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<td>26</td>
<td></td>
</tr>
<tr>
<td>8/8/2003</td>
<td>4181339-4</td>
<td>similar Plan b</td>
<td>26</td>
<td></td>
</tr>
</tbody>
</table>

9/2/2005 4764187-3  Plan b  Ectopic
5/10/2006 4999818-6  Plan b  Ectopic
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 Ethinylin 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 Ethinylin 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.
A. Patient Information
1. Patient identifier:  
2. Age at onset of event: 19 YR  
3. Sex: X female  
4. Weight: lbs  
   in confidence: Unknown  
   Date of birth: Unknown

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 (within 30 days)
   X life-threatening
   X hospitalization - initial or prolonged
   X recovered
   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.

C. Suspect medication(s)
1. Name (give labeled strength & mfr/labl./if known)
   X TRINORDIOL (0.05MG LNG/0.05MG E.E., 0.075 LNG/0.04MG E.E.,
   0.125MG LNG/0.03MG E.E.)

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

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

4. Diagnosis for use (indication)
   X Unknown

5. Event abated after use stopped or dose reduced
   X yes

6. Lot # (if known)

7. Exp. date (if known)

8. Event reappeared after reintroduction
   X yes
   X no

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
   X study
   X literature
   X consumer
   X health professional
   X user facility
   X company representative
   X distributor
   X other:

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

5. FDA # 19-192

6. 8 IND # PLAB #

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

2. Health professional?
   Yes

3. Occupation
   N/A

4. Initial reporter also sent report to FDA
   Yes

5. Dates of treatment
   [Redacted]
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)
ZOEVIRAX 800 mg QID ORAL (04/00/96 to 04/00/97)
A. Patient information
1. Patient identifier 
2. Age at time of event: 23 YR
3. Sex: female
4. Weight: 129 lbs

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
   - life-threatening (must in days/months/year)
   - hospitalization - inpatient or prolonged
   - required intervention to prevent permanent impairment or damage
   - other:

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

5. Describe event or problem
The patient, with Down's Syndrome, presented to the ER unresponsive with DNR 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.

C. Suspect medication(s)
1. Name (give strength & maker/labeler, if known)
   - TRIFASIL-28 TABLETS

2. Dose, frequency & route used:
   - 1 TABLET ONCE DAILY ORAL
   - 08/08/96 to 04/14/97

3. Therapy dates (if unknown, give duration):
   - 08/08/96 to 04/14/97

4. Diagnosis for use (indication)
   - REGULATE MENSES/DYSMENORRHEA

5. Event aborted after use stopped or dose reduced:
   - yes
   - no
   - doesn't apply

6. Lot # (if known)
   - 1

7. Exp. date (if known)
   - 1

8. Event reappearance after reintroduction:
   - yes
   - no
   - doesn't apply

9. NDC # for product problems only (if known)
   - 0

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 CHESTERTOWN ROAD
   ST. DAVIDS, PA. 19087

KAREL F. BERNARDI, PH.D.

2. Phone number
   (610) 902-3760

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)
   04/24/97

5. IND No.
   19-190

6. PL No.
   PLX

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

8. Event reviewed after reintroduction:
   - yes
   - no
   - doesn't apply

9. Mfr. report number
   8-97116-249N

10. Adverse event term(s)
    PULMONARY EMBOLUS

E. Initial reporter
1. Name, address & phone #

2. Health professional?
   - yes
   - no

3. Occupation
   Pharmacist

4. Initial report also sent to FDA
   - yes
   - no
Box 8.6 - Relevant Tests/Laboratory Data, including dates (Continuation)

<table>
<thead>
<tr>
<th>DATE</th>
<th>TEST</th>
<th>RESULT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Provisional autopsy report</td>
<td>Coiled thrombus in main pulmonary artery occluding both right and left</td>
</tr>
<tr>
<td></td>
<td></td>
<td>pulmonary arteries with partial organization of thrombus in secondary</td>
</tr>
<tr>
<td></td>
<td></td>
<td>branch of left pulmonary artery; peripheral wedge infarct of lower left</td>
</tr>
<tr>
<td></td>
<td></td>
<td>lung lobe</td>
</tr>
</tbody>
</table>

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

LEVOHYDROXINE 0.075 mg
IRON SUPPLEMENT

DEC 01 1997
### ADVERSE EXPERIENCE REPORT

#### REACTION INFORMATION

<table>
<thead>
<tr>
<th>1. PATIENT INITIALS</th>
<th>2. COUNTRY</th>
<th>3. DATE OF BIRTH</th>
<th>4-5. AGE UNITS</th>
<th>6. SEX</th>
<th>7. EXPERIENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Day</td>
<td>Month</td>
<td>33Yr</td>
<td>F</td>
</tr>
</tbody>
</table>

#### 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 Micronor (0.15mg levonorgestrel/0.03mg ethinyl estradiol) (equivalent to Nordestyl 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].

#### 13 RELEVANT TESTS/LABORATORY DATA

None Provided.

#### SUSPECT DRUG(S) INFORMATION

14. **SUSPECT DRUG(S) INCLUDING ACTIVE SUBSTANCE(S):**

- NORGESTREL (0.15MG LEVONORGESTREL/0.03MG ETHINYL ESTRADIOL, TABLET)

15. DAILY DOSE(S):

- 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINISTRATION:

- Oral

17. INDICATION(S) FOR USE:

- [Redacted]

18. THERAPY DATES (FROM/TO):

- 00-UNK-1997 / 20-APR-2001

19. THERAPY DURATION:

- 3 Yr

#### CONCOMITANT DRUG(S) AND HISTORY

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

Unknown

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

UNK

### IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

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

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

24b. MFR CONTROL NO.:

HQ2066614JUN2001

24c. DATE RECEIVED BY MANUFACTURER:

14-Jun-2001

24d. REPORT SOURCE:

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

Date of this report:

15-Jun-2001

25a. REPORT TYPE:

[X] INITIAL

[ ] FOLLOWUP

### OTHER REFERENCE NUMBERS:

Regulatory Authority (RA) (via Schering AG):
01/01822-CDS

DSS

JUN 19 2001

CDR/CDE-H

JUN 1 5 2001

DATE SENT TO FDA
### Individual Safety Report

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>16 Years</td>
<td>Female</td>
<td>154.3 lbs</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>70.0 lbs</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5. Adverse event or product problem</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adverse event and/or Product problem (e.g., defect/malfunction)</td>
</tr>
<tr>
<td>[X] Death</td>
</tr>
</tbody>
</table>

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

### Case Description

This report was received by King Pharmaceuticals, Inc. on 10/28/2004 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 1/3/2004 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 6/1/2001, closed fracture of the right fifth metatarsal, tonsillitis diagnosed on 2/5/2003 and treated with penicillin, and a recurrence of tonsillitis symptoms on continued in additional info section...

### Concomitant medications and therapy dates (exclude treatment of event)

- **NORDETTE-21 (LEVONORGEST) (continued)**
- **1 tablet, gd, Oral**
- **01/13/2004 to 03/31/2004**

---

**G. All Manufacturers**

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

   King Pharmaceuticals, Inc.
   501 Fifth Street
   Bristol, TN 37620 UNITED STATES

2. Phone number

   916537005

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

   07/14/2004

5. ANOVA #: 18-668

6. IF IND, protocol #

   pro-1938

7. Type of report (check all that apply)

   [ ] 5-day
   [ ] 15-day
   [ ] 10-day
   [ ] periodic

8. Adverse event term(s)

   Pulmonary Infarction, Pulmonary embolism, chest pain, dyspnoea, cough, and granuloma NOS, pulmonary oedema NOS, continued in additional info section...

9. MIF report number

   K9200400695

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

   - **NORDETTE-21 (LEVONORGEST) (continued)**
   - **1 tablet, gd, Oral**
   - **01/13/2004 to 03/31/2004**

---

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

26-Jul-2004 13:14

JUL 27 2004
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 119/77 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 36 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

<table>
<thead>
<tr>
<th>#</th>
<th>Date</th>
<th>Test / Assessment / Notes</th>
<th>Results</th>
<th>Normal High / Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>[redacted]</td>
<td>Electrocardiogram</td>
<td>Nothing abnormal detected</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>[redacted]</td>
<td>Post mortem</td>
<td>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</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>[redacted]</td>
<td>Paracetamol level</td>
<td>4 mg/l</td>
<td>6 2</td>
</tr>
</tbody>
</table>

No other drugs were detected in the blood.

B7. OTHER RELEVANT HISTORY

<table>
<thead>
<tr>
<th>#</th>
<th>Start/Stop Date</th>
<th>Condition Type / Condition</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>UNK</td>
<td>Historical Condition</td>
<td>Left ankle injury: rupture of lateral collateral ligament.</td>
</tr>
</tbody>
</table>

JUL 27 2004 DSS

JUL 28 2004
## Individual Safety Report

### Experience Report (continued)

<table>
<thead>
<tr>
<th>No.</th>
<th>Condition</th>
<th>Status</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>UNK</td>
<td>Historical Condition</td>
<td>Foot fracture</td>
</tr>
<tr>
<td>3</td>
<td>UNK</td>
<td>Historical Condition</td>
<td>Tonsillitis</td>
</tr>
<tr>
<td>5</td>
<td>UNK</td>
<td>Current Condition</td>
<td>Overweight</td>
</tr>
</tbody>
</table>

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

G8. ADVERSE EVENT TERMS (cont.)
Pericardial effusion

**JUL 2 7 2004**

26-Jul-2004 13:14
### A. Patient Information

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>UNK</td>
<td>16 Years</td>
<td>female</td>
<td>UNK lbs</td>
</tr>
</tbody>
</table>

### B. Adverse event or product problem

- **Event Type**: Adverse event
- **Product Problem**: Pulmonary embolism

### Case Description:

This report was received by King Pharmaceuticals, Inc. on 10/15/2004 via fax from Barlex Laboratories. A regulatory authority reported that a 16-year-old female patient received oral levonorgestrel/ethinyl estradiol 1 tablet daily starting 13JAN2004 for oral contraception. There were no concomitant medications or significant past medical history. On 03/31/2004, 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.

### Relevant tests/laboratory data, including dates

None.

### Other relevant history, including preexisting medical conditions

None.

---

### C. Suspect medication(s)

<table>
<thead>
<tr>
<th>1. Name (give labeled strength and formulation, if known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORDETTE-21(LEVONORGEST (continued))</td>
</tr>
</tbody>
</table>

### D. Date of event

03/31/2004

### E. Initial reporter

- **Name & address**: [Redacted]
- **Phone**: [Redacted]
- **Health professional?**: Yes
- **Occupation**: Other Manufacturer
- **Initial reporter also sent report to FDA**: Yes

### Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.
C1. Name (cont.)
Suspect Medication #1: NORDETTE -21(LEVONORGESTREL, ETHINYLESTRADIOL) Tablet
The FDA Safety Information and Adverse Event Reporting Program

<table>
<thead>
<tr>
<th>A. PATIENT INFORMATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Patient Identifier</td>
</tr>
<tr>
<td>2. Age at Time of Event: UNK</td>
</tr>
<tr>
<td>3. Sex (\checkmark) Female</td>
</tr>
<tr>
<td>4. Weight UNK or UNK</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>B. ADVERSE EVENT OR PRODUCT PROBLEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Adverse Event (\checkmark) Death</td>
</tr>
<tr>
<td>2. Outcomes Attributed to Adverse Event (Check all that apply)</td>
</tr>
<tr>
<td>3. Date of Event (mo/day/year) UNK</td>
</tr>
<tr>
<td>4. Date of This Report (mo/day/year) 02/01/2006</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C. SUSPECT MEDICATION(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Name (Give labeled strength &amp; refill if known)</td>
</tr>
<tr>
<td>2. Dose, Frequency &amp; Route Used</td>
</tr>
<tr>
<td>3. Therapy Dates (if unknown, give duration)</td>
</tr>
<tr>
<td>4. Diagnosis for Use (Indication)</td>
</tr>
<tr>
<td>5. Event Altered After Use Stopped or Dose Reduced?</td>
</tr>
<tr>
<td>6. Lot # (if known)</td>
</tr>
<tr>
<td>7. Exp. Date (if known)</td>
</tr>
<tr>
<td>8. Event Reappeared After Reintroduction?</td>
</tr>
<tr>
<td>9. NDC(s) (For product problems only)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>G. ALL MANUFACTURERS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Contact Office - Name/Address (and Manufacturing Site for Devices)</td>
</tr>
<tr>
<td>2. Phone Number 20193030302</td>
</tr>
<tr>
<td>3. Report Source (Check all that apply)</td>
</tr>
<tr>
<td>4. Date Received by Manufacturer (mo/day/year) 01/26/2006</td>
</tr>
<tr>
<td>5. IF IND, Give Protocol # Pre-1938</td>
</tr>
<tr>
<td>6. Type of Report (Check all that apply)</td>
</tr>
<tr>
<td>7. Other Relevant History, Including Presenting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatocellular dysfunction, etc.)</td>
</tr>
<tr>
<td>8. Other Relevant History, Including Presenting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatocellular dysfunction, etc.)</td>
</tr>
<tr>
<td>9. Manufacturer Report Number 006392</td>
</tr>
</tbody>
</table>

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 (Microgynon, 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 Presenting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatocellular dysfunction, etc.)
#1 UNK, Historical Memo, History of drug related leukopenia (Azathioprine)

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 03 2006
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 erthematosus
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

Page 1 of 1

A. Patient information
1. Patient identifier
2. Age at time of event or Date of birth:
3. Sex
4. Weight
   ☐ male
   ☐ female
   153 lbs

B. Adverse event or product problem
1. Adverse event and/or Product problem (e.g., defects/malfunctions)
2. Outcomes attributed to adverse event
   ☐ death
   ☐ dis ease
   ☐ congenital anomaly
   ☐ life-threatening
   ☐ hospitalization – initial or prolonged
   ☐ other:

3. Date of event
   2-20-03

4. Date of this report
   2-21-03

5. Describe event or problem

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

6. Relevant tests/laboratory data, including dates

DSS
FEB 28 2003

C. Suspect medication(s)
1. Name (give labeled strength & mfr/labeler, if known)
   #1
   Nordette 21 day
   Ortho Novum 150 28 day

2. Dose, frequency & route used
   #1
   1 po QD

3. Therapy dates (if unknown, give duration):
   #1
   1 po QD
   #2
   unknown

4. Diagnosis for use (indication)
   menorrhagia
   menorrhagia

5. Event abated after use stopped or dose reduced
   ☐ yes
   ☐ no
   ☐ doesn’t apply

6. Lot # (if known)
   #1
   N/A
   #2
   N/A

7. Exp. date (if known)
   #1
   N/A
   #2
   N/A

8. Event reappeared after reintroduction
   ☐ 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

RECEIVED
MEdWAtCH Ctu
FEB 28 2003

2. Type of device

3. Manufacturer name & address

4. Operator of device
   ☐ health professional
   ☐ lay user/patient
   ☐ other

5. Expiration date
   ☐ month

6. Model #

7. If implanted, g date
   ☐ month

8. If explanted, g date
   ☐ month

9. Device available for evaluation?
   ☐ yes
   ☐ no
   ☐ returned to manufacturer

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

E. Reporter (see confidentiality section on back)
1. Name, address & phone

2. Health professional?
   ☐ yes
   ☐ no

3. Occupation
   ☐ mEdicAte
   ☐ phAmmo

4. Also reported to
   ☐ mEdicAte
   ☐ phAmmo

5. If you do NOT want your identity disclosed to the manufacturer, place an “X” in this box.

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

1. Patient identifier: UNK
2. Age at time of event: UNK
3. Sex: female
4. Weight: UNK lbs

**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)
   - death
   - disability
   - congenital anomaly
   - life-threatening
   - required intervention to prevent permanent impairment/damage
   - hospitalization-initial or prolonged
   - recovered
   - other:
3. Date of event (month/day/year): UNK
4. Date of the report (month/day/year): 11/23/1999

**Description of event or problem**

STROKE. Information has been received from an attorney regarding an unidentified female patient (age unspecified) who had been prescribed Triphas-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 8 tablets. The interval at which the patient took the tablets is unknown. Twelve days after receiving Triphas-28 therapy the patient suffered a stroke and died. No further information was provided.

**Relevant laboratory data, including dates**

None provided.

**Other relevant history, including pre-existing 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.
**ADVERSE EXPERIENCE REPORT**

I. REACTION INFORMATION

<table>
<thead>
<tr>
<th>1. PATIENT INITIALS</th>
<th>a. COUNTRY</th>
<th>2. DATE OF BIRTH</th>
<th>2a. AGE UNITS</th>
<th>3. SEX</th>
<th>4-6. EXPERIENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>France</td>
<td></td>
<td></td>
<td>F</td>
<td>38Yr</td>
</tr>
</tbody>
</table>

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/0.0125MG 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)

<table>
<thead>
<tr>
<th>8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>☑ PATIENT DIED</td>
</tr>
<tr>
<td>☑ INVOLVED OR PROLONGED INPATIENT HOSPITALIZATION</td>
</tr>
<tr>
<td>☑ INVOLVED PERSISTENCE OF SIGNIFICANT DISABILITY OR INCAPACITY</td>
</tr>
<tr>
<td>☑ LIFE THREATENING</td>
</tr>
<tr>
<td>☑ NONE OF THE ABOVE</td>
</tr>
<tr>
<td>☑ RECOVERED</td>
</tr>
</tbody>
</table>

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/0.0125MG LNG/0.03MG EE, TABLET) |

15. DAILY DOSE(S)

| #1 |

16. ROUTE(S) OF ADMINISTRATION

| #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/MON/YY)

| TYLENOL (PARACETAMOL), Unknown |

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

| UNK |

IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

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

<table>
<thead>
<tr>
<th>WYETH LABS (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>201 King of Prussia</td>
</tr>
<tr>
<td>Sixth Floor</td>
</tr>
<tr>
<td>Radnor, PA 19087-5114</td>
</tr>
</tbody>
</table>

24b. MFR CONTROL NO

| HQ4722412DEC2000 |

24c. DATE RECEIVED BY MANUFACTURER

| 20-Dec-2000 |

24d. REPORT SOURCE

| ☐ STUDY |
| ☐ CONSUMER |
| ☑ LITERATURE |
| ☑ REGULATORY |
| ☐ HEALTH |
| ☐ PROFESSIONAL |
| ☐ LICENSE |

25a. REPORT TYPE

| ☑ INITIAL |
| ☑ FOLLOWUP |

25c. DATE SENT TO FDA

| DEC 28 2000 |

26c. RECIPT NO

| DEC 29 2000 |

26d. CHECK FOR DRUG RECALL RECOMMENDATION

| A | B |

27a. NOTifier's Signature

| DSS |

27b. Date

| DEC 29 2000 |

27c. Signature

| ☑ ☑ |
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)

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Data</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laboratory test abnormal NOS</td>
<td>Autopsy showed diffuse capillary thrombi involving most organs and confirmed diagnosis of thrombotic microangiopathy.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelet count decreased</td>
<td>10 Giga L</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DSS
JAN 02 2001

DEC 29 2000
Fatal thrombotic thrombocytopenic purpura: Role of oral contraceptives?

Zenut M. Lamaison D. Merle P. Souweine B. -Caillaud D

Therapie 55(3):413, Abstr: 42b, 2000 May-Jun
4th Annual Congress of French Society of Pharmacology, Rouen, 10-12 Apr 2000

A severe thrombopenia (10 giga/1) 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 eye ground minor bleeding otherwise clinical examination and cranial tomodensitometry were normal. Additional investigation showed hemolytic anemia and the presence of schizontes, 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) (CISZ) 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 (WISOWSKI DK and GREEN L., 1995). Another case of TTP has been mentioned in a 18 old girl on low dose oral progestatives (CAILLARD S., 1998).
MED WATCH
THE FDA MEDICAL PRODUCTS REPORTING PROGRAM
Page 1 of 2

A. Patient Information
1. Patient initials: [Confidential]
2. Age at time of event: 34 years
3. Sex: Female
4. Weight: 70 lbs

B. Adverse event or product problem
1. Adverse event and/or product problem e.g., (defects/malfunctions)
   - death
   - life-threatening
   - hospitalization - Initial or prolonged

2. Outcomes attributed to adverse event
   - disability
   - congenital anomaly
   - required intervention to prevent permanent impairment/damage
   - other:

3. Date of event: 10 Apr 2000
4. Date of this report: 24 Jan 2000

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. 061); and follow-up #4 on 03 Jan 01 (serial no. 068).

   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. Physican 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, no risk factors, multipara (2 children), allergy to penicillin.
   No clotting disorder in known.

C. Suspect medication(s)
1. Name (give labeled strength & mfclabeler, if known):
   #1 MIRENA (levonorgestrel)

   #2

   #3

   #4

   #5

   #6

   #7

   #8

   #9

   #10

G. All manufacturers
1. Contact office - name/address & mfg site for device(s)
   Berlex Laboratories, Inc.
   300 Fairfield Road
   Wayne, NJ 07470
   USA

2. Phone number: (888) 237-5394

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

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

5. Similar to:
   A/NDA # 21-225
   IND
   PLA
   pre-1938
   OTC
   product

6. Adverse event term(s)
   EMB PULM
   THROMBOPHLEB DEEP
   CONVULS
   HEART ARREST

E. Reporter
1. Name, address & phone #
   <redacted>

2. Health professional?
   Yes [ ] No [ ]

3. Occupation
   Physician

4. Initial reporter also
   sent report to FDA
   Yes [ ] No [ ] unk
B.5. Describe event or problem

Gynecologist's written report:
Patient suffered from cardiac arrest in ____. 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 ____. When emergency physician arrived husband had already performed CPR for 15 minutes because of apnea/difficult breathing. An incubation 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 26 2001
A. Patient Information

1. Patient Initials
   - [__________]
2. Age at time of event: 45 years
3. Sex: ☐ female
   ☑ male
4. Weight: 60 lbs
   ☐ 180 lbs

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)
   □ disability
   □ congenital anomaly
   □ required intervention to prevent permanent impairment/damage
   □ hospitalization - initial or prolonged
   □ other: death 2001

C. Suspect medication(s)

1. Name (give labeled strength & mf/labeler, if known)
   #1 MIRANOVA (levonorgestrel, ethinyloestradiol)

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

3. Therapy dates (if unknown, give duration)
   #1 1996 - approx. 5 years
   #2

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

5. Event started after use stopped or dose reduced
   #1 Yes #2 No

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

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

8. NDC # - for product problems only (if known)
   #1
   #2

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

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

D. All manufacturers

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

3. Report source (check all that apply)
   ☑ Foreign
   ☐ Study
   ☐ Literature
   ☐ Consumer
   ☐ Health professional
   ☐ User facility
   ☐ Company representative
   ☐ Other:

4. Date received by manufacturer (MM/DD/YYYY)
   26 Mar 2001

5. Similar to:
   (A/NDA # 20-860)

6. If IND, protocol #
   IND #
   PLA #
   pre-1938 ☐ yes
   OTC ☐ product
   ☐ yes

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

8. Adverse event term(s)
   HEART FAIL RIGHT

E. Reporter

1. Name, address, phone #
   [__________]

2. Health professional? ☐ yes ☑ no
3. Occupation ☐ Physician

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

Country of origin: Germany
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.
**ADVERSE EXPERIENCE REPORT**

### REACTION INFORMATION

<table>
<thead>
<tr>
<th>1. PATIENT INITIALS</th>
<th>2. COUNTRY</th>
<th>2a. DATE OF BIRTH</th>
<th>2a. AGE</th>
<th>3. SEX</th>
<th>4-6. EXPERIENCE</th>
<th>8-12. CHECK ALL APPROPRIATE TO ADVERSE REACTION</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Denmark</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>7. DESCRIBE EXPERIENCE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PULMONARY EMBOLISM</td>
</tr>
</tbody>
</table>

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 Nordenesta 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].

### SUSPECT DRUG(S) INFORMATION

<table>
<thead>
<tr>
<th>14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1: MICROGYNON (0.15MG LEVONORGESTREL/0.03MG ETHINYL Estradiol, TABLET)</td>
</tr>
</tbody>
</table>

### SUSPECT DRUG(S) INFORMATION

<table>
<thead>
<tr>
<th>15. DAILY DOSE(S)</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1: 1 Tablet 1x per 1 Day</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>16. ROUTE(S) OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1: Oral</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>18. THERAPY DATES (FROM TO)</th>
</tr>
</thead>
<tbody>
<tr>
<td># 1: 00-JUN-1997 / 20-APR-2001</td>
</tr>
</tbody>
</table>

### CONCOMITANT DRUG(S) AND HISTORY

<table>
<thead>
<tr>
<th>22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DAY/MON/YY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
</tr>
</tbody>
</table>

### OTHER RELEVANT HISTORY (e.g. diagnosis, allergies, pregnancy within last month of period, etc.)

UNK

---

### RECEIVED

**JUN 1 8 2001**

**CDR/CGER**

---

### ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

<table>
<thead>
<tr>
<th>24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VERSTSPHARMA (RA)</td>
</tr>
<tr>
<td>101 Kli. Nr. 15</td>
</tr>
<tr>
<td>Gt. Kli. Nr. 15</td>
</tr>
<tr>
<td>Radnor, PA 19087-5114</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>24c. DATE RECEIVED BY MANUFACTURER</th>
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<tbody>
<tr>
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<tr>
<th>24d. REPORT SOURCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>X CONSUMER REGULATORY AUTHORITY</td>
</tr>
</tbody>
</table>

<table>
<thead>
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<th>25. REPORT TYPE</th>
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</thead>
<tbody>
<tr>
<td>INITIAL</td>
</tr>
</tbody>
</table>

---

**DSS**

**JUN 1 9 2001**

**JUN 1 5 2001**

**DATE SENT TO FDA**
THE FDA MEDICAL PRODUCTS REPORTING PROGRAM
Page 1 of

A. Patient information

1. Patient initials

2. Age at time of event: 40 years
   - or -
   Date of birth: Unknown

3. Sex
   - or -
   Female

4. Weight
   - or -
   Lbs

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)
   - disability
   - congenital anomaly
   - required intervention to prevent permanent impairment/damage
   - hospitalization - initial or prolonged
   - other:

3. Date of event
   - or -
   (dd Mon yyyy)
   Unknown

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

C. Suspect medication(s)

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

2. Dose, frequency & route used
   - or -
   0.02 mg intraterine

3. Therapy dates
   (if unknown, give duration)
   - or -
   20 Jul 2000 - 27 Jul 2001

4. Diagnosis for use (indication)
   - reduction of menstrual flow

5. Event abated after use stopped or dose reduced
   - yes
   - no
   - doesn't apply

6. Lot # (if known)
   - Unknown

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

D. Description of 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 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 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 the patient died.

Outcome: died

E. Relevant past/laboratory data, including dates

None reported

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

G. All manufacturers

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

2. Phone number
   (888)237-5394

3. Report source
   - foreign
   - study
   - literature
   - consumer

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

5. Similar to
   - (A)NDA # 21-225
   - IND 
     PLA 

6. If IND, protocol #

7. Type of report
   (check all that apply)
   - 5-day
   - 10-day periodic
   - Initial
   - follow-up

8. Adverse event term(s)
   - PANCREATITIS

E. Reporter

1. Name, address & phone #

Country of origin: Brazil

FDA
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 22 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

FDA

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 2 2001
ADVERSE EXPERIENCE REPORT

1. PATIENT INITIALS: Canada

2. DATE OF BIRTH: Day: 11 Month: SEP

3. AGE: 20Yr

4. SEX: Female

5. EXPERIENCE: Day: 11 Month: SEP Year: 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), Flosnase (fluticasone propionate), Clozaril (clozapine), and 'Serequel'. The patient experienced a seizure (convulsions NOS) on 13-SEP-2001 and was taken to the hospital. The following day her blood pressure dropped (blood pressure decreased). Subsequently, the patient died on 13-SEP-2001. According to the coroner, the cause of death was a pulmonary embolism (pulmonary embolism).

13. RELEVANT TESTS/LABORATORY DATA
   None provided.

14. SUSPECT DRUG(S) INFORMATION
   ALESSE-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)

   15. DAILY DOSES:
   #1 Tablet 1x per 1 Day

   16. ROUTES(S) OF ADMINISTRATION
   #1 Oral

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

   18. THERAPY DATES (FROM/TO):
   #1 00-Mar-2001 / 00-UNK-2001

   19. THERAPY DURATION
   #1 Unknown

II. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DAW/MONTH):

   EFFEXOR XR (VENLAFAXINE HYDROCHLORIDE), Unknown
   TOPAMAX (TOPIMARATE), Unknown
   FLOSNASE (FLUTICASONE PROPIONATE), Unknown
   CLOZARIL (CLOZAPINE), Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnosis, allergies, 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 19087-514

24b. MFR CONTROL NO.
   HQ5992414SEP2001

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

DSS
SEP 20 2001

SEP 21 2001
SEP 19 2001
DATE SENT TO FDA
Box 22 - CONCOMITANT DRUGS AND DATES OF ADMINISTRATION

CLONAZEPAM (CLONAZEPAM), Unknown
For use by user-facilities, distributors and manufacturers for MANDATORY reporting Berlex Laboratories

Page 1 of 5

INDIVIDUAL SAFETY REPORT

The FDA Medical Products Reporting Program

396141-9-66-81

1. Name (give labeled strength & manufacturer, if known)
   #1. Levetiracetam (LEVONO) (continued)

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

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

4. Diagnosis for use (Indication)
   #1. UNK

5. Event labeled after use
   stoppage or dose reduced
   #1. No doesn't apply

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

7. Exp. Date (if known)
   #1. UNK

8. Event happened after 
   start of treatment
   #1. Yes no doesn't apply

9. NDC # -- for product problems only (if known)
   #1. Yes no doesn't apply

10. Concurrent medical products and therapy dates (exclude treatment of event)
   TYLENOL EXTRA-STRENGTH UNK to UNK (FERROSULFATE (FERROSULFATE) UNK to UNK continued in additional info section)

G. All Manufacturers

1. Contact office - name/address (if mailing site for device)
   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"
   "intraservice"
   "consumer"
   "health"
   "professional"
   "user facility"
   "company representative"
   "distributor"
   "other"

4. Data received by manufacturer
   07/26/2002

5. FDA
   IND: 20-860
   FDA #: PLA # OTC product
   pre-9388
   yes

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

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

E. Initial reporter

1. Name & address
   phone
   UNK

2. Health professional?
   yes no

3. Occupation
   Professor / Faculty member

4. Initial reporter also sent report to FDA
   yes no
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 Levilite 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.
<table>
<thead>
<tr>
<th></th>
<th>Date</th>
<th>Test / Assessment / Notes</th>
<th>Results</th>
<th>Normal High / Low</th>
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</thead>
<tbody>
<tr>
<td>6</td>
<td></td>
<td>Stool</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>No ova or parasites; Clostridium difficile negative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td></td>
<td>AST (SGOT)</td>
<td>65 U/L</td>
<td>42 U/L</td>
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<tr>
<td></td>
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<td></td>
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<td>10 U/L</td>
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<td>8</td>
<td></td>
<td>ALT (SGPT)</td>
<td>138 U/L</td>
<td>33 U/L</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>7 U/L</td>
</tr>
<tr>
<td>9</td>
<td></td>
<td>Hemoglobin</td>
<td>8.0 g/dL</td>
<td>16.1 g/dL</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12.0 g/dL</td>
</tr>
<tr>
<td>10</td>
<td></td>
<td>Hematocrit</td>
<td>28.5%</td>
<td>48.0%</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>36.0%</td>
</tr>
<tr>
<td>11</td>
<td></td>
<td>Thrombin time</td>
<td>100.0s</td>
<td>10.7s</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>8.9s</td>
</tr>
<tr>
<td>12</td>
<td></td>
<td>Antithrombin III</td>
<td>0.92 U/ml</td>
<td>1.29 U/ml</td>
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<td></td>
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<td></td>
<td>0.95 U/ml</td>
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<td>13</td>
<td></td>
<td>Anti-phospholipid: IgG</td>
<td>2 GPL</td>
<td>11 GPL</td>
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<td></td>
<td></td>
<td></td>
<td>0 GPL</td>
</tr>
<tr>
<td>14</td>
<td></td>
<td>Anti-phospholipid: IgM</td>
<td>5 MPL</td>
<td>13 MPL</td>
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<tr>
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<td></td>
<td></td>
<td>0 MPL</td>
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<tr>
<td>15</td>
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<td>Anti-cardiolipid: IgG</td>
<td>10 GPA</td>
<td>&lt;25 GPA</td>
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<tr>
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<td>Anti-cardiolipid: IgM</td>
<td>4 MPA</td>
<td>&lt;10 MPA</td>
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<tr>
<td>17</td>
<td></td>
<td>Anti-cardiolipid: IgA</td>
<td>3 APA</td>
<td>&lt;12 APA</td>
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<td>Anti-phosphatidyserine: IgG</td>
<td>20 GPS</td>
<td>&lt;10 GPS</td>
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<tr>
<td>19</td>
<td></td>
<td>Anti-phosphatidyserine: IgM</td>
<td>17 MPS</td>
<td>&lt;26 MPS</td>
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<tr>
<td>20</td>
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<td>Anti-Beta2GPI: IgG</td>
<td>3 SGA</td>
<td>9 SGA</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>0 SGA</td>
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<tr>
<td>21</td>
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<td>Anti-Beta2GPI: IgM</td>
<td>9 SMA</td>
<td>26 SMA</td>
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<td></td>
<td></td>
<td>0 SMA</td>
</tr>
<tr>
<td>22</td>
<td></td>
<td>Anti-Beta2GPI: IgA</td>
<td>7 SA</td>
<td>19 SA</td>
</tr>
<tr>
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<td></td>
<td></td>
<td></td>
<td>0 SA</td>
</tr>
<tr>
<td>23</td>
<td></td>
<td>LAC screening (DW ratio)</td>
<td>DSS</td>
<td>No Clot</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>&lt;1.5</td>
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AUG 09 2002

AUG 13 2002
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<tr>
<th>Test</th>
<th>Value</th>
<th>Reference</th>
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<tr>
<td>Hexagonal phospholipid</td>
<td>No Clot</td>
<td>8s</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>4.0 mg/dL</td>
<td>36.3 mg/dL</td>
</tr>
<tr>
<td>Reptilase time</td>
<td>12.2s</td>
<td>21.8s</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>439 mg/dL</td>
<td>450 mg/dL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>180 mg/dL</td>
</tr>
<tr>
<td>HPIA</td>
<td>0.1</td>
<td>0.5</td>
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<tr>
<td></td>
<td></td>
<td>0.0</td>
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<tr>
<td>TAT</td>
<td>74.9</td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1.3</td>
</tr>
<tr>
<td>D-DIMQ</td>
<td>7.0</td>
<td>0.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.0</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>Arg506Gln</td>
<td>Heterozy</td>
</tr>
<tr>
<td></td>
<td>Arg506</td>
<td>Homozygous</td>
</tr>
<tr>
<td>Factor II Leiden</td>
<td>G20210</td>
<td>Homozygous</td>
</tr>
<tr>
<td></td>
<td>G20210</td>
<td>Homozygous</td>
</tr>
<tr>
<td>Methylene tetrahydrofolate reductase</td>
<td>C677</td>
<td>Homozygous</td>
</tr>
<tr>
<td></td>
<td>C677</td>
<td>Homozygous</td>
</tr>
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**B7. OTHER RELEVANT HISTORY**

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<tr>
<th>#</th>
<th>Start/Stop Date</th>
<th>Condition Type / Condition</th>
<th>Notes</th>
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<tbody>
<tr>
<td>1</td>
<td>UNK Ongoing</td>
<td>Historical Condition</td>
<td>chronic anemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Anaemia NOS</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>UNK Ongoing</td>
<td>Historical Condition</td>
<td>history of uterine leiomyomas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Uterine fibroids</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>UNK Ongoing</td>
<td>Historical Condition</td>
<td>attributed to a history of uterine leiomyomas</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Dysfunctional uterine bleeding</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>UNK Ongoing</td>
<td>Other</td>
<td>one full term pregnancy at 31 years of age</td>
</tr>
<tr>
<td>5</td>
<td>UNK Ongoing</td>
<td>Family History</td>
<td>Diabetes mellitus NOS</td>
</tr>
<tr>
<td>6</td>
<td>UNK Ongoing</td>
<td>Family History</td>
<td>Hypertension NOS</td>
</tr>
<tr>
<td>7</td>
<td>UNK Ongoing</td>
<td>Family History</td>
<td>Coronary artery disease NOS</td>
</tr>
<tr>
<td>8</td>
<td>UNK Ongoing</td>
<td>Factor V deficiency</td>
<td>patient is heterozygous for Arg506Gln mutation of the Factor V gene (Factor V Leiden mutation)</td>
</tr>
</tbody>
</table>
C1. Name (cont.)
Suspect Medication #1: Levlute 21 or 28(LEVONORGESTREL, ETHINYLESTRADIOL) Coated tablet

C10. CONCOMITANT MEDICAL PRODUCTS

COMPZINE (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
INTERNATIONAL ADVERSE EXPERIENCE REPORT

1. PATIENT INITIALS: 
2. DATE OF BIRTH: Day 14
   Month: JAN
   Year: 2002
3. AGE UNITS: 30Yr
4. EXPERIENCE ONSET: Day 14
   Month: JAN
   Year: 2002

7. DESCRIBE EXPERIENCE(S): Cerebral infarction; Carotid artery thrombosis; Convulsions NOS

Information was received from a regulatory authority (bp), 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 Marcipin (desogestrel/ethyl estradiol) for 4 months in 2000. Therapy with Triul (0.05mg levonorgestrel/0.03mg ethinyl estradiol) for 1 tablet daily, Concomitant therapy included Pipam (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)

13. RELEVANT TEST/LABORATORY DATA
   See following page.

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

15. DAILY DOSE(S)
   #1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINISTRATION
   #1 Oral

17. INDICATION(S) FOR USE
   #1 Menometrorrhagia

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

23. OTHER RELEVANT HISTORY (e.g., diagnosis, allergies, pregnancy with last month of period, etc.)
   CONCURRENCE CONDITIONS:
   Depression NOS; 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

24b. MFR CONTROL NO.

24c. DATE RECEIVED BY MANUFACTURER

07-Aug-2002

24d. REPORT SOURCE

☐ STUDY
☐ LITERATURE
☐ REGULATORY AUTHORITY
☐ HEALTH PROFESSIONAL
☐ LICENSE

25a. REPORT TYPE

☐ INITIAL
☐ FOLLOWUP

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

AUG 1 6 2002
AUG 1 4 2002
AUG 1 5 2002
ADVERSE EXPERIENCE REPORT

Manufacturer Control Number: HQ3635207AUG2002

Box # 7 - DESCRIBE EXPERIENCE(S)

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

Box # 13 - RELEVANT TESTS/LABORATORY DATA

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Date</th>
<th>Result</th>
<th>Normal Range</th>
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</thead>
<tbody>
<tr>
<td>Blood cholesterol</td>
<td></td>
<td>normal</td>
<td></td>
</tr>
</tbody>
</table>

DSS
AUG 16 2002

AUG 15 2002
Individual Safety Report

A. Patient information
1. Patient Identifier or event date: 42 Years
2. Age at time of event: UNK
3. Sex: female
4. Weight: UNK

B. Adverse event or problem
1. Adverse event and/or Product problem
2. Outcomes attributed to adverse event
   - death
   - congenital anomaly
   - required intervention to prevent permanent impairment
   - hospitalization - initial or prolonged
   - other
3. Date of event: 07/18/2002
4. Date of this report: 02/19/2003
5. Describe event or problem
   Fatal pulmonary embolism

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


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

C. Suspect medication(s)
1. Name (give labeled strength & mfbr/labeler, if known)
   #1. Mirena (LEVONORGESTREL) (continued)

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

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

4. Diagnosis for use (indication)
   - Menorrhagia / contraception

5. Event reported after use
   - doesn't apply

G. All manufacturers
1. Contact office - name/address & mailing site for devices
   Berlex Laboratories
2. Phone number
   +1 8882375394
6. West Belt
   Wayne, NJ 07470-6806 UNITED STATES

C. Initial reporter
1. Name & address
   Name and address withheld.
2. Health professional?
   yes
3. Occupation
   Health Care Professional
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
**ADVERSE EXPERIENCE REPORT**

**1. PATIENT INITIALS**
United Kingdom

**2. DATE OF BIRTH**
Day: 00
Month: JAN
Year: 2003

**1a. AGE UNITS**
31Yr

**3. SEX**
F

**4-6. EXPERIENCE ONSET**

**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 athero-sclerosis (atherosclerosis) in hospital. 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 TEST/LABORATORY DATA**
See following page.

**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 ADMINISTRATION**

#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

**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. medical diagnoses, allergies, pregnancy with last month of period, etc.)**

CONCURRENT CONDITIONS:

Obesity (LLT: Obesity); Smoker (LLT: Cigarette smoker); Atherosclerosis (LLT: Atherosclerosis)

---

**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. #1 NDA: 18-668

**24b. MPR CONTROL NO.**
H05YE651625PBB03

**24c. DATE RECEIVED BY MANUFACTURER**
24-FEB-2003

**24d. REPORT SOURCE**

- [ ] STUDY
- [X] LITERATURE
- [X] HEALTH PROFESSIONAL

**24e. REPORT TYPE**

- [X] INITIAL
- [ ] FOLLOWUP

---

**DSS**

MAR 06 2003
Box # 7 - DESCRIBE EXPERIENCE(S) (Continuation)

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

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

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Date</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure (LLT: Blood pressure)</td>
<td>130/71 mm Hg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body mass index (LLT: Body mass index)</td>
<td>28</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
1. **PATIENT INITIALS**
   - Japan

2. **COUNTRY**
   - [Country Details]

3. **DATE OF BIRTH**
   - [Birth Details]

4. **AGE**
   - [Age Details]

5. **EXPERIENCE ONSET**
   - [Onset Details]

6-12. **CHECK ALL APPROPRIATE TO ADVERSE REACTION**
   - [Checkmark Details]

7. **DESCRIBE EXPERIENCE**
   - Myocardial infarction (LLT: Myocardial Infarction); Sinus arrhythmia (LLT: Sinus arrhythmia); Electrocardiogram T wave abnormal (LLT: Electrocardiogram T wave abnormal)
   - [Details]

Follow-up information was received from a gynecologist 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 "Tridrilol 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)

13. **RELEVANT TESTS/LABORATORY DATA**
   - See following page.

14. **SUSPECT DRUG(S) INFORMATION**

   - #1 TriDolol-28 (levonorgestrel/ethinyl estradiol/INERT, TABLET)

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

16. **ROUTE(S) OF ADMINISTRATION**
   - #1 Oral

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

18. **THERAPY DATES (FROM/TO)**
   - #1 22-Sep-1999 / 00-Mar-2002

19. **THERAPY DURATION**
   - #1 29 hth

20. **DID REACTION ABATE AFTER STOPPING DRUG?**
   - [Data]

21. **DID REACTION REAPPEAR AFTER REINTRODUCTION?**
   - [Data]

23. **OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, 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)**
   - [Manufacturer Details]

   **24b. MFR CONTROL NO.**
   - [Control Number]

   **24c. DATE RECEIVED BY MANUFACTURER**
   - [Date]

   **24d. REPORT TYPE**
   - [Select]

   **24e. REPORT SOURCE**
   - [Select]

   **24f. OTHER REFERENCE NUMBERS**
   - [Reference Numbers]

   **Date of this report**
   - [Date]

   **X INITIAL**
   - [Initial]

   **FOLLOWUP**
   - [Select]

   **OCT 31 2003**
   - [Date Sent to FDA]

   **NOV 03 2003**
   - [Date]
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 environment 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 on [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)

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Date</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrocardiogram(LLT: Electrocardiogram)</td>
<td></td>
<td>normal</td>
<td>sinus arrhythmia and T wave abnormal</td>
</tr>
</tbody>
</table>

SUSPECT DRUG(S) INFORMATION
(Continuation)

14. SUSPECT DRUG(S)

# 1.2  TRIDIO 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 04 2003

NOV 03 2003
# Individual Safety Report

**A. Patient Information**

- **Patient identifier**: [Redacted]
- **Age at time of event**: 40 Years
- **Sex**: Female
- **Weight**: 143.3 lbs or 65.0 kg

**B. Adverse event or product problem**

1. **Adverse event** and/or **Product problem** (e.g., defects/malfunctions):
   - Death
   - Hospitalization - initial or prolonged
   - Other

2. **Outcomes attributed to adverse event** (check all that apply):
   - Disability
   - Congenital anomaly
   - Life-threatening
   - Required intervention to prevent permanent impairment/damage
   - Medically Significant

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

**C. Suspect medication(s)**

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

2. **Dose, frequency & route used**
   - 20 (continued)

3. **Therapy dates (if unknown, give duration)**
   - 11/13/2003 to 11/18/2003

4. **Diagnosis for use (indication)**
   - Menorrhagia

5. **Event observed after use**
   - Stopped or dose reduced
   - None
   - Does not apply

6. **Lot @ (if known)**
   - UNK

7. **Exp. date (if known)**
   - UNK

8. **Event reappeared after reintroduction**
   - None
   - Does not apply

9. **NDC @ for product problems only (if known)**

10. **Concomitant medical products & therapy dates (exclude treatment of event)**
    - NONE

**G. All Manufacturers**

1. **Contact office - name/address (& mfr/site for device)**
   - Berlex Laboratories
   - Harri Haltajavri, M.D.
   - Director, Medical Assessment
   - harri.bala.jarvi@berlex.com
   - Fax: 1 973 335 5315
   - Global Med. Safety Surveillance, 6 West Belt Way, NJ 07470-6806 UNITED STATES

2. **Phone number**
   - +1 888 237 3594

3. **Source (if different from mfr)**
   - Foreign
   - COI

4. **Date received by manufacturer**
   - 11/19/2003

5. **ANDA #**
   - NDA 21-225

6. **IND #**
   - PLA #

7. **Type of report**
   - OTC
   - Yes

8. **Adverse event term(s)**
   - Septic shock, Salpingitis NOS, Myometritis, Leukopenia NOS, Dysmenorrhea NOS, Abdominal pain NOS

9. **Mr. report number**
   - CO-SHR-03-017632

**E. Initial reporter**

1. **Name & address**
   - UNK

2. **Health professional?**
   - No

3. **Occupation**
   - Health Care Professional

4. **Initial reporter also sent report to FDA**
   - Yes

---

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.
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 hypochondrium, 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 findings: 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 possibly related to treatment with Mirena.

B6. LABORATORY DATA

<table>
<thead>
<tr>
<th>#</th>
<th>Date</th>
<th>Test / Assessment / Notes</th>
<th>Results</th>
<th>Normal High / Low</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td></td>
<td>Coagulation test</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>changes noted (unspecified)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td>Leucocytes</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>abnormal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>leucopenia with 40% of &quot;cayados&quot;</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

B7. OTHER RELEVANT HISTORY

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

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 02 2003
**MEDWATCH**

**THE FDA MEDICAL PRODUCTS REPORTING PROGRAM**

**Page 1 of 2**

### A. Patient Information

1. **Patient identifier**
   - [Image]

2. **Age at time of event**
   - 34 years

3. **Sex**
   - [Female]

4. **Weight**
   - 220.5 lbs

5. **Date of birth**
   - [Redacted]

### B. Adverse event or product problem

1. **Adverse event**
   - [Severe headache, brain edema, death]

2. **Outcomes attributed to adverse event**
   - [Death]
   - [Congenital anomaly]

3. **Date of event**
   - 04/02/2004

4. **Date of this report**
   - 06/16/2004

### C. Suspect medications(s)

1. **Name**
   - giletrile	h (if known)

2. **Dosage, frequency & route used**
   - [Levonorgestrel]

3. **Therapy dates (if unknown, give duration)**
   - [11/1/2003, duration UNK]

### D. Description of event or problem

**Event Verbatim (PREFERRED TERM)**
- 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

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...

### E. Initial reporter

1. **Name & address**
   - [Redacted]

2. **Health professional?**
   - [Yes]

3. **Occupation**
   - [Physician]

4. **Initial reporter also sent report to FDA**
   - [No]
**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 had severe headache for one week. She vomited once during the night. Afterwards, pronounced brain edema. 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

<table>
<thead>
<tr>
<th>C1. Name (cont.)</th>
<th>Suspect Medication #1: Mirena(LEVONORGESTREL) IUS</th>
</tr>
</thead>
<tbody>
<tr>
<td>C2. Dose, frequency &amp; route used (cont.)</td>
<td>Suspect Medication #1: 20 µg/day, cont. intra-uterine</td>
</tr>
</tbody>
</table>

---

**DSS**

**JUN 21 2004**

---

**JUN 17 2004**
### Individual Safety Report

**Facilities manufacturers for**

**Bexar Laboratories**

**THE FDA MEDICAL PRODUCTS REPORTING PROGRAM**

1. **Patient Information**
   1. **Patient identifier**
   2. **Age at time of event:** 24 years
   3. **Sex:**
      - female
      - male
   4. **Weight:**
      - 240.0 lbs
      - 108.8 kg

2. **Adverse event or product problem**
   1. Adverse event
   2. **Product problem (e.g., defect/malfunction)**

3. **Outcomes attributed to adverse event**
   - death
   - congenital abnormality
   - required intervention to prevent permanent impairment/damage
   - hospitalization - initial or prolonged

4. **Date of event**
   - 06/08/2004

5. **Date of this report**
   - 09/24/2004

6. **Describe event or problem**
   - Event Verbal [PREFERRED TERM] (Related symptoms if any separated 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 clot in the brain with severe headache, vomiting, and lethargy in an overweight 24-year-old Caucasian female who received ethinyl estradiol/levonorgestrel (Levon 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 Lever 28 for contraception. Approximately 3 months later, 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...

7. **Relevant tests/laboratory data, including dates**
   - NI

8. **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, Qosity (continued)

### C. Suspect medication(s)

1. **Name (give labeled strength & mf/labeler, if known)**
   - Levon 28 (ETHINYLESTRAD)

2. **Dose, frequency & route used**
   - 1 tab(s), (continued)
   - 03/2004 to 06/2004

3. **Therapy dates if unknown, give duration**
   - #1: 03/2004 to 06/2004

4. **Diagnosis for use (Indication)**
   - Oral contraception

5. **Event abated after use stopped or dose reduced**
   - #1: yes

6. **Event reappeared after reintroduction**
   - #1: yes

7. **NDC # - for product problems only if known**
   - #1: UNK

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

### G. All Manufacturers

1. **Contact office - name/address & mailing site for devices**
   - Bexar Laboratories
   - Harti Helaifar, M.D.
   - Director, Medical Assessment
   - hartihelaifar@bexar.com
   - Fax: +1 973 305 5315
   - Global Med. Safety Surveillance, 6 West Belt Wayne, NJ 07470-6608 UNITED STATES

2. **Phone number**
   - +1 8882375394

3. **Report source (check all that apply)**
   - device
   - study
   - literature
   - consumer
   - health professional
   - user facility
   - company representative
   - distributor
   - other

4. **Date received by manufacturer**
   - 09/15/2004

5. **IND #**
   - #1938

6. **Type of report (check all that apply)**
   - 5-day: yes
   - 15-day: yes

7. **Adverse event term(s)**
   - Cerebral thrombosis, Haemorrhagic stroke, Cardiac failure

8. **NIF report number**
   - US-2004-028202

### E. Initial reporter

- **Name & address**
- **Phone #**

### DSS
- **UNITED STATES**
- **SEP 0 7 2006**

- **2. Health professional?**
  - yes
  - no

- **3. Occupation**
  - nurse

- **4. Initial reporter also sent report to FDA**
  - yes
  - no
  - unk
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 Levolen 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 hemorrhagic 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 Levolen 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

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

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

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

DSS

SEP 29 2004
Individual Safety Report

INTERNATIONAL ADVERSE EXPERIENCE REPORT

1. PATIENT INITIALS: France
2. DATE OF BIRTH: Day Month Year
3. AGE UNITS: 32Yr
4. SEX: F
5. EXPERIENCE ONSET: Day Month Year 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 (APSSAPS) regarding a 32-year-old female patient who received Adepa (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 2003). 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.

13. RELEVANT TESTS/LABORATORY DATA
See following page.

II. SUSPECT DRUG(S) INFORMATION
14. SUSPECT DRUG(S) (INCLUDE ACTIVE SUBSTANCE(S))
   #1 ADEPA (LEVONORGESTREL/ETHINYL ESTRADIOL, TABLET, 0)

15. DAILY DOSE(S)
   #1 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINISTRATION
   #1 Oral

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

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

19. THERAPY DURATION
   #1 Several years

III. CONCOMITANT DRUG(S) AND HISTORY
22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DATE/YY)
   LOVENOX (HEPARIN-FRACTION, SODIUM SALTS), one injection of 0.20 ml, 00-Oct-2004 / 00-Oct-2004

OTHER RELEVANT HISTORY (e.g. diagnoses, allergies, 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

24b. MFR CONTROL NO.

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

24d. REPORT SOURCE
   X CONSUMER
   LITERATURE
   HEALTH
   PROFESSIONAL

24e. REPORT TYPE
   X INITIAL
   FOLLOWUP

OTHER REFERENCE NUMBERS:
Reg Authority Ref Num - TS0500028

DATE SENT TO FDA
FEB 25 2005

DSS
MAR 1 2005
**International Adverse Experience Report**

**1. Reaction Information**

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<thead>
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<td>Sweden</td>
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</tr>
</tbody>
</table>

*7. Describe experience(s):*

**PULMONARY EMBOLISM (LIT: PULMONARY EMBOLISM)**

(LLL = 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/0.175mg 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)

**13. Relevant Test/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 Administration**

- #1 Unknown

**17. Indication(s) for Use**

- #1

**18. Therapy Dates (From TO)**

- #1 Unknown

**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)

Unknown

23. Other Relevant History (e.g. diagnosis, allergies, pregnancy within 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

**Other Reference Numbers:**

Regulatory Authority (HP) - 032127

**Other Data**

Local Marketing No.

81 NDA 19-192

24d. Date Received By Manufacturer

21-Mar-2005

24c. Report Source

- [X] Study

- [ ] Literature

- [X] Health Professional

- [ ] Consumer

- [ ] Regulatory Authority

- [ ] License

**Date of this report**

01-Apr-2005

**Report Type**

- [X] Initial

- [ ] Followup

**Received**

APR 04 2005

CDR/CDER

**Other Data**

APR 04 2005

DSS

APR 05 2005
1. PATIENT INITALS: [Canada]

2. DATE OF BIRTH: [Day], [Month], [Year]
3. AGE: 26Yr
4. EXPERIENCE ONSET: [Day], [Month], [Year]

5. 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

6. DESCRIBE EXPERIENCE:
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)

7. RELEVANT TESTING/LABORATORY DATA
None Provided.

8. SUSPECT DRUG(S) INFORMATION
\#1 ALESSE-28 (LEVONORGESTREL/ETHINYL ESTRADIOL/INERT, TABLET)

9. DAILY DOSE(S)
\#1 1 Tablet 1x per 1 Day

10. ROUTE(S) OF ADMINISTRATION
\#1 Oral

11. INDICATION(S) FOR USE
\#1 Menorrhagia (LLT: Menorrhagia)

12. THERAPY DATES (FROM/TO)
\#1 Unknown

13. THERAPY DURATION
\#1 3 Mth

14. CONCOMITANT DRUG(S) AND HISTORY

15. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DA/MON YYYY)
NONE (NONE), Unknown

16. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)
CONCURRENT CONDITIONS:
Obesity (LLT: Obesity); Smoker (LLT: Smoker); Alcohol use (LLT: Alcohol use)

17. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER

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

19. MFR CONTROL NO.
HQWY8731113MAY05

20. DATE RECEIVED BY MANUFACTURER
24-May-2005

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

22. REPORT TYPE
- [ ] INITIAL
- [X] FOLLOW UP

23. DATE SENT TO FDA
JUN 06 2005

24. OTHER REFERENCE NUMBERS:
Affiliate Ref Num

25. RECEIVED
JUN 06 2005

CDR/CDER

26. JUN 03 2005

DSS

JUN 06 2005
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.
Patient Information

1. Patient identifier
   - 31 Years

2. Age at time of event: 31 Years
   - Date of birth: UNK
   - Sex: Female
   - Weight: 25 lbs

3. Suspect medication(s)

   1. Name (give labeled strength & mtls/ingredients, if known):
      - Seasonale (LEVONORGESTRE (continued))

   2. Dose, frequency & route used:
      - UNK, UNK, Oral

   3. Therapy dates (if unknown, give duration): -/2004, duration UNK

   4. Diagnosis for use (indication):
      - UNK

   5. Event lasted after use stopped or dose reduced:
      - Yes
      - Does not apply

   6. Event reappeared after reintroduction:
      - Yes
      - Does not apply

   7. Concomitant medical products & therapy (excl. of treatment of event):
      - N/A

   8. All Manufacturers
      - Barr Laboratories
      - Salvatore Peritore, R.Ph.

5. Adverse event or product problem

   2. Outcomes attributed to adverse event:
      - Disability
      - Congenital anomaly
      - Required intervention to prevent permanent impairment & damage
      - Hospitalization - initial or prolonged
      - Other: Medically Significant

6. Date of event: 12/25/2004

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

8. Relevant tests/laboratory data, including dates:
   - NI

9. Other relevant history, including pre-existing medical conditions:
   - NI

10. Medical history:
    - 3. Diseases:
    - 4. Procedures:

11. Initial report:
    - 1. Name & address:
      - Phone #
      - Address:
      - City, State, ZIP:
      - Telephone:
      - Fax:

12. Health professional:
    - Yes
    - No

13. Other:

Submission of a report does not constitute an admission that the medical personnel, user facility, distributor, manufacturer or product caused or contributed to the event.
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
A. PATIENT INFORMATION
1. Patient Identifier: 
   | 2. Age at Time of Event:  |
   | Date of Birth: | 
   | 3. Sex | 4. Weight 169 lbs |

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)
   - Disability
   - Congenital Anomaly
   - Life-threatening
   - Hospitalization - initial or prolonged
   - Other:
3. Date of Event (mod/day/year): 6/12/05
4. Date of This Report (mod/day/year): 8/1/05
5. Describe Event or Problem
   - Fatal pulmonary thromboembolism
   - of deep venous thrombosis

DSS
AUG 11 2005

6. Relevant Tests/Laboratory Data, Including Dates
   - Cadiac ekg - enlarged right ventricle
   - Elevated D-dimer
   - Improvement after TNK therapy
   - Improvable minor brain injury

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, hepatocerebral dysfunction, etc.)
   - Factor V Leiden heterozygote
   - MTHFR C677T heterozygote

C. SUSPECT MEDICATION(S)
1. Name (Give trade name & manufacturer, if known)
   - Levora, 2.8
2. Dose, Frequency & Route Used
   - Once daily, oral
3. Therapy Dates (if unknown, give duration)
   - 7 years
4. Diagnosis for Use (Indication)
   - Birth control
5. Event Abated After Use Stopped or Dose Reduced?
   - Yes No
6. Lot # (if known)
   - TEV 995
7. Exp. Date (if known)
   - 3/07
8. Event Reappeared After Reintroduction?
   - Yes No
9. NDC# (For product problems only)
   - 
10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
    - Oral supplements: Papaya Enzyme, Milk Thistle, Polysorbate 80, Leucine, Ester-C, Colloidal Silver

D. SUSPECT MEDICAL DEVICE
1. Brand Name
2. Type of Device
3. Manufacturer Name, City and State
4. Model # Lot # Expiration Date (mod/day/year)
5. Operator of Device
   - Health Professional
   - Lay User/Patient
   - Other:
6. If Implanted, Give Date (mod/day/year)
7. If Implanted, Give Date (mod/day/year)
8. Is this a Single-Use Device that was Reprocessed and Reused on a Patient?
   - Yes No
9. If Yes to Implanted above, Is the Device a Type of Reprocessor
   - Recycle

E. REPORTER (See confidentiality section on back)
1. Name and Address
2. Phone #
3. Occupation
4. Also Reported to:
   - Manufacturer
   - User Facility
   - Distributor/Importer

Form FDA 3500 (12/03) Submission of a report does not constitute an admission that medical personnel or the product caused or contributed to the event.
**U.S. Department of Health and Human Services**

**Individual Safety Report**

**4954000-3-08-31**

**ADVERSE EVENT REPORTING PROGRAM**

**A. PATIENT INFORMATION**

1. Patient Identification:
   - Name:
   - Address:
   - Phone:

2. Age and Sex:
   - Age at Time of Event:
   - Sex:
   - Date of Birth:

3. Date of Event:
   - Date:
   - Month:
   - Year:

4. Weight:
   - Lbs:
   - Kgs:

B. ADVERSE EVENT OR PRODUCT PROBLEM

1. Adverse Event and/or Product Problem:
   - Disability:
   - Congenital Anomaly:
   - Required Intervention to Prevent Permanent Impairment:
   - Other:

2. Outcomes Attributed to Adverse Event:
   - Death:
   - Life-threatening (Requiring hospitalization or medical evaluation by health professional):
   - Hospitalization:

3. Date of Event:
   - Date:
   - Month:
   - Year:

4. Date of This Report:
   - Date:
   - Month:
   - Year:

5. Describe Event or Problem:
   - Event Summary (PREFERRED TERM): 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 2008 the occurrence of a rapid course of septicemia (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 information.

6. Relevant Tests/Laboratory Data, Including:
   - NI:

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

C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & manufacture, if known):
   - Mirena (LEVONORGESTREL) (continued):

2. Dose, Frequency & Route Used:
   - Dose:
   - Route:

3. Therapy Dose (If unknown, give duration):
   - Duration:

4. Diagnosis for Use (Indication):
   - UNK:

5. Event Abated After Use:
   - Stopped or Dose Reduced:

6. Lot # (If known):
   - UNK:

7. Exp. Date (If known):
   - UNK:

8. Event Resumed After Reintroduction:
   - Yes:

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

10. Concomitant Medical Problems 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:
   - Foreign:
   - GBR:

4. Date Received by Manufacturer:
   - 03/14/2006

5. IND #:
   - MNDG # NDA 21-225

6. IF IND, Give Protocol #:
   - PRE-1938

7. Type of Report:
   - Yes:

8. Adverse Event Term(s):
   - Streptococcal sepsis

E. INITIAL REPORTER

1. Name and Address:
   - Phone # Withheld:

2. Health Professional:
   - Yes:

3. Occupation
   - health care professional:

4. Initial Reporter:
   - Yes:
   - No:

**FDA**

**REceived**

**MAR 2 2 2006**

**MAR 2 3 2006**

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

<table>
<thead>
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<th>C1. Name (cont.)</th>
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<tr>
<td>Suspect Medication #1: Mirena(LEVONORGESTREL) IUS</td>
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<table>
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<tr>
<th>C2. Dose, frequency &amp; route used (cont.)</th>
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</thead>
<tbody>
<tr>
<td>Suspect Medication #1: 20 µg/day, cont. intra-uterine</td>
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</tbody>
</table>
A. PATIENT INFORMATION
1. Patient Identifier: [Redacted]
2. Age at Time of Event: 42 years
3. Sex: Female
4. Weight: 158.6 lbs

B. ADVERSE EVENT OR PRODUCT PROBLEM
1. Adverse Event: [Redacted]
2. Outcomes Attributed to Adverse Event: [Redacted]
3. Date of Event (month/year): UNK

C. SUSPECT MEDICATION(S)
1. Name (Give labeled strength & mf if known)
   a. Mirena(LEVONORGESTREL) (continued)

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

3. Therapy Dates (if unknown, give duration)
   a. 01/1/2003, duration UNK

4. Diagnosis for Use (Indication)
   a. UNK

5. Event Altered After Use
   a. No

6. Lot # (if known)
   a. UNK

7. Exp. Date (if known)
   a. UNK

8. Event Reappeared After Readministration?
   a. No

C. SUSPECT MEDICATION(S)
   a. [Redacted]

10. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
    a. [Redacted]

G. ALL MANUFACTURERS
1. Contact Office - Name/Address (and Manufacturing Site for Device)
   a. Berlex Inc.
   b. Stephen Heaton, M.D.
   c. Director, Medical Assessment
   d. Stephen_Heaton@Berlex.com
   e. Fax: +1 973 487 2914
   f. Global Med. Safety Surveillance, P.O. Box 1000
   g. Montville, NJ 07045-1000
   h. UNITED STATES

4. Data Received by Manufacturer (month/year) [Redacted]
5. A/NDA # NDA 21-225
6. IND # [Redacted]
7. Type of Report (Check all that apply)
   a. OTC Product
   b. Yes
   c. 5-day
   d. 15-day
   e. Periodic
   f. Initial
   g. Follow-up
   h. [Redacted]

E. INITIAL REPORTER
1. Name and Address
   a. Name and address withheld.

2. Health Professional? [Redacted]
3. Occupation
   a. [Redacted]
4. Initial Reporter Also Sent Report to FDA
   a. No

Submission of a report does not constitute an admission that medical personnel, user facility, distributor, manufacturer, or product caused or contributed to the event.
B5. EVENT DESCRIPTION (cont.)

occurrence of a rapid course of septicemia (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 septicemia 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. (31 Mar 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

07-Apr-2006 07:27
The reporter did not provide an assessment of the relationship of event to treatment of Mirena.

B7. OTHER RELEVANT HISTORY

<table>
<thead>
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<th>#</th>
<th>Start/Stop Date</th>
<th>Condition Type / Condition</th>
<th>Notes</th>
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<td>1</td>
<td>UNK</td>
<td>concurrent condition</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Body mass index</td>
<td></td>
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<td></td>
<td></td>
<td>Suppl. (31 Mar 2006): BMI = 24.57 (71 kg, 170 cm)</td>
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<tr>
<td>2</td>
<td>-/-/1995</td>
<td>procedure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ovarian cystectomy</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Suppl. (31 Mar 2006) Ovarian cystectomy whilst pregnant</td>
<td></td>
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<tr>
<td>3</td>
<td>-/-/1995</td>
<td>historical condition</td>
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<tr>
<td></td>
<td>UNK</td>
<td>Pregnancy</td>
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<tr>
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<td>Suppl. (31 Mar 2006)</td>
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<tr>
<td>4</td>
<td>UNK</td>
<td>procedure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Caesarean section</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Suppl. (31 Mar 2006)</td>
<td></td>
</tr>
</tbody>
</table>

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
my daughter was on seasonale for about 6 wks when she died of a DVT. The doctors said the cause was birth control pills.
PULMONARY EMBOLISM (LIT: PULMONARY EMBOLISM)
(LIT = 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 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
(continued))

13. RELEVANT TESTS/LABORATORY DATA
None Provided.

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

15. DAILY DOSE(S)
#1 unknown

16. ROUTE(S) OF ADMINISTRATION
#1 Oral

17. INDICATION(S) FOR USE
#1 Prophylaxis (LIT: Prevention)

18. THERAPY DATES (FROM/TO)
#1 13-Nov-1995 / UNK

19. THERAPY DURATION
#1 Unknown

20. DID REACTION ABATE
AFTER STOPPING DRUG?

21. DID REACTION REAPPEAR
AFTER REINTRODUCTION?

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event): (DAVICOPEX)
ZOLOFT (SERTRALINE HYDROCHLORIDE). Unknown

23. OTHER RELEVANT HISTORY (e.g. diagnoses, allergies, pregnancy within last month of period, etc.)
PAST CONDITIONS:
Normal delivery (LIT: Normal birth); Idiopathic thrombocytopenic purpura (LIT: Idiopathic thrombocytopenic purpura); infection (LIT: Infection); Splenectomy (LIT: Splenectomy)

24. NAME AND ADDRESS OF MANUFACTURER (Include Zip Code)
Wyeth Pharmaceuticals INC.
P.O. Box 7687
Philadelphia, PA 19101-7687

25. REPORT SOURCE
□ STUDY
□ LITERATURE
□ CONSUMER
□ PROFESSIONAL
□ REGULATORY AUTHORITY
□ HEALTH PROFESSIONAL
□ LICENSE

26. DATE RECEIVED BY MANUFACTURER
10-Aug-2006

27. DATE OF LAST COMMUNICATION TO MANUFACTURER
16-Aug-2006

28. REPORT TYPE
□ INITIAL
□ FOLLOWUP

DSS
AUG 1 8 2006

AUG 1 7 2006
Box # 7 - DESCRIBE EXPERIENCE(S)

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 [Blank]. The patient experienced stomach sickness on 17-May-2006. On the morning on [Blank] the patient experienced abdominal pain, nausea, vomit, ready to faint and respiratory arrest. All resuscitation in the home failed. The patient died on [Blank].

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.

DSS
AUG 18 2006

AUG 17 2006
MEDWATCH
The FDA Safety Information and Adverse Event Reporting Program

A. PATIENT INFORMATION
1. Patient Identifier: 
2. Age at Time of Event: 21 Years
3. Sex: Female
4. Weight: 125.0 lbs
   or
   56.7 kg
   or
   in confidence

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)
   - Disability
   - Congenital Anomaly
   - Required Intervention to Prevent Permanent Impairment/Damage
3. Death (Specify)
4. Life-threatening (Specify)
5. Hospitalization - initial or prolonged
6. Other:

3. Date of Event (month/day/year)
   02/28/2006
4. Date of This Report (month/day/year)
   08/29/2006

5. Describe Event or Problem
   [Preferred Term] (Related symptoms if any separated by commas)
   Urinary tract infection, Urinary tract infection, Dysuria, Haematuria, Flu, Influenza, Pyrexia, Chills, Headache

6. Heavy, prolonged uterine bleeding, Menorrhagia
   Pelvic pain, Pelvic pain
   Bloody (Abdominal distension)
   Took unapproved Amphetamine [Drug use for unknown indication]
   Cardiac arrhythmia, Arrhythmia
   Spotting, Menorrhagia

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 that 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 information section).

6. Relevant Tests/Laboratory Data, Including Dates
   #1 [ ] Comprehensive Drug Panel (continued)
   #2 [ ] Pregnancy test Negative
   #3 [ ] Rapid Flu test Negative

7. Other Relevant History, Including Preexisting Medical Conditions (e.g., race, pregnancy, smoking and alcohol use, hepatic dysfunction, etc.)
   #1 UNK Historical Condition, (continued)
   #2 [ ] to UNK Historical Condition, (continued)
   #3 [ ] to UNK Historical Condition, (continued)
   #4 [ ] to UNK Historical Condition, (continued)
   continued in additional information section...

8. Concomitant Medical Products and Therapy Dates (Exclude treatment of event)
   ORAL CONTRACEPTIVE NOS (ORAL CONTRACEPTIVE NOS) UNK to UNK

9. NDC# (For product problems only)

G. ALL MANUFACTURERS
1. Contact Office - Name, Address (and Manufacturing Site for Devices)
   Barr Laboratories
   400 Chestnut Ridge Road
   Woodcliff Lake, NJ 07677-7888 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 (month/day/year)
   08/16/2006

5. (ANDA # 21-045)
   IND #
   PLA #
   Pre-1993
   # Yes
   # Product
   # Yes

6. If IND, Give Protocol #
   007819

8. Adverse Event Terms (a)
   Urinary tract infection, Influenza, Mononucleosis, Pyrexia, Chills, Pelvic pain, Abdominal distension, Headache, continued in additional information section...

E. INITIAL REPORTER
1. Name and Address
   [ ]
   UNITED STATES

2. Health Professional? [ ] Yes [ ] No
3. Occupation
   Consumer
4. Initial Reporter Also Sent Report to FDA [ ] Yes [ ] No [ ] UNK
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 02/08/2006, the patient was examined for sore throat and congestion, GualMax-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. GualMax-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 unlabelled event.

### B6. LABORATORY DATA

<table>
<thead>
<tr>
<th>#</th>
<th>Date</th>
<th>Test / Assessment / Notes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>[REDACTED]</td>
<td>Comprehensive Drug Panel</td>
<td>Positive</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1- Amphetamines</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>2- Pseudoephedrine 1059 ng/mL</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>3- Caffeine</td>
<td></td>
</tr>
</tbody>
</table>

### B7 OTHER RELEVANT HISTORY

<table>
<thead>
<tr>
<th>#</th>
<th>Start/Stop Date</th>
<th>Condition Type / Condition</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>UNK</td>
<td>Historical Condition, Light smoking and light alcohol use</td>
<td>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)</td>
</tr>
<tr>
<td>2</td>
<td>[REDACTED]</td>
<td>Procedure</td>
<td></td>
</tr>
</tbody>
</table>

Autopsy report-Cause of death: [REDACTED]

29-Aug-2006 12:06
**Individual Safety Report**

**Experience Report**
(continued)

<table>
<thead>
<tr>
<th>No.</th>
<th>Historical Condition</th>
<th>Event Details</th>
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<tr>
<td>3</td>
<td>UNK</td>
<td>Annual exam- normal</td>
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<tr>
<td>4</td>
<td>UNK</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>5</td>
<td>UNK</td>
<td>Chlamydia</td>
</tr>
<tr>
<td>6</td>
<td>UNK</td>
<td>Herpes</td>
</tr>
<tr>
<td>7</td>
<td>UNK</td>
<td>Sore throat, congestion Temp 98, BP 98/54</td>
</tr>
<tr>
<td>8</td>
<td>UNK</td>
<td>Clinic visit</td>
</tr>
<tr>
<td>9</td>
<td>UNK</td>
<td>LMP</td>
</tr>
<tr>
<td>10</td>
<td>UNK</td>
<td>Clinic visit</td>
</tr>
<tr>
<td>11</td>
<td>UNK</td>
<td>Clinic visit</td>
</tr>
<tr>
<td>12</td>
<td>UNK</td>
<td>Clinic visit</td>
</tr>
</tbody>
</table>

C1. **Name (cont.)**
Suspect Medication #1: Plan B(LEVONORGESTREL) Tablet, 0.75mg
Suspect Medication #2: ORTHO TRI-CYCLEN LO()

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

**DSS**
**AUG 31 2006**

**AUG 30 2006**

29-Aug-2006 12:08
### Block C - Additional Dosage Regimens

<table>
<thead>
<tr>
<th>Suspect Product</th>
<th>2. Dose, Frequency &amp; Route Used (If unknown, give duration)</th>
<th>3. Therapy dates</th>
<th>6. Lot # (If known)</th>
<th>7. Exp. Date (If known)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1 Plan B Regimen # 2</td>
<td>2 Tablet, single, Oral</td>
<td>03/27/2006 to 03/27/2006</td>
<td>T54395C</td>
<td>UNK</td>
</tr>
</tbody>
</table>

DSS

AUG 31 2006

29-Aug-2006 12:06
For VOLUNTARY reporting of adverse events, product problems and product use errors

D. SUSPECT PRODUCT(S)
1. Name, Strength, Manufacturer (and product label)
   a. LEVONORGESTREL (Plan B) - Gedeon Richter, Ltd.
   b. Duramed Pharmaceuticals, Inc.

2. Date or Amount
   a. 0.75 mg.
   b. 0.75 mg.

3. Route
   a. oral
   b. oral

4. Event Before Use, After Use, Stopped or Does Not Apply?
   a. Yes
   b. No
   c. Doesn't Apply

5. Event Reapplied After Reintroduction?
   a. Yes
   b. No
   c. Doesn't Apply

6. Event and Reason for Use (Indication)
   a. Emergency Contraceptive
   b. Emergency Contraceptive

7. Lot #
   a. 
   b. 

8. Expiration Date
   a. 
   b. 

E. SUSPECT MEDICAL DEVICE
1. Brand Name
2. Common Device Name
3. Manufacturer Name, City and State

F. OTHER (CONSUMER) MEDICAL PRODUCTS
Product names and therapy dates (include treatment of event)

Ortho Tricycles 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
2. Health Professional?
   a. Yes
   b. No
3. Occupation
   a. Non-Healthcare Professional
4. Also Reported to:
   a. Manufacturer
   b. User Facility
   c. Distributor/Importer

ATTACHMENT
ISR # 5095100-X
DATE: 5/09/05

C. PRODUCT AVAILABILITY
Product Available for Evaluation? (Do not send product to FDA)
   a. Yes
   b. No
   c. Returned to Manufacturer on

7. Other Relevant History, including Preexisting Medical Conditions (e.g., allergies, race, pregnancy, smoking and alcohol use, Atrial fibrillation, etc.)
   Light smoking and light alcohol use

6. Relevant Tests/Laboratory Data, Including Dates
   See attached autopsy report/blood toxicology screen
DEPARTMENT OF PATHOLOGY

AUTOPSY REPORT

NAME: [Redacted]
AGE: 21
SEX: F
PROSECTOR: [Redacted]
Assistant: [Redacted]

AUTOPSY NO: [Redacted]
DATE: [Redacted]
TIME: 8:30 am
CORONER: [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

[Redacted] M.D.
Forensic Pathologist

COMPLETED: [Redacted]
CIRCUMSTANTIAL SUMMARY

was a 21 year old white female found dead in her room at a Sorority on the morning of . According to investigators from the Police Department and 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 .

IDENTIFICATION

On at 8:30 AM, a complete post mortem examination was performed on the body of , who was identified by a toe tag. Persons present for the autopsy included as autopsy assistant, Coroner Dept. Coroner and Police Dept. Officer .

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 thrombembolism. 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 antrhacotic 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, pelvis, 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 Police Department and the 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.
<table>
<thead>
<tr>
<th>Analyte Name</th>
<th>Result</th>
<th>Cut-off</th>
<th>Units</th>
<th>Therapeutic Range</th>
<th>Loc</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMPHETAMINES</td>
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<td>50</td>
<td>ng/mL</td>
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<td>Pseudoephedrine</td>
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<td>1059</td>
<td>ng/mL</td>
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<tr>
<td>BARBITURATES</td>
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</table>
### Laboratory Specimen No: [Redacted]  Date Collected: [Redacted]

#### Container(s) Received:
- 01: Red Top Tube  Vitreous

#### Test(s) Requested:
- 70570  Autopsy Panel, Volatiles (550V1)

<table>
<thead>
<tr>
<th>Analyte Name</th>
<th>Result</th>
<th>Cut-off</th>
<th>Units</th>
<th>Therapeutic Range</th>
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<td>% (w/v)</td>
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</table>

The Specimen identified by this Laboratory Specimen Number has been handled and analyzed in accordance with all applicable requirements.

**Laboratory Case #: [Redacted]**

**Signature of Certifying Scientist**

Page: 2 of 2
### Individual Safety Report

#### Acute Problem

<table>
<thead>
<tr>
<th>Medication</th>
<th>Start</th>
<th>#</th>
</tr>
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<tbody>
<tr>
<td></td>
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</table>

#### Continuing Problems / Conditions / Medications

<table>
<thead>
<tr>
<th>Date</th>
<th>Condition</th>
<th>Lat</th>
<th>Start</th>
<th>Medication / Treatment</th>
<th>Stop</th>
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<tbody>
<tr>
<td></td>
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</tr>
</tbody>
</table>

#### Tobacco Use / Amount

**Emergency Treatment Date**

- [ ] Diabetes
- [ ] Contact Lenses
- [ ] Rem Dentures / Bridges

**Prostheses, specify**

- [ ] Hepatitis B, other
- [ ] Varicella Vax

**Current Tetracycline**

**N/A (date)**

**Allergy or Intolerance / Reason / Date Noted**

- [ ] **N/A (date)**
Subjective

Chief Complaint: 

Current medication: 

Med allergies: 

General: 

Ears: 

Nose: 

Facial Pain: 

Throat: 

Chest: 

PMH: 

Other Hx: 

If PMHx of Asthma complete section below:

Age of onset ______ date of most recent asthma episode 

Resp Sx freq: 

Trigger: 

Home PEF: 

Previous Tx: 

Other: 

URI/ASTHMA FORM

[✓] = Present 
[ ] = Absent 
+PPD = Not asked or not applicable
Individual Safety Report

Objective
VS: BP 80/60 P 98 RR __ PEF Pred. PEF Distress __

Ear Canal: R - X NL □ Red □ Swollen □ Exudate □ Wax L - X NL □ Red □ Swollen □ Exudate □ Wax

Ear Drum: R - X NL □ Red □ Effusion □ Retraction L - X NL □ Red □ Effusion □ Retraction

Nasal: □ NL □ Red □ Pale □ Swollen X Discharge Color clear □ Sinus tenderness

Throat: □ NL □ Red □ Lymphoid hypertrophy □ Ulcerations X Discharge Color clear

Tonsils: □ NL □ Absent □ Small □ Moderate □ Large □ Exudate

Neck: □ NL □ Accessory muscle use □ Decreased ROM

Cerv. Nodes: □ NL □ Enlarged □ Tend - R □ AC □ PC

Chest: X NL □ Wheezing □ Rales □ Rhonchi □ Clears w/cough □ Other

Cardiac: X NL □ NE □ Irregular rhythm □ Irregular rate □ Murmur □ Other

Other PE

In-office Tx: □ None □

Lab/Testing
□ Strep. rapid/cult □ Mono □ CBC X Rapid Flu No
□ Other

Assessment
□ URI □ Tonsillitis/Pharyngitis □ Sinusitis □ Acute bronchitis □ Allergic rhinitis □ Other

□ ASTHMA □ acute exacerbation □ mild intermittent □ persistent - mild □ moderate □ severe; □ OM - L R

Plan: Guainax 1.5 PO BID #20
Nearsyn 10 and PO BID 1ST \Sheathing

□ Pt. education given □ Handout □ Influenza Vaccine

□ Call if not improving in \□ Appointent □ Asthma educ. □ Referral

□ Push Fluids □ Call for test results □ Additional Dictation

Signature: [15/7]
Subjective

Chief Complaint: net throat congestion ___________ Today

Current medication: Cephalexin 500 ___________ LMP: ___________

Med allergies: NKA ___________ Cl: ___________

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 - sp prod both ___________ ☑ SOB □ Wheeze □ Tightness □ Pain

PMH: □ Asthma □ Abn Heart valve □ +PPD ☑ Cigarettes - 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 ___________

11:42AM

/ASTHMA FORM

□ / Present
Objective S:
BP 84/60 P 99 RR PEF Pred. PEF Distress - none mild mod sev □ O2Sat 90%(RA)

Ear Canal: R √ NL □ Red □ Swollen □ Exudate □ Wax L 65 NL □ Red □ Swollen □ Exudate □ Wax

Ear Drum: R 65 NL □ Red □ Effusion □ Retraction L 65 NL □ Red □ Effusion □ Retraction

Nasal: □ NL □ Red □ Pale □ Swollen □ Discharge Color clean □ Sinus tenderness

Throat: □ NL □ Red □ Lymphoid hypertrophy □ Ulcerations □ Discharge Color clean

Tonsils: □ NL □ Absent □ Small □ Moderate □ Large □ Exudate

Neck: □ NL □ Accessory muscle use □ Decreased ROM

S erv. Nodes: □ NL □ Enlarged □ Tender R L □ □ PC

N eust: □ NL □ Wheezing □ Rales □ Rhonchi □ Clears w/cough □ Other

Cardiac: □ NL □ NE □ Irregular rhythm □ Irregular rate □ Murmur □ Other

Other PE

n-office Tx: □ None □

ab/Testing
1) Strep. rapid/cult □ Mono □ CBC □ Rapid Flu □ Other

Assessment
1) URI □ Tonsillitis/Pharyngitis □ Sinusitis □ Acute bronchitis □ Allergic rhinitis □ Other

2) ASTHMA □ acute exacerbation □ mild intermittent □ persistent - mild moderate severe; □ OM - L R

Plan

1) Pt. education given □ Handout □ Cold □ Influenza Vaccine

2) Call if not improving in □ Referral □ Asthma educ.

1) Push Fluids □ Call for test results □ Additional Dictation

Signature: [1/5/7]
SUBJECTIVE: I saw [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 Tussilonex 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
To: [redacted]

[Redacted]
At instructed Z-Pak still working on it today. Coughing Advair 1 puff b.i.d. Office of Dr. [redacted] 7:00 to 1 bypass. Same cough in refill. No cough

P.O. [redacted] [redacted]

[Redacted]

[Redacted]
[Redacted]

P. Ven [redacted] never picked up.
# A. PATIENT INFORMATION

1. Patient Identifier --
   2. Age at Time of Event: 26 years
   3. Sex --
   4. Weight --
   5. Height --

# B. ADVERSE EVENT OR PRODUCT PROBLEM

1. Adverse Event and/or Product Problem (e.g., side effects/illnesses)
   2. Outcomes Attributed to Adverse Event (Check all that apply):
      - Death: UNK
      - Life-Threatening
      - Hospitalization
      - Disability
      - Congenital Anomaly
      - Required Intervention to Prevent Permanent Impairment/Damage
      - Other:
   3. Date of Event (month/year): UNK
   4. Date of This Report (month/year): 11/20/2006

# C. SUSPECT MEDICATION(S)

1. Name (Give labeled strength & NDC number, if known)
   - Mirena (LEVONORGESTREL)
   2. Dose, Frequency & Route Used (If unknown, give duration)
   3. Therapy Dates (If unknown, give duration)

# G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site
   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

# E. INITIAL REPORTER

1. Name and Address
   Name and address withheld.

2. Health Professional? No
3. Occupation company sales representative
4. Initial Reporter Also Sent Report to FDA No

---

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

The FDA Safety Information and Adverse Event Reporting Program

Page 1 of 2

A. PATIENT INFORMATION

1. Patient Identifier: [Redacted]
2. Age at Time of Event: 31 Years
3. Sex: [Female]
4. Weight: UNK lbs

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
   - life-threatening
   - hospitalization

3. Date of Event (month/year): [Redacted]
4. Date of This Report (month/year): 04/24/2007

5. Event Description or Problem (Check all that apply)
   - cerebrovascular accident
   - stroke
   - cerebrovascular accident
   - hemorrhage
   - intracranial pressure
   - swelling

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...

F. INITIAL REPORTER

1. Name and Address
   - Phone: UNK
   - UNITED STATES

2. Health Professional? [No]
3. Occupation
   - Consumer

4. Initial Reporter Also Sent Report to FDA
   - [No]

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

C. SUSPECT MEDICATION(S)

1. Name (Clue labeled strength & mf(kalbe): if known)
   - Seasonique/LEVONORGESTR

2. Dose, Frequency & Route Used
   - UNK, UNK, Oral

3. Therapy Dates (if unknown, give duration (from/to or best estimate)
   - UNK

4. Diagnosis for Use (Indication)
   - Oral contraception

5. Event Abated After Use
   - stopped or dose reduced?
   - [No]

G. ALL MANUFACTURERS

1. Contact Office - Name/Address (and Manufacturing Site for Devices)
   - Barr Laboratories
   - Anthony Oelidip, PharmD, MPH
   - VP, Drug Safety and Risk Management
   - 400 Chestnut Ridge Road
   - Woodcliff Lake, NJ 07677-7668 UNITED STATES

2. Phone Number
   - 2019303446

3. Event Reappeared After Reintroduction?
   - [No]

9. Manufacturer Report Number
   - 012396

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

24-Apr-2007 14:02

APR 2 5 2007 DSS
APR 27 2007
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 _______. 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

The FDA Safety Information and Adverse Event Reporting Program

A. PATIENT INFORMATION
1. Patient Identifier:
   - Name: [redacted]
   - Date of Birth: 20yo
2. Age at Time of Event, or Date of Birth:
   - Female
3. Sex: Female
4. Weight:
   - 150 lb

B. ADVERSE EVENT, PRODUCT PROBLEM OR ERROR
1. Check all that apply:
   - Adverse Event
   - Product Use Error
   - Problem with Different Manufacturer of Same Medicine
2. Outcomes Attributed to Adverse Event:
   - Death: [redacted]
   - Disability or Permanent Damage
   - Life-threatening
   - Congenital Anomaly/Birth Defect
   - Other Serious (Impairment Medical Event)
   - Required Intervention to Prevent Permanent Impairment (Device)
3. Date of Event:
   - 07/20/2007
4. Date of this Report:
   - 07/20/2007

5. Describe Event, Problem or Product Use Error:
   Safety Evaluation Follow-up Report for ISRs
   5962812-0-00-01. Contacting Providing Follow-up information:
   [redacted] (consumer). Date contacted: 11/27/2006. PT term from original ISRs: 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 RR & pronounced dead. She went on a long plane flight on her honeymoon. Previously been on long plane flights (Africa, China) with no problems. Attachment: follow-up letter.

C. PRODUCT AVAILABILITY
1. Product Available for Evaluation? (Do not send product to FDA):
   - Yes
   - No
   - Returned to Manufacturer:

D. SUSPECT PRODUCT(S)
1. Name, Strength, Manufacturer (from product label):
   - Seasonale
   - 
2. Dose or Amount:
   - 
3. Dates of Use (If unknown, give duration) from/to (or best estimate):
   - 11/05-11/06 (5-6 wks)
4. Diagnosis or Reason for Use (Indication):
   - 
5. Event Altered After Use Stopped or Does Reducing?
   - 
6. Lot #:
   - 
7. Expiration Date:
   - 
8. Operator of Device:
   - 
9. Other:
   - 
10. IF Implanted, Give Date (mm/dd/yyyy):
11. IF Explanted, Give Date (mm/dd/yyyy):

E. SUSPECT MEDICAL DEVICE
1. Brand Name:
2. Common Device Name:
3. Manufacturer Name, City and State:

F. OTHER (CONCOMITANT) MEDICAL PRODUCTS
1. Product names and therapy dates (exclude treatment of event):
   - None

G. REPORTER (See confidentiality section on back)
1. Name and Address:
   - [redacted]
2. Health Professional:
   - Yes
   - No
3. Occupation:
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:

[Signature]

RECEIVED
JUL 23 2007
MEDWATCH CTU

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.
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?

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 and pronounced dead.

DSS

JUL 25 2007
6. Does your daughter have any previous history of clotting events? Is there a family history of clotting events? 
   There is no family history of 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" 180 lbs + 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 (covered) 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,

[Signature]

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
**ADVERSE EXPERIENCE REPORT**

**REACTION INFORMATION**

<table>
<thead>
<tr>
<th>1. PATIENT INITALS</th>
<th>2. DATE OF BIRTH</th>
<th>3. AGE</th>
<th>4. SEX</th>
<th>5. EXPERIENCE</th>
<th>6-12 CHECK ALL APPLICABLE TO ADVERSE REACTION</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>Day</td>
<td>Month</td>
<td>27 Yr</td>
<td>F</td>
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</tbody>
</table>

1. 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 (equivlent to Norlestrin) 1 Tabid daily for contraception was begun in FEB-1999 and ceased on 08-Oct-1999. Concomitant therapy included NONE. The patient became pregnant (unintended pregnancy) with tripilals in SEP-1999 and death of one embryo (intra-uterine death) was suspected. An ultrasound antral screen confirmed a gestational age of 4-5 weeks. Schering Ref. 0-99/00866-CDS.

13. RELEVANT TESTS/LABORATORY DATA

See following page.

**SUSPECT DRUG(S) INFORMATION**

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

1. NORDETT-21 TABLET (LEVOMESTRREL, ETHINYL ESTRADIOL)

15. DAILY DOSE(S):

1. 1 Tablet 1x per 1 Day

16. ROUTE(S) OF ADMINISTRATION:

1. Oral

17. INDICATION(S) FOR USE:

1. Contraception NOS

18. THERAPY DATES (BEGIN/DURATION):

1. CD-Feb-1999 / 08-Oct-1999

19. THERAPY DURATION:

1. 8 Mth.

20. DID REACTION ABATE AFTER STOPPING DRUG?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

21. DID REACTION REAPPEAR AFTER REINTRODUCTION?

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
<th>N/A</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

**CONCOMITANT DRUG(S) AND HISTORY**

22. CONCOMITANT DRUGS AND DATES OF ADMINISTRATION (Exclude those used to treat event) (DAMOCYR)

NONE. Unknown

33. OTHER RELEVANT HISTORY (e.g. diagnosis, allergies, pregnancy with last menstruation, etc.)

(cont'd)

35. OTHER DIAGNOSIS:

Multinarrus

PREGNANCY:

1999-01-08

**IV. ONLY FOR REPORTS SUBMITTED BY MANUFACTURER**

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

WYETH LAMS (RA)

J.C. Pagner Chester

Rt. Davids, PA 19087

Local Marketing No.

NDA 18-668

24b. MEDICAL NO.

R0472304NOV1999

25. DATE RECEIVED BY MANUFACTURER:

02-Nov-1999

26. REPORT SOURCE:

<table>
<thead>
<tr>
<th>STUDY</th>
<th>CONSUMER</th>
<th>LITERATURE</th>
<th>REGULATORY</th>
<th>AUTHORITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>NO</td>
<td>X</td>
<td>X</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

26a. REPORT TYPE:

<table>
<thead>
<tr>
<th>INITIAL</th>
<th>FOLLOWUP</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

OTHER REFERENCE NUMBERS:

Business Partner (HP) (via Schering AG) - 99/00866

CENTER FOR DRUG EVALUATION AND RESEARCH

REC'D

NOV 12 1999

CUR

NOV 1 1999
<table>
<thead>
<tr>
<th>Test Name</th>
<th>Result</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ultrasound</td>
<td>Gestational age is 4-5 weeks.</td>
<td></td>
</tr>
</tbody>
</table>

**Adverse Experience Report**

Manufacturer Code: HQ4572304NOV999

Box # 13 - TESTS/LABORATORY DATA (Continuation)

Box # 23 - PREGNANT HISTORY (Continuation)

Confirmation: Ultrasound

Nov 12 1993
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
Initial or Follow-up ISR: Follow-up
eSub ISR: Yes
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: [Blacked Out]
Gender: Female
Weight: 65 Kilogram
Event Start Date: 05/05/2005
Health Prof.: YES
Occupation: OTHER HEALTH PROFESSIONAL

Reporter Information:
Reporter Name: [Blacked Out]
Reporter Org.:
Reporter Street:
Reporter Zip:
Reporter Phone:
Reporter City:
Reporter State: UNITED KINGDOM
Reporter Country: UNITED KINGDOM

Product(s)
HUMIRA

Dosage Text
Role
P
Route SUBCUTANEOUS
Lot # UNKNOWN
NDC #
Indication(s) RHEUMATOID ARTHRITIS
Therapy Start Date 05/09/2003
Therapy End Date
Interval 1st Dose to Event

Reaction(s)
ACTH STIMULATION TEST ABNORMAL
BLOOD POTASSIUM INCREASED

ReC

Relevant Laboratory

Test Date 05/05/2005
Test Name Body height
Result 165
Unit CM
Normal Low Range
Normal High Range
Info Avail Y/N

Test Date 05/05/2005
Test Name Potassium
Result Increased
Unit
Normal Low Range
Normal High Range
Info Avail Y/N

Test Date 05/05/2005
Test Name Synacthen test
Result Long
Unit
Normal Low Range
Normal High Range
Info Avail Y/N

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 05/05/2005
End Date 05/05/2005
Continuing
Comment

Note: If a field is blank, there is no data for that field.
### HYPERTENSION

#### PEPTIC ULCER

<table>
<thead>
<tr>
<th>Medical History Product(s)</th>
<th>Start Date</th>
<th>End Date</th>
<th>Indication(s)</th>
<th>Reaction(s)</th>
</tr>
</thead>
</table>

**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:**
## Patient Information:
- **Patient ID:**
- **Age:** 41 YR
- **Gender:** Female
- **DoB:**
- **Event Start Date:**
- **Health Prof.:** NO

## Reporter Information:
- **Reporter Name:**
- **Reporter Org.:**
- **Reporter Address:**
- **Reporter Phone:**
- **Reporter City:**
- **Reporter State:**
- **Reporter Country:** BRAZIL
- **Occupation:** CONSUMER OR OTHER NON HEALTH PROFESSIONAL

## Product(s) Reaction(s)

<table>
<thead>
<tr>
<th>Product(s)</th>
<th>Role</th>
<th>Dosage Text</th>
<th>Route</th>
<th>Lot #</th>
<th>NDC #</th>
<th>Indication(s)</th>
<th>Therapy Start Date</th>
<th>Therapy End Date</th>
<th>Interval 1st Dose to Event</th>
<th>DeC</th>
<th>ReC</th>
</tr>
</thead>
<tbody>
<tr>
<td>MIRENA</td>
<td>P</td>
<td>20 μUg/day, cont</td>
<td>INTRA-UTERINE</td>
<td></td>
<td></td>
<td></td>
<td>09/01/2002</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Relevant Laboratory
- **Test Name:** DEATH

## Relevant Medical History

## Disease/Surgical Procedure

## Medical History Product(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 μg/day, cont via intra-uterine for an unspecified indication. On an unspecified date the patient experienced unspecified death. The patient died from...

### Note:
If a field is blank, there is no data for that field.

06/01/2008
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: