
NI

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 UNK, allergy (None)
#2 UNK, historical condition (continued)
#3 UNK, social circumstance, Non-smoker
#4 UNK, concurrent condition, Obesity (continued)
continued in additional info section...

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1. Levlen 28(ETHINYLESTRAD (continued)
#2.

2. Dose, frequency & route used
#1. 1 tab(s), (continued)
#2.

3. Therapy dates (if unknown, give duration)
#1. 03/--/2004 to 06/09/2004
#2.

4. Diagnosis for use (indication)
#1. Oral contraception
#2.

5. Event abated after use stopped or dose reduced
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

6. Lot# (if known)
#1. UNK
#2.

7. Exp. date (if known)
#1. UNK
#2.

8. Event reappeared after reintroduction
#1. ☐ yes ☐ no ☒ doesn't apply
#2. ☐ yes ☐ no ☐ doesn't apply

9. NDC# - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
No Concomitant Medication UNK to UNK

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Berlex Laboratories
Harri Helajarvi, M.D.
Director, Medical Assessment
harri.helajarvi@berlex.com
Fax: +1 973 305 5315
Global Med. Safety Surveillance, 6 West Belt
Wayne, NJ 07470-6806 UNITED STATES

2. Phone number: +1 8882375394

3. Report source (check all that apply)
☐ foreign ☐ study ☐ literature ☐ consumer ☒ health professional ☐ user facility ☐ company representative ☐ distributor ☐ other:

4. Date received by manufacturer: 09/15/2004

5. (A)NDA # NDA 18-782
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
☐ 5-day ☒ 15-day ☐ 10-day ☐ periodic ☐ initial ☒ follow-up # 1

8. Adverse event term(s)
Cerebral thrombosis, Haemorrhagic stroke, Cardiac failure

9. Mfr. report number
US-2004-028202

E. Initial reporter

1. Name & address: [redacted] UNITED STATES
phone # [redacted]

DSS

SEP 2 9 2004

2. Health professional ? ☒ yes ☐ no

3. Occupation: nurse

4. Initial reporter also sent report to FDA ☐ yes ☐ no ☒ unk

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

3500A - Facsimile

24-Sep-2004 08:07

SEP 2 7 2004

Additional Information

B5. EVENT DESCRIPTION (cont.)

patient reportedly died from blood clots in the brain on [redacted] Treatment was not specified.

Suppl. (15 SEP 2004): On 01 MAY 2004, the patient initiated Levlen 28 for contraception (correction from previous report). The 24 year-old obese (correction from previous report) patient also experienced a massive stroke identified on a CT scan on [redacted] It was determined the patient experienced a hemorragic stroke after the rapid development of the blood clots. There was no known previous history of deep vein thrombosis, cerebral vascular accident, or coronary artery disease. The patient was treated with unspecified "clot busting medication" and underwent a surgical procedure to insert a shunt to drain fluid. A nurse confirmed the patient's date of death was [redacted].

Suppl. (23 SEP 2004): The nurse stated the morbidly obese patient (BMI = 43.9) did not have any infection and was a "healthy" female. She also stated the physician did not identify any coagulopathy or coagulation problems. The death certificate reportedly stated the patient died from a hemorrhagic stroke due to a blood clot that resulted in heart failure.

No additional information is expected.

Case closed.

Reporter's Comment:
The nurse stated the physician suspected a probable relationship between the patient's death and treatment with Levlen 28 because the patient developed blood clots rapidly which caused a hemorrhagic stroke that ultimately lead to her death and heart failure.

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
2	UNK	historical condition	Patient had no reported health problems
4	UNK	concurrent condition Obesity	Suppl. (15 SEP 2004): BMI = 43.9 (108.8 kg, 157.5 cm), morbid obesity
5	[redacted] UNK	AE Dx procedure Computerised tomogram abnormal	Suppl. (15 SEP 2004): Showed a massive stroke
6	UNK	AE Tx procedure Shunts	Suppl. (15 SEP 2004):
7	--/--/1999 --/--/2004	past drug name DEPO PROVERA	Suppl. (15 SEP 2004):

C1. Name (cont.)
Suspect Medication #1: Levlen 28(ETHINYLESTRADIOL, LEVONORGESTREL) coated tablet

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 1 tab(s), 1x/day, Oral

DSS

SEP 29 2004

SEP 27 2004

Wyeth

INTERNATIONAL ADVERSE EXPERIENCE REPORT

Individual Safety Report

4596309-1-00-01

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH Day	Month	Year	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET Day	Month	Year
	France				32Yr	F	00	OCT	2004

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM(LLT:ACUTE MASSIVE PULMONARY EMBOLISM); Cardio-respiratory arrest(LLT:Cardio-respiratory arrest)
[LLT = Lowest Level Term]

Information was received from a healthcare professional via French regulatory authority (AFSSAPS) regarding a 32-year-old female patient who received Adepal (0.15mg levonorgestrel/0.03mg ethinyl estradiol/0.2mg levonorgestrel/0.04mg ethinyl estradiol tablet) therapy and experienced massive pulmonary embolism and cardio-respiratory arrest.
MEDICAL HISTORY:
The patient's concurrent illness includes varicose vein for which she underwent varicose vein operation (in [redacted]. The patient had a body mass index of 27, she did not suffer from dyslipidemia or arterial hypertension, she had no personal or family history of thrombosis.

(cont'd)

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED A PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- [X] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA

See following page.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 ADEPAL (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET, 0)

(cont'd)

15. DAILY DOSE(S)

#1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINSTRATION

#1 Oral

17. INDICATION(S) FOR USE

#1 Contraception(LLT:Contraception)

18. THERAPY DATES (FROM/TO)

#1 Unknown

19. THERAPY DURATION

#1 several years

20. DID REACTION ABATE AFTER STOPPING DRUG?

- [ ] YES [ ] NO [X] N/A

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

- [ ] YES [ ] NO [X] N/A

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

LOVENOX (HEPARIN-FRACTION, SODIUM SALT), one injection of 0.20 ml, 00-Oct-2004 / 00-Oct-2004

RECEIVED
FEB 23 2005

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

CONCURRENT CONDITIONS:
Varicose vein(LLT:Varicose veins of lower extremities)

PAST CONDITIONS:
Varicose vein operation(LLT:Varicose vein operation)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
P.O. Box 7667
Philadelphia, PA 19101-7667

OTHER REFERENCE NUMBERS:
Reg Authority Ref Num - TS0500028

Local Marketing No.: #1 NDA 19-192

24b. MFR CONTROL NO.: FRWYE444721FEB05

24c. DATE RECEIVED BY MANUFACTURER: 21-Feb-2005

24d. REPORT SOURCE

- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [X] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [ ] LICENSE

Date of this report: 25-Feb-2005

25a. REPORT TYPE

- [X] INITIAL
- [ ] FOLLOWUP

FEB 25 2005
DATE SENT TO FDA

DSS

FEB 28 2005

MAR - 1 2005

Wyeth

Wyeth Pharmaceuticals Inc.
Box 8299
PHILADELPHIA, PA 19101

Individual Safety Report
4628502-3-00-01

INTERNATIONAL ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET (Day / Month / Year)
	Sweden		33Yr	F	

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM (LLT: PULMONARY EMBOLISM)
[LLT = Lowest Level Term]

This case was reversioned in order to correct data entry errors.
Information was received from a healthcare professional via a regulatory authority regarding a 33-year-old female patient who received Trinordiol (0.05mg levonorgestrel/0.03mg ethinyl estradiol/0.075mg levonorgestrel/0.04mg ethinyl estradiol/0.125mg levonorgestrel/0.03mg ethinyl estradiol tablet) therapy and experienced pulmonary embolism.
MEDICAL HISTORY:
Relevant medical history was not provided.
PRODUCT DETAILS:
Indication, dose and dates of Trinordiol therapy were not provided.
CONCOMITANT THERAPY:
(cont'd)

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED A PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

13. RELEVANT TESTS/LABORATORY DATA
None Provided.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))
#1 TRINORDIOL (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET)

15. DAILY DOSE(S)
#1

16. ROUTE(S) OF ADMINSTRATION
#1 Unknown

17. INDICATION(S) FOR USE
#1

18. THERAPY DATES (FROM/TO)
#1 Unknown

19. THERAPY DURATION
#1 Unknown

20. DID REACTION ABATE AFTER STOPPING DRUG?
[ ] YES [ ] NO [X] N/A

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
[ ] YES [ ] NO [X] N/A

III. CONCOMITANT DRUG(S) AND HISTORY

RECEIVED
APR 04 2005
CDR / CDER

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)
Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)
UNK

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
WYETH PHARMACEUTICALS INC.
P.O. Box 7667
Philadelphia, PA 19101-7667

APR 04 2005

OTHER REFERENCE NUMBERS:
Regulatory Authority (HP) - 032127

Local Marketing No.
#1 NDA 19-192

24b. MFR CONTROL NO.
SEWYE526423MAR05

APR 01 2005
DATE SENT TO FDA

DSS
APR 05 2005

24c. DATE RECEIVED BY MANUFACTURER
21-Mar-2005

24d. REPORT SOURCE
[ ] STUDY [ ] CONSUMER
[ ] LITERATURE [X] REGULATORY AUTHORITY
[X] HEALTH PROFESSIONAL [ ] LICENSE

Date of this report
01-Apr-2005

25a. REPORT TYPE
[X] INITIAL [ ] FOLLOWUP

Individual Safety Report — Wyeth Pharmaceuticals Inc.

4686111-4-00-01

IN

ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET (Day / Month / Year)
[redacted]	Canada		26Yr	F	

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED A PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

7. DESCRIBE EXPERIENCE(S)

MESENTERIC OCCLUSION(LLT:MESENTERIC ARTERY THROMBOSIS); Aspiration(LLT:Aspiration)
[LLT = Lowest Level Term]

Additional information was received from a healthcare professional regarding patient demographics and autopsy results.
Information was received from a healthcare professional regarding a 26-year-old female patient who received Alesse-28 (0.1mg levonorgestrel/0.02mg ethinyl estradiol/inert tablet) therapy and experienced fresh thrombosis of the superior mesenteric artery and died after using Alesse for approximately 3 months.
MEDICAL HISTORY:
The patient's concurrent illnesses include obesity, smoker and alcohol use.
PRODUCT DETAILS:
Indication for Alesse-28 was menorrhagia. Duration of therapy was 3 months. Dose regimen was 1 tablet 1 time per day (oral).
(cont'd)

13. RELEVANT TESTS/LABORATORY DATA

None Provided.

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 ALESSE-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG? [ ] YES [ ] NO [X] N/A

15. DAILY DOSE(S)	16. ROUTE(S) OF ADMINSTRATION
#1 1 Tablet 1x per 1 Day	#1 Oral

17. INDICATION(S) FOR USE

#1 Menorrhagia(LLT:Menorrhagia)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? [ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)	19. THERAPY DURATION
#1 Unknown	#1 3 Mth

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

NONE (NONE), Unknown

RECEIVED
JUN 0 6 2005
CDR / CDER

23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)

CONCURRENT CONDITIONS:
Obesity(LLT:Obesity); Smoker(LLT:Smoker); Alcohol use(LLT:Alcohol use)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH PHARMACEUTICALS INC.
P.O. Box 7667
Philadelphia, PA 19101-7667

OTHER REFERENCE NUMBERS:
Affiliate Ref Num

Local Marketing No.	24b. MFR CONTROL NO.
#1 NDA 20-683	HQWYE731113MAY05

24c. DATE RECEIVED BY MANUFACTURER: 24-May-2005

24d. REPORT SOURCE: [ ] STUDY [ ] CONSUMER [ ] LITERATURE [ ] REGULATORY AUTHORITY [X] HEALTH PROFESSIONAL [ ] LICENSE

Date of this report: 03-Jun-2005

25a. REPORT TYPE: [ ] INITIAL [X] FOLLOWUP

JUN 0 3 2005
DATE SENT TO FDA

DSS
JUN - 8 2005

JUN 0 6 2005

Individual Safety Report

4686111-4-00-02

ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: HQWYE731113MAY05

Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

CONCOMITANT THERAPY:
Patient was not taking concomitant therapy.
EVENT DETAILS:
The autopsy cause of death was reported as "ischemic bowel disease with extensive ischemia of the small bowel due to fresh thrombosis of the superior mesenteric artery (mesenteric occlusion) associated with terminal aspiration (aspiration) of foreign material". No further details were provided.

4734121-0-00-01

MEDWATCH

THE FDA MEDICAL PRODUCTS REPORTING PROGRAM

use by user-facilities,
ors and manufacturers for
NDATORY reporting

Page 1 of 4

Reisys International, Inc
FDA Facsimile Approval: 11-JUN-1999

Mfr report # 005287

UF/Dist report #

FDA Use Only

A. Patient Information

1. Patient identifier [redacted] In confidence

2. Age at time of event: 31 Years
or Date of birth: UNK

3. Sex: ☒ female ☐ male

4. Weight: UNK lbs or UNK kgs

B. Adverse event or product problem

1 ☒ Adverse event and/or ☐ Product problem(e.g., defects/malfunction)

2. Outcomes attributed to adverse event (check all that apply)

☒ death [redacted]
☒ life-threatening
☐ hospitalization - initial or prolonged
☐ disability
☐ congenital anomaly
☐ required intervention to prevent permanent impairment/damage
☒ other: Medically Significant

3. Date of event: --/--/2004

4. Date of this report: 07/28/2005

5. Describe event or problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any seperated by commas)

Blood clot in the leg[Deep vein thrombosis]
Blood clot in heart[Intracardiac thrombus]
Blood clot in lung[Pulmonary embolism]
Cardiac arrest[Cardiac arrest]
Brain damage[Brain damage]

Case Description:
Information was received regarding a 31 year old female patient that was prescribed Seasonale (levonorgestrel, ethinylestradiol) Tablets 0.15/0.03 mg for an unknown indication. Therapy with Seasonale was initiated in the Fall of 2004. It was reported the patient developed a blood clot in the leg that traveled to her heart causing cardiac arrest. She was resuscitated, but suffered severe brain damage. The clot traveled to her lungs. Five weeks later, on [redacted] she expired. No additional information was available.

continued in additional info section...

6. Relevant tests/laboratory data, including dates
NI

7. Other relevant history, including preexisting medical conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
NI

JUL 29 2005

C. Suspect medication(s)

1. Name (give labeled strength & mfr/labeler, if known)
#1. Seasonale(LEVONORGESTRE (continued)
#2.

2. Dose, frequency & route used
#1. UNK, UNK, Oral
#2.

3. Therapy dates (if unknown, give duration)
#1. --/--/2004, duration UNK
#2.

4. Diagnosis for use (indication)
#1. UNK
#2.

5. Event abated after use stopped or dose reduced
#1. ☐ yes ☐ no ☐ doesn't apply UNK
#2. ☐ yes ☐ no ☐ doesn't apply

6. Lot# (if known)
#1. UNK
#2.

7. Exp. date (if known)
#1. UNK
#2.

8. Event reappeared after reintroduction
#1. ☐ yes ☐ no ☐ doesn't apply UNK
#2. ☐ yes ☐ no ☐ doesn't apply

9. NDC# - for product problems only (if known)

10. Concomitant medical products and therapy dates (exclude treatment of event)
NI

G. All Manufacturers

1. Contact office - name/address (& mfring site for devices)
Barr Laboratories
Salvatore Peritore, R.Ph.

400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677-7668 UNITED STATES

2. Phone number
2019303302

3. Report source (check all that apply)
☐ foreign
☐ study
☒ literature
☐ consumer
☒ health professional
☐ user facility
☐ company representative
☐ distributor
☐ other:

4. Date received by manufacturer
07/26/2005

5. (A)NDA # 21-544
IND #
PLA #
pre-1938 ☐ yes
OTC product ☐ yes

6. If IND, protocol #

7. Type of report (check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ periodic
☒ initial ☐ follow-up #

8. Adverse event term(s)
Deep vein thrombosis, Intracardiac thrombus, Pulmonary embolism, Cardiac arrest, Brain damage

9. Mfr. report number
005287

E. Initial reporter

1. Name & address
[redacted]
UNITED STATES

phone # [redacted]

2. Health professional ?
☒ yes ☐ no

3. Occupation
Other Health Professional

4. Initial reporter also sent report to FDA
☐ yes ☐ no ☒ unk

FDA
3500A - Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

28-Jul-2005 12:35

DSS

AUG 0 9 2005

DSS

Additional Information

B5. EVENT DESCRIPTION (cont.)

MedWatch Case Comment:
Submission of this 15-day report does not constitute an admission that the reported event is an unlabeled event.

C1. Name (cont.)
Suspect Medication #1: Seasonale(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet, 0.15/0.03mg

G3. Report source literature description

Journal: Virginia Pilot Newspaper 07/26/2005
Author: Mary Ann Bromley
Title: Unnecessary tragedies from the birth control patch

U.S. Department of Health and Human Services

Individual Safety Report

4743529-9-00-01

VOLUNTARY reporting of events and product problems

CDER

Page 1 of 1 CBER

Form Approved: OMB No. 0910-0291, Expires: 03/31/05
See OMB statement on reverse.

FDA USE ONLY

Triage unit sequence # 255859

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. Patient Identifier: [redacted] In confidence
2. Age at Time of Event: or Date of Birth: [redacted]
3. Sex: ☑ Female ☐ Male
4. Weight: 168 lbs or ____ kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☑ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)
- ☑ Death: [redacted] (mo/day/yr)
- ☐ Life-threatening
- ☐ Hospitalization - Initial or prolonged
- ☐ Disability
- ☐ Congenital Anomaly
- ☐ Required Intervention to Prevent Permanent Impairment/Damage
- ☐ Other: _____

3. Date of Event (mo/day/year): 6/23/05

4. Date of This Report (mo/day/year): 8/4/05

5. Describe Event or Problem

Fatal pulmonary thromboembolism of deep venous thrombosis.

DSS

AUG 11 2005

6. Relevant Tests/Laboratory Data, Including Dates

[redacted] - Cardiac echo - enlarged right ventricle
- Elevated D-dimer
- Improvement of respiratory function after TNK therapy
- Irreversible anoxic brain injury.

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

[redacted] (Post mortem)
Factor V Leiden heterozygote
MTHFR C677T heterozygote

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)
#1 Levora-28
#2

2. Dose, Frequency & Route Used
#1 Once daily, oral
#2

3. Therapy Dates (If unknown, give duration) from/to (or best estimate)
#1 ~7 years
#2

4. Diagnosis for Use (Indication)
#1 Birth control
#2

5. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☑ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot # (if known)
#1 TEV003
#2

7. Exp. Date (if known)
#1 3/07
#2

8. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☑ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC# (For product problems only)
- -

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
Oral supplements: Papaya Enzyme, Milk Thistle, Probiotic acidophilus, Lecithin, Esker-C, Colloidal Silver

D. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Type of Device
3. Manufacturer Name, City and State
4. Model # / Lot # / Catalog # / Expiration Date (mo/day/yr) / Serial # / Other #
5. Operator of Device: ☐ Health Professional ☐ Lay User/Patient ☐ Other:
6. If Implanted, Give Date (mo/day/yr)
7. If Explanted, Give Date (mo/day/yr)
8. Is this a Single-use Device that was Reprocessed and Reused on a Patient? ☐ Yes ☐ No
9. If Yes to Item No. 8, Give Name and Address of Reprocessor

RECEIVED

AUG 10 2005

MEDWATCH CTU

10. Device Available for Evaluation? (Do not send to FDA) ☐ Yes ☐ No ☐ Returned to Manufacturer on: _____ (mo/day/yr)
11. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)

E. REPORTER (See confidentiality section on back)

1. Name and Address: [redacted] MD [redacted] USA
Phone #: [redacted]
2. Health Professional? ☑ Yes ☐ No
3. Occupation: Medical Examiner
4. Also Reported to: ☐ Manufacturer ☐ User Facility ☐ Distributor/Importer
5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

FDA

Mail to: **MedWatch** 5600 Fishers Lane Rockville, MD 20852-9787 -or- FAX to: 1-800-FDA-0178

U.S. Department of Health and Human Services

Individual Safety Report

4954000-3-00-01

Adverse Event Reporting Program

...Focus by user-facilities, ...utors and manufacturers ATORY reporting ...lerlex Inc.

Page 1 of 2

Relays International, Inc., FDA Facsimile Approval: 30-JUN-1998

Mfr Report # GB-2006-005656

UF/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier: -- In confidence

2. Age at Time of Event: UNK or Date of Birth: UNK

3. Sex: ☒ Female ☐ Male

4. Weight: UNK lbs or UNK kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

☒ Death UNK (mo/day/yr)
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Disability
☐ Congenital Anomaly
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Other:

3. Date of Event (mo/day/year): UNK

4. Date of This Report (mo/day/year): 03/21/2006

5. Describe Event or Problem

Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

rapid course of septicaemia (ascending genital infection via post-mortem, Group A streptococcal sepsis with micro-abscess in several body areas, i.e. lung tissue)[Streptococcal sepsis]

Case Description:
A health care professional reported on 14 Mar 2006 the occurrence of a rapid course of septicaemia (ascending genital infection identified via post-mortem, Group A Streptococcal sepsis with micro-abscess in several body areas, e.g. lung tissue) resulting in death in a female patient in her 40's who was prescribed levonorgestrel (Mirena, IUS).

The patient's past medical history, concurrent medical conditions, and concomitant medications were not reported. It was not reported if Mirena was used previously and tolerated.

On an unspecified date in 2003 the patient received
continued in additional info section...

6. Relevant Tests/Laboratory Data, Including Dates
NI

RECEIVED MAR 2 2 2006 CDER/CDR

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
NI

DSS MAR 2 3 2006

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)
#1. Mirena(LEVONORGESTREL) (continued)
#2.

2. Dose, Frequency & Route Used
#1. 20 (continued)
#2.

3. Therapy Dates (If unknown, give duration) from/to (or best estimate)
#1. --/--/2003, duration UNK
#2.

4. Diagnosis for Use (Indication)
#1. UNK
#2.

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot # (If known)
#1. UNK
#2.

7. Exp. Date (If known)
#1. UNK
#2.

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
NI

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Berlex Inc.
Stephen Heaton, M.D.
Director, Medical Assessment
Stephen_Heaton@Berlex.com
Fax: +1 973 487 2914
Global Med. Safety Surveillance, P.O. Box 1000
Montville, NJ 07045-1000 UNITED STATES

2. Phone Number: +1 8882375394

3. Report Source (Check all that apply)
☒ Foreign GBR
☐ Study
☐ Literature
☐ Consumer
☒ Health Professional
☐ User Facility
☐ Company Representative
☐ Distributor
☐ Other:

4. Date Received by Manufacturer (mo/day/yr): 03/14/2006

5. (A)NDA # NDA 21-225
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ Periodic
☒ Initial ☐ Follow-up #

8. Adverse Event Term(s)
Streptococcal sepsis

9. Manufacturer Report Number
GB-2006-005656

E. INITIAL REPORTER

1. Name and Address
Name and address withheld.

Phone # Withheld

2. Health Professional? ☒ Yes ☐ No

3. Occupation: health care professional

4. Initial Reporter Also Sent Report to FDA ☐ Yes ☐ No ☒ Unk

FDA 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

21-Mar-2006 06:58

MAR 2 2 2006

DSS MAR 2 3 2006

Additional Information

B5. EVENT DESCRIPTION (cont.)

levonorgestrel (Mirena) via intra-uterine route of administration for an unspecified indication.

On an unspecified date the patient developed a rapid course of septicaemia which was identified as an ascending genital infection via post-mortem. The post-mortem established a Group A Streptococcal sepsis with micro-abscesses in several body areas (e.g.lung tissue), resulting in death.

The patient died from the Group A Streptococcal sepsis on an unspecified date.

No additional information was provided. Further information requested and will be furnished upon receipt.

Reporter's Comment:
The reporter did not provide an assessment of the relationship of event to treatment of Mirena.

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 µg/day, cont, Intra-uterine

U.S. Department of Health and Human Services

Individual Safety Report

4975478-5-00-01

...se by user-facilities, ...stributors and manufacturers ...NDATORY reporting

Berlex Inc.

Relsys International, Inc., FDA Facsimile Approval: 30-JUN-1999

Mfr Report # GB-2006-005656

Mfr/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event: / or Date of Birth:	3. Sex	4. Weight
-- In confidence	42 years / UNK	☒ Female ☐ Male	156.6 lbs or 71.0 kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

- ☒ Death [redacted] (mo/day/yr)
- ☐ Life-threatening
- ☐ Hospitalization - initial or prolonged
- ☐ Disability
- ☐ Congenital Anomaly
- ☐ Required Intervention to Prevent Permanent Impairment/Damage
- ☒ Other: Medically Significant

3. Date of Event (mo/day/year): UNK

4. Date of This Report (mo/day/year): 04/07/2006

5. Describe Event or Problem

Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Group A streptococcal sepsis (unwell,lethargic, dizzy, lightheaded, flulike, diarrhea, temp 39, pulse 100, pulmonary edema, abscess on ovary with coccal bacteria)[Streptococcal sepsis]
pelvic inflamatory disease (both ovaries oedematous and inflammed, falloplan tubes appear oedematous and inflammed, uterus inflammed)[Pelvic inflammatory disease]
peritonitis (peritoneal cavity contained purulent fluid, inflammation of peritoneum)[Peritonitis]
left ovary contained benign cystic teratoma[Dermoid cyst of ovary]
right ovary contained haemorrhagic cyst[Haemorrhagic ovarian cyst]
right adrenal gland showed 20mm nodule[Adrenal mass]

Case Description:
A health care professional reported on 14 Mar 2006 the
continued in additional info section...

CDER/CDR
APR 10 2006
RECEIVED

6. Relevant Tests/Laboratory Data, Including Dates

#1 [redacted] Body temperature 39 , Suppl. ([redacted])
#2 [redacted] Heart rate 100 , Suppl. ([redacted])
#3 [redacted] Blood pressure 120/80 , Suppl. ([redacted])

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)

#1 UNK concurrent condition, (continued)
#2 --/--/1995 to --/--/1995 procedure, (continued)
#3 --/--/1995 to UNK historical condition, (continued)
#4 UNK, procedure, Caesarean section (continued)

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)

#1. Mirena(LEVONORGESTREL) (continued)
#2.

2. Dose, Frequency & Route Used
#1. 20 (continued)
#2.

3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. --/--/2003, duration UNK
#2.

4. Diagnosis for Use (Indication)
#1. UNK
#2.

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot # (If known)
#1. UNK
#2.

7. Exp. Date (If known)
#1. UNK
#2.

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
NI

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)

Berlex Inc.
Stephen Heaton, M.D.
Director, Medical Assessment
Stephen_Heaton@Berlex.com
Fax: +1 973 487 2914
Global Med. Safety Surveillance, P.O. Box 1000
Montville, NJ 07045-1000 UNITED STATES

2. Phone Number: +1 8882375394

3. Report Source (Check all that apply)
☒ Foreign GBR ☐ Study ☐ Literature ☐ Consumer ☒ Health Professional ☐ User Facility ☐ Company Representative ☐ Distributor ☐ Other:

4. Date Received by Manufacturer(mo/day/yr): 03/31/2006

5. (A)NDA # NDA 21-225
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
☐ 5-day ☒ 15-day ☐ 10-day ☐ Periodic ☐ Initial ☒ Follow-up # 1

8. Adverse Event Term(s)
Streptococcal sepsis, Pelvic inflammatory disease, Peritonitis, Dermoid cyst of ovary, Haemorrhagic ovarian
continued in additional info section...

9. Manufacturer Report Number
GB-2006-005656

E. INITIAL REPORTER

1. Name and Address
Name and address withheld.

Phone # Withheld

APR 10 2006

2. Health Professional?	3. Occupation	4. Initial Reporter Also Sent Report to FDA
☒ Yes ☐ No	health care professional	☐ Yes ☐ No ☒ Unk

FDA

3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

DSS

Additional Information

B5. EVENT DESCRIPTION (cont.)

occurrence of a rapid course of septicaemia (ascending genital infection identified via post-mortem, Group A Streptococcal sepsis with micro-abscess in several body areas, e.g. lung tissue) resulting in death in a female patient in her 40's who was prescribed levonorgestrel (Mirena, IUS).

The patient's past medical history, concurrent medical conditions, and concomitant medications were not reported. It was not reported if Mirena was used previously and tolerated.

On an unspecified date in 2003 the patient received levonorgestrel (Mirena) via intra-uterine route of administration for an unspecified indication.

On an unspecified date the patient developed a rapid course of septicaemia which was identified as an ascending genital infection via post-mortem. The post-mortem established a Group A Streptococcal sepsis with micro-abscesses in several body areas (e.g.lung tissue), resulting in death.

The patient died from the Group A Streptococcal sepsis on an unspecified date.

No additional information was provided. Further information requested and will be furnished upon receipt.

Suppl. (31Mar 2006): Additional information provided by the physician including the post-mortem report.

This 42 year-old female patient's medical history included an ovarian cystectomy while pregnant in 1995 and then had a caesarean delivery. There was no other record of any other significant gynecological or obstetric history. There was no other past history of note. The patient's body mass index (BMI) was 24.57. In April 2005 she was noted to have no problems with her IUD.

On [redacted] this patient felt unwell, lethargic, dizzy, lightheaded, had complained of flu-like symptoms for the past 7 days and had diarrhea 4 times in 24 hours before she was seen by a doctor the day before she was found dead. The patient was seen by a physician the night before she died and was described as being fully alert and oriented with a temperature of 39, pulse of 100, blood pressure 120/80, her mouth was dry, her chest was clear, her abdomen was soft and non-tender, there was no neck stiffness or photophobia. A diagnosis of gastroenteritis was made by the physician and the following morning after a sudden deterioration in her health she was found dead at her home in bed on [redacted].

A post-mortem examination was performed on [redacted]. Head and neck examination resulted in normal findings. Chest examination revealed cut lung surfaces expressing straw colored fluid in keeping with pulmonary edema. The lower trachea and main bronchi contained some purulent material. Cardiac examination results were normal. Abdominal examination revealed the peritoneal cavity contained some purulent fluid primarily within the pelvis with inflammation of the peritoneum. The uterus contained an intrauterine contraceptive device. Both ovaries were oedematous and inflamed. The left ovary contained a benign cystic teratoma and the right ovary contained a haemorrhagic cyst. Both fallopian tubes also appeared oedematous and inflamed. One of the ovaries contains a small abscess in which a number of bacteria with a coccal morphology were identified. Sections from the pelvic organs showed inflammation of the uterus, fallopian tubes, and ovaries. The right adrenal gland showed a 20mm diameter nodule and the left appeared normal. Swabs taken from the peritoneum, IUD, and lung tissue showed Group A haemolytic streptococcus present.

Post mortem examination showed the patient died as a result of sepsis following infection with Group A streptococcus. The infection appeared to have been primarily centered within the pelvis involving the uterus., fallopian tubes, and ovaries. As noted, the organism was also isolated from the IUD device.

The post mortem report stated it appeared most likely that the infection of the pelvic organs was a direct result of an ascending genital tract infection and death was directly attributable to Group A streptococcal sepsis which was secondary to pelvic inflammatory disease and peritonitis.

No additional information was reported.

APR 1 0 2006

Reporter's Comment:

DSS

ADD 1 1 2006

The reporter did not provide an assessment of the relationship of event to treatment of Mirena.

B7. OTHER RELEVANT HISTORY

#	Start/Stop Date	Condition Type / Condition	Notes
1	UNK	concurrent condition Body mass index	Suppl. (31 Mar 2006): BMI = 24.57 (71 kg, 170 cm)
2	--/--/1995 --/--/1995	procedure Ovarian cystectomy	Suppl. (31 Mar 2006) Ovarian cystectomy whilst pregnant
3	--/--/1995 UNK	historical condition Pregnancy	Suppl. (31 Mar 2006)
4	UNK	procedure Caesarean section	Suppl. (31 Mar 2006)

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 µg/day, cont, Intra-uterine

G8. ADVERSE EVENT TERMS (cont.)
cyst, Adrenal mass

APR 1 0 2006

DSS
APR 1 1 2006

Individual Safety Report

5060812-0-00-01

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

/OLUNTARY reporting of adverse events, product problems and product use errors

Internet Submission - Page 1

Form Approved: OMB No. 0910-0291, Expires: 10/31/08
See OMB statement on reverse.

FDA USE ONLY
Triage unit sequence # 281347

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event, or Date of Birth:	3. Sex	4. Weight
girl In confidence	20 Years	☑ Female ☐ Male	150 lb or ____ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☑ Adverse Event ☐ Product Problem *(e.g., defects/malfunctions)*
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event *(Check all that apply)*

☑ Death: [redacted] *(mm/dd/yyyy)*
☐ Disability or Permanent Damage
☐ Life-threatening
☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - initial or prolonged
☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event *(mm/dd/yyyy)*	4. Date of this Report *(mm/dd/yyyy)*
	07/19/2006

5. Describe Event, Problem or Product Use Error

my daughter was on seasonale for about 6 wks when she died of a DVT. The doctors said the cause was birth control pills.

RECEIVED
JUL 20 2006
MEDWATCH CTU

More

6. Relevant Tests/Laboratory Data, Including Dates

More

7. Other Relevant History, Including Preexisting Medical Conditions *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

DSS
JUL 21 2006

More

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*

☐ Yes ☑ No ☐ Returned to Manufacturer on: ____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. Name, Strength, Manufacturer *(from product label)*
#1 seasonale unknown
#2

2. Dose or Amount	Frequency	Route
#1		
#2		

3. Dates of Use *(If unknown, give duration)* from/to *(or best estimate)*
#1 12/01/2005 -- 4 to 6 wks [redacted]
#2 --

4. Diagnosis or Reason for Use *(Indication)*
#1 birth control
#2

5. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☑ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

8. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☑ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #	7. Expiration Date
#1	#1
#2	#2

9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name
seasonale
3. Manufacturer Name, City and State

4. Model #	Lot #	5. Operator of Device
Catalog #	Expiration Date *(mm/dd/yyyy)*	☑ Health Professional ☐ Lay User/Patient
Serial #	Other #	☐ Other:

6. If Implanted, Give Date *(mm/dd/yyyy)*	7. If Explanted, Give Date *(mm/dd/yyyy)*

8. Is this a Single-use Device that was Reprocessed and Reused on a Patient?
☐ Yes ☑ No

9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*

My daughter died of a DVT the doctors said was because of the use of seasonale birth control pill. She had been on it for 5 to 6 wks.

More

G. REPORTER *(See confidentiality section on back)*

1. Name and Address
[redacted]

Phone # [redacted]
E-mail [redacted]

2. Health Professional?	3. Occupation	4. Also Reported to:
☐ Yes ☑ No	Other Health	☐ Manufacturer ☐ User Facility ☐ Distributor/Importer

5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

FORM FDA 3500 (8/05) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

Wyeth

Individual Safety Report

5086087-4-00-01

INTERNATIONAL ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS	1a. COUNTRY	2. DATE OF BIRTH (Day / Month / Year)	2a. AGE UNITS	3. SEX	4-6. EXPERIENCE ONSET (Day / Month / Year)
	Sweden	[redacted] / [redacted] / [redacted]	32Yr	F	20 / MAY / 1996

7. DESCRIBE EXPERIENCE(S)

PULMONARY EMBOLISM(LLT:PULMONARY EMBOLISM)
[LLT = Lowest Level Term]

This case was considered medically important.
Information was received from a healthcare professional via a regulatory authority regarding a 32-year-old female patient who received Trinordiol (0.05mg levonorgestrel/0.03mg ethinyl estradiol/0.075mg levonorgestrel/0.04mg ethinyl estradiol/0.125mg levonorgestrel/0.03mg ethinyl estradiol tablet) therapy and experienced pulmonary embolism.
MEDICAL HISTORY:
The patient has a past history of normal delivery, splenectomy, infection (Severe infections the last one six months before the death.) and idiopathic thrombocytopenic purpura. Past therapies included Trinordiol (0.05mg levonorgestrel/0.03mg ethinyl estradiol/0.075mg levonorgestrel/0.04mg ethinyl
(cont'd)

13. RELEVANT TESTS/LABORATORY DATA
None Provided.

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- [X] PATIENT DIED
- [ ] INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- [ ] INVOLVED A PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY
- [ ] LIFE THREATENING
- [ ] NONE OF THE ABOVE
- [ ] RECOVERED

II. SUSPECT DRUG(S) INFORMATION

14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))
#1 TRINORDIOL (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET)

20. DID REACTION ABATE AFTER STOPPING DRUG?
[ ] YES [ ] NO [X] N/A

15. DAILY DOSE(S)
#1 unknown

16. ROUTE(S) OF ADMINSTRATION
#1 Oral

17. INDICATION(S) FOR USE
#1 Prophylaxis(LLT:Prevention)

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?
[ ] YES [ ] NO [X] N/A

18. THERAPY DATES (FROM/TO)
#1 13-Nov-1995 / UNK

19. THERAPY DURATION
#1 Unknown

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)
ZOLOFT (SERTRALINE HYDROCHLORIDE), Unknown

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AUG 17 2006
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23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergics, pregnancy with last month of period, etc.)
PAST CONDITIONS:
Normal delivery(LLT:Normal birth); Idiopathic thrombocytopenic purpura(LLT:Idiopathic thrombocytopenic purpura); Infection(LLT:Infection); Splenectomy(LLT:Splenectomy)

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
WYETH PHARMACEUTICALS INC.
P.O. Box 7667
Philadelphia, PA 19101-7667

OTHER REFERENCE NUMBERS:
Regulatory Authority (HP) - 062587
Affiliate Ref Num - S06272

Local Marketing No.
#1 NDA 19-192

24b. MFR CONTROL NO.
SEWYE670311AUG06

24c. DATE RECEIVED BY MANUFACTURER
10-Aug-2006

24d. REPORT SOURCE
- [ ] STUDY
- [ ] CONSUMER
- [ ] LITERATURE
- [X] REGULATORY AUTHORITY
- [X] HEALTH PROFESSIONAL
- [ ] LICENSE

DSS
AUG 18 2006

AUG 16 2006
DATE SENT TO FDA

Date of this report
16-Aug-2006

25a. REPORT TYPE
- [X] INITIAL
- [ ] FOLLOWUP

AUG 17 2006

Wyeth

Individual Safety Report

5086087-4-00-02

INTERNATIONAL ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: SEWYE678311AUG06

Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

estradiol/0.125mg levonorgestrel/0.03mg ethinyl estradiol tablet).
PRODUCT DETAILS:
Indication for Trinordiol was prophylaxis. Therapy began on 13-Nov-1995. Dose regimen was not provided.
CONCOMITANT THERAPY:
Concomitant therapy included Zoloft (sertraline hydrochloride).
EVENT DETAILS:
The patient experienced pulmonary embolism (pulmonary embolism) on [redacted]. The patient experienced stomach sickness on 17-May-2006. On the morning on [redacted] the patient experienced abdominal pain, nausea, vomit, ready to faint and respiratory arrest. All resuscitation in the home failed. The patient died on [redacted].
The cause of death was reported as pulmonary embolism and the autopsy cause of death was pulmonary embolism. According to the autopsy they found both new and old clots. The right thigh was swollen. They who made the autopsy thought that the embolism came from the right femoral vein.

5095100-X-00-01

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

For use by user-facilities, importers, distributors and manufacturers for MANDATORY reporting

Ralsys International, Inc., FDA Facsimile Approval 11-JUN 1999

Mfr Report # 007819

Uf/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier [redacted] In confidence

2. Age at Time of Event: 21 Years or Date of Birth: [redacted]

3. Sex: ☒ Female ☐ Male

4. Weight: 125.0 lbs or 56.7 kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

☒ Death [redacted] (mo/day/yr)
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Disability
☐ Congenital Anomaly
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Other:

3. Date of Event (mo/day/year): 02/28/2006

4. Date of This Report (mo/day/year): 08/29/2006

5. Describe Event or Problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Urinary tract infection[Urinary tract infection] ([Dysuria], [Haematuria])
Flu[Influenza] ([Pyrexia], [Chills], [Headache])
Heavy, prolonged menstrual bleeding[Menorrhagia]
Pelvic pain[Pelvic pain]
Bloating[Abdominal distension]
Took unprescribed Amphetamine[Drug use for unknown indication]
Cardiac arrhythmia[Arrhythmia]
Spotting[Metrorrhagia]

Case Description:
Information was received regarding a 21-year-old female patient prescribed Plan B (levonorgestrel tablets, 0.75 mg) for emergency contraception. It was reported the patient had unprotected sexual intercourse on unspecified dates in 2006. The patient took Plan B on 02/28/2006 and 03/29/2006 (dosage
continued in additional info section...

6. Relevant Tests/Laboratory Data, Including Dates
#1 [redacted] Comprehensive Drug Panel (continued)
#2 [redacted] Pregnancy test Negative
#3 [redacted] Rapid Flu test Negative

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AUG 30 2006
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7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
#1 UNK Historical Condition, (continued)
#2 [redacted] to [redacted] Procedure, (continued)
#3 [redacted] to UNK Historical Condition, (continued)
#4 [redacted] o UNK Historical Condition, (continued)
continued in additional info section...

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known) (Regimens Continued)
#1. Plan B(LEVONORGESTREL) (continued)
#2. ORTHO TRI-CYCLEN LO() (continued)

2. Dose, Frequency & Route Used
#1 2 (continued)
#2. UNK, UNK, Oral

3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. 02/10/2006 to 02/10/2006
#2. 05/31/2005, duration UNK

4. Diagnosis for Use (Indication)
#1. Emergency contraception
#2. Oral contraception

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply UNK

6. Lot # (If known)
#1. T543958
#2. UNK

7. Exp. Date (If known)
#1. UNK
#2. UNK

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply UNK

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
ORAL CONTRACEPTIVE NOS (ORAL CONTRACEPTIVE NOS) UNK to UNK
continued in additional info section...

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Barr Laboratories

400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677-7668 UNITED STATES

2. Phone Number: 2019303302

3. Report Source (Check all that apply)
☐ Foreign
☐ Study
☐ Literature
☒ Consumer
☒ Health Professional
☐ User Facility
☐ Company Representative
☐ Distributor
☐ Other

4. Date Received by Manufacturer(mo/day/yr): 08/16/2006

5. (A)NDA # 21-045
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ Periodic
☐ Initial ☒ Follow-up #2

8. Adverse Event Term(s)
Urinary tract infection, Influenza, Menorrhagia, Pyrexia, Chills, Pelvic pain, Abdominal distension, Headache,
continued in additional info section...

9. Manufacturer Report Number
007819

E. INITIAL REPORTER

1. Name and Address
[redacted]
[redacted]
[redacted] UNITED STATES

Phone # [redacted]

2. Health Professional?
☐ Yes ☒ No

3. Occupation
Consumer

4. Initial Reporter Also Sent Report to FDA
☒ Yes ☐ No ☐ Unk

FDA 3500A (6/2005)

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

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29-Aug-2006 12:06

Additional Information

B5. EVENT DESCRIPTION (cont.)

not provided). It was reported the patient experienced heavy menstrual bleeding, a swollen, and a painful, inflamed pelvic area, on 04/01/2006. The patient developed fever, chills and headache, on 04/04/2006. On [redacted] the patient expired due to cardiac arrhythmia.

06/30/2006- Additional information was received from the reporter. The patient had been taking an unspecified antibiotic for a urinary tract infection. Oral contraceptives were taken daily for at least five years. There were episodes of sexual intercourse in 02/2006 and 03/2006. Plan B (dosage unknown) was taken for contraceptive protection, due to the antibiotic use, on 02/28/2006 and again on 03/29/2006. On 04/01/2006, the patient's menstrual period started, described as a heavy and prolonged flow and included pelvic pain and pelvic swelling described as bloating. On 04/03/2006, the patient took a single dose of an unspecified amphetamine (not prescribed for her) for an unknown indication. She developed fever and chills on 04/04/2006 and started taking Tylenol Cold and Sinus tablets. The campus clinic prescribed unspecified medications (never filled) and instructed her to rest, as she may be "coming down with the flu." On [redacted] the patient expired. Pathology autopsy results indicated cardiac arrhythmia was the cause of death. A Comprehensive Drug Panel report indicated positive amphetamine, caffeine and pseudoephedrine levels. Additional information has been requested.

07/07/2006-See attached reports.

07/24/2006- Final autopsy report was received. See attached report.

08/04/2006- [redacted] records received. Medical history, medication history, correct dates (02/10/2006, 03/27/2006) and Lot numbers for Plan B were provided.

08/16/2006- Additional information was received. Clinic notes were provided. On 02/06/2006, the patient was examined for sore throat and congestion, GuaiMax-D was prescribed. On 02/28/2006, symptoms of a UTI started. Sulfamethoxazole & Trimethoprim was prescribed on 03/04/2006. On 03/08/2006, the patient experienced burning on urination and hematuria. She was resistant to the Sulfamethoxazole & Trimethoprim, therefore Cipro was prescribed on 03/08/2006. Pyridium and Macrobid were prescribed on 03/10/2006. The patient started spotting on 03/29/2006, secondary to Ortho Tri-Cylen Lo and antibiotics. On 04/04/2006, the patient went to the clinic with flu symptoms. A Rapid Flu test was negative. GuaiMax-D and Delsyn were prescribed for probable flu, but never filled. The patient expired on [redacted] No additional information is expected.

MedWatch Case Comment:
Submission of this 15-day report does not constitute an admission that the reported event is an unlabeled event.

B6. LABORATORY DATA

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	[redacted]	Comprehensive Drug Panel 1- Amphetamines 2- Pseudoephedrine 1059 ng/mL 3- Caffeine	Positive	

B7. OTHER RELEVANT HISTORY

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#	Start/Stop Date	Condition Type / Condition	Notes
1	UNK	Historical Condition Light smoking and light alcohol use	
2	[redacted]	Procedure	1-Early autolytic changes, diffuse (explanation-due to body lying in warm room for 24 hours) 2- Pulmonary congestion, marked (explanation- could be due to a number of unspecified reasons) 3- Hepatic congestion and mild chronic inflammation, periportal (explanation- possible early viral hepatitis) 4-Pseudoephedrine 1059 ng/ml (explanation- although high, thought to be non-significant)
	[redacted]	Autopsy report-Cause of	

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AUG 3 1 2006

		death-cardiac arrythmia, Manner of Death-Natural	
3	[redacted] UNK	Historical Condition Annual exam- normal	Received Rx for OrthoTri-Cyclen Lo
4	[redacted] UNK	Historical Condition Urinary tract infection	Received Rx for Sulfamethoxazole &Trimethoprim #6 [redacted] Received Rx for Cipro 500 mg x3 (03/08/06) for continuing symptoms of UTI [redacted] referred to family MD for continuing symptoms of UTI
5	[redacted] UNK	Historical Condition Chlamydia	
6	[redacted] UNK	Historical Condition Herpes	
7	[redacted] UNK	Historical Condition Clinic visit	Sore throat, congestion Temp 98, BP 98/54
8	[redacted] UNK	Historical Condition Clinic visit	Symptoms of burning on urination/hematuria, started on [redacted], Cipro prescribed.
9	[redacted] UNK	Historical Condition LMP	
10	[redacted] UNK	Historical Condition Clilnic visit	Urinary tract infection, last dose of Cipro [redacted] Pyridium and Macrobid prescribed. Bp 124/78
11	[redacted] UNK	Historical Condition Clinic visit	Vaginal spotting, for past week. Just started new pack of Ortho Tri-Cyclen Lo-dysfunctional uterine bleeding secondary to Ortho Tri-Cyclen Lo and antibiotics.
12	[redacted] UNK	Historical Condition Clinic visit	Complaining of Flu symptoms. Temp 98.6, BP 96/56. GualMax-D and Delsiyn prescribed (never filled as per family).

C1. Name (cont.)
Suspect Medication #1: Plan B(LEVONORGESTREL) Tablet, 0.75mg
Suspect Medication #2: ORTHO TRI-CYCLEN LO()

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C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 2 Tablet, single, Oral

C10. CONCOMITANT MEDICAL PRODUCTS

TYLENOL COLD MEDICATION (CHLORPHENAMINE MALEATE, PSEUDOEPHEDRINE HYDROCHLORIDE) 04/01/2006 to 04/05/2006
AMPHETAMINE UNK to UNK
VITAMINS UNK to UNK

AUG 3 0 2006

VALTREX (VALACICLOVIR HYDROCHLORIDE) UNK to UNK
CIPRO 03/08/2006 to UNK
SULFAMETHOXAZOLE W/TRIMETHOPRIM (SULFAMETHOXAZOLE, TRIMETHOPRIM) 03/04/2006 to UNK

G8. ADVERSE EVENT TERMS (cont.)
Drug use for unknown indication, Arrhythmia, Metrorrhagia, Dysuria, Haematuria

Block C - Additional Dosage Regimens

Suspect Product	2. Dose, Frequency & Route Used	3. Therapy dates (if unknown, give duration)	6. Lot # (if known)	7. Exp. Date (if known)
#1 Plan B Regimen # 2	2 Tablet, single, Oral	03/27/2006 to 03/27/2006	T54395C	UNK

DSS
AUG 3 1 2006

AUG 3 0 2006

Individual Safety Report

5095100-X-01-01

Form Approved: OMB No. 0910-0291, Expires: 10/31/08
See OMB statement on reverse.

S. Department of Health and Human Services

MEDWATCH

For VOLUNTARY reporting of adverse events, product problems and product use errors

he FDA Safety Information and
dverse Event Reporting Program

Page ___ of ___

FDA USE ONLY

Triage unit
sequence #

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event, or Date of Birth:	3. Sex	4. Weight
[redacted] in confidence	21	☑ Female ☐ Male	115 lb or ___ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☑ Adverse Event ☐ Product Problem (e.g., defects/malfunctions)
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event (Check all that apply)

☑ Death: [redacted] (mm/dd/yyyy) ☐ Disability or Permanent Damage
☐ Life-threatening ☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - initial or prolonged ☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event (mm/dd/yyyy): [redacted]

4. Date of this Report (mm/dd/yyyy): 06/26/2006

5. Describe Event, Problem or Product Use Error

Following 2nd time pills were taken on 3-29-06 patient experienced heavy menstrual bleeding, pelvic area was swollen, painful and inflamed starting 04/01/2006; chills, fever and headache started on 04/04/2006 and eventual death [redacted] Concern with lack of long term study of suspect product safety and possible serious side effects not adequately described in the product label or other materials.

Patient was healthy prior to taking 2nd dose, and family and friends that knew her and saw her prior to her death are convinced that her death is directly related to her use of the drug.

6. Relevant Tests/Laboratory Data, Including Dates

See attached autopsy report/blood toxicology screen [redacted]

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)

Light smoking and light alcohol use

C. PRODUCT AVAILABILITY

Product Available for Evaluation? (Do not send product to FDA)

☐ Yes ☑ No ☐ Returned to Manufacturer on: ___ (mm/dd/yyyy)

D. SUSPECT PRODUCT(S)

1. Name, Strength, Manufacturer (from product label)

#1 Levonorgestrel(Plan B) Gedeon Richter, Ltd. and

#2 Duramed Pharmaceuticals, Inc.

2. Dose or Amount	Frequency	Route
#1 0.75 m.g.	one time use	oral
#2 0.75 m.g.	one time use	oral

3. Dates of Use (If unknown, give duration) from/to (or best estimate)

#1 02/28/2006

#2 03/29/2006

4. Diagnosis or Reason for Use (Indication)

#1 Emergency Contraceptive

#2 Emergency Contraceptive

5. Event Abated After Use Stopped or Dose Reduced?

#1 ☐ Yes ☑ No ☐ Doesn't Apply

#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #

#1

#2

7. Expiration Date

#1

#2

8. Event Reappeared After Reintroduction?

#1 ☐ Yes ☐ No ☐ Doesn't Apply

#2 ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE

1. Brand Name

2. Common Device Name

3. Manufacturer Name, City and State

4. Model #	Lot #	5. Operator of Device
Catalog #	Expiration Date (mm/dd/yyyy)	☐ Health Professional ☐ Lay User/Patient ☐ Other:
Serial #	Other #	

6. If Implanted, Give Date (mm/dd/yyyy)

7. If Explanted, Give Date (mm/dd/yyyy)

8. Is this a Single-use Device that was Reprocessed and Reused on a Patient?
☐ Yes ☐ No

9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates (exclude treatment of event)

Ortho Tricyclen Low - Age 16 to event date
Tylenol cold and sinus 04/01/2006 to event date

G. REPORTER (See confidentiality section on back)

1. Name and Address

[redacted]

Fax: [redacted]

Phone # [redacted]

E-mail [redacted]

2. Health Professional?	3. Occupation	4. Also Reported to:
☐ Yes ☑ No	Non-Healthcare Professional	☑ Manufacturer ☐ User Facility ☐ Distributor/Importer

5. If you do NOT want your identity disclosed to the manufacturer, place an "X" in this box: ☐

ATTACHMENT
ISR # 5095100-X
DATE: [illegible]

Individual Safety Report
5095100-X-01-03

[redacted] HOSPITAL
[ ]

DEPARTMENT OF PATHOLOGY
[redacted]

AUTOPSY REPORT

AUTOPSY NO: [redacted]

NAME: [redacted]

DATE: [redacted]

AGE: 21

TIME: 8:30 am

SEX: F

CORONER: [redacted]

PROSECTOR: [redacted]
Assistant: [redacted]

ANATOMIC FINDINGS

1. Early autolytic changes, diffuse
2. Pulmonary congestion, marked
3. Hepatic congestion and mild chronic inflammation, periportal

TOXICOLOGY

Pseudoephedrine 1059 ng/ml (Ther 200-800)

CAUSE OF DEATH

Consistent with cardiac arrhythmia

MANNER OF DEATH

Natural

[/S/]

[redacted] M.D.
Forensic Pathologist

COMPLETED: [redacted]

CIRCUMSTANTIAL SUMMARY

[redacted] was a 21 year old white female found dead in her room at a [redacted] Sorority on the morning of [redacted]. According to investigators from the [redacted] Police Department and [redacted] Coroner, she had been complaining of an upper respiratory infection and had visited the student health center. She had also apparently taken OTC cold medication, and remarked to a friend that she intended to take a large quantity of Adderal to help her finish a school project. No signs of foul play were noted at the scene. Due to the circumstances of the death, the Coroner was notified and an autopsy authorized.

DOCUMENTS AND EVIDENCE EXAMINED

Telephone and additional conversations with [redacted].

IDENTIFICATION

On [redacted] at 8:30 AM, a complete post mortem examination was performed on the body of [redacted] who was identified by a toe tag. Persons present for the autopsy included [redacted] as autopsy assistant, [redacted] Coroner [redacted] Dept. Coroners [redacted] and [redacted], and [redacted] Police Dept. Officer [redacted]

CLOTHING AND VALUABLES

The deceased is received wearing a black fleece jacket, black t-shirt, gray sweat pants, and white socks. Valuables included a white metal with white stone ring on the left middle finger, a small white metal nose stud in the left side, and a metal and plastic navel stud. A woven and plastic bracelet is on the left wrist and a green and blue braided bracelet is on the left ankle.

EXTERNAL EXAMINATION.

The body is that of a well developed, well nourished, white female adult appearing the stated age of 21 years. The body length is 62 inches and the estimated body weight is 125 pounds. Scalp hair is bleached blonde with dark roots. Jaundice is not present in the skin or sclerae.

The head is normocephalic. The irides are green and the sclerae are white. The pupils are equal in diameter. There are no contact lenses present and there are no conjunctival petechiae. The nose is normal. There is blood in the nares and mouth. Teeth are present. There is no denture. Oral hygiene is good. The ears are pierced.

There is no significant increase in the anteroposterior diameter of the chest. The breasts are symmetrical without palpable masses. The abdomen is not distended. The external genitalia are those of a shaved female adult. The anus is not dilated and has no evidence of injury. The extremities are symmetric and there are no significant deforming injuries.

The following scars, nevi and tattoos are present: there is a pigmented nevus on the right knee.

SIGNS OF DEATH: Rigor mortis is generalized and post mortem lividity is purple and fixed on the

anterior surface of the body.

ARTIFACTS: No artifacts of medical or post mortem care are present.

No artifacts of putrefaction are present.

INJURIES

No external or internal injuries are identified.

INTERNAL EXAMINATION

SEROUS CAVITIES: The body cavities are opened with a standard Y- shaped incision. The cranial cavity is opened with a coronal incision of the scalp and removal of the calvarium. An odor like alcohol is not apparent in the body cavities. The lungs are well aerated and fill the pleural cavities. There is no evidence of pneumothorax. There is no blood or effusion in either pleural cavity. There are no pleural adhesions. There is no blood or excess fluid in the pericardial sac. There is no evidence of pericarditis. There is no evidence of peritonitis. There is no blood in the peritoneal cavity. There is no ascitic fluid. After removal of the organs from the body, inspection of the serous cavities reveals no evidence of fracture of the ribs, sternum, clavicles, vertebral column or pelvic bones. Contusion hemorrhage is not present in the body walls.

NECK ORGANS: The larynx and trachea are in the midline. No significant hemorrhage is present in the skin, fat or sternocleidomastoid muscles of the anterior neck. The thyroid gland is symmetrical and composed of reddish-brown parenchyma.

There is no hemorrhage in the intrinsic muscles of the larynx. There is no obstruction of the respiratory tract in the nasopharynx, larynx or trachea. There is scant mucus in the larynx. The mucosa of the hypopharynx, larynx and trachea is smooth and glistening without ulceration or tumor. Cervical lymph nodes are appropriate for age. No fractures or dislocations of the cervical vertebrae are detected.

HEART: The 240 gram heart is in usual position with respect to the great vessels and chest cavity. The left ventricle is not significantly hypertrophied and the cardiac chambers are not dilated. On opening the aorta and pulmonary trunk, there is no evidence of air embolism and there is no evidence of pulmonary thromboembolism. There is no evidence of pericarditis. The circumflex coronary artery arises from the left main coronary. The coronary arteries are examined by multiple cross-sections. There is no significant atherosclerotic plaque in the major coronary arteries.

Thrombosis of the coronary arteries is not present. The cardiac valve leaflets are delicate. The circumferences of the cardiac valves are within normal limits for age and heart size. There is no softening or mottling of the myocardium due to recent myocardial infarction or necrosis. There is no myocardial fibrosis. There is no myocardial contusion. There are no defects in the atrial or ventricular septae. Autolysis is mild to moderate.

VASCULAR SYSTEM: The aorta and its main branches show mild yellow streak atherosclerosis. There is no evidence of aneurysm, coarctation, dissection or laceration of the aorta. The renal arteries are not stenotic.

LUNGS: The combined weight of the lungs is 1260 grams. The trachea is complete, without malformation, from the larynx to the carina. There is no aspirated gastric material and no aspirated blood in the trachea. The distal bronchi contain scant mucus. The pleural surfaces are smooth and glistening. No petechiae are visible. The lungs and hilar nodes are not significantly anthracotic and there is no bullous emphysema. On cut section, there is no aspirated blood apparent in alveoli. Pneumonia is not recognized. There is no focal consolidation and no tumor. There is mild passive congestion of the lungs. There is no evidence of pulmonary edema. There is no pulmonary contusion. Pulmonary thromboemboli are not present. There is no putrid gas cavitation.

LIVER: The 1410 gram liver has a smooth capsular surface. On cut section, the parenchyma is reddish-brown and has a lobular architecture. The liver is mildly passively congested. Metastatic tumor is not present. The hepatic duct is patent. The gallbladder is present. There are no gallstones. Autolysis of the liver is mild.

PANCREAS: The pancreas is appropriate in shape and size with respect to total body fat stores. On cut surface, it is lobular with interspersed fat without focal calcification, fibrosis, hemorrhage or fat necrosis. Autolysis is mild.

GASTROINTESTINAL SYSTEM: The esophagus is lined with glistening white mucosa. The stomach is coarsely rugated. The stomach contains 25 ml of particulate food matter. There is no odor like alcohol in the stomach. No pills or pill residues are present. There are no erosions or ulcers in the stomach or duodenum. The small bowel and colon are intact without perforation, diverticula or palpable tumors. The vermiform appendix is present.

SPLEEN: The 250 gram spleen is composed of red and white trabecular pulp. There is no laceration of the splenic capsule. Autolysis is not significant.

ADRENALS: Two adrenals are present with golden brown cortex and white medulla. No cortical nodules are present in either adrenal. Autolysis is not significant.

URINARY TRACT: The right kidney weighs 130 grams, the left kidney 110 grams. The two kidneys, ureters and bladder are present in their usual positions without dilatation. The kidneys are symmetrical in shape and size. The capsules strip from the cortices with ease and the cortical surfaces are smooth. On cut section, the cortex appears of ample thickness and the medulla appears ample. The kidneys are congested. There are no stones or tumors in the kidneys, pelves, ureters or bladder. Autolysis of the kidneys is not significant. The bladder contains scant yellow urine.

REPRODUCTIVE SYSTEM: The uterus, fallopian tubes and ovaries are present. They are of usual size and shape for age. No tumors are present. There is no evidence of current pregnancy.

CENTRAL NERVOUS SYSTEM: There is no hemorrhage in the scalp or galea. The dura, removed by stripping from the calvarium and base of the skull, shows no epidural or subdural hemorrhage. The cerebral and cerebellar hemispheres of the 1340 gram brain are symmetrical. The leptomeninges are transparent and can be stripped with ease. There is no subarachnoid hemorrhage. There is no flattening of the gyri and no widening of the sulci. The major vessels at the base of the brain have a usual anatomic distribution and there is no significant atherosclerosis. The cranial nerves are symmetrical and intact. There is no evidence of herniation at any of the portals of the brain. On serial coronal sectioning of the brain, there is no evidence of contusion, edema,

hemorrhage, tumor, atrophy, infection or infarction in the cerebrum, cerebellum and brain stem. There are no fractures of the convexity or base of the skull. The craniocervical junction demonstrates a usual range of motion. The spinal cord is not examined.

PHOTOGRAPHS: Autopsy photography is taken by the [redacted] Police Department and the [redacted] County Coroner's Office.

SPECIMENS FOR FIREARMS EXAMINATION OR TRACE EVIDENCE: None.

SPECIMENS FOR TOXICOLOGY: Blood (central) and Urine.

MICROSCOPIC EXAMINATION

HEART: Heart sections are histologically within normal limits.

LUNGS: Pulmonary sections show congestion.

LIVER: Hepatic sections demonstrate the presence of mild periportal inflammatory infiltrates, chronic, without additional pathologic change..

SPLEEN: Splenic sections show depletion of white pulp elements..

ADRENALS: Adrenal sections are histologically within normal limits.

KIDNEYS: Renal sections are histologically within normal limits.

PANCREAS: Pancreatic sections show autolysis but are otherwise histologically within normal limits.

THYROID: Thyroid sections are histologically within normal limits.

CENTRAL NERVOUS SYSTEM: Representative CNS sections are histologically within normal limits.

Individual Safety Report

5095100-X-01-08

[redacted]

LABORATORY CASE NUMBER: [redacted]

Client Account: [redacted]
Physician:
Report To: [redacted] CORONER-IN
ATTN: [redacted]
[redacted]
[redacted]
Fx: 1-[redacted]

Subject's Name: [redacted]
Agency Case #: [redacted]
Date Of Death: [redacted]
Test Reason: Not given
Investigator:
Date Received: [redacted]
Date Reported: [redacted]

Laboratory Specimen No: [redacted]
Container(s) Received:
01: Red Top Bottle Blood, AUTOPSY

Date Collected: [redacted]
Test(s) Requested:
70510 Comprehensive Drug Panel (550B)

Analyte Name	Result	Cut-off	Units	Therapeutic Range	Loc
AMPHETAMINES	POSITIVE	50	ng/mL		
Pseudoephedrine	POSITIVE	50	ng/mL	200-800	
Pseudoephedrine, Quant	1059		ng/mL		
BARBITURATES	Negative	1	ug/mL		
BENZODIAZEPINES	Negative	150	ng/ml		
CANNABINOIDS	Negative	20	ng/ml		
COCAINE/METABOLITES	Negative	50	ng/ml		
FENTANYL	Negative	1	ng/ml		
METHADONE	Negative	50	ng/ml		
OPIATES	Negative	20	ng/ml		
OXYCODONE/METABOLITE	Negative	20	ng/ml		
PHENCYCLIDINE	Negative	50	ng/ml		
PROPOXYPHENE	Negative	100	ng/ml		
SALICYLATES	Negative	10	ug/ml		
TRICYCLIC ANTIDEPRESSANTS	Negative	20	ng/mL		
ALCOHOLS	Negative	0.02	% (w/v)		
STIMULANTS	POSITIVE				
Caffeine	POSITIVE				
NARCOTICS	Negative				
SEDATIVES/HYPNOTICS	Negative				
ANTIDEPRESSANTS	Negative				
ANALGESICS	Negative				
ANESTHETICS	Negative				
CARDIOVASCULAR AGENTS	Negative				
ANTIHISTAMINES	Negative				
ANTICONVULSANTS	Negative				
ANTIPSYCHOTICS	Negative				

[redacted]

Laboratory Case #: [redacted]
Print Date/Time: [redacted]

Individual Safety Report

5095100-X-01-09

[redacted]

Laboratory Specimen No: [redacted]

Date Collected: [redacted]

Container(s) Received:

01: Red Top Tube Vitreous

Test(s) Requested:

70570 Autopsy Panel, Volatiles (550V1)

Analyte Name	Result	Cut-off	Units	Therapeutic Range	Loc
ALCOHOLS	Negative	0.02	% (w/v)		
Methanol	Negative	0.02	% (w/v)		
Ethanol	Negative	0.02	% (w/v)		
Acetone	Negative	0.02	% (w/v)		
Isopropanol	Negative	0.02	% (w/v)		

The Specimen identified by this Laboratory Specimen Number has been handled and analyzed in accordance with all applicable requirements.

[redacted]

Laboratory Case #: [redacted]

Print Date/Time: [redacted]

[redacted]

Signature of Certifying Scientist

Individual Safety Report

5095100-X-01-10

ACUTE PROBLEM	DATE (initial visit per episode)						
Viral URI c̄ pharyngitis	[redacted]						
L ear wax							
Post-infectious cough / URI							
URI							
Bronchitis							

Medication	Start	#	Medication	Start	#	Medication	Start
Guaifenex D	[redacted]						
Duradex							
[illegible]							
Tessalon Perles							
Tussionex	"						
Advair	"						
Tussionex	[redacted]						
Zpak							
Advair 100/50							
Guaifenex D	[redacted]						
Guaifenex D							
[illegible]							

CONTINUING PROBLEMS / CONDITIONS / MEDICATIONS

Date	Condition	Lat	Start	Medication / Treatment	Stop
	Contraception	A		Ortho Tri-Cyclen Lo	

Tobacco Use / Amount:

DATE	SIGNIFICANT PAST HISTORY, SURGERIES, ETC.

Emergency Treatment Data

☐ Glasses ☐ Contact Lenses ☐ Rem Dentures / Bridges

☐ Anisocoria, specify

☐ Prosthesis, specify

☐ Hepatitis B series ☐ Varicella Vax

Current Tetanus: [redacted]

ALLERGY or INTOLERANCE / RXN / DATE NOTED

[redacted]

NKMA (date) [redacted]

HMR

Individual Safety Report

5095100-X-01-11

Date & Time	Intls & Clinic	Temp	BP	Ht & Wt	Dict & Intls	Notes
						OD 20/10 OS 20/10 OU 20/10 c cor @ [illegible]
		97[3]	92/58		BH	Meds: O.T. [illegible] LMP: 4 wks All: Ø
						will call to R/S. 4:00pm spoke w/pt - forgot -
		pt N/S appt			-	rescheduled for 5/4 @ 1045 - Doing well [illegible]
						Dr. [redacted] cc: cough ~~[illegible]~~ or sinus
		98	98/64			SEE UR FORM [redacted]
						Cancelled c Dr. [redacted] Southwest Med W/C
						SEE UR FORM cBeckman
		98[2]	100/68			Dr. [redacted] See URI form Approved
		98.3	102/66			Ebling CC: c/o coughing until vomits
		drinking coffee 98	98/70	132	[illegible]	white [illegible] NA NKMA Med -
						Tussionex; Tricodene LO Age-20
						LMP: 11-9-65 Smoker-Occasionally
						CI - Ø [illegible]
						Peak Flow Actual 400 Pred ~ 430
						[redacted]
						SEE UR FORM [redacted]
		99[0]	98/54			
						SEE UR FORM
		98	96/56			

Individual Safety Report

5095100-X-01-12

Subjective

Chief Complaint: fever stuffy nose Duration: Today

Current medication: Arthrotec 50 Rheumatrex LMP: 2 wk

Med allergies: NKDA CI: Ø

General: ☐ No Sx ☒ Fever ☒ Fatigue ☒ Myalgia ☐ Dizziness/lightheadedness ☒ Headache ☒ Appetite

Ears: ☒ No Sx ☐ Pain – R L ☐ Fullness – R L ☐ Hearing loss – R L ☐ Popping – R L

Nose: ☐ No Sx ☒ Stuffy ☒ Drainage_____ ☒ Runny ☐ Sneezing ☐ Itching

Facial Pain: ☒ No Sx ☐ Maxillary – R L ☐ Frontal – R L ☐ Between eyes ☐ Upper teeth ☐ Worse bending

Throat: ☒ No Sx ☐ Pain_____ ☐ Swollen glands ☐ Post nasal drainage ☐ Itching ☐ Scratchy

Chest: ☐ No Sx ☒ Cough – (dry) prod both _____ ☐ SOB ☐ Wheeze ☐ Tightness ☐ Pain

PMH: ☐ Asthma ☐ Abn Heart valve ☐ +PPD ☒ Cigarettes 1 cig/day ppd x __yrs. ☐ Mono ☐ Envir Allergy

☐ Recurrent strep ☐ Flu shot ☐ H/O GERD ☐ H/O Ent Surgery _____

Other Hx: Pt thinks she has Flu

If PMHx of Asthma complete section below:

Age of onset _____ date of most recent asthma episode _____

Resp Sx freq: ☐ Daytime_____ ☐ Nighttime_____

Trigger: ☐ Allergy_____ ☐ Activity ☐ Resp infection ☐ Other_____

Home PEF: ☐ No ☐ Yes – most recent_____ Personal best_____ ☐ Spacer use

Previous Tx: ☐ Steroid – oral inhaled ☐ Bronchodilator – short long ☐ Oral anti-inflam

☐ Anti-histamine ☐ Other_____ ☐ Hospitalization_____ ☐ Intubated_____

[redacted]

[151]

URI/ASTHMA FORM

[√] = Present
[ ] = Absent
~~+PPD~~ = Not asked or not applicable

4

Individual Safety Report

5095100-X-01-13

Objective

VS: BP 96/66 T 98.6 P___ RR___ PEF___ Pred. PEF___ Distress – (none) mild mod sev ☐ O_2Sat___(RA)

Ear Canal: R – ☒ NL ☐ Red ☐ Swollen ☐ Exudate ☐ Wax L – ☒ NL ☐ Red ☐ Swollen ☐ Exudate ☐ Wax

Ear Drum: R – ☒ NL ☐ Red ☐ Effusion ☐ Retraction L – ☒ NL ☐ Red ☐ Effusion ☐ Retraction

Nasal: ☐ NL ☐ Red ☐ Pale ☐ Swollen ☒ Discharge Color clear ☐ Sinus tenderness_____

Throat: ☐ NL ☐ Red ☐ Lymphoid hypertrophy ☐ Ulcerations ☒ Discharge Color clear

Tonsils: ☐ NL ☐ Absent ☒ Small ☐ Moderate ☐ Large ☐ Exudate_____

Neck: ☒ NL ☐ Accessory muscle use ☐ Decreased ROM

Cerv. Nodes: ☐ NL ☒ Enlarged ☒ L ☐ Tender – R L ☒ AC ☐ PC

Chest: ☒ NL ☐ Wheezing ☐ Rales ☐ Rhonchi ☐ Clears w/cough ☐ Other_____

Cardiac: ☒ NL ☐ NE ☐ Irregular rhythm ☐ Irregular rate ☐ Murmur Other_____

Other PE _____

In-office Tx: ☐ None ☐ _____

Lab/ Testing

☐ Strep. rapid/cult___ ☐ Mono___ ☐ CBC_____ ☒ Rapid Flu Neg ☐ Other_____

Assessment

☒ URI ☐ Tonsillitis/Pharyngitis ☐ Sinusitis ☐ Acute bronchitis ☐ Allergic rhinitis ☐ Other_____

☐ ASTHMA - ☐ acute exacerbation ☐ mild intermittent ☐ persistent – mild moderate severe; ☐ OM – L R

Plan Guaimax D 1 PO BID #20

Delsym 10 ml PO BID 1ST DC Smoking

☐ Pt. education given _____ ☐ Handout _____ ☐ Influenza Vaccine

☒ Call if not improving in 1 wk ☐ Appointment _____ ☐ Asthma educ. Referral _____

☒ Push Fluids ☐ Call for test results ☐ Additional Dictation Signature

[151]

Individual Safety Report

5095100-X-01-14

Subjective

Chief Complaint: sore throat congestion Duration: Today

Current medication: ortho tricyclen LO LMP: [redacted]

Med allergies: NKDA CI: Ø

General: ☐ No Sx ☐ Fever ☒ Fatigue ☒ Myalgia ☐ Dizziness/lightheadedness ☒ Headache ☒ ↓ Appetite

Ears: ☒ No Sx ☐ Pain – R L ☐ Fullness – R L ☐ Hearing loss – R L ☐ Popping – R L

Nose: ☐ No Sx ☒ Stuffy ☒ Drainage _____ ☒ Runny ☐ Sneezing ☐ Itching

Facial Pain: ☒ No Sx ☐ Maxillary – R L ☐ Frontal – R L ☐ Between eyes ☐ Upper teeth ☐ Worse bending

Throat: ☐ No Sx ☒ Pain _____ ☒ Swollen glands ☒ Post nasal drainage ☐ Itching ☐ Scratchy

Chest: ☐ No Sx ☒ Cough – dry prod both _____ ☐ SOB ☐ Wheeze ☐ Tightness ☐ Pain

PMH: ☐ Asthma ☐ Abn Heart valve ☐ +PPD ☒ Cigarettes 4 cig/wd ppd x __yrs. ☐ Mono ☐ Envir Allergy

☐ Recurrent strep ☐ Flu shot ☐ H/O GERD ☐ H/O Ent Surgery _____

Other Hx: _____

_____

_____

If PMHx of Asthma complete section below:

Age of onset _____ date of most recent asthma episode _____

Resp Sx freq: ☐ Daytime _____ ☐ Nighttime _____

Trigger: ☐ Allergy _____ ☐ Activity ☐ Resp infection ☐ Other _____

Home PEF: ☐ No ☐ Yes – most recent _____ Personal best _____ ☐ Spacer use

Previous Tx: ☐ Steroid – oral inhaled ☐ Bronchodilator – short long ☐ Oral anti-inflam

☐ Anti-histamine ☐ Other _____ ☐ Hospitalization _____ ☐ Intubated _____

[redacted] 11:48AM [redacted]

[redacted]/ASTHMA FORM

+ √ ◇ ↳ Present

Individual Safety Report
5095100-X-01-15

Objective

S: BP 98/54 T 99° P___ RR___ PEF___ Pred. PEF___ Distress – none mild mod sev ☐ O_2Sat___(RA)

ar Canal: R – ☒ NL ☐ Red ☐ Swollen ☐ Exudate ☐ Wax L – ☒ NL ☐ Red ☐ Swollen ☐ Exudate ☐ Wax

ar Drum: R – ☒ NL ☐ Red ☐ Effusion ☐ Retraction L – ☒ NL ☐ Red ☐ Effusion ☐ Retraction

lasal: ☐ NL ☐ Red ☐ Pale ☐ Swollen ☒ Discharge Color clear ☐ Sinus tenderness_____

hroat: ☐ NL ☒ Red ☐ Lymphoid hypertrophy ☐ Ulcerations ☒ Discharge Color clear

onsils: ☐ NL ☐ Absent ☒ Small ☐ Moderate ☐ Large ☐ Exudate_____

leck: ☒ NL ☐ Accessory muscle use ☐ Decreased ROM

erv. Nodes: ☐ NL ☒ Enlarged – (B L) ☐ Tender – R L ☒ AC ☐ PC

hest: ☒ NL ☐ Wheezing ☐ Rales ☐ Rhonchi ☐ Clears w/cough ☐ Other_____

ardiac: ☒ NL ☐ NE ☐ Irregular rhythm ☐ Irregular rate ☐ Murmur Other_____

ther PE _____

_____

n-office Tx: ☐ None ☐ _____

ab/ Testing

] Strep. rapid/cult___ ☐ Mono___ ☐ CBC_____ ☐ Rapid Flu_____ ☐ Other_____

Assessment

URI ☐ Tonsillitis/Pharyngitis ☐ Sinusitis ☐ Acute bronchitis ☐ Allergic rhinitis ☐ Other_____

] ASTHMA - ☐ acute exacerbation ☐mild intermittent ☐ persistent – mild moderate severe; ☐ OM – L R

lan Guaimax D 1 PO BID #20

_____

] Pt. education given _____ ☒ Handout cold ☐ Influenza Vaccine

Call if not improving in 1 wk ☐ Appointment _____ ☐ Asthma educ. Referral _____

] Push Fluids ☐ Call for test results ☐ Additional Dictation Signatur

[/S/]

Individual Safety Report

5095100-X-01-16

[redacted]

SUBJECTIVE: I saw [redacted] on 1[redacted] and at that time she had had a cough for 4-5 days. I thought it was viral and symptomatic care was recommended. She was given a script for Tussionex to use at bedtime. She comes in today stating that the cough is more frequent. She has paroxysms of coughing, sometimes 20-30 minutes at a time, and sometimes will vomit after coughing. Occasionally there is some mucus produced, but it is mostly clear. She has noticed fatigue, does not know if she has had a fever. She still has some nasal congestion, but denies sinus pain. The patient has no history of asthma, but has used an inhaler before when she has been ill.

OBJECTIVE: Peak flow 400, predicted 430. She appears in no distress. TMs are normal. Nose real red with swollen turbinates. Throat clear. Neck no adenopathy. Chest has good expansion and clear to auscultation. No wheezes, rales or rhonchi heard.

ASSESSMENT: BRONCHITIS.

PLAN:

1. Z-Pak.
2. Advair 100-50, 1 puff b.i.d., #3.
3. She is to let me know if this not improving in 5-6 days.

[redacted], M.D.

Dictated: [redacted]
2:13 pm
DVI Job # [redacted]

[redacted]

1:50 pm — TC: [redacted] (P.N [redacted]) Pt. states finished Z-Pak yesterday. Continues Advair 1 puff bid - Not seeing great improvement. Still noting cough- more it is loose- but unable to cough up sputum. No fever. Did not rest a great deal over weekend due to work. A [redacted] consulted. Pt. advised Z-Pak still working up to ~ 10 day. Continue Advair 1 puff bid. Rx Tussionex 2 yz ½ to 1 tsp q 6-8 pm cough - no refills. Non-smkr. PA + Lat CXR - Order to IUMC Radiology.

pm — PVD B[redacted] /S. Gipson, M.

[redacted]

SPN 11-14-05. Pt. did not return for chest x-ray. Notified by IUMC Radiology. Order destroyed.

— PVD B[redacted] /S. Gipson, M.

[redacted] -- Rx for Tussionex written [redacted] never picked up.

Individual Safety Report

5161338-5-00-01

U.S. Depar

MEDWATCH

The FDA Safety Information and Adverse Event Reporting Program

ties, anufacturers for MANDATORY reporting Berlex Inc.

RECEIVED

Page 1 of 2

Raleye International, Inc., FDA Facsimile Approval: 30-JUN-1998

Mfr Report # CA-2006-035391

UF/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier -- In confidence

2. Age at Time of Event: 26 years or Date of Birth: UNK

3. Sex ☒ Female ☐ Male

4. Weight UNK kgs

CDR/CDER

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

☒ Death UNK (mo/day/yr)
☐ Life-threatening
☐ Hospitalization - initial or prolonged
☐ Disability
☐ Congenital Anomaly
☐ Required Intervention to Prevent Permanent Impairment/Damage
☐ Other:

3. Date of Event (mo/day/year) UNK

4. Date of This Report (mo/day/year) 11/20/2006

5. Describe Event or Problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

ruptured cerebral aneurysm[Ruptured cerebral aneurysm]

Case Description:
This report describes the occurrence of ruptured cerebral aneurysm in a 26 year-old female patient who was prescribed levonorgestrel (Mirena, IUS). This report was received on 14 Nov 2006 from a patient and has not been verified by a physician or other health care professional.

There was no past medical history reported. There were no concurrent conditions reported. The patient received no concomitant medication. It was not reported if Mirena was used previously and tolerated.

On an unspecified date the patient received the first dose of levonorgestrel (Mirena) at 20 µg/day, cont via intra-uterine route of administration for contraception.
continued in additional info section...

6. Relevant Tests/Laboratory Data, Including Dates
NI

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
NI

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)
#1. Mirena(LEVONORGESTREL) (continued)
#2.

2. Dose, Frequency & Route Used
#1. 20 (continued)
#2.

3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. UNK
#2.

4. Diagnosis for Use (Indication)
#1. Contraception
#2.

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot # (if known)
#1. UNK
#2.

7. Exp. Date (if known)
#1. UNK
#2.

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
No Concomitant Medication UNK to UNK

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Berlex Inc.
Claudia Schoenig-Diesing, M.D.
Director, Medical Assessment
Claudia_Schoenig@Berlex.com
Fax: +1 973 487 2914
Global Med. Safety Surveillance, P.O. Box 1000
Montville, NJ 07045-1000 UNITED STATES

2. Phone Number
+1 8882375394

3. Report Source (Check all that apply)
☒ Foreign CAN
☐ Study
☐ Literature
☐ Consumer
☐ Health Professional
☐ User Facility
☐ Company Representative
☐ Distributor
☐ Other:

4. Date Received by Manufacturer(mo/day/yr)
11/14/2006

5. (A)NDA # US:NDA 21-225
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
☐ 5-day ☒ 15-day
☐ 10-day ☐ Periodic
☒ Initial ☐ Follow-up #

8. Adverse Event Term(s)
Ruptured cerebral aneurysm

9. Manufacturer Report Number
CA-2006-035391

E. INITIAL REPORTER

1. Name and Address
Name and address withheld.

Phone # Withheld

DSS
NOV 22 2006

2. Health Professional?
☐ Yes ☒ No

3. Occupation
company sales representative

4. Initial Reporter Also Sent Report to FDA
☐ Yes ☐ No ☒ Unk

FDA
3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.

NOV 2 1 2006

Additional Information

B5. EVENT DESCRIPTION (cont.)

On an unspecified date the patient developed a ruptured cerebral aneurysm, resulting in death.

The patient died from ruptured cerebral aneurysm. It was not reported if an autopsy was performed. Death occurred on an unspecified date, after treatment with Mirena was started.

The dosage of Mirena was not changed. Dechallenge for Mirena was not applicable. Rechallenge for Mirena was not applicable.

Further information will be requested by the sales representative.

C1. Name (cont.)
Suspect Medication #1: Mirena(LEVONORGESTREL) IUS

C2. Dose, frequency & route used (cont.)
Suspect Medication #1: 20 µg/day, cont, Intra-uterine

...ment of Health and Human

MEDWATC..

The FDA Safety Information and Adverse Event Reporting Program

Individual Safety Report

5314285-0-00-01

for MANDATORY reporting

Page 1 of 2

Releya International, Inc., FDA Facsimile Approval: 11-JUN-1999

Mfr Report # 012396

UF/Importer Report #

FDA Use Only

A. PATIENT INFORMATION

1. Patient Identifier [redacted] In confidence

2. Age at Time of Event: 31 Years or Date of Birth: [redacted]

3. Sex: ☒ Female ☐ Male

4. Weight: UNK lbs or UNK kgs

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. ☒ Adverse Event and/or ☐ Product Problem (e.g., defects/malfunctions)

2. Outcomes Attributed to Adverse Event (Check all that apply)

- ☒ Death [redacted] (mo/day/yr)
- ☐ Life-threatening
- ☒ Hospitalization - initial or prolonged
- ☐ Disability
- ☐ Congenital Anomaly
- ☐ Required Intervention to Prevent Permanent Impairment/Damage
- ☐ Other:

3. Date of Event (mo/day/year) [redacted]

4. Date of This Report (mo/day/year) 04/24/2007

5. Describe Event or Problem
Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas)

Stroke[Cerebrovascular accident]
Passed out[Loss of consciousness]
Blood clot in neck[Thrombosis]
Multiple blood clots in brain[Cerebral thrombosis]
Pressure in brain[Intracranial pressure increased]
Swelling of brain[Brain oedema]

Case Description:
Information was received regarding a 31-year-old female patient prescribed Seasonique (levonorgestrel, ethinyl estradiol) tablets for oral contraception. Therapy dates and dosages are unknown. It was reported the patient passed out and was taken to the hospital on an unspecified date. At the hospital, it was discovered the patient had a blood clot in her neck. It was discovered the clot had spread to her brain causing severe damage. It was reported the patient underwent surgery to relieve the pressure on her brain by having the continued in additional info section...

6. Relevant Tests/Laboratory Data, Including Dates
NI

7. Other Relevant History, Including Preexisting Medical Conditions (e.g. allergies, race, pregnancy, smoking and alcohol use, hepatic/renal dysfunction, etc.)
NI

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & mfr/labeler, if known)
#1. Seasonique(LEVONORGESTR (continued)
#2.

2. Dose, Frequency & Route Used
#1. UNK, UNK, Oral
#2.

3. Therapy Dates (if unknown, give duration) from/to (or best estimate)
#1. UNK
#2.

4. Diagnosis for Use (Indication)
#1. Oral contraception
#2.

5. Event Abated After Use Stopped or Dose Reduced?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot # (if known)
#1. UNK
#2.

7. Exp. Date (if known)
#1. UNK
#2.

8. Event Reappeared After Reintroduction?
#1. ☐ Yes ☐ No ☒ Doesn't Apply
#2. ☐ Yes ☐ No ☐ Doesn't Apply

9. NDC# (For product problems only)

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
NI

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
Barr Laboratories
Anthony Oladipo, PharmD, MPH
VP, Drug Safety and Risk Management
400 Chestnut Ridge Road
Woodcliff Lake, NJ 07677-7668 UNITED STATES

2. Phone Number
2019303446

3. Report Source (Check all that apply)
- ☐ Foreign
- ☐ Study
- ☐ Literature
- ☒ Consumer
- ☐ Health Professional
- ☐ User Facility
- ☐ Company Representative
- ☐ Distributor
- ☐ Other:

4. Date Received by Manufacturer(mo/day/yr)
04/11/2007

5. (A)NDA # 21-840
IND #
PLA #
Pre-1938 ☐ Yes
OTC Product ☐ Yes

6. If IND, Give Protocol #

7. Type of Report (Check all that apply)
- ☐ 5-day ☒ 15-day
- ☐ 10-day ☐ Periodic
- ☒ Initial ☐ Follow-up #

8. Adverse Event Term(s)
Cerebrovascular accident, Loss of consciousness, Thrombosis, Cerebral thrombosis, Intracranial pressure continued in additional info section...

9. Manufacturer Report Number
012396

E. INITIAL REPORTER

1. Name and Address
[redacted]
UNITED STATES

Phone # UNK

2. Health Professional?
☐ Yes ☒ No

3. Occupation
Consumer

4. Initial Reporter Also Sent Report to FDA
☐ Yes ☐ No ☒ Unk

FDA 3500A Facsimile

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.

APR 25 2007

DSS

APR 27 2007

24-Apr-2007 14:02

Additional Information

B5. EVENT DESCRIPTION (cont.)

right half of her skull removed. It was reported the patient was induced into a coma to stop the blood flow and three unspecified surgeries were performed. Multiple clots were found on the left side of her brain. The brain swelling continued and the patient was on life support. She subsequently died on [redacted]. It was reported the cause of death was stroke. Additional information was requested.

MedWatch Case Comment:
Submission of this 15-day report does not constitute an admission that the reported event is an unlabeled event.

C1. Name (cont.)
Suspect Medication #1: Seasonique(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet

G8. ADVERSE EVENT TERMS (cont.)
increased, Brain oedema

Individual Safety Report

5399025-1-00-01

1/3

308592

Form Approved: OMB No. 0910-0291, Expires: 10/31/08
See OMB statement on reverse.

Y reporting of
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CDER

The FDA Safety Information and Adverse Event Reporting Program

Page 1 of 1

FDA USE ONLY

Triage unit sequence #

PLEASE TYPE OR USE BLACK INK

A. PATIENT INFORMATION

1. Patient Identifier	2. Age at Time of Event, or Date of Birth:	3. Sex	4. Weight
girl In confidence	[redacted] - 20yo	☑ Female ☐ Male	150 lb or ____ kg

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR

Check all that apply:

1. ☑ Adverse Event ☐ Product Problem *(e.g., defects/malfunctions)*
☐ Product Use Error ☐ Problem with Different Manufacturer of Same Medicine

2. Outcomes Attributed to Adverse Event *(Check all that apply)*
☑ Death: [redacted] *(mm/dd/yyyy)* ☐ Disability or Permanent Damage
☐ Life-threatening ☐ Congenital Anomaly/Birth Defect
☐ Hospitalization - Initial or prolonged ☐ Other Serious (Important Medical Events)
☐ Required Intervention to Prevent Permanent Impairment/Damage (Devices)

3. Date of Event *(mm/dd/yyyy)*	4. Date of this Report *(mm/dd/yyyy)*
	07/20/2007

5. Describe Event, Problem or Product Use Error

Safety Evaluator Follow-up Report for ISR# 5060812-0-00-01. Contact Providing Follow-up information: [redacted] (consumer). Date contacted: 11/27/2006. PT term from original ISR:Deep vein thrombosis. Follow-up information: Started Seasonale in Nov 2005, was on no other drugs. Did not previously use birth control, had no pregnancies, births or complications. Brought to ER & pronounced dead. She went on a long plane flight on her honeymoon [redacted]. Previously been on long plan flights (Africa, China) with no problems. Attachment: follow-up letter.

6. Relevant Tests/Laboratory Data, Including Dates

7. Other Relevant History, Including Preexisting Medical Conditions *(e.g., allergies, race, pregnancy, smoking and alcohol use, liver/kidney problems, etc.)*

No previous pregnancies, births or complications. No family history of clotting events. in 'perfect health' per reporter.

C. PRODUCT AVAILABILITY

Product Available for Evaluation? *(Do not send product to FDA)*

☐ Yes ☐ No ☐ Returned to Manufacturer on: ____ *(mm/dd/yyyy)*

D. SUSPECT PRODUCT(S)

1. Name, Strength, Manufacturer *(from product label)*
#1 Seasonale
#2

2. Dose or Amount	Frequency	Route
#1		
#2		

3. Dates of Use *(If unknown, give duration)* from/to *(or best estimate)*
#1 11/05-1/1/06 (5-6 wks)
#2

5. Event Abated After Use Stopped or Dose Reduced?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

4. Diagnosis or Reason for Use *(Indication)*
#1 birth control
#2

8. Event Reappeared After Reintroduction?
#1 ☐ Yes ☐ No ☐ Doesn't Apply
#2 ☐ Yes ☐ No ☐ Doesn't Apply

6. Lot #	7. Expiration Date
#1	#1
#2	#2

9. NDC # or Unique ID

E. SUSPECT MEDICAL DEVICE

1. Brand Name
2. Common Device Name
3. Manufacturer Name, City and State

4. Model #	Lot #	6. Operator of Device
Catalog #	Expiration Date *(mm/dd/yyyy)*	☐ Health Professional ☐ Lay User/Patient ☐ Other:
Serial #	Other #	

6. If Implanted, Give Date *(mm/dd/yyyy)* 7. If Explanted, Give Date *(mm/dd/yyyy)*

8. Is this a Single-use Device that was Reprocessed and Reused on a Patient?
☐ Yes ☐ No

9. If Yes to Item No. 8, Enter Name and Address of Reprocessor

RECEIVED
JUL 23 2007
MEDWATCH CTU

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS

Product names and therapy dates *(exclude treatment of event)*

None

G. REPORTER *(See confidentiality section on back)*

1. Name and Address
[redacted] U.S.

Phone #	E-mail

2. Health Professional?	3. Occupation	4. Also Reported to:
☐ Yes ☐ No		☐ Manufacturer ☐ User Facility ☐ Distributor/Importer

5. If you do NOT want your identity disclosed to the manufacturer, place an 'X' in this box: ☐

FORM FDA 3500 (10/05) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.

DSS

NOV 2 5 2007

Individual Safety Report

5399025-1-00-02

308592

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993
September 11, 2006

[redacted]

RE: Case Number [redacted]

Dear Ms. [redacted],

I recently received a report you submitted to MedWatch of fatal deep vein thrombosis associated with the use of Seasonale. Additional clinical information would be useful in evaluating your report; to assist you in making your response, a copy of the report is included. **The privacy of reporting persons and institutions as well as patients is protected from public disclosure.** For your convenience, space has been provided for any information that is available on the following subjects; alternatively, providing a copy of the hospital discharge summary (if you were hospitalized) or any other relevant medical records would be appreciated. Or, you may ask your health care provider to complete this letter.

1. What were the exact dates of Seasonale therapy in relation to the adverse event?

My daughter started taking Seasonale in Nov. 2005 - She died [redacted]

2. Was your daughter receiving other drugs concomitantly? If so, please provide the dates of therapy and the indication for use for these drugs.

She was on no other drugs

3. If your daughter previously used hormonal contraceptives, please list the brand names, dates of therapy and reason for discontinuation.

She used no previous birth control.

4. Please list your daughter's previous gynecologic history, including the number of pregnancies, the number of births, and any complications during pregnancy.

She had no pregnancies, births or complications of any kind.

5. How was the deep vein thrombosis diagnosed and treated?

She was brought into the ER + pronounced dead.

DSS

JUL 25 2007

Individual Safety Report

5399025-1-00-03

308592

6. Does your daughter have any previous history of clotting events? Is there a family history of clotting events? There is no family history & my daughter was in perfect health as far as we knew.

7. Does your daughter have any other medical history that might be relevant to this event? Please provide your daughter's height and weight.

She was 5'7", 150 pds & beautiful!

8. Did your daughter have any prolonged travel, physical trauma, bed rest or inactivity prior to the event? Please describe her smoking history.

She went on a long plane flight on her honeymoon ([redacted]). She had been on previous long plane flights (Africa, China) with no problems.

I appreciate your assistance and am truly interested in as much of the requested information as you can provide. You may provide your response via facsimile at 301-796-9721 or mail at the address listed below.

Sincerely yours,

[redacted] Pharm.D.

[redacted] Pharm.D.
Food and Drug Administration
Office of Drug Safety
10903 New Hampshire Ave Bldg
WO22 Rm 3487; Mailstop 3411
Silver Spring, MD 20993-0002

DSS

MAY 05 2009

Individual Safety Report

3396782-0-00-01

INTERNATIONAL ADVERSE EXPERIENCE REPORT

I. REACTION INFORMATION

1 PATIENT INITIALS	1a COUNTRY	2. DATE OF BIRTH (Day / Month)	2a. AGE UNITS	3. SEX	4-6 EXPERIENCE (Day / Month / Year)
	Brazil		27 Yr	F	00 / UNK / 1999

8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION

- ☐ PATIENT DIED
- ☐ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION
- ☐ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY
- ☐ LIFE THREATENING
- ☒ NONE OF THE ABOVE
- ☐ RECOVERED

7 DESCRIBE EXPERIENCE(S)

INTRA-UTERINE DEATH; Unintended pregnancy; Multiple pregnancy

Information was received on 03-Nov-1999 from a healthcare professional via Schering AG Germany concerning a 27 yr old female patient. The patient's concurrent history includes Multiparity. Therapy with MICROGYNON (equivalent to Nordette-21) (1 tablet daily) for Contraception NOS began in FEB-1999 and ceased on 8-OCT-1999. Concomitant therapy included NONE. The patient became pregnant (Unintended pregnancy) with triplets in SEP-1999 and death of one embryo (Intra-uterine death) was suspected. An Ultrasound antenatal screen confirmed a gestational age of 4-5 weeks. Schering Ref. #-99/00886-CDS.

13 RELEVANT TESTS/LABORATORY DATA

See following page.

II. SUSPECT DRUG(S) INFORMATION

14 SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))

#1 NORDETTE-21 TABLET (LEVONORGESTREL, ETHINYL ESTRADIOL)

20. DID REACTION ABATE AFTER STOPPING DRUG? ☐ YES ☐ NO ☒ N/A

15 DAILY DOSE(S)

#1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINSTRATION

#1 Oral

17 INDICATION(S) FOR USE

#1 Contraception NOS

21. DID REACTION REAPPEAR AFTER REINTRODUCTION? ☐ YES ☐ NO ☒ N/A

18 THERAPY DATES (FROM/TO)

#1 CC-Feb-1999 / 08-Oct-1999

19. THERAPY DURATION

#1 8 Mth

III. CONCOMITANT DRUG(S) AND HISTORY

22 CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MO/YR)

NONE, Unknown

23 OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) (cont'd)

CONCURRENT CONDITIONS:
Multiparous

PREGNANCY:
LMP: 10/08/1999

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

24a. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)

WYETH LABS (RA)
170 Radnor Chester
St. Davids, PA 19087

OTHER REFERENCE NUMBERS:
Business Partner (BP) (via Schering AG) - 99/00886

Local Marketing No	24b. MFR CONTROL NO.
NDA 18-668	HQ4572304NOV1999

24c DATE RECEIVED BY MANUFACTURER	24d. REPORT SOURCE
03-Nov-1999	☐ STUDY ☐ CONSUMER ☐ LITERATURE ☐ REGULATORY AUTHORITY ☒ HEALTH PROFESSIONAL ☒ LICENSE

NOV 1 1 1999
DATE SENT TO FDA

25a. REPORT TYPE ☒ INITIAL ☐ FOLLOWUP

CENTER FOR DRUG EVALUATION AND RESEARCH REC'D NOV 12 1999 CDR

NOV 12 1999

...Safety Report...

3396... -00-02

ADVERSE ...ERIENCE REPORT

Manufacturer Co... : HQ4572304NOV1999

Box # 13 - ...ESTS/LABORATORY DATA (Continuation)

Test Name / Date	Result	Normal Range
Ultrasound ... 00-...	...l screen Gestational age is 4-5 weeks.	

Box # 23 - ...ANT HISTORY (Continuation)

Conception ...: [redacted]
Delivery ...
Confirmat...: Ultrasound

NOV 12 1993

Adverse Event Reporting System (AERS)

ISR Information Report for ISR #(s)

5088172-X 5337347-0

Run by: STEPPER
Date Run: 06/01/2008
Total ISRs: 2

FDA - Adverse Event Reporting System (AERS)

ISR Information Report for ISR #5088172-X

ISR Information:

ISR #: 5088172-X
Case #: 5926485
ISR Type: Expedited (15-Day)
FDA Rcvd. Date: 08/24/2006
Outcome(s): HO

Best Rep. ISR: Yes
eSub ISR: Yes

Initial or Follow-up ISR: Follow-up
Verbatim Follow-up #:

Manufacturer Information:

Sender Mfr: ABBOTT
Mfr. Control #: GB-ABBOTT-05P-167-0317426-00
Mfr. Rcvd. Date: 08/15/2006
Primary Suspect (A)NDA/PLA #:

Patient Information:

Patient ID: UNKNOWN
Age: 77.45 YR
DoB: [redacted]
Gender: Female
Weight: 65 Kilogram
Event Start Date: 05/05/2005

Reporter Information:

Reporter Name: [redacted]
Reporter Org.:
Reporter Street:
Reporter Zip:
Reporter Phone:
Reporter City:
Reporter State:
Reporter Country: UNITED KINGDOM
Health Prof.: YES
Occupation: OTHER HEALTH PROFESSIONAL

Product(s)	Role	Dosage Text	Route	Lot #	NDC #	Indication(s)	Therapy Start Date	Therapy End Date	Interval 1st Dose to Event	DeC	ReC
HUMIRA	P		SUBCUTANEOUS	UNKNOWN		RHEUMATOID ARTHRITIS	05/09/2003				

Reaction(s) **ReC**

ACTH STIMULATION TEST ABNORMAL

BLOOD POTASSIUM INCREASED

Relevant Laboratory

Test Date	Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail Y/N
	Body height	165	CM			
05/05/2005	Potassium	Increased				
05/05/2005	Synacthen test	Long				

Relevant Medical History

The patient has a history of rheumatoid arthritis since 1993, hypertension since 1996, and peptic ulcer disease since 2003. BSRBR patient number: 0002999

Disease/Surgical Procedure	Start Date	End Date	Continuing	Comment

HYPERTENSION

PEPTIC ULCER

Medical History Product(s)	Start Date	End Date	Indication(s)	Reaction(s)

Event/Problem Narrative

Report from the United Kingdom of increased blood potassium level and long synacthen test coincident with ADALIMUMAB (HUMIRA PRE-FILLED SYRINGE) therapy. On 09 May 2003, the patient began HUMIRA PRE-FILLED SYRINGE therapy for rheumatoid arthritis. On [redacted] the patient was hospitalized for increased blood potassium level and long synacthen test. The events of increased blood potassium level and long synacthen test resolved. The reporting healthcare professional believed the events of increased blood potassium level and long synacthen test were not related to HUMIRA PRE-FILLED SYRINGE therapy. Follow-up information received on 15 Aug 2006: This case was determined to be a duplicate of AER 06P-167-0339103-00, which will be invalidated. Information from both cases will be combined into this case.

Study Report?: No

Study Name:

Study Type:

Sponsor Study #:

Protocol #:

IND #:

Literature Text:

FDA - Adverse Event Reporting System (AERS)
ISR Information Report for ISR #5337347-0

ISR Information:

ISR #: 5337347-0
Case #: 6321897
ISR Type: Expedited (15-Day)
FDA Rcvd. Date: 05/29/2007
Outcome(s): DE

Best Rep. ISR: No
eSub ISR: Yes

Initial or Follow-up ISR: Initial
Verbatim Follow-up #:

Manufacturer Information:

Sender Mfr: BERLEX
Mfr. Control #: BR-SHR-BR-2007-018677
Mfr. Rcvd. Date: 05/22/2007
Primary Suspect (A)NDA/PLA #: 021225

Patient Information:

Patient ID: [redacted]
Age: 41 YR
DoB: [redacted]
Gender: Female
Weight:
Event Start Date:

Reporter Information:

Reporter Name:
Reporter Org.:
Reporter Street:
Reporter Zip:
Reporter Phone:
Reporter City:
Reporter State:
Reporter Country: BRAZIL
Health Prof.: NO
Occupation: CONSUMER OR OTHER NON HEALTH PROFESSIONAL

Product(s)	Role	Dosage Text	Route	Lot #	NDC #	Indication(s)	Therapy Start Date	Therapy End Date	Interval 1st Dose to Event	DeC	ReC
MIRENA	P	20 Âµg/day, cont	INTRA-UTERINE				09/01/2002				

Reaction(s) **ReC**
DEATH

Relevant Laboratory

Test Date	Test Name	Result	Unit	Normal Low Range	Normal High Range	Info Avail Y/N

Relevant Medical History

Disease/Surgical Procedure	Start Date	End Date	Continuing	Comment

Medical History Product(s)	Start Date	End Date	Indication(s)	Reaction(s)

Event/Problem Narrative

This report describes the occurrence of unspecified death in a 41 year-old female who had levonorgestrel (Mirena, IUS) inserted. This report was received on 22 May 2007 via patient support program from a company representative and has not been verified by a physician or other health care professional. The company became aware of this case after receiving back the patient support program magazine from the Post Office. They informed that it could not be delivered because the patient died. There was no medical history, concurrent conditions or concomitant medications reported. It was not reported if Mirena was used previously and tolerated. In Sep-2002 the patient received the first dose of levonorgestrel (Mirena) at 20 Âµg/day, cont via intra-uterine for an unspecified indication. On an unspecified date the patient experienced unspecified death. The patient died from

unspecified death. It was not reported if an autopsy was performed. Death occurred on an unspecified date, after treatment with Mirena was started.

Study Report?: Yes

Study Name:
Study Type: OTHER STUDIES
Sponsor Study #:

Protocol #:
IND #:

Literature Text: