THALOMID® (thalidomide) Pregnancy Exposure Registry

Version 2

Celgene Corporation
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1. Introduction

Thalidomide was introduced in West Germany by Chemie Grunenthal in the 1950s, and was used widely as a sedative and as an anti-inflammatory agent outside the United States. Thalidomide was withdrawn from the market in 1961 because of its teratogenic effects, notably phocomelia, which became known (McBride, 1961). Thalidomide was never released in the United States as a sedative or marketed for any indication prior to the discovery of its teratogenic effects.

The FDA approved THALOMID® (thalidomide) capsules for U.S. prescription market availability on 16 Jul 1998. Thalidomide is indicated for the acute treatment of cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL). Thalidomide is not indicated as monotherapy for ENL in the presence of moderate to severe neuritis. Thalidomide is also indicated as maintenance therapy for prevention and suppression of the cutaneous manifestations of ENL recurrence. On 25 May 2006, the FDA granted accelerated approval for thalidomide in combination with dexamethasone for the treatment of multiple myeloma.

1.1. THALOMID Pregnancy Prevention REMS Program

Because of the known teratogenic effects of thalidomide and in an effort to prevent to the greatest extent possible any chance of embryo-fetal exposure to thalidomide, THALOMID® (thalidomide) is approved for marketing only under a special restricted distribution program approved by the FDA. Under this program, the System for Thalidomide Education and Prescribing Safety (THALOMID REMS™), only prescribers and pharmacies certified with the program are allowed to prescribe and dispense the product. In addition, patients must be advised of, agree to, and comply with the requirements of the THALOMID REMS™ program. To monitor patient compliance with the THALOMID REMS™ program, all patients must complete the THALOMID REMS™ program and participate in a mandatory and confidential surveillance registry.

In the THALOMID REMS™ program, a female patient of reproductive potential (FRP) is defined as a sexually mature female who has not undergone a hysterectomy, bilateral oophorectomy, or who has not been postmenopausal naturally for at least 24 consecutive months (i.e., who has had menses at some time in the preceding 24 consecutive months). Enrolled FRP need to complete a brief, confidential telephone survey monthly before a prescription can be written for the medication. The FRP must have a thorough understanding of the need for 2 of the recommended forms of birth control beginning at least 4 weeks before therapy, and continuing during therapy (including any necessary dose interruptions) and for at least 4 weeks following discontinuation of therapy with

THALOMID®. The FRP must have negative pregnancy tests within 24 hours prior to receiving an initial prescription for THALOMID®. Pregnancy tests must be sensitive to 50mIU/mL. A pregnancy test is to be performed weekly during the first 4 weeks, then repeated every 4 weeks in FRP with regular menstrual cycles. If menstrual cycles are irregular, testing should occur every 2 weeks. In the event of pregnancy, the FRP should discontinue THALOMID®. Pregnancy testing and counseling should be performed if a patient misses her period or if there is any abnormality in her pregnancy test or in her menstrual bleeding. All cases of pregnancy should be reported to FDA MedWatch at 1-800-FDA-1088 and to Celgene at 1-888-423-5436.

2. Objective

Celgene is committed to investigating any reports of possible embryo-fetal exposure to THALOMID® (thalidomide) whether it is the patient or the patient's partner.

The objectives of the THALOMID® Pregnancy Exposure Registry are:

- to monitor pregnancy outcomes (should one occur) in female patients of reproductive potential and female partners of patients who are exposed to THALOMID® and
- to understand the root cause for the pregnancy.

3. Methods

Pregnancy is identified as any of the following:

- Pregnancy of a patient
- Pregnancy of a female partner of a patient taking THALOMID®

Reports of pregnancy may be received from the THALOMID REMS™ program in the United States, Celgene Pregnancy Prevention Plan programs in the rest of the world (ROW), company representatives, clinical trials (US and ROW), or directly from consumer and health care professionals. Specifications for handling pregnancy reports are included in every Celgene study protocol. All reports of pregnancy in a female patient or partner of patient will be actively monitored. Contact information of health care providers and patients will be retrieved from United States Risk Management System (US RMS) database for reports from the commercial environment and from Celtrak (repository of study information) for reports from clinical trials. Health care providers (HCP; clinical trial investigator, prescriber, obstetrician, neonatologist, pediatrician) will be contacted to obtain pregnancy background, pregnancy outcome, pregnancy follow-up and infant outcome information; patients and male patients of pregnant partners will be contacted (when appropriate) to obtain pregnancy information to the extent permitted by local regulations/laws will permit. A letter with the Pregnancy Background Form will be sent initially to the health care provider (prescriber, clinical trial investigator, and obstetrician) and a letter with the Pregnancy Follow-up Form will be sent every trimester or until the outcome is known. A letter with the Pregnancy Form for patient or male patient of pregnant partner will be sent (when appropriate) within 30 days after a report of a confirmed pregnancy. A letter with the Pregnancy Outcome Form for HCP (prescriber, clinical trial investigator, obstetrician, neonatologist, pediatrician) will be sent within 30 days after expected delivery. A letter with the Pregnancy Outcome Form for patient/male patient of partner will be sent (when appropriate) within 30 days after expected delivery. A letter with the Infant Follow-up Form will be sent to the pediatrician or primary care physician every quarter until the infant is a year old.

All pregnancy cases are entered in the Global Drug Safety database. The Drug Safety Specialist (DSS) or designee will process the completed forms and follow-up with the HCP and patient or male patient of pregnant partner.

The following forms will be used to monitor the pregnancy and pregnancy outcome:

- Pregnancy Background Form for HCP,
- Pregnancy Follow-up Form for HCP,
- Pregnancy Outcome Form for HCP,
- Pregnancy Background Form for Patient or Male Patient of Pregnant Partner
- Pregnancy Outcome Form for Patient or Male Patient of Pregnant Partner, and
- Infant Follow-up Form for Primary Care Physician or Pediatrician.

The Pregnancy Background Form for Patient or Male Patient of Pregnant Partner will be utilized for the root cause analysis of pregnancy. The letters and the forms are found in Appendix 1 and the definition of terms is found in Appendix 2.

The processes are presented in Figure 1, Figure 2 and Figure 3.

3.1 Pregnancy/Pregnancy Background

3.1.1 Health Care Providers

- When a pregnancy is reported, the Drug Safety Specialist (DSS) or designee will make an outbound call to the reporter to verify the pregnancy. If there is no response, the DSS or designee will make another outbound call to the reporter to verify the pregnancy.
- If the pregnancy is verified, the DSS will generate a letter and a Pregnancy Background Form that will be sent to the health care provider (HCP; prescriber, clinical trial investigator, obstetrician, primary care physician).
- If no response is received within 30 days, the letter and Pregnancy Background Form will be resent.
- If there is no response to the second letter within 30 days, an outbound call will be made to the HCP (prescriber, clinical trial investigator, obstetrician, primary care physician) requesting that the Pregnancy Background Form be completed.
- If there is no response to the outbound call from the obstetrician/primary care physician within 30 days, all contacts and attempts will be documented in the case.
- If there is no response to the outbound call from the clinical trial investigator, the clinical study manager will be contacted to assist in obtaining the response from the clinical trial investigator.
- If there is no response to the outbound call from the prescriber within 30 days, he or she will be flagged. When the flagged prescriber request for a prescription authorization, the call will be directed to the DSS or designee who will remind the prescriber to complete the Pregnancy Background Form.

- If there is no response within 30 days, the DSS or designee will document all contacts and attempts. If the completed Pregnancy Background Form is received, the DSS or designee will unflag the Prescriber.
- The DSS or designee will process the completed Pregnancy Background Form.

3.1.2 Patient and Male Patient of Pregnant Partner

- A letter and a Pregnancy Background Form for patient and male patient of pregnant partner will be sent (when appropriate) within 30 days after a report of confirmed pregnancy to patients enrolled in the THALOMID REMS™ program. The letter and the form for patient and male patient of pregnant partner will be sent to the clinical trial investigator for completion of the study subject at the next study visit. The Pregnancy Background Form will collect information for the root cause analysis of pregnancy.
- If no response is received within 30 days, the letter and Pregnancy Background Form will be resent.
- If there is no response to the second letter within 30 days, an outbound call will be made to the patient/male patient of pregnant partner for patients enrolled in the THALOMID REMS™ program requesting that the Pregnancy Background Form be completed and to the clinical trial investigator to remind the study subject to complete the form at the next study visit.
- If there is no response to the outbound call from the patient/male patient of pregnant partner within 30 days, the study manager will be contacted to assist in obtaining the response.
- If there is no response to the outbound call from the patient/male patient of pregnant partner within 30 days, all contacts and attempts will be documented in the case.
- The DSS or designee will process the completed Pregnancy Background Form.

3.2 Pregnancy Follow-up

- A Pregnancy Follow-up Form will be sent to the obstetrician/primary care physician every trimester or until the outcome is known.
- If the obstetrician/primary care physician does not respond within 30 days, the letter and Pregnancy Follow-up Form will be resent.
- If there is no response to the second letter, an outbound call will be made to the obstetrician/primary care physician requesting the completion of the Pregnancy Follow-up Form.
- If no response is received within 30 days, all contacts and attempts will be documented in the case.
- The DSS or designee will process the completed Pregnancy Follow-up Form.

3.3 Pregnancy Outcome

3.3.1 Health Care Providers

- For confirmed pregnancies, Pregnancy Outcome Form for HCP (prescriber, clinical trial investigator, obstetrician, neonatologist, pediatrician, primary care physician) will be sent within 30 days after the expected date of delivery.
- If the HCP (prescriber, clinical trial investigator, obstetrician, neonatologist, pediatrician, primary care physician) does not respond within 30 days, the letter and Pregnancy Outcome Form will be resent.
- If there is no response to the second letter, an outbound call will be made to the HCP (prescriber, clinical trial investigator, obstetrician, neonatologist, pediatrician, primary care physician) requesting the completion of the Pregnancy Outcome Form.
- If there is no response from the clinical trial investigator, the study manager will be contacted to assist in obtaining the response.
- If there is no response from the obstetrician/neonatologist/pediatrician/primary care physician/clinical trial investigator within 30 days, all contacts and attempts will be documented in the case.
- If there is no response from the Prescriber within 30 days, the prescriber will be flagged. When the flagged prescriber request for a prescription authorization, the call will be directed to the DSS or designee who will remind the prescriber to complete the Pregnancy Outcome Form.
- If there is no response within 30 days, the DSS or designee will document all contacts and attempts. If the completed Pregnancy Outcome Form is received, the DSS or designee will unflag the Prescriber.
- The DSS or designee will process the completed Pregnancy Outcome Form.

3.3.2 Patient and Male Patient of Pregnant Partner

- A Pregnancy Outcome Form for patient and male patient of pregnant partner will be sent (when appropriate) within 30 days after the expected date of delivery.
- If the patient and male patient of pregnant partner do not respond within 30 days, the letter and Pregnancy Outcome Form will be resent.
- If there is no response to the second letter, an outbound call will be made to the patient and male patient of pregnant partner requesting the completion of the Pregnancy Outcome Form.
- If no response is received within 30 days, all contacts and attempts will be documented in the case.
- The DSS or designee will process the completed Pregnancy Outcome Form.

3.4 Infant Follow-up

- The DSS or designee will send a letter and an Infant Follow-up Form to the primary care physician or pediatrician quarterly until the infant is a year old. The first letter will be sent 3 months after birth.
- If there is no response within 30 days, the DSS or designee will re-send the letter and the Infant Follow-up Form.
- If there is no response to the second letter, an outbound call will be made to the primary care physician or pediatrician requesting the completion of the Infant Follow-up Form.
- If no response is received within 30 days, all contacts and attempts will be documented in the case.
- The DSS or designee will process the completed Infant Follow-up Form.

4. Data Analysis

Descriptive statistics will be the primary approach for summarizing data from the pregnancy exposure registry.

Subjects' age, duration of thalidomide treatment, and weeks of gestational age at exposure will be summarised using descriptive statistics for continuous variables, while gender, indication for thalidomide use, concomitant medications, type of delivery, pregnancy outcome, obstetrical history, adverse events during pregnancy, embryo-fetal outcome, infant status, and cytogenetic abnormalities will be summarised with descriptive statistics appropriate for categorical data. The information will be separately provided for female patients and for male patients and their pregnant partners as appropriate for the variable of interest.

The pregnancy proportion for female patient of reproductive potential (FRP) will be determined by dividing the total number of FRP experiencing at least one pregnancy over the total FRP population. The pregnancy proportion will be stratified by prescribing environment (e.g., patients exposed to commercially marketed thalidomide, patients exposed to thalidomide in clinical trials under IND applications]. Because of the unique denominator data available in the United States, these analyses will be conducted separately for patients in the THALOMID REMS™ program. Patients with more than one exposed pregnancy will be tabulated.

The Pregnancy Background Form completed by the patient or male patient of pregnant partner will be utilized to analyze root cause for the pregnancy. The forms of birth control; unprotected sex; reasons for unprotected sex; receipt, reading, and understanding of the medication guide, source of knowledge about contraception, and understanding of the risk of pregnancy during thalidomide use will be summarized with descriptive statistics.

The CDC birth defects code list will be used for classifying any reported congenital anomalies.

5. Individual Case Reports

Initial pregnancy cases must be reported (notification) to the FDA within 24 hours of receipt followed by a 15-day alert report. Any follow-up information received must be submitted as a follow-up 15-day alert report.

For all Celgene products where there is a regulatory commitment for 24-hour notification (i.e., lenalidomide, thalidomide) or a requirement in the clinical study protocol for immediate notification, all Celgene personnel, including affiliates and licensed partners, shall inform Global Drug Safety or the appropriate Celgene Drug Safety department worldwide **IMMEDIATELY** by a telephone call followed by electronic transmission (email or facsimile) of a serious adverse event report of any possible exposure of a pregnant woman to the Celgene product.

6. Status Reports

The status report will be included in the THALOMID® periodic safety report. The status report will include the following:

- Number of pregnancies in patients and partners of patients with outcome known (stratified by live birth, spontaneous abortions, elective terminations, fetal deaths/stillbirths)
- Number of pregnancies with outcome pending
- Number of pregnancies lost to follow-up
- Pregnancy proportions for FRP patients and for male patients, stratified by prescribing environment
- Number of females of reproductive potential exposed for postmarketing and clinical trials (US and ROW*) during the time period
- Number of males exposed for postmarketing and clinical trials (US and ROW*) during the time period

*Note: THALOMID REMS™ is unique to the United States. In other countries where THALOMID® is marketed, such controlled distribution may not be possible because of legal restraints. Hence, accurate data on patient demographics will not be available.

For pregnancies with known outcome, the status report will include line listings and summaries of:

- Demographics, obstetrical and medical history of mothers
- Weeks of gestational age at exposure
- Type, dose and duration of exposure
- Weeks of gestational age at completion or termination of pregnancy
- For live births and deaths/stillbirths, whether multiple birth, small for gestational age, pre-term delivery and congenital anomalies or other embryo-fetal abnormalities
- For spontaneous abortions and elective terminations, abnormalities in products of conception

7. Registry Discontinuation

The pregnancy registry will be evaluated annually to determine if the feasibility of collecting information has diminished to unacceptable levels because of low exposure rates or loss to follow-up

8. REFERENCES

CDC. Metropolitan Atlanta Congenital Defects Program Procedure Manual, 1993;A32-A100(77):488-7160.

EMEA Committee for Medicinal Products for Human Use: *Guideline on the Exposure to Medicinal Products During Pregnancy: Need for Post-Authorization Data.* London, UK. 14 Nov 2005.

Food and Drug Administration. *Guidance for Industry Establishing Pregnancy Exposure Registries*. Rockville, MD. August 2002.

Investigator's Brochure for Thalidomide. Summit, NJ: Celgene Corporation, 06 Mar 2007.

McBride WG. Thalidomide and congenital abnormalities. The Lancet. December 1961:1358.

THALOMID REMS™ Starter Kit

THALOMID® [Full Prescribing Information]. Summit, NJ: Celgene Corporation; 2005.

Figure 1: Pregnancy Background and Follow-Up Process Flow - HCP

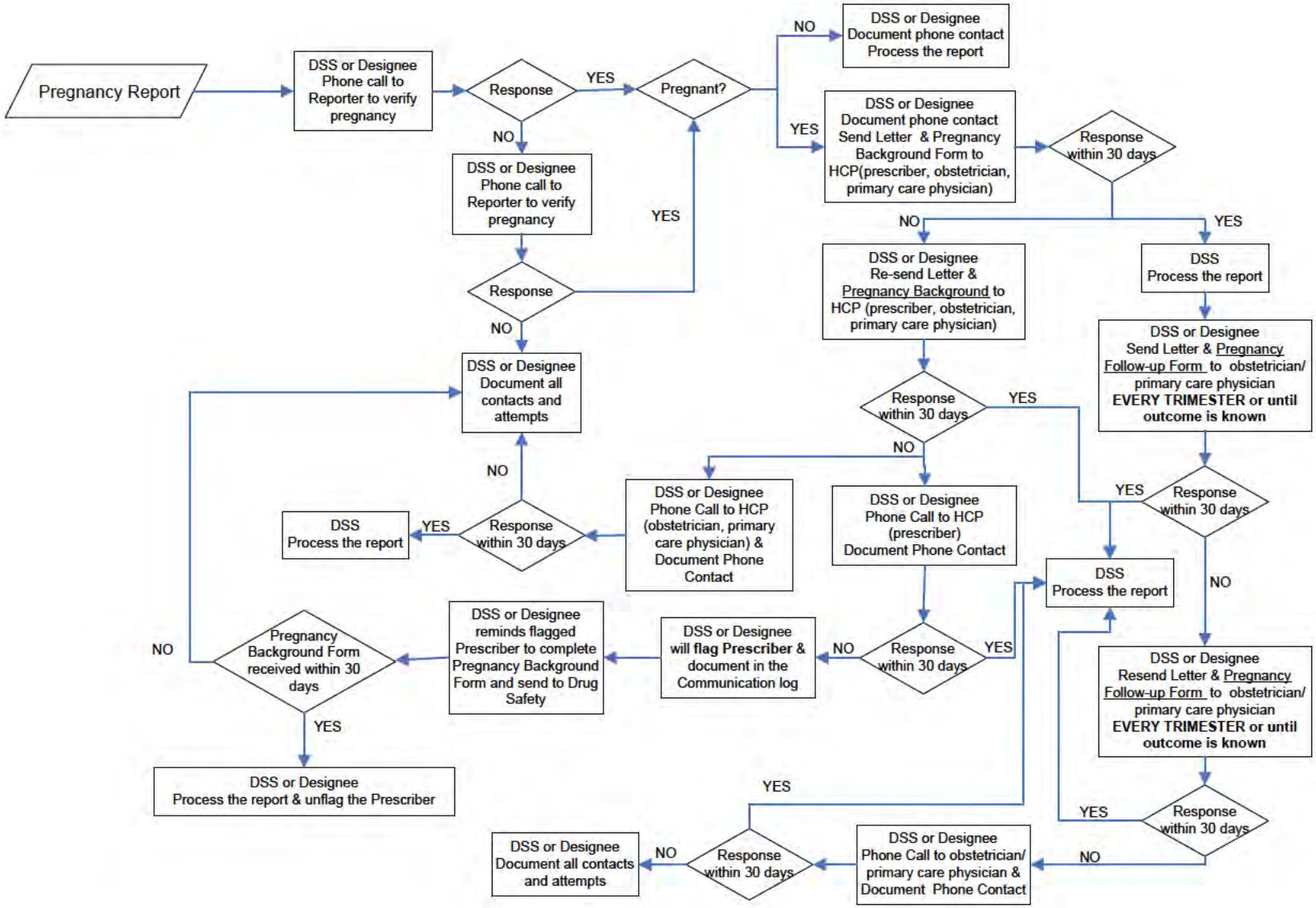


Figure 2: Pregnancy Outcome and Infant Follow-Up Process Flow - HCP

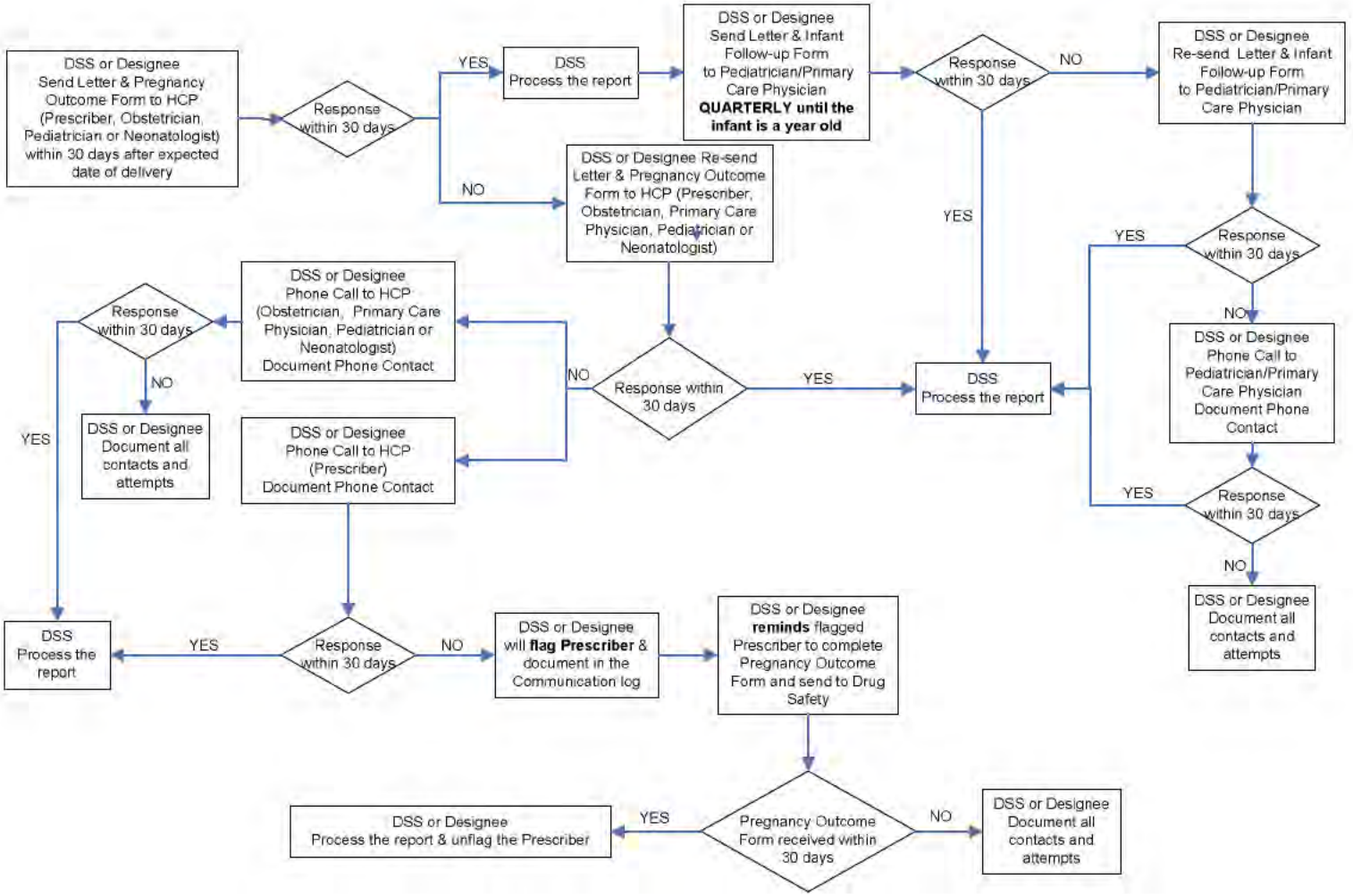
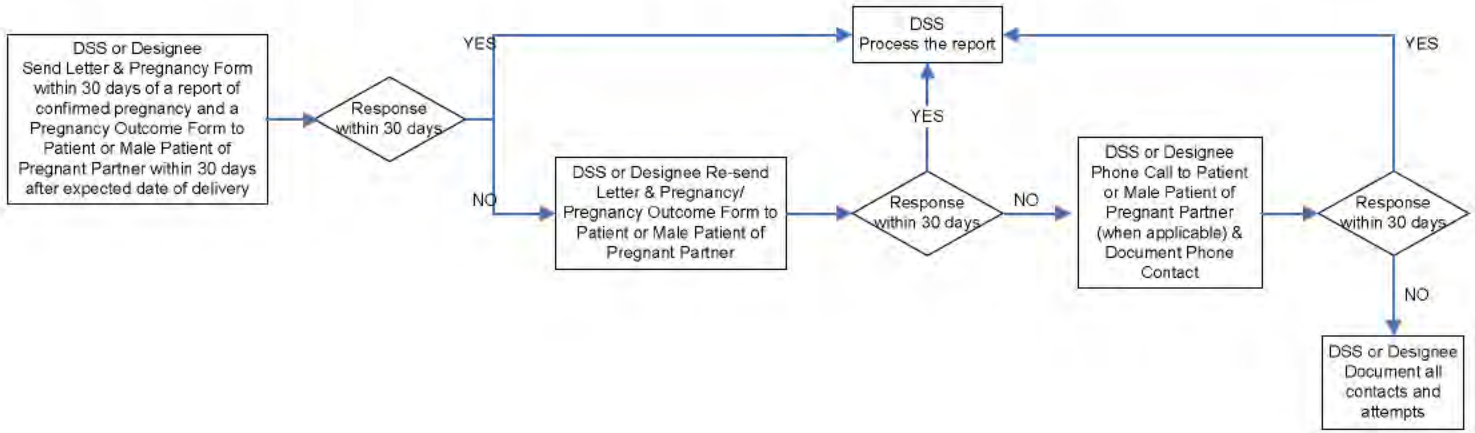


Figure 3: Pregnancy/Pregnancy Outcome Process Flow -Patient and Male Patient of Pregnant Partner



Appendix 1: Pregnancy Letters and Questionnaires

Name, MD [Prescriber/Clinical trial investigator/
Obstetrician/Pediatrician/Neonatologist/Primary Care Physician)
Attn: Name
Address:

DDMMYYYY

Re: Patient Identifier: [patient identifier]
Patient DOB, Patient sex
Drug: [Primary Suspect Product Name]
Our Manufacturer Control No (MCN): [MCN]

Dear Dr. [Selected Reporter]

The Celgene Corporation Drug Safety Department has received a report of a pregnancy regarding your patient [patient identifier].

Celgene is committed to investigating any reports of possible embryo-fetal exposure to our products whether it be the patient or patient's partner. In order to perform a thorough evaluation and to meet our regulatory reporting requirements throughout the world, we are interested in obtaining additional details regarding this patient. Please be assured that all information will be treated in the strictest of confidence.

Please complete the enclosed Event-Specific Questionnaire for HCP – Pregnancy Background (Patient or Partner of Patient)/ Event-Specific Questionnaire for HCP - Pregnancy Outcome (Patient or Partner of Patient)/ Event-Specific Questionnaire for HCP - Pregnancy Follow-up (Patient or Partner of Patient)/ Event-Specific Questionnaire for Primary Care Physician or Pediatrician Infant Follow-up, date and sign the form(s) and return to Celgene Drug Safety via mail (self-addressed envelope provided), or FAX to (908) 673-9115. Please provide our Manufacturer Control No. as stated above in all communications regarding this case.

If you are aware that further information will not be available, it would be helpful if you could indicate that to us, including the reason if complete information cannot be provided.

If you have any questions, please do not hesitate to contact me at 1-800-640-7854.

Thank you in advance for your assistance.

Name of Specialist
Title

Name of Patient
Address:

DDMMYYYY

Re: Patient Identifier: [patient identifier]
Patient DOB, Patient sex
Drug: [Primary Suspect Product Name]
Our Manufacturer Control No (MCN): [MCN]

Dear [Patient's Name]

The Celgene Corporation Drug Safety Department has received a report of your [your partner's pregnancy].

Celgene is committed to investigating any reports of possible embryo-fetal exposure to our products whether it be the patient or patient's partner. In order to perform a thorough evaluation and to meet our regulatory reporting requirements throughout the world, we are interested in obtaining additional details regarding your [your partner's] pregnancy. Please be assured that all information will be treated in the strictest of confidence.

Please complete the enclosed Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner – Pregnancy Background/ Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner – Pregnancy Outcome Form and return to Celgene Drug Safety via mail (self-addressed envelope provided), or FAX to (908) 673-9115.

If you have any questions, please do not hesitate to contact me at 1-800-640-7854.

Thank you in advance for your assistance.

Name of Specialist
Title

Event-Specific Questionnaire for HCP – Pregnancy Background

(Patient or Partner of Patient)

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

MCN:				
Reporter Information				
REPORTER NAME:				
ADDRESS:		CITY, STATE, ZIP, COUNTRY:		
PHONE NO.:		FAX NO.:		
Obstetrician Information (Please provide)				
OBSTETRICIAN NAME:				
ADDRESS:		CITY, STATE, ZIP, COUNTRY:		
PHONE NO.:		FAX NO.:		
Patient Information				
PATIENT ID:	DATE OF BIRTH:	ETHNICITY: ☐ WHITE ☐ AFRICAN-AMERICAN ☐ ASIAN ☐ OTHER, SPECIFY:		
Partner of Patient Information ☐ Not applicable				
DATE OF BIRTH:	ETHNICITY: ☐ WHITE ☐ AFRICAN-AMERICAN ☐ ASIAN ☐ OTHER, SPECIFY:			
Patient Treatment Information: THALOMID®				
LOT NO.	EXPIRY DATE:	DOSE:	FREQUENCY:	ROUTE:
START DATE		STOP DATE		
INDICATION FOR USE				

CYTOGENETIC ABNORMALITIES: ☐ NO ☐ YES, IF YES, SPECIFY:					
Current Pregnancy					
Date of last menstrual period:		Estimated Delivery Date:			
Pregnancy Test	*REFERENCE RANGE*	*DATE*			
Urine Qualitative					
Serum quantitative					
Prenatal Tests					
	Date	*Result*			
Ultrasound					
Ultrasound					
Ultrasound					
Amniocentesis					
Maternal Serum AFP					
Pregnancy History					
No. of previous pregnancies: Date of last pregnancy:		No. of Full term deliveries:		No. of Pre-term births:	
No. of fetal deaths:		No. of living children:		No. of abortions: Elective Spontaneous	
Type of delivery: Vaginal:	C-section:	Other:, specify			
Did birth defect occur in any previous pregnancy? ☐ No ☐ Yes ☐ Unknown If Yes, specify					

Did a stillbirth or miscarriage occur in any previous pregnancy? No ☐ Yes ☐ Unknown ☐

1) If Yes, in what week of pregnancy did the stillbirth or miscarriage occur? _____ week

2) Was there any birth defect noted? Specify:

Relevant Medical History

	Date of Diagnosis		*Date of Diagnosis*
Cancer ☐ No ☐ Yes, if yes, specify _____			

Social History

Alcohol ☐ No ☐ Yes, if yes, amount/unit consumed per day:

Tobacco ☐ No ☐ Yes	IV or recreational drug use ☐ No ☐ Yes, specify

Family History: Congenital Abnormalities ☐ No ☐ Yes, specify:

Medications/Treatments (including herbal, alternative and over the counter medicines and dietary supplements) During Pregnancy

Drug	*Start Date*	*Stop Date/ Continuing*	*Indication*

Adverse Event(s) During Pregnancy

Event(s)	Serious		Serious Criteria[1]	Start Date	Stop Date	Causal Relationship to Celgene Product		
	No	Yes				Yes	No	If No, what medications, disease states etc played a role in the event.

[1] Serious Criteria: **1**) death, **2**) life-threatening, **3**) required inpatient hospitalization or prolongation of existing hospitalization, **4**) a persistent or significant disability/incapacity, **5**) a congenital anomaly/birth defect, **6**) medically significant

SIGNATURE OF PERSON COMPLETING THIS FORM **DATE**

MCN:

**Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner–
Pregnancy Background**

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

Date _____

Name of Patient or Name of Male Patient of Partner _____

For a better understanding of pregnancy among patients or partners of patients on Thalomid® and for further improvement of the THALOMID REMS™ program, please complete the following questions.

1. What forms of birth control have you been using while on THALOMID® before you/your partner got pregnant? Please check all that applies.

☐ IUD

☐ Hormonal (birth control pills, hormonal patches, injections, implants)

☐ Tubal ligation

☐ Partner's vasectomy

☐ Latex condom

☐ Diaphragm

☐ Cervical cap or shield

☐ Spermicide or sponge

☐ Withdrawal

2. Were you or your partner at any time during use of THALOMID® without contraception for even one day?

☐ No, please proceed to Q5

☐ Yes, please answer Q3, Q4, Q5, and Q6

3. How often did you have unprotected sexual intercourse?

☐ multiple times

☐ once a week

☐ once every 2 weeks

☐ once a month

☐ not at all

☐ other, specify _____

4. Why did you or your partner interrupt or stop using contraception?

☐ wanted a child

☐ partner disapproved

☐ side effects

☐ health concerns

☐ inconvenient to use

☐ other, specify _____

5. Where did most of your knowledge about contraception during THALOMID® use come from?

☐ physician who prescribed THALOMID®

☐ THALOMID REMS™ Patient Resource Pack

☐ THALOMID® Medication Guide

☐ Other, specify _____

6. Do you feel you and/or your partner had good understanding of the risk of pregnancy during THALOMID® use?

☐ Yes

☐ No

☐ Don't know

Event-Specific Questionnaire for HCP – Pregnancy Follow-up

(Patient or Partner of Patient)

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

Date:	**Period Covered: [Date] to [Date]**
Reporter Information	
REPORTER NAME:	
ADDRESS:	CITY, STATE, ZIP, COUNTRY:
PHONE NO.:	FAX NO.:
Name of Patient or Pregnant Partner of Male Patient	
Current Pregnancy	
Prenatal Tests	

	Date	*Result*
Ultrasound		
Ultrasound		
Ultrasound		
Amniocentesis		
Maternal Serum AFP		
Other tests, specify		

Medications/Treatments (including herbal, alternative and over the counter medicines and dietary supplements) During Pregnancy

DRUG	*START DATE*	*STOP DATE/ CONTINUING*	*INDICATION*

Adverse Event(s) During Pregnancy

Event(s)	Serious		Serious Criteria[1]	Start Date	Stop Date	Causal Relationship to Celgene Product		
	No	Yes				Yes	No	If No, what medications, disease states etc played a role in the event.

[1] Serious Criteria: **1**) death, **2**) life-threatening, **3**) required inpatient hospitalization or prolongation of existing hospitalization, **4**) a persistent or significant disability/incapacity, **5**) a congenital anomaly/birth defect, **6**) medically significant

Signature of Person Completing this Form ..... **Date** .....

MCN:

Event-Specific Questionnaire for HCP – Pregnancy Outcome

(Patient or Partner of Patient)

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

Reporter Information			
REPORTER NAME:			
ADDRESS:			CITY, STATE, ZIP, COUNTRY:
PHONE NO.:			FAX NO.:
Patient Information			
PATIENT ID:	DATE OF BIRTH:		ETHNICITY: ☐WHITE ☐AFRICAN-AMERICAN ☐OTHER, SPECIFY:
Partner of Patient Information ☐ Not applicable			
DATE OF BIRTH:			ETHNICITY: ☐WHITE ☐AFRICAN-AMERICAN ☐OTHER, SPECIFY:
Pregnancy Outcome			
DATE OF DELIVERY:			GESTATION AGE AT DELIVERY:
	No	**Yes**	
Normal	☐	☐	
C-section	☐	☐	
Induced	☐	☐	
Ectopic pregnancy	☐	☐	
Elective termination	☐	☐	Date:
Spontaneous abortion (≤20 weeks)	☐	☐	Weeks from LMP:
Fetal death/stillbirth (>20 weeks)	☐	☐	

Were the products of conception examined?	☐	☐	If yes, was the fetus normal? ☐ Yes ☐ No ☐ Unknown If no, describe:
Obstetrics Information			
	No	**Yes**	
Complications during pregnancy	☐	☐	If yes, please specify
Complications during labor/delivery	☐	☐	If yes, please specify
Post-partum maternal complications	☐	☐	If yes, please specify
Embryo-fetal Outcome			
	No	**Yes**	
LIVE NORMAL INFANT	☐	☐	
FETAL DISTRESS	☐	☐	
INTRA-UTERINE GROWTH RETARDATION	☐	☐	
NEONATAL COMPLICATIONS	☐	☐	IF YES, PLEASE SPECIFY:
BIRTH DEFECT NOTED?	☐	☐	IF YES, PLEASE SPECIFY:
Sex: ☐ Male ☐ Female		**Birth Weight:** __lbs _ oz. or __ kg	**Length:** _____inches or ___ cm.
Apgar Score:	Unknown:	1 min:	5 min: 10 min:

SIGNATURE OF PERSON COMPLETING THIS FORM **DATE**

.....

MCN:

Event-Specific Questionnaire for Patient or Male Patient of Pregnant Partner–Pregnancy Outcome

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

Date _____

Name of Patient or Name of Male Patient of Partner _____

Please provide the outcome of your or your partner's pregnancy.

☐ Normal baby

☐ Abnormal baby, please specify defect_____

☐ Therapeutic abortion

Please specify any abnormality of the fetus if known: _____

☐ Spontaneous abortion or miscarriage

Please specify any abnormality of the fetus if known: _____

Event-Specific Questionnaire for Primary Care Physician or Pediatrician – Infant Follow-up

Telephone: (908) 673-9667

Fax: (908) 673-9115

Email: Drugsafety@celgene.com

Date: _____

Name of Patient or Name of Male Patient of Partner (Mother)_____

Name of Infant (if known) _____

Please provide information for the period from [**Date]** to [**Date**].

Anomalies Diagnosed Since Initial Report:

_____

☐ None

Developmental Assessment:

☐ Normal

☐ Abnormal, specify _____

Infant Illnesses, Hospitalizations, Drug Therapies:

Infant Illnesses	**Hospitalized?**	**Drug Therapies**

	☐ Yes ☐ No	
	☐ Yes ☐ No	
	☐ Yes ☐ No	
	☐ Yes ☐ No	
	☐ Yes ☐ No	

SIGNATURE OF PERSON COMPLETING THIS FORM **DATE**

Appendix 2: Definitions

Fetus: covers the whole prenatal development from the conception until birth.

Pregnancy outcome: the end products of pregnancy which include three main categories: fetal death, termination of pregnancy and live birth.

- Fetal death (intrauterine death, in utero death): death prior to complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy; the death is indicated by the fact that after such separation the fetus does not show any evidence of life (WHO ICD 10).
  - Early fetal death (before 20 completed weeks of gestation) comprises ectopic pregnancy and miscarriage
  - Late fetal death (after 20 completed weeks of gestation) – known as stillbirth

Miscarriage: spontaneous abortion, molar pregnancy

Termination of pregnancy (induced abortion, elective abortion): artificial interruption of pregnancy

Live birth: the complete expulsion or extraction from its mother of a product of conception, irrespective of the duration of pregnancy, which, after such separation, breathes or shows any evidence of life (WHO ICD 10)

Gestational age or length: duration of gestation is measured from the first day of the last normal menstrual period. Gestation age is expressed in completed days or completed weeks (e.g., events occurring 280 to 286 days after the onset of the last menstrual period are considered to have occurred at 40 weeks of gestation).

Last menstrual period (LMP): according to international consensus, the gestational age is measured from the first day of the LMP.

Birth weight: the initial weight of the infant at birth

Pre-term baby (previously premature birth): less than 37 completed weeks (less than 259 days) of gestation

Term birth: from 37 to less than 42 completed weeks (259 to 293 days)

Post-term birth: 42 completed weeks or more (294 days or more)

Low birth weight: less than 2,500 gram (up to and including 2,499 g) of body weight of the newborn at birth

Intrauterine growth retardation (small for gestational age): the observed weight of a live born infant or size of a fetus is lower than expected on the basis of gestational age.