Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G001 – Subject Consent Confirmation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __--__ __ __ __ -- __ __ __ -- __

Section B: CONSENT

B1. Has the subject signed a consent form? ☐Yes$_1$ ☐No$_2$

B2. Has the subject signed HIPAA authorization? ☐Yes$_1$ ☐No$_2$

B3. Was signed copy of consent given to subject? ☐Yes$_1$ ☐No$_2$

B4. Date Consent Signed: __ __ / __ __ / __ __ __ __

B5. Date IRB approval of consent expires: __ __ / __ __ / __ __ __ __

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G002 – Subject Consent, Eligibility and Randomization Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline..... (GBSL)

A3. Date form completed: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person completing form: ____ ____ ____

Section B: CONSENT

B1. Has the subject signed a consent form? Yes..... 1

B2. Date consent signed: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section C: INCLUSION CRITERIA	**Yes**	**No**
C1. Has the subject undergone dose-intensive chemotherapy **OR** hematopoietic stem cell transplantation within 60 days prior to eligibility determination?	1	2
C2. Does the subject have an ANC count <500/mm^3 **AND** is the subject expected to remain neutropenic for at least five days?	1	2
C3. Does the subject have a fungemia, bacteremia, invasive tissue bacterial infection, or proven/probable invasive tissue fungal infection conformed by a culture, histopathologic, or radiologic criteria as defined in Appendix A of the Granulocyte Protocol?	1	2

Section D: EXCLUSION CRITERIA	**Yes**	**No**
D1. Is the subject unlikely to survive for the next five days?	1	2
D2. Was this subject previously enrolled in the Granulocyte Study?	1	2

Section E: ELIGIBILITY STATUS

E1. Date eligibility status determined: __ __ / __ __ / __ __ __ __ ***(mm/dd/yyyy)***

E2. Time eligibility status determined: ___ ___ : ___ ___ ***(24 hour clock)***

Section F: ELIGIBILITY Labs

Please provide the subject's most recent ANC count (must be within 24 hours of randomization) used to determine the patient's eligibility (question B2):

Test	a. Date Collected *(mm/dd/yyyy)*	b. Time Collected *(24-hour clock)*	c. Value	d. Units
F1. ANC Count	__ __ / __ __ / __ __ __ __	___ ___ : ___ ___	__ __ . __ __	X 109 cells/L

Section G: STRATIFICATION

G1. Risk Status: Stem cell transplantation or relapsed Leukemia 1

Other 2

G2. Type of Infection: Invasive mold infection 1

Other 2

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G002 – Subject Consent, Eligibility and Randomization Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....(GBSL)

A3. Initial Assessment Date:__ __ / __ __ / __ __ __ __

Section B: CONSENT

B1. Has the subject signed a consent form? Yes ..... 1 No ..... 2 **(End)**

B2. Date consent signed: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section C: INCLUSION CRITERIA	**Yes**	**No**
C1. Has the subject undergone dose-intensive chemotherapy **OR** hematopoietic stem cell transplantation within 90 days prior to eligibility determination?	1	2
C2. Does the subject have an ANC count <500/mm^3 (0.5 x 10^9 cells/L) **AND** is the subject expected to remain neutropenic for at least five days?	1	2
C3. Does the subject have a fungemia, bacteremia, invasive tissue bacterial infection, proven invasive tissue fungal infection, or probable invasive tissue fungal infection as defined in Appendix A of the RING Study Protocol?	1	2

Section D: EXCLUSION CRITERIA	**Yes**	**No**
D1. Is the subject unlikely to survive for the next five days?	1	2
D2. Was this subject previously enrolled in the RING Study?	1	2

Section E: ELIGIBILITY STATUS and LABS

E1. Date eligibility status determined: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

E2. Time eligibility status determined: ___ ___ : ___ ___ *(24 hour clock)*

E3. Most recent ANC count **prior to eligibility determination** (C2): __ . __ __ __ x 10^{9}cells/L

E4a. Date sample collected: __ __/__ __/__ __ __ __ E4b. Time sample collected: __ __ : __ __

Section F: RANDOMIZATION

F1. Does the subject have a more recent ANC result available (after ANC value reported in E3 but prior to randomization)? Yes ..... 1 No ..... 2 **(G1)**

F2. Most recent ANC count **prior to randomization**: __ . __ __ __ x 10^{9}cells/L

F3a. Date sample collected: __ __/__ __/__ __ __ __ F3b. Time sample collected: __ __ : __ __

Section G: STRATIFICATION

G1. Risk Status:	Stem cell transplantation or relapsed Leukemia	1
	Other	2
G2. Type of Infection:	Invasive mold infection	1
	Other	2

Section H: SIGNATURE

H1. Approved by: Initials ____ ____ ____ H2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G002 – Subject Consent, Eligibility and Randomization Form

Version A: 05/15/2007

Purpose of this form:

1) To confirm that a patient (or the patient's legal guardian, if applicable) and the Site Investigator have signed an Informed Consent document indicating that the patient has agreed to participate in the RING Study
2) To document the eligibility status of the patient based on all inclusion and exclusion criteria. This form must be completed for every patient who signs an Informed Consent document.
3) To record the stratification criteria for a subject considered eligible for randomization.

When to complete this form: This form must be completed during the screening/eligibility phase of the study, after the subject has signed a Consent/Assent document.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: CONSENT

B1. Indicate that the subject (or the subject's legal guardian) signed an Informed Consent document. This form is only to be completed if a subject signs a Consent document. If a consent form was not signed, go to the end of the form.

B2. Record the date the subject (or the subject's legal guardian) signed the Informed Consent document.

SECTION C: INCLUSION CRITERIA

C1. Indicate if the subject has undergone dose-intensive chemotherapy **OR** had a hematopoietic stem cell transplantation within 60 days prior to eligibility determination.

C2. Indicate if the subject has an ANC count less than 500/mm^3 (0.5 x 10^9 cells/L) **AND** is expected to remain neutropenic for at least five days.

C3. Indicate if the subject has a fungemia, bacteremia, invasive tissue bacterial infection, or proven/probable invasive tissue fungal infection as defined in Appendix A of the Granulocyte Protocol.

SECTION D: EXCLUSION CRITERIA

D1. Indicate if the subject is unlikely to survive for the next 5 days.

D2. Indicate if the subject was previously enrolled in the RING Study.

SECTION E. ELIGIBILITY STATUS

E1. Record the date the subject's eligibility status was determined in mm/dd/yyyy

E2. Record the time the subject's eligibility status was determined using to a 24-hour clock.

E3. Record the lab result used to determine if the subject's ANC count is less than 500/mm^3 (0.5 x 10^9 cells/L; inclusion criterion C2). This test must be done in the 24 hours prior to eligibility determination (as recorded in fields E1 and E2), and may be extracted from the subject's medical record. If the subject has not had this test done within the 24 hours prior to eligibility determination, draw a blood sample for the test to determine if the subject is eligible for the study.

E4a-b. Record the date and time the specimen was collected in mm/dd/yyyy.

SECTION F: STRATIFICATION

F1. Circle the number that corresponds to the subject's risk status. Category "1" includes subjects who have relapsed leukemia, subjects who have had a stem cell transplant, and subjects who are neutropenic due to preparation for a stem cell transplant.

F2. Circle the number that that best describes the subject's study-qualifying infection, as documented on Form G007.

SECTION G: SIGNATURE

G1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

G2. Record the date the form was approved using mm/dd/yyyy.

RING Study

Form G002 – Subject Consent, Eligibility and Randomization Form

Version B: 12/30/2009

Purpose of this form:

1) To confirm that a patient (or the patient's legal guardian, if applicable) and the Site Investigator have signed an Informed Consent document indicating that the patient has agreed to participate in the RING Study
2) To document the eligibility status of the patient based on all inclusion and exclusion criteria. This form must be completed for every patient who signs an Informed Consent document.
3) To record the stratification criteria for a subject considered eligible for randomization.

When to complete this form: This form must be completed during the screening/eligibility phase of the study, after the subject has signed a Consent/Assent document.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the subject's initial assessment date.

SECTION B: CONSENT

B1. Indicate that the subject (or the subject's legal guardian) signed an Informed Consent document. This form is only to be completed if a subject signs a Consent document. If a consent form was not signed, go to the end of the form.

B2. Record the date the subject (or the subject's legal guardian) signed the Informed Consent document.

SECTION C: INCLUSION CRITERIA

C1. Indicate if the subject has undergone dose-intensive chemotherapy **OR** had a hematopoietic stem cell transplantation within 90 days prior to eligibility determination.

C2. Indicate if the subject has an ANC count less than 500/mm^3 (0.5 x 10^9 cells/L) **AND** is expected to remain neutropenic for at least five days.

C3. Indicate if the subject has a fungemia, bacteremia, invasive tissue bacterial infection, or proven/probable invasive tissue fungal infection as defined in Appendix A of the Granulocyte Protocol.

SECTION D: EXCLUSION CRITERIA

D1. Indicate if the subject is unlikely to survive for the next 5 days.

D2. Indicate if the subject was previously enrolled in the RING Study.

SECTION E. ELIGIBILITY STATUS

E1. Record the date the subject's eligibility status was determined in mm/dd/yyyy

E2. Record the time the subject's eligibility status was determined using to a 24-hour clock.

E3. Record the most recent ANC prior to determining eligibility. Record the lab result used to determine if the subject's ANC count is less than 500/mm^3 (0.5 x 10^9 cells/L; inclusion criterion C2).

E4a-b. Record the date and time the specimen was collected.

SECTION E. RANDOMIZATION

F1. Does the subject have a more recent ANC result available (after ANC value reported in E3) prior to randomization?

F2. If the subject has a more recent ANC count result after ANC value reported in E3 and prior to randomization, record that result. Subjects must be consented and randomized within 3 days of eligibility determination. At randomization, the subject's ANC count must be <500/ mm^3 otherwise the subject may not be randomized.

F3a-b. Record the date and time the specimen was collected.

SECTION G: STRATIFICATION

G1. Circle the number that corresponds to the subject's risk status. Category "1" includes subjects who have relapsed leukemia, subjects who have had a stem cell transplant, and subjects who are neutropenic due to preparation for a stem cell transplant.

G2. Circle the number that that best describes the subject's study-qualifying infection, as documented on Form G007.

SECTION H: SIGNATURE

H1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

H2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G004 – Baseline Demographics and Medical History Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline..... (GBSL)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: DEMOGRAPHICS

B1. Date of birth: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

B2. Gender: Male..... 1 Female..... 2

B3. Ethnic Origin Hispanic/Latino ..... 1 Not Hispanic/Latino 2

Not obtained/Unknown..... -8 Refused ..... -7

B4. Race:	Yes	No	Refused	Unknown/ Not Obtained
a. American Indian or Alaska Native	1	2	-7	-8
b. Asian	1	2	-7	-8
c. Black or African American	1	2	-7	-8
d. Native Hawaiian or Other Pacific Islander	1	2	-7	-8
e. White	1	2	-7	-8
f. Other	1	2 **(B5a)**	-7 **(B5a)**	-8 **(B5a)**

B4f1. Specify Other: _____

B5a. Weight in kilograms: ___ ___ ___ • ___ kilograms = pounds X 0.4536

B5b. Weight in pounds: ___ ___ ___ • ___ pounds = kilograms X 2.205

Section C: PRIMARY DIAGNOSIS

C1. Date of primary diagnosis: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C2. Primary Diagnosis: ***(circle one)***

Acute Lymphocytic Leukemia..... 01
Acute Nonlymphocytic Leukemia..... 02
Chronic Myelogenous Leukemia 03
Chronic Lymphocytic Leukemia..... 04
Chronic Myelomonocytic Leukemia 05
Non-Hodgkin's Lymphoma 06
Other (specify)..... 99➔

Hodgkin's Lymphoma 07
Myelodysplasia..... 08
Myeloma..... 09
Non-Hematopoietic Solid Tumor..... 10
Aplastic anemia 11
Sickle cell disease 12
Specify other: _____

__ __ -__ __ __ __- __ __ __- __

Section D: MEDICAL HISTORY

	Yes	No	Unknown
D1. Does the subject have a known history of granulocyte transfusions?	1	2	-8
D2. Does the subject have a known history of granulocyte reaction?	1	2	-8
D3. For female subjects only: has the subject ever been pregnant?	1	2 **(D4)**	-8 **(D4)**

D3a. Number of pregnancies (including miscarriages and abortions): ___ ___

D4. What is the subject's CMV status? Positive..... 1
Negative 2

D4a. Date of most recent CMV test: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D5. Date of current neutropenia onset (ANC < $0.5x10^9$/L): __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D6. Cause of subject's current neutropenia: Chemotherapy only ..... 1 **(E1)**
Infection..... 2 **(E1)**
HST (or preparation for HST)..... 3

D6a. Date of most recent or planned transplant: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D6b. Type of transplant: Allogeneic 1
Autologous ..... 2 **(D6d)**
Syngeneic ..... 3 **(D6d)**
Other: ..... 99➔➔ Specify: _____ **(D6d)**

D6c. If Allogeneic, match: Matched related 1
Mismatched related..... 2
Matched unrelated..... 3
Mismatched unrelated 4
Other ..... 99➔➔ Specify: _____

D6d. Stem cell source: Peripheral blood stem cells 1
Blood from one umbilical cord ... 2
Blood from ≥ 2 umbilical cords .. 3
Bone marrow..... 4
Other ..... 99➔➔ Specify:_____

D6e. Product Manipulation: No manipulation 1
T-cell depletion..... 2
CD34 selected 3
Other:..... 99➔➔ Specify: _____

D6f. Type of conditioning therapy: Myeloablative..... 1
Non-myeloablative..... 2

__ __ -__ __ __ __- __ __ __- __

Section D: MEDICAL HISTORY, cont.

D6g. Did the subject receive Total Body Irradiation within 3 months of the onset of current infection?	Yes ..... 1 No 2
D6h. Has the subject received one or more HSTs prior to this admission?	Yes ..... 1 No ..... 2 **(E1)**

D6h 1. If yes, number of previous HSTs: ___ ___

Section E: SIGNATURE

E1. Approved by: Initials ____ ____ ____ E2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G004 – Baseline Demographics and Medical History Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: DEMOGRAPHICS

B1. Date of birth: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

B2. Gender: Male .....1 Female 2

B3. Ethnic Origin Hispanic/Latino.....1 Not Hispanic/Latino 2

Not obtained/Unknown .....-8 Refused.....-7

B4. Race:	Yes	No	Refused	Unknown/ Not Obtained
a. American Indian or Alaska Native	1	2	-7	-8
b. Asian	1	2	-7	-8
c. Black or African American	1	2	-7	-8
d. Native Hawaiian or Other Pacific Islander	1	2	-7	-8
e. White	1	2	-7	-8
f. Other	1	2 **(B5a)**	-7 **(B5a)**	-8 **(B5a)**

B4f1. Specify Other: _____

B5a. Weight in kilograms: ___ ___ ___ • ___ kilograms = pounds X 0.4536

B5b. Weight in pounds: ___ ___ ___ • ___ pounds = kilograms X 2.205

Section C: PRIMARY DIAGNOSIS

C1. Date of primary diagnosis: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C2. Primary Diagnosis: ***(circle one)***

Acute Lymphocytic Leukemia 01
Acute Nonlymphocytic Leukemia.....02
Chronic Myelogenous Leukemia.....03
Chronic Lymphocytic Leukemia 04
Chronic Myelomonocytic Leukemia 05
Non-Hodgkin's Lymphoma 06
Other (specify).....99➔

Hodgkin's Lymphoma 07
Myelodysplasia 08
Myeloma..... 09
Non-Hematopoietic Solid Tumor 10
Aplastic anemia 11
Sickle cell disease 12
Specify other: _____

__ __ -__ __ __ __- __ __ __- __

Section D: MEDICAL HISTORY

	Yes	No	Unknown
D1. Does the subject have a known history of granulocyte transfusions?	1 **(D1a)**	2	-8
D1a. Date of most recent granulocyte transfusion __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy) or (mm/yyyy) or (yyyy)*			
D2. Does the subject have a known history of granulocyte reaction?	1	2	-8
D3. For female subjects only: has the subject ever been pregnant?	1	2 **(D4)**	-8 **(D4)**

D3a. Number of pregnancies (including miscarriages and abortions): ___ ___

D4. What is the subject's CMV status? Positive 1
Negative 2

D4a. Date of most recent CMV test:..... __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D5. Date of current neutropenia onset (ANC < $0.5x10^9$/L): __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D6. Cause of subject's current neutropenia:
Chemotherapy only..... 1 **(E1)**
Infection..... 2 **(E1)**
HST (or preparation for HST)..... 3

D6a. Date of most recent or planned transplant: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

D6b. Type of transplant:
Allogeneic 1
Autologous ..... 2 **(D6d)**
Syngeneic ..... 3 **(D6d)**
Other: ..... 99➔➔ Specify: _____ **(D6d)**

D6c. If Allogeneic, match:
Matched related..... 1
Mismatched related 2
Matched unrelated..... 3
Mismatched unrelated 4
Other ..... 99➔➔ Specify: _____

D6d. Stem cell source:
Peripheral blood stem cells..... 1
Blood from one umbilical cord.... 2
Blood from ≥ 2 umbilical cords... 3
Bone marrow..... 4
Other .....99➔➔ Specify:_____

D6e. Product Manipulation:
No manipulation 1
T-cell depletion..... 2
CD34 selected..... 3
Other:..... 99➔➔ Specify: _____

D6f. Type of conditioning therapy:
Myeloablative..... 1
Non-myeloablative 2

__ __ -__ __ __ __- __ __ __- __

Section D: MEDICAL HISTORY, cont.

D6g. Did the subject receive Total Body Irradiation within 3 months of the onset of current infection?	Yes.....1 No 2
D6h. Has the subject received one or more HSTs prior to this admission?	Yes.....1 No .....2 **(E1)**
D6h1. If yes, number of previous HSTs: ___ ___	

Section E: SIGNATURE

E1. Approved by: Initials ____ ____ ____ E2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Form G004 – Baseline Demographics and Medical History Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to collect demographic information and medical history for a subject enrolled in the RING study.

When to complete this form: This form must be completed during the baseline phase of the study, after the subject has signed a Consent/Assent document.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: DEMOGRAPHICS

B1. Record the subject's date of birth in mm/dd/yyyy format.

B2. Record the subject's gender.

Questions B3 and B4a-f must be self-reported or self-identified by the subject or the subject's legal guardian. This may be accomplished by asking the subject to circle the appropriate answers on the form or by a staff member conducting an interview with the subject.

B3. Record the subject's ethnic origin.

B4a-f. Record the subject's race. The subject may identify him/herself as one or more than one race. If the subject provides a racial category not in this list, circle 'Yes' for other (B4f) and write the category in the line provided in B4f1.

B5a. Record the subject's weight in kilograms.

B5b. Record the subject's weight in pounds.

SECTION C: PRIMARY DIAGNOSIS

C1. Record the date of the subject's primary diagnosis. If the date of the subject's diagnosis is unknown, enter 08/08/0808 ("don't know"). ***Note:*** this field will accept partial dates if the month/year or just year of diagnosis is known. Therefore, the date can be entered in the formats: mm/dd/yyyy, mm/yyyy or yyyy.

C2. Record the subject's primary diagnosis by circling one number in the list provided. If the subject's primary diagnosis is not listed, circle "Other (99)" and record the primary diagnosis in the space provided.

SECTION D: MEDICAL HISTORY

D1. Indicate if the subject has a known history of granulocyte transfusions.

D2. Indicate if the subject has a known history of granulocyte transfusion reactions.

D3. For female subjects only: Indicate if the subject was ever pregnant. If a subject has been pregnant, record the number of pregnancies in D3a. This number should include all pregnancies, including those that ended in elective, spontaneous, or therapeutic abortions.

D4. Indicate the subject's CMV status.

D4a. Record the date of the subject's most recent CMV test.

D5. Record the onset date of this episode of neutropenia in mm/dd/yyyy format.

D6. Indicate the cause of the subject's current neutropenia. If the cause is chemotherapy only ("1") or infections ("2"), skip to question E1.

D6a. If the subject has a hematopoietic stem cell transplant (HST) (or preparation for a hematopoietic stem cell transplant), record the date of the transplant (or planned transplant) in mm/dd/yyyy format. Per protocol, this date must be within 60 days of enrollment (randomization) in the RING Study.

D6b. Indicate the type of transplant that is planned or that the subject received. If the subject will receive/received autologous, syngeneic or another type of transplant, go to question D6d.

D6c. If the subject received an allogeneic match, indicate the donor type. Mismatched related is defined as: not HLA matched, but donor biologically related.

D6d. Indicate the stem cell source(s). If the subject will receive/received stem cells from more than one source select "other" and write in the sources in the space provided.

D6e. Indicate the product manipulation method.

D6f. Indicate the type of conditioning.

D6g. Indicate if the subject received Total Body Irradiation within 3 months prior to the onset of the current infection.

D6h. Indicate if the subject received one or more hematopoietic stem cell transplants (HST) prior to this admission. If yes, indicate the number of previous HSTs.

SECTION E: SIGNATURE

E1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

E2. Record the date the form was approved using mm/dd/yyyy.

Form G004 – Baseline Demographics and Medical History Form

Version B: 03/23/2011

Purpose of this form: The purpose of this form is to collect demographic information and medical history for a subject enrolled in the RING study.

When to complete this form: This form must be completed during the baseline phase of the study, after the subject has signed a Consent/Assent document.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: DEMOGRAPHICS

B1. Record the subject's date of birth in mm/dd/yyyy format.

B2. Record the subject's gender.

Questions B3 and B4a-f must be self-reported or self-identified by the subject or the subject's legal guardian. This may be accomplished by asking the subject to circle the appropriate answers on the form or by a staff member conducting an interview with the subject.

B3. Record the subject's ethnic origin.

B4a-f. Record the subject's race. The subject may identify him/herself as one or more than one race. If the subject provides a racial category not in this list, circle 'Yes' for other (B4f) and write the category in the line provided in B4f1.

B5a. Record the subject's weight in kilograms.

B5b. Record the subject's weight in pounds.

SECTION C: PRIMARY DIAGNOSIS

C1. Record the date of the subject's primary diagnosis. If the date of the subject's diagnosis is unknown, enter 08/08/0808 ("don't know"). ***Note:*** this field will accept partial dates if the month/year or just year of diagnosis is known. Therefore, the date can be entered in the formats: mm/dd/yyyy, mm/yyyy or yyyy.

C2. Record the subject's primary diagnosis by circling one number in the list provided. If the subject's primary diagnosis is not listed, circle "Other (99)" and record the primary diagnosis in the space provided.

SECTION D: MEDICAL HISTORY

D1. Indicate if the subject has a known history of granulocyte transfusions. If yes, answer question D1a.

D1a. Indicate date of most recent known granulocyte transfusion. This filed will capture any date information available (mm/dd/yyyy; mm/yyyy; yyyy).

D2. Indicate if the subject has a known history of granulocyte transfusion reactions.

D3. For female subjects only: Indicate if the subject was ever pregnant. If a subject has been pregnant, record the number of pregnancies in D3a. This number should include all pregnancies, including those that ended in elective, spontaneous, or therapeutic abortions.

D3a. Indicate number of pregnancies include miscarriages and abortions.

D4. Indicate the subject's CMV status.

D4a. Record the date of the subject's most recent CMV test.

D5. Record the onset date of this episode of neutropenia in mm/dd/yyyy format.

D6. Indicate the cause of the subject's current neutropenia. If the cause is chemotherapy only ("1") or infections ("2"), skip to question E1.

D6a. If the subject has a hematopoietic stem cell transplant (HST) (or preparation for a hematopoietic stem cell transplant), record the date of the transplant (or planned transplant) in mm/dd/yyyy format. Per protocol, this date must be within 60 days of enrollment (randomization) in the RING Study.

D6b. Indicate the type of transplant that is planned or that the subject received. If the subject will receive/received autologous, syngeneic or another type of transplant, go to question D6d.

D6c. If the subject received an allogeneic match, indicate the donor type. Mismatched related is defined as: not HLA matched, but donor biologically related.

D6d. Indicate the stem cell source(s). If the subject will receive/received stem cells from more than one source select "other" and write in the sources in the space provided.

D6e. Indicate the product manipulation method.

D6f. Indicate the type of conditioning.

D6g. Indicate if the subject received Total Body Irradiation within 3 months prior to the onset of the current infection.

D6h. Indicate if the subject received one or more hematopoietic stem cell transplants (HST) prior to this admission. If yes, indicate the number of previous HSTs.

SECTION E: SIGNATURE

E1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

E2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G005 –Symptoms & Signs Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....GBSL
Measurement.....GMMT

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: SYMPTOMS/SIGNS

B1. Indicate data collection date:
Baseline (Day 1).....1 *(Narrative required)*
+2 weeks (Day 14 +/- 2 days).....2 *(Narrative encouraged)*
+4 weeks (Day 28 +/- 2 days).....3 *(Narrative encouraged)*
End of study (Day 42).....4 *(Narrative required)*

B2. Indicate subject's Zubrod score (circle one number):

0.....Asymptomatic
1.....Symptomatic, fully ambulatory
2.....Symptomatic, in bed < 50% of the day
3.....Symptomatic, in bed > 50% of the day but not bedridden
4.....Bedridden
5.....Dead **(C1)**

	Yes	**No**	**Unknown/ not Assessed**
B3. (Baseline measurement only) Did the subject have a fever (≥100.4°F or 38°C) within 7 days prior to clinical diagnosis of this infection?	1	2	-8
B4. Does the subject have Graft vs. Host Disease (GVHD)?	1	2 **(B5)**	
B4a. Indicate grade of GVHD: _____			
Lower respiratory tract symptoms/signs & physical findings	**Yes**	**No**	**Unknown/ not Assessed**
B5. Does the subject have any lower respiratory tract symptoms/signs?	1	2 **(B6)**	
B5a. Is the subject on a ventilator?	1	2	-8

__ - ____ __ - __ __ __ __ - __ __

Lower respiratory tract symptoms/signs & physical findings (cont.)

B5b. What is the subject's Fi02? ___ ___ ___ % ☐ Unknown .....-8

B5c. What is the subject's oxygen saturation? ___ ___ ___ % ☐ Unknown.....-8

B5d. What is the subject's respiratory rate? ___ ___ ___ breaths/minute

	Yes	No	Unknown/ not Assessed
B5e. Dyspnea?	1	2	-8
B5f. Hemoptysis?	1	2	-8
B5g. Other (specify)	1	2 **(B5h)**	-8

B5g1. Specify symptom/sign: _____

B5h. Comment on lower respiratory tract symptoms/signs:

_____

_____

Nasal/Sinus symptoms/signs	Yes	No	Unknown / Not Assessed
B6. Does the subject have any nasal/sinus symptoms/signs?	1	2 **(B7)**	
B6a. Epistaxis	1	2	-8
B6b. Nose ulceration or eschar of nasal mucosa	1	2	-8
B6c. Periorbital swelling	1	2	-8
B6d. Maxillary tenderness	1	2	-8
B6e. Black necrotic lesions or perforation of hard palate	1	2	-8
B6f. Other (specify)	1	2 **(B6g)**	-8

B6f1. Specify symptom: _____

B6g. Comment on nasal/sinus symptoms/signs:

_____

_____

CNS symptoms/signs	Yes	No	Unknown / Not Assessed
B7. Does the subject have any CNS symptoms/signs?	1	2 **(B8)**	
B7a. Focal neurological symptoms and signs (including focal seizures, hemiparesis, cranial nerve palsies)	1	2	-8
B7b. Mental status changes (including speech)	1	2	-8
B7c. Meningeal irritation findings	1	2	-8
B7d. Headaches	1	2	-8

__ - ____ __ - __ __ __ __ - __ __

CNS symptoms/signs(cont.)	**Yes**	**No**	**Unknown / Not Assessed**
B7e. Photophobia	1	2	-8
B7f. Other (specify)	1	2 **(B7g)**	-8
B7f1. Specify symptom/sign: _____			
B7g. Comment on CNS symptoms/signs: _____ _____			

Other symptoms/signs	**Yes**	**No**	**Unknown / Not Assessed**
B8. Intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis	1	2	-8
B9. Papular or nodular skin lesions without any other explanation	1	2	-8
B10. Does the subject have any other symptoms/signs related to their infection?	1	2 **(B11)**	
B10a. Specify symptom/sign: _____			
B10b. Specify symptom/sign: _____			
B11. General comments: _____ _____			

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G005 –Symptoms & Signs Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline ..... GBSL
Measurement..... GMMT

A3. Form completion date: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: SYMPTOMS/SIGNS

B1. Indicate data collection timepoint: Baseline (Day 1).....1 *(Narrative required)*
+2 weeks (Day 14 +/- 2 days) .....2 *(Narrative encouraged)*
+4 weeks (Day 28 +/- 2 days) .....3 *(Narrative encouraged)*
End of study (Day 42).....4 *(Narrative required)*

B1a. Collection Date: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

B2. Indicate subject's Zubrod score (circle one number):

0..... Asymptomatic
1..... Symptomatic, fully ambulatory
2..... Symptomatic, in bed < 50% of the day
3..... Symptomatic, in bed > 50% of the day but not bedridden
4..... Bedridden
5..... Dead **(C1)**

	Yes	**No**	**Unknown/ not Assessed**
B3. (Baseline measurement only) Did the subject have a fever (≥100.4°F or 38°C) within 7 days prior to clinical diagnosis of this infection?	1	2	-8
B4. Does the subject have Graft vs. Host Disease (GVHD)?	1	2 **(B5)**	
B4a. Indicate grade of GVHD: _____			
Lower respiratory tract symptoms/signs & physical findings	**Yes**	**No**	**Unknown/ not Assessed**
B5. Does the subject have any lower respiratory tract symptoms/signs?	1	2 **(B6)**	
B5a. Is the subject on a ventilator?	1	2	-8

__ __ - __ __ __ __ - __ __ __ - __

Lower respiratory tract symptoms/signs & physical findings (cont.)			
B5b. What is the subject's Fi02? ___ ___ ___ % ☐ Unknown .....-8			
B5c. What is the subject's oxygen saturation? ___ ___ ___ % ☐ Unknown.....-8			
B5d. What is the subject's respiratory rate? ___ ___ ___ breaths/minute			
	Yes	**No**	**Unknown/ not Assessed**
B5e. Dyspnea?	1	2	-8
B5f. Hemoptysis?	1	2	-8
B5g. Other (specify)	1	2 **(B5h)**	-8
B5g1. Specify symptom/sign: _____			
B5h. Comment on lower respiratory tract symptoms/signs: _____ _____			

Nasal/Sinus symptoms/signs	**Yes**	**No**	**Unknown / Not Assessed**
B6. Does the subject have any nasal/sinus symptoms/signs?	1	2 **(B7)**	
B6a. Epistaxis	1	2	-8
B6b. Nose ulceration or eschar of nasal mucosa	1	2	-8
B6c. Periorbital swelling	1	2	-8
B6d. Maxillary tenderness	1	2	-8
B6e. Black necrotic lesions or perforation of hard palate	1	2	-8
B6f. Other (specify)	1	2 **(B6g)**	-8
B6f1. Specify symptom/sign: _____			
B6g. Comment on nasal/sinus symptoms/signs: _____ _____			

CNS symptoms/signs	**Yes**	**No**	**Unknown / Not Assessed**
B7. Does the subject have any CNS symptoms/signs?	1	2 **(B8)**	
B7a. Focal neurological symptoms and signs (including focal seizures, hemiparesis, cranial nerve palsies)	1	2	-8
B7b. Mental status changes (including speech)	1	2	-8
B7c. Meningeal irritation findings	1	2	-8
B7d. Headaches	1	2	-8

__ __ - __ __ __ __ - __ __ __ - __

CNS symptoms/signs(cont.)	**Yes**	**No**	**Unknown / Not Assessed**
B7e. Photophobia	1	2	-8
B7f. Other (specify)	1	2 **(B7g)**	-8
B7f1. Specify symptom/sign: _____			
B7g. Comment on CNS symptoms/signs: _____ _____			

Other symptoms/signs	**Yes**	**No**	**Unknown / Not Assessed**
B8. Intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis	1	2	-8
B9. Papular or nodular skin lesions without any other explanation	1	2	-8
B10. Does the subject have any other symptoms/signs related to their infection?	1	2 **(B11)**	
B10a. Specify symptom/sign: _____			
B10b. Specify symptom/sign: _____			

B11. Was the subject an inpatient or outpatient on date specified on B1a?

Inpatient..... 1

Outpatient..... 2

B12. General comments:

_____

_____

Section C: SIGNATURE

C1. Approved by: Initials _____ _____ _____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G005 – Symptoms & Signs Documentation Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document symptoms and signs that the subject experiences while an inpatient on the RING Study.

When to complete this form: This form must be completed at baseline (Day 1), 2 weeks after baseline (Day 14), 4 weeks after baseline (Day 28), and at the end of the study (Day 42).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. Indicate the event the form was completed for: if the collection date is Baseline (Day 1) select "Baseline"; otherwise, select "Measurement".

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: SYMPTOMS/SIGNS

B1. Indicate the collection date for the data contained on the form. The baseline measurement must be completed on day 1. The 2 week, 4 week and end of study must be completed on the date indicated +/- 2 days (i.e. 2 week measurement can be completed on days 10 – 16).

B2. Indicate the subject's Zubrod score by circling one number on the scale provided. If the Zubrod score is 5 (dead), skip to question C1.

B3. At baseline, indicate if the subject had a fever within the 7 days prior to the clinical diagnosis of the study-qualifying infection. Fever is defined as a temperature $\geq$ 100.4°F or 38°C. If this is the 2 week, 4 week, or end of study measurement skip to question B4.

B4. Indicate if the subject has Graft vs. Host Disease (GVHD). If the subject does have GVHD, record the grade of GVHD in question B4a. If the subject does not, skip to question B5.

B5. Indicate if the subject had any lower respiratory tract symptoms/signs or physical findings on the measurement day. If not, skip to question B6.

B5a. Indicate if the subject was on a ventilator on the measurement day.

SECTION B: SYMPTOMS/SIGNS, cont.

Questions B5b-d: if more than one measurement is made on the day of evaluation (00:00 – 23:59), report the measurement obtained closest to 0800 local time (either before or after 0800).

B5b. Record the subject's Fraction of Inspired Oxygen (Fi02), if known.

B5c. Record the subject's oxygen saturation, if known.

B5d. Record the subject's respiratory rate.

B5e. Indicate if the subject experienced dyspnea on the measurement day.

B5f. Indicate if the subject experienced hemoptysis on the measurement day.

B5g. Indicate if the subject experienced another respiratory symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B5h. Record any relevant comment on the subject's respiratory symptoms/signs.

B6. Indicate if the subject had any nasal/sinus symptoms or signs on the measurement day. If not, skip to question B7.

B6a. Indicate if the subject experienced epistaxis on the measurement day.

B6b. Indicate if the subject had a nose ulceration or eschar of the nasal mucosa on the measurement day.

B6c. Indicate if the subject had any periorbital swelling on the measurement day

B6d. Indicate if the subject had maxillary tenderness on the measurement day.

B6e. Indicate if the subject had black necrotic lesions or perforation of the hard palate.

B6f. Indicate if the subject had another nasal/sinus symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B6g. Record any relevant comment on the subject's nasal/sinus symptoms/signs.

B7. Indicate if the subject had any CNS symptoms or signs on the measurement day. If not, skip to question B8.

B7a. Indicate if the subject had any focal neurological symptoms and signs on the measurement day. This includes focal seizures, hemiparesis, and cranial nerve palsies.

B7b. Indicate if the subject had any mental status changes on the measurement day, including speech changes.

B7c. Indicate if the subject had meningeal irritation findings on the measurement day.

B7d. Indicate if the subject had any headaches on the measurement day.

SECTION B: SYMPTOMS/SIGNS, cont.

B7e. Indicate if the subject had photophobia on the measurement day.

B7f. Indicate if the subject had another CNS symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B7g. Record any relevant comment on the subject's CNS symptoms/signs.

B8. Indicate if the subject had any intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis on the measurement day.

B9. Indicate if the subject had any popular or nodular skin lesions without any other explanation (other than study-qualifying infection) on the measurement day.

B10. Indicate if the subject had any other symptom/sign related to their study-qualifying infection on the measurement day. If not, skip to question B11.

B11. Record any general comments related to the subjects symptoms/signs.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form.

C2. Record the date the form was approved using mm/dd/yyyy. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

Form G005 – Symptoms & Signs Documentation Form

Version B: 09/4/2009

Purpose of this form: The purpose of this form is to document symptoms and signs that the subject experiences while an inpatient on the RING Study.

When to complete this form: This form must be completed at baseline (Day 1), 2 weeks after baseline (Day 14), 4 weeks after baseline (Day 28), and at the end of the study (Day 42).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. Indicate the event the form was completed for: if the collection date is Baseline (Day 1) select "Baseline"; otherwise, select "Measurement".

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: SYMPTOMS/SIGNS

Form completion note: to answer the questions in section B, review the subject's medical record and speak to their care providers. If a particular event is not noted in the medical record, it may be assumed that the event did not take place, and the question can be answered "No". Select "unknown" if you are unable to determine the response to the question.

B1. Indicate the collection date for the data contained on the form. The baseline measurement must be completed on day 1. The 2 week, 4 week and end of study must be completed on the date indicated +/- 2 days (i.e. 2 week measurement can be completed on days 10 – 16).

B1a. Indicate exact date collection was made.

B2. Indicate the subject's Zubrod score by circling one number on the scale provided. If the Zubrod score is 5 (dead), skip to question C1.

B3. At baseline, indicate if the subject had a fever within the 7 days prior to the clinical diagnosis of the study-qualifying infection. Fever is defined as a temperature $\geq$ 100.4°F or 38°C. If this is the 2 week, 4 week, or end of study measurement skip to question B4.

B4. Indicate if the subject has Graft vs. Host Disease (GVHD). If the subject does have GVHD, record the grade of GVHD in question B4a. If the subject does not, skip to question B5.

B5. Indicate if the subject had any lower respiratory tract symptoms/signs or physical findings on the measurement day. If not, skip to question B6.

B5a. Indicate if the subject was on a ventilator on the measurement day.

SECTION B: SYMPTOMS/SIGNS, cont.

Questions B5b-d: if more than one measurement is made on the day of evaluation (00:00 – 23:59), report the measurement obtained closest to 0800 local time (either before or after 0800).

B5b. Record the subject's Fraction of Inspired Oxygen (Fi02), if known.

B5c. Record the subject's oxygen saturation, if known.

B5d. Record the subject's respiratory rate.

B5e. Indicate if the subject experienced dyspnea on the measurement day.

B5f. Indicate if the subject experienced hemoptysis on the measurement day.

B5g. Indicate if the subject experienced another respiratory symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B5h. Record any relevant comment on the subject's respiratory symptoms/signs.

B6. Indicate if the subject had any nasal/sinus symptoms or signs on the measurement day. If not, skip to question B7.

B6a. Indicate if the subject experienced epistaxis on the measurement day.

B6b. Indicate if the subject had a nose ulceration or eschar of the nasal mucosa on the measurement day.

B6c. Indicate if the subject had any periorbital swelling on the measurement day

B6d. Indicate if the subject had maxillary tenderness on the measurement day.

B6e. Indicate if the subject had black necrotic lesions or perforation of the hard palate.

B6f. Indicate if the subject had another nasal/sinus symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B6g. Record any relevant comment on the subject's nasal/sinus symptoms/signs.

B7. Indicate if the subject had any CNS symptoms or signs on the measurement day. If not, skip to question B8.

B7a. Indicate if the subject had any focal neurological symptoms and signs on the measurement day. This includes focal seizures, hemiparesis, and cranial nerve palsies.

B7b. Indicate if the subject had any mental status changes on the measurement day, including speech changes.

B7c. Indicate if the subject had meningeal irritation findings on the measurement day.

B7d. Indicate if the subject had any headaches on the measurement day.

SECTION B: SYMPTOMS/SIGNS, cont.

B7e. Indicate if the subject had photophobia on the measurement day.

B7f. Indicate if the subject had another CNS symptom or sign on the measurement day. If so, specify the symptom/sign in the space provided.

B7g. Record any relevant comment on the subject's CNS symptoms/signs.

B8. Indicate if the subject had any intraocular findings suggestive of hematogenous fungal chorioretinitis or endophthalmitis on the measurement day.

B9. Indicate if the subject had any popular or nodular skin lesions without any other explanation (other than study-qualifying infection) on the measurement day.

B10. Indicate if the subject had any other symptom/sign related to their study-qualifying infection on the measurement day. If not, skip to question B11.

B10a. Specify the other symptom/sign related to the study-qualifying infection.

B10b. Specify another symptom/sign related to the study-qualifying infection, if applicable. If the subject does not have another symptom/sign, enter -1 (not applicable).

B11. Indicate if the patient was in-patient or out-patient on date specified on B1a.

B12. Record any general comments related to the subjects symptoms/signs.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G006 – Eligibility, Study Qualifying Infection Documentation and Randomization Form

TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....(GBSL)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: INCLUSION CRITERIA	**Yes**	**No**
B1. Does the subject have severe neutropenia (ANC count <500/mm^3 (0.5 x 10^9 cells/L) due to marrow failure caused by underlying disease or therapy?	1	2
B2. Does the subject have a proven invasive fungal infection, probable invasive fungal infection, presumptive invasive fungal infection, probable endemic mycosis, typhlitis, proven invasive bacterial tissue infection of chest and/or sinuses, proven invasive tissues infection of other location, presumptive invasive bacterial tissue infection of chest and/or sinuses, presumptive invasive tissue infection of other location, or Bacteremia as defined in Appendix A of the RING Study Protocol?	1	2

Section C: EXCLUSION CRITERIA	**Yes**	**No**
C1. Is the subject unlikely to survive for the next five days?	1	2
C2. Is there evidence that the subject will <u>not</u> be neutropenic for at least 5 days?	1	2
C3. Was this subject previously enrolled in the RING Study?	1	2

Section D: INFECTION INFORMATION

D1. Type of infection:

Proven invasive fungal infection……..... 1 **(Complete Section D)**
Probable invasive fungal infection……..... 2 **(Complete Sections E, F, G)**
D1a. Is this infection a mold? Yes…….1 No…....2
Presumptive invasive fungal infection…..... ..... 3 **(Complete Sections E & G)**
Probable Endemic Mycosis .... 4 **(Complete Section E & Question G6)**
Typhlitis…….…… ..... 5 **(Complete Section H)**
Proven Invasive Bacterial Tissue Infection of Chest and/or Sinuses..... 6 **(Complete Section I)**
Proven Invasive Bacterial Tissue Infection of Other Location…….. 7 **(Complete Section I)**
Presumptive Invasive Bacterial Tissue Infection of Chest and/or Sinuses 8 **(Complete Section I)**
Presumptive Invasive Bacterial Tissue Infection of Other Location……..... 9 **(Complete Section I)**
Bacteremia……..... 10 **(Complete Section J)**

D2. Site of infection: Bloodstream.....1
Pulmonary/Chest 2
Facial.....3
Sinus.....4
Localized skin or soft tissue 5
CNS.....6
Disseminated (more than one site) ....7➔Specify sites:_____
Other.....99➔Specify: _____

For ***proven invasive fungal infections***, is the causative agent:

D3. Mold Yes.....1 No.....2 (D4)

D3a. Identify the specific agent:

Aspergillus 1
Zygomycetes..... 2
Fusarium..... 3
Scedosporium..... 4
Mold not otherwise specified.... 5
Other ..... 99 ➔➔ D3a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

D3b. Histopathologic, cytopathologic, or direct microscopic examination of a specimen obtained by a needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage	Yes..... 1	No 2
D3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine	Yes..... 1	No 2

D3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes..... 1 **(K1)**	No ..... 2 **(K1)**

D4. Yeast Yes .....1 No 2 (D5)

D4a. Identify the specific agent:

Candida 1

Non-Candida ..... 99 ➔➔ D4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

D4b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen from a normally sterile site (other than mucous membranes) showing yeast cells e.g. *Cryptococcus* species indicated by encapsulated budding yeasts, *Candida* species showing pseudohyphae or true hyphae	Yes..... 1	No 2
D4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly placed, <24 hours ago, drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes..... 1	No 2
D4d. Blood culture that yields yeast (e.g. *Cryptococcus* species, *Candida* species), or yeast-like fungi (e.g. *Trichosporon* spp.)	Yes..... 1	No 2
D4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes..... 1 **(K1)**	No ..... 2 **(K1)**

D5. Endemic Fungal Infection Yes..... 1 No 2 (K1)

D5a. Identify the specific agent:

Paracoccidioidomycosis 1

Coccidioidomycosis..... 2

Other ..... 99 ➔➔ D5a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply in a host with an illness consistent with endemic mycosis:

D5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms with a truly distinctive appearance characteristic of dimorphic fungi, such as *Coccidioides* species spherules, *Blastomyces dermatitidis* thick-walled broad-based budding yeasts, *Paracoccidioides brasiliensis* multiple budding yeast cells, and, in the case of histoplasmosis, the presence of characteristic intracellular yeast forms in a phagocyte in a peripheral blood smear or in tissue macrophages	Yes..... 1	No 2
D5c. Recovery in culture from a specimen obtained from the affected site	Yes..... 1	No 2
D5d. Recovery in culture from a specimen obtained from the blood	Yes..... 1	No 2

D5e. Paracoccidioidomycosis: demonstration in 2 consecutive serum samples of a precipitin band to paracoccidioidin concurrently in the setting of an ongoing infection disease process OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process	Yes..... 1 **(K1)**	No ..... 2 **(K1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion. For *presumptive invasive fungal infection,* subjects must have at least one host factor and one clinical criterion. For *probable endemic mycoses infection,* subjects must have at least one host factor criterion and a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive *Histoplasma* antigen test result from urine, blood or CSF.

Section E: HOST FACTORS

Identify the criteria that apply to the infection by answering yes or no to each question

E1. E1a. Does the subject have relapsed or refractory acute leukemia or MDS and a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease? (presumptive invasive fungal infection)	Yes ..... 1 **(E2)**	No 2
E1b. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease? (probable invasive fungal infection)	Yes 1	No 2
E2. Has the subject received an allogeneic stem cell transplant?	Yes 1	No 2
E3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes 1	No 2
E4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues) during the past 90 days?	Yes 1	No 2
E5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes 1	No 2

Section F: MICROBIOLOGICAL CRITERIA

Identify the criteria that apply to the infection by answering yes or no to each question

F1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes 1	No 2

F2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid, bronchial brush, or sinus aspirate samples? F2a. Specify organism identified: _____	Yes.... 1 **(F2a)**	No 2
F3. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF?	Yes.....1	No 2
F4. Does the subject have Beta-D-glucan detected in serum?	Yes.....1	No 2

Section G: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
G1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes.....1	No..... 2 **(G2)**
G1a. Is there presence of one of the following imaging signs on CT: • dense, well defined nodule(s) with or without a halo sign; • air crescent sign; • cavity	Yes.....1	No..... 2
G2. Does the subject have ***tracheobronchitis***?	Yes.....1	No.... 2 **(G3)**
G2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes.....1	No..... 2
G3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes.....1	No.... 2 **(G4)**
G3a. Is there imaging showing sinusitis **AND** at least one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer with black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes.....1	No..... 2
G4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes.....1	No.... 2 **(G5)**
G4a. Are there focal lesions on imaging?	Yes.....1	No..... 2
G4b. Is there meningeal enhancement on MRI or CT?	Yes.....1	No..... 2
G5. Does the subject have signs/symptoms of ***Disseminated candidiasis?*** *(At least one of the following after an episode of candidemia within the previous 2 weeks):*	Yes.....1	No.... 2 **(K1)**
G5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen?	Yes.....1	No..... 2
G5b. Does the subject have progressive retinal exudates on ophthalmologic examination?	Yes...1	No.... 2
G6. Does the subject have a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive *Histoplasma* antigen test result from urine, blood or CSF?	Yes...1 **(K1)**	No.... 2 **(K1)**

Section H: TYPHLITIS		
Identify the criteria that apply to the infection by answering yes or no to each question		
H1. Is there evidence compatible with disease by imaging techniques? (document on G014)	Yes…...1	No……2
H2. Does the subject have clinical signs and symptoms compatible with disease?	Yes…1 **(K1)**	No…2 (K**1**)

Section I: INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
I1. Does the subject have a pure or predominant culture from normally sterile site **or** BAL (bronchoalveolar lavage) **or** a blood culture of an organism that is a plausible cause of the infection (for example, isolation of Streptococcus pneumoniae from blood in a subject with pneumonia)? I1a. Specify organism identified: _____	Yes..1 **(I1a)**	No.....2
I2. Is there evidence compatible with disease by imaging techniques? (document on G014)	Yes…...1	No……2
I3. Does the subject have clinical signs and symptoms compatible with localized bacterial infection (e.g. sinusitis, pneumonia, intra-abdominal abscess, perirectal cellulitis/ecthyma/abscess, lesions with crepitation or blebs, multiple skin lesions with bacteremia)?	Yes…1 **(K1)**	No…2 **(K1)**

Section J: BACTEREMIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
J1. Does the subject have a positive isolate from bacterial blood cultures indicative of serious infection (e.g. gram negative Bacteremia or S. aureus Bacteremia) [coagulase-negative staphylococcal bacteremias are excluded])? J1a. Specify organism identified: _____	Yes..1**(J1a)**	No ... 2
J2. Does the subject have ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention)?	Yes….1	No….2
J3. Has subject had persistent fever for 48 hours and more than one positive culture from the same organism, in spite of appropriate antimicrobial therapy? The second positive culture must be from a sample obtained at least 20 hours after the sample for the initial culture was drawn. The most recent culture results available at the time eligibility is determined must be positive.	Yes....1	No….2
J4. Have the subject's signs and symptoms been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours?	Yes….1	No….2

Section K: ELIGIBILITY STATUS and LABS

K1. Date eligibility status determined: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

K2. Time eligibility status determined: ___ ___ : ___ ___ *(24 hour clock)* **(N1 if not eligible)**

K3. Most recent ANC count **prior to eligibility determination** (B1): __ . __ __ __ x 10^9cells/L

K4a. Date sample collected: __ __/__ __/__ __ __ __ K4b. Time sample collected: __ __ : __ __

Section L: STRATIFICATION

L1. Risk Status: Stem cell transplantation or relapsed Leukemia 1
Other 2

Section M: RANDOMIZATION

M1. Does the subject have a more recent ANC result available (after ANC value reported in K3 but prior to randomization)? Yes .....1 No.....2 **(N1)**

M2. Most recent ANC count **prior to randomization**: __ . __ __ __ x 10^9cells/L

M3a. Date sample collected: __ __/__ __/__ __ __ __ M3b. Time sample collected: __ __ : __ __

Section N: SIGNATURE

N1. Approved by: Initials ____ ____ ____ N2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Form G006 – Eligibility, Study Qualifying Infection Documentation and Randomization Form

Version A: 03/23/2011

Purpose of this form: The purpose of this form is to capture eligibility, document the subject's study-qualifying infection and randomization.

When to complete this form: This form must be completed and data entered at baseline (Day 1).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: When answering the questions on this form, select "No" if a particular test was not done to prove the subject's study qualifying infection.

SECTION B: INCLUSION CRITERIA

B1. Indicate if the subject has an ANC count less than 500/mm^3 (0.5 x 10^9 cells/L) due to marrow failure caused by underlying disease or therapy.

B2. Indicate if the subject has a proven, probable or presumptive invasive fungal infection, probable endemic mycosis, typhlitis, proven or presumptive invasive bacterial infection of the chest and/or sinuses, proven or presumptive invasive bacterial infection other location or bacteremia as defined in Appendix A of the RING Protocol.

SECTION C: EXCLUSION CRITERIA

C1. Indicate if the subject is unlikely to survive for the next 5 days.

C2. Indicate if there is evidence that the subject will not be neutropenic for at least 5 days.

C3. Indicate if the subject was previously enrolled in the RING Study.

SECTION D: INFECTION INFORMATION

D1. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section D
- Probable invasive fungal infection, complete Sections E, F, G
  D1a. Indicate if above infection is mold
- Presumptive invasive fungal infection, complete Section E & G
- Probable endemic mycosis, complete Section E & Question G6
- Typhlitis, complete Section H
- Proven invasive bacterial tissue infection of chest and/or sinuses, complete Section I
- Proven invasive bacterial tissue infection, other location, complete Section I
- Presumptive invasive bacterial tissue infection of chest and/or sinuses, complete Section I
- Presumptive invasive bacterial tissue infection other location, complete Section I
- Bacteremia, complete Section J

D2. Indicate the site of the subject's study-qualifying infection. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

D3. Indicate if the subject's study-qualifying infection is a mold infection. If it is not, skip to question D4.

D3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

D3b-d. Answer yes or no to each question D3b, D3c, and D3d to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question D3b-d must be answered yes.

After completing question D3d, skip to question K1.

D4. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question D5.

D4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

D4b-e. Answer yes or no to each question D4b, D4c, D4d, and D4e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question D4b-e must be answered yes.

After completing question D4e, skip to question K1.

D5. Indicate if the subject's study-qualifying infection is endemic fungal infection. If it is not, skip to question K1 – the subject is not eligible for the RING Study.

D5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

D5b-e. Answer yes or no to each question D5b, D5c, D5d, and D5e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question D5b-e must be answered yes.

After completing question D5e, skip to question K1.

To qualify for the RING study based on probable invasive fungal infections, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion. To qualify based on *presumptive invasive fungal infection,* subjects must have at least one host factor and one clinical criterion. To qualify based on *probable endemic mycoses infection,* subjects must have at least one host factor criterion and a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive *Histoplasma* antigen test result from urine, blood or CSF.

SECTION E: HOST FACTORS.

E1a. Indicate if the subject has had a recent history of relapsed or refractory acute leukemia or MDS and a recent history of neutropenia (neutropenia in this case is defined as ANC < $500/mm^3$ (0.5×10^9 cells/L) for >10 days) temporarily related to the onset of fungal disease (presumptive invasive fungal infection). If yes, skip to E2. If no, answer E1b.

E1b. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease (probable invasive fungal infection). Neutropenia in this case is defined as an ANC < $500/mm^3$ (0.5×10^9 cells/L) for >10 days.

E2. Indicate if the subject has received an allogeneic stem cell transplant.

E3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks.

E4. Indicate if the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues) during the past 90 days.

E5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION F: MICROBIOLOGICAL CRITERIA

F1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

F2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples. If yes answer F2a.

F2a. Specify organism identified.

F3. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF.

F4. Indicate if the subject had Beta-D-glucan detected in serum.

SECTION G: CLINICAL CRITERIA

G1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to question G2.

G1a. Indicate if the subject has any of the following "specific" imaging signs on CT: dense, well defined nodule(s) with or without a halo sign, air crescent sign or cavity.

G2. Indicate whether or not the subject has tracheobronchitis. If not, skip to question G4.

G2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

G3. Indicate if the subject has signs/symptoms of a sinonasal infection? If not, skip to question G4.

G3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer with black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

G4. Indicate if the subject has signs/symptoms of a CNS infection. If not, skip to question G5.

G4a. Indicate if the subject has focal lesions on imaging.

G4b. Indicate if there is meningeal enhancement on MRI or CT. If the subject has not had an MRI or CT answer No (2).

G5. Indicate if the subject has signs/symptoms of Disseminated candidiasis. If not, skip to question K1.

G5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen.

G5b. Indicate if the subject has progressive retinal "cotton wool" exudates on ophthalmologic examination.

G6. Indicate if the subject has a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive histoplasm antigen test result from urine, blood or CSF.

After completing Question G6, Skip to Question K1.

SECTION H: TYPHLITIS

H1. Indicate if the subject has evidence compatible with disease by imaging techniques. If yes, document on form G014.

H2. Indicate if subject has clinical signs and symptoms compatible with disease.

To qualify for the RING study based on typhlitis subjects must answer yes to both H1 and H2.

After completing Question H2, Skip to Question K1.

SECTION I: INVASIVE BACTERIAL TISSUE INFECTION

I1. Indicate if subject has a pure or predominant culture from normally sterile site or BAL or blood culture of an organism that is a plausible cause of the infection (for example, isolation of Streptococcus pneumonia from blood in subject with pneumonia). If yes, answer question I1a.

I1a. Specify organism identified.

I2. Indicate if the subject has evidence compatible with disease by imaging techniques. If so, document on Form G014

I3. Does the subject have clinical signs and symptoms compatible with localized bacterial infection (e.g., sinusitis, pneumonia, intra-abdominal abscess, perirectal cellulitis/ecthyma/abscess, lesions with crepitation or blebs, multiple skin lesions with bacteremia)?

To qualify for the RING study based on a *proven invasive bacterial tissue infection of chest and/or sinuses*, subjects must be able to answer yes to questions I1, I2 and I3. To qualify based on *proven invasive bacterial tissue other* subjects must be able answer yes to questions I1 and I3. To qualify based on *presumptive invasive bacterial tissue of chest and/or sinuses,* subjects must be able to answer yes to questions I2 and I3 and to qualify based on *presumptive invasive bacterial tissue other* subject must be able to answer yes to question I3.

After completing Question I3, Skip to Question K1.

SECTION J: BACTEREMIA

J1. Indicate if the subject has a positive isolate from bacterial blood culture indicative of serious infection (e.g. gram negative bacteremia or S. aureus bacteremia) [coagulase-negative staphylococcal bacteremias are excluded]. If yes, answer question J1a and document on G012.

J1a. Specify organism identified.

J2. Indicate if the subject has ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention).

J3. Indicate if the subject has had a persistent fever for 48 hours and more than one positive culture from the same organism in spite of appropriate antimicrobial therapy.

- The second positive culture must be from a sample obtained at least 20 hours after results of initial culture were known; the last culture with known results prior to eligibility determination must be positive.

J4. Indicate if the subject's signs and symptoms have been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours.

SECTION K. ELIGIBILITY STATUS and LABS

K1. Record the date the subject's eligibility status was determined in mm/dd/yyyy

K2. Record the time the subject's eligibility status was determined using to a 24-hour clock.

K3. Record the most recent ANC prior to determining eligibility. Record the lab result used to determine if the subject's ANC count is less than 500/mm^3 (0.5 x 10^9 cells/L; inclusion criterion C2).

K4a-b. Record the date and time the specimen was collected.

Once determined to be eligible for the study, subjects must be consented (if not previously consented) and randomized within 7 days. The 7-day period will start with the first time the patient meets the eligibility criteria as per the report time of the relevant test results. For presumptive invasive tissue bacterial or fungal infections, the 7-day period will start when the clinical team determines that the subject meets all eligibility criteria. RING study staff must document the date and time this decision is made in the subject's study files or medical records.

SECTION G: STRATIFICATION

L1. Circle the number that corresponds to the subject's risk status. Category "1" includes subjects who have relapsed leukemia, subjects who have had a stem cell transplant, and subjects who are neutropenic due to preparation for a stem cell transplant. Category "2" is all others.

SECTION M. RANDOMIZATION

M1. Does the subject have a more recent ANC result available (after ANC value reported in K3) prior to randomization? If answered no, skip to N1.

M2. If the subject has a more recent ANC count result after ANC value reported in K3 and prior to randomization, record that result. Subjects must be consented and randomized within 3 days of eligibility determination. At randomization, the subject's ANC count must be <500/ mm^3 otherwise the subject may not be randomized.

M3a-b. Record the date and time the specimen was collected.

SECTION N: SIGNATURE

N1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

N2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G007 – Baseline Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline..... GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: INFECTION INFORMATION

B1. Site of infection:
- Bloodstream 1
- Pulmonary 2
- Facial/sinus 3
- Localized skin or soft tissue 4
- CNS..... 5
- Disseminated (more than one site) .... 6➔Specify sites:_____
- Other ..... 99➔Specify: _____

B2. Type of infection:
- Proven invasive fungal infection 1
- Probable invasive fungal infection .....2 **(Go to Section C)**
- Bacteremia .....3 **(Go to Section F)**
- Invasive bacterial tissue infection .....4 **(Go to Section G)**

For ***proven invasive fungal infections***, is the causative agent:

B3. Mold Yes..... 1 No..... 2 (B4)

B3a. Identify the specific agent:
- Aspergillus 1
- Zygomycetes 2
- Fusarium..... 3
- Scedosporium..... 4
- Mold not otherwise specified.... 5
- Other ..... 99 ➔➔ B3a1: Specify Other: _____

__ - __ __ __ - __ __ __ __ - __ __

Indicate whether the following EORTC/MSG criteria apply:

B3b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen showing hyphal or melanized yeast-like forms with evidence of associated tissue damage (either microscopically or as an infiltrate or lesion by imaging)	Yes 1	No..... 2
B3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine.	Yes 1	No..... 2
B3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes ..... 1 **(H1)**	No..... 2 **(H1)**

B4. Yeast Yes .....1 No 2 (B5)

B4a. Identify the specific agent:

Candida 1

Non-Candida ..... 99 ➔➔ B4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

B4b. Histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site (mucous membranes excluded) showing yeast cells e.g. Cryptococcus species indicated by encapsulated budding yeasts, Candida species showing pseudohyphae or true hyphae	Yes 1	No..... 2
B4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly (<24h) placed drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes 1	No..... 2
B4d. Blood culture that yields yeast (e.g. Cryptococcus species, Candida species), or yeast-like fungi (e.g. Trichosporon spp.)	Yes 1	No..... 2
B4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes ..... 1 **(H1)**	No..... 2 **(H1)**

B5. Dimorphic Fungal Infection Yes ..... 1 No 2 (H1)

B5a. Identify the specific agent:

histoplasmosis 1

coccidioidomycosis 2

Other ..... 99 ➔➔ B5a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms (if culture is sterile or not obtained)	Yes 1	No..... 2
B5c. Proven by recovery in culture from a specimen obtained from the affected site, and the host must at the same time have an illness consistent with a fungal infectious disease	Yes 1	No..... 2

__ - __ __ __ - __ __ __ __ - __ __

B5d. Blood culture that yields an agent of endemic mycosis	Yes 1	No..... 2
B5e. Histoplasmosis: diagnosis of disseminated disease can be established by means of a positive Histoplasma antigen EIA test on CSF, urine or serum, or by showing the presence of characteristic intracellular yeast forms in a peripheral blood smear or in bone marrow. OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise in the coccidioidal antibody titer measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process.	Yes ..... 1 **(H1)**	No..... 2 **(H1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion

Section C: HOST FACTORS		
Identify the criteria that apply to the infection by answering yes or no to each question		
C1. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease?	Yes..... 1	No 2
C2. Has the subject received an allogeneic stem cell transplant?	Yes..... 1	No 2
C3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes..... 1	No 2
C4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, nucleoside analogues) during the past 90 days?	Yes..... 1	No 2
C5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes..... 1	No 2

Section D: MICROBIOLOGICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
D1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes..... 1	No 2
D2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples?	Yes..... 1	No 2
D3. Did the subject have a biopsy of skin ulcers or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion?	Yes..... 1	No 2
D4. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours?	Yes..... 1	No 2
D5. Does the subject have Beta-D-glucan detected in serum?	Yes..... 1	No 2

__ - __ __ __ - __ __ __ __ - __ __

Section E: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
E1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes..... 1	No ....2 **(E2)**
E1a. Are any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity?	Yes..... 1	No 2
E1b. Is a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis?	Yes..... 1	No 2
E2. Does the subject have ***tracheobronchitis***?	Yes..... 1	No ....2 **(E3)**
E2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes..... 1	No 2
E3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes..... 1	No ....2 **(E4)**
E3a. Is there imaging showing sinusitis **AND** one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer, black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes..... 1	No 2
E4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes..... 1	No ....2 **(E5)**
E4a. Are there focal lesions on imaging?	Yes..... 1	No 2
E4b. Is there meningeal enhancement on MRI or CT?	Yes..... 1	No 2
E5. Does the subject have signs/symptoms of ***Disseminated candidiasis?***	Yes..... 1	No ....2 **(H1)**
E5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen and has the patient had candidemia within the previous 2 weeks?	Yes..... 1	No 2
E5b. Does the subject have progressive "cotton wool" exudates on ophthalmologic examination?	Yes... 1**(H1)**	No ....2 **(H1)**

Section F: BACTEREMIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
F1. Does the subject have a positive isolate from bacterial blood cultures indicative of serious infection (e.g., gram negative bacteremia, S. aureus bacteremia)?	Yes... 1	No .. 2 **(H1)**
F2. Does the subject have bacteremia with hemodynamic instability?	Yes... 1	No .. 2 **(F4)**
F3. Has the subject been unresponsive to appropriate clinical and antimicrobial management for > 24 hours?	Yes... 1(**H1)**	No .. 2 **(H1)**
F4. Does the subject have bacteremia that has persisted for 72 hours in spite of appropriate antimicrobial therapy?	Yes... 1(**H1)**	No .. 2 **(H1)**

__ - __ __ __ - __ __ __ __ - __ __

Section G: INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
G1. Does the subject have clinical signs and symptoms compatible with disease (e.g., sinusitis, pneumonia, intra-abdominal abscess)?	Yes..... 1	No 2
G2. Is there radiographic evidence of disease?	Yes..... 1	No 2
G3. Does the subject have a pure or predominant culture from sterile site biopsy or bronchoalveolar lavage (BAL)?	Yes..... 1	No 2
G4. Does the subject have a positive blood culture with an organism that is a plausible cause of infection (e.g. isolation of Streptococcus pneumoniae from blood in a subject with pneumonia)?	Yes..... 1	No 2
G5. Does the subject have typhlitis (neutropenic enterocolitis) with signs and symptoms compatible with disease and typical radiographic evidence of disease (with or without culture confirmation)?	Yes..... 1	No 2

Section H: SIGNATURE

H1. Approved by: Initials ____ ____ ____ H2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G007 – Baseline Study Qualifying Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline ..... GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: INFECTION INFORMATION

B1. Site of infection:
- Bloodstream 1
- Pulmonary 2
- Facial/sinus 3
- Localized skin or soft tissue 4
- CNS 5
- Disseminated (more than one site) .... 6➔Specify sites: _____
- Other ..... 99➔Specify: _____

B2. Type of infection:
- Proven invasive fungal infection..... 1
- Probable invasive fungal infection ..... 2 **(Go to Section C)**
- Bacteremia ..... 3 **(Go to Section F)**
- Invasive bacterial tissue infection..... 4 **(Go to Section F)**

For ***proven invasive fungal infections***, is the causative agent:

B3. Mold **Yes ..... 1** **No ..... 2 (B4)**

B3a. Identify the specific agent:
- Aspergillus 1
- Zygomycetes..... 2
- Fusarium 3
- Scedosporium 4
- Mold not otherwise specified..... 5
- Other ..... 99 ➔➔ B3a1: Specify Other: _____

__ __ - __ __ __ __ - __ __ __ - __

Indicate whether the following EORTC/MSG criteria apply:

B3b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen showing hyphal or melanized yeast-like forms with evidence of associated tissue damage (either microscopically or as an infiltrate or lesion by imaging)	Yes..... 1	No..... 2
B3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine.	Yes..... 1	No..... 2
B3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes..... 1 **(G1)**	No..... 2 **(G1)**

B4. Yeast Yes .....1 No 2 (B5)

B4a. Identify the specific agent:

Candida..... 1

Non-Candida ..... 99 ➔➔ B4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

B4b. Histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site (mucous membranes excluded) showing yeast cells e.g. Cryptococcus species indicated by encapsulated budding yeasts, Candida species showing pseudohyphae or true hyphae	Yes..... 1	No..... 2
B4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly (<24h) placed drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes..... 1	No..... 2
B4d. Blood culture that yields yeast (e.g. Cryptococcus species, Candida species), or yeast-like fungi (e.g. Trichosporon spp.)	Yes..... 1	No..... 2
B4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes..... 1 **(G1)**	No..... 2 **(G1)**

B5. Dimorphic Fungal Infection Yes ..... 1 No 2 (G1)

B5a. Identify the specific agent:

histoplasmosis 1

coccidioidomycosis 2

Other ..... 99 ➔➔ B5a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms (if culture is sterile or not obtained)	Yes..... 1	No..... 2
B5c. Proven by recovery in culture from a specimen obtained from the affected site, and the host must at the same time have an illness consistent with a fungal infectious disease	Yes..... 1	No..... 2

B5d. Blood culture that yields an agent of endemic mycosis	Yes..... 1	No..... 2
B5e. Histoplasmosis: diagnosis of disseminated disease can be established by means of a positive Histoplasma antigen EIA test on CSF, urine or serum, or by showing the presence of characteristic intracellular yeast forms in a peripheral blood smear or in bone marrow. OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise in the coccidioidal antibody titer measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process.	Yes..... 1 **(G1)**	No..... 2 **(G1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion

Section C: HOST FACTORS		
Identify the criteria that apply to the infection by answering yes or no to each question		
C1. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease?	Yes..... 1	No 2
C2. Has the subject received an allogeneic stem cell transplant?	Yes..... 1	No 2
C3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes..... 1	No 2
C4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, nucleoside analogues) during the past 90 days?	Yes..... 1	No 2
C5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes..... 1	No 2

Section D: MICROBIOLOGICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
D1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes..... 1	No 2
D2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples?	Yes..... 1	No 2
D3. Did the subject have a biopsy of skin ulcers or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion?	Yes..... 1	No 2
D4. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours?	Yes..... 1	No 2
D5. Does the subject have Beta-D-glucan detected in serum?	Yes..... 1	No 2

__ __ - __ __ __ __ - __ __ __ - __

Section E: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
E1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes..... 1	No .... 2 **(E2)**
E1a. Are any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity?	Yes..... 1	No 2
E1b. Is a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis?	Yes..... 1	No 2
E2. Does the subject have ***tracheobronchitis***?	Yes..... 1	No .... 2 **(E3)**
E2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes..... 1	No 2
E3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes..... 1	No .... 2 **(E4)**
E3a. Is there imaging showing sinusitis **AND** one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer, black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes..... 1	No 2
E4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes..... 1	No .... 2 **(E5)**
E4a. Are there focal lesions on imaging?	Yes..... 1	No 2
E4b. Is there meningeal enhancement on MRI or CT?	Yes..... 1	No 2
E5. Does the subject have signs/symptoms of ***Disseminated candidiasis?***	Yes..... 1	No .... 2 **(G1)**
E5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen and has the patient had candidemia within the previous 2 weeks?	Yes..... 1	No 2
E5b. Does the subject have progressive "cotton wool" exudates on ophthalmologic examination?	Yes... 1**(G1)**	No .... 2 **(G1)**

Section F: BACTEREMIA AND INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
F1. Does the subject have typhlitis (neutropenic enterocolitis)?	Yes…...1	No .. ….2
F2. Does the subject have a pure or predominant culture from normally sterile site or BAL (bronchoalveolar lavage)?	Yes…...1	No .. ….2
F3. Does the subject have a positive isolate from blood cultures associated with type of infection (invasive tissue infection) or indicative of serious infection (bacteremia)?	Yes…...1	No……2
F4. Is study qualifying infection an infection of the chest or sinuses?	Yes…...1	No……2
F5. Is there radiographic evidence of disease? (document on G014)	Yes…...1	No……2

F6. Does the subject have ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention)?	Yes…...1	No……2
F7. Has subject had persistent fever for 48 hours and more then one positive culture from the same organism in spite of appropriate antimicrobial therapy?	Yes..…1	No .. …2
F8. Does the subject have clinical signs and symptoms compatible with disease?	Yes..…1	No .. …2
F9. Have the subject's signs and symptoms been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours?	Yes..…1	No……2

Section G: SIGNATURE

G1. Approved by: Initials ____ ____ ____ G2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G007 – Baseline Infection Documentation

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document the subject's study-qualifying infection.

When to complete this form: This form must be completed and data entered at baseline (Day 1), prior to randomization.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: INFECTION INFORMATION

B1. Indicate the site of the subject's infection. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

B2. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section B
- Probable invasive fungal infection, complete Sections C, D and E
- Bacteremia, complete Section F
- Invasive bacterial tissue infection, complete Section G

B3. Indicate if the subject's study-qualifying infection is a mold infection. If it is not, skip to question B4.

B3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

SECTION B: INFECTION INFORMATION, cont.

B3b-d. Answer yes or no to each question B3b, B3c, and B3d to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B3b-d must be answered yes.

After completing question B3d, skip to question H1.

B4. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question B5.

B4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

B4b-e. Answer yes or no to each question B4b, B4c, B4d, and B4e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B4b-e must be answered yes.

After completing question B4e, skip to question H1.

B5. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question H1 – the subject is not eligible for the RING Study.

B5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

B5b-e. Answer yes or no to each question B5b, B5c, B5d, and B5e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B5b-e must be answered yes.

After completing question B5e, skip to question H1.

To qualify for the RING Study based on a "probable invasive fungal infection" subjects must have at least one host factor (i.e. at least one question in Section C must be answered "yes"), one microbiologic criterion (i.e. at least one question in Section D must be answered "yes"), and one clinical criterion (i.e. at least one question in Section E must be answered "yes").

SECTION C: HOST FACTORS

C1. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease. Neutropenia in this case is defined as an ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days.

C2. Indicate if the subject has received an allogeneic stem cell transplant.

C3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks. Subjects with allergic bronchopulmonary aspergillosis are excluded from this criterion.

C4. Indicate if, in the past 90 days, the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues).

C5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION D: MICROBIOLOGICAL FACTORS

D1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

D2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples.

D3. Indicate if the subject had a biopsy of skin ulcers, or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion.

D4. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours.

D5. Indicate if the subject had Beta-D-glucan detected in serum?

SECTION E: CLINICAL FACTORS

E1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to question E2.

E1a. Indicate if the subject has any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity.

E1b. Indicate if the subject has a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis.

E2. Indicate whether or no the subject has tracheobronchitis. If not, skip to question E3.

E2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

E3. Indicate if the subject has signs/symptoms of a sinonasal infection? If not, skip to question E4.

E3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer, black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

E4. Indicate if the subject has signs/symptoms of a CNS infection? if not, skip to question E5.

E4a. Indicate if the subject has focal lesions on imaging?

E4b. Indicate if there is meningeal enhancement on MRI or CT? If the subject has not had an MRI or CT answer No (2).

E5. Indicate if the subject has signs/symptoms of Disseminated candidiasis? If not, skip to question H1. The subject is not eligible for the RING Study.

E5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen **AND** has had candidemia within the previous 2 weeks?

E5b. Indicate if the subject has progressive "cotton wool" exudates on ophthalmologic examination.

After completing Question E5b, Skip to Section H.

SECTION F: BACTEREMIA

F1. Indicate if the subject has a positive isolate from bacterial blood cultures indicative of serious infection (for example, gram negative bacteremia, S. aureus bacteremia). If not, the subject is not eligible for the RING Study.

F2. Indicate if subject has bacteremia with hemodynamic instability. If not, skip to question F4.

F3. Indicate if the subject has been unresponsive to appropriate clinical and antimicrobial management for > 24 hours. If not, the subject is not eligible for the RING Study.

F4. Indicate if the subject has bacteremia that has persisted for 72 hours in spite of appropriate antimicrobial therapy? If not, the subject is not eligible for the RING Study.

SECTION G: INVASIVE BACTERIAL TISSUE INFECTION

G1. Indicate if the subject has clinical signs and symptoms compatible with disease (e.g., sinusitis, pneumonia, intra-abdominal abscess). If not, skip to question H1, the subject is not eligible for the RING Study.

G2. Indicate if there is radiographic evidence of disease. If not, skip to question H1, the subject is not eligible for the RING Study.

G3. Indicate if the subject have a pure or predominant culture from sterile site biopsy or bronchoalveolar lavage (BAL).

G4. Indicate if the subject has a positive blood culture with an organism that is a plausible cause of infection (e.g. isolation of Streptococcus pneumoniae from blood in a subject with pneumonia).

G5. Indicate if the subject has typhlitis (neutropenic enterocolitis) with signs and symptoms compatible with disease and typical radiographic evidence of disease (with or without culture confirmation)?

Note: to qualify for the RING Study, a subject must have either typlitis (“Yes” to question G5) or clinical signs/symptoms compatible disease and radiographic evidence (“Yes” to questions G1 and G2) **AND** a positive biopsy site or BAL culture or a positive blood culture (“Yes to either G3 or G4).

SECTION H: SIGNATURE

H1. Enter the initials of the person approving the form.

H2. Record the date the form was approved using mm/dd/yyyy. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

Form G007 – Baseline Study Qualifying Infection Documentation

Version B: 12/30/2009

Purpose of this form: The purpose of this form is to document the subject's study-qualifying infection.

When to complete this form: This form must be completed and data entered at baseline (Day 1), prior to randomization.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: When answering the questions on this form, select "No" if a particular test was not done to prove the subject's study qualifying infection.

SECTION B: INFECTION INFORMATION

B1. Indicate the site of the subject's study-qualifying infection. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

B2. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section B
- Probable invasive fungal infection, complete Sections C, D and E
- Bacteremia, complete Section F
- Invasive bacterial tissue infection, complete Section F

B3. Indicate if the subject's study-qualifying infection is a mold infection. If it is not, skip to question B4.

B3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

SECTION B: INFECTION INFORMATION, cont.

B3b-d. Answer yes or no to each question B3b, B3c, and B3d to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B3b-d must be answered yes.

After completing question B3d, skip to question G1.

B4. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question B5.

B4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

B4b-e. Answer yes or no to each question B4b, B4c, B4d, and B4e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B4b-e must be answered yes.

After completing question B4e, skip to question G1.

B5. Indicate if the subject's study-qualifying infection is a dimorphic fungal infection. If it is not, skip to question H1 – the subject is not eligible for the RING Study.

B5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

B5b-e. Answer yes or no to each question B5b, B5c, B5d, and B5e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B5b-e must be answered yes.

After completing question B5e, skip to question G1.

To qualify for the RING Study based on a "probable invasive fungal infection" subjects must have at least one host factor (i.e. at least one question in Section C must be answered "yes"), one microbiologic criterion (i.e. at least one question in Section D must be answered "yes"), and one clinical criterion (i.e. at least one question in Section E must be answered "yes").

SECTION C: HOST FACTORS

C1. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease. Neutropenia in this case is defined as an ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days.

C2. Indicate if the subject has received an allogeneic stem cell transplant.

C3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks. Subjects with allergic bronchopulmonary aspergillosis are excluded from this criterion.

C4. Indicate if, in the past 90 days, the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues).

C5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION D: MICROBIOLOGICAL FACTORS

D1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

D2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples.

D3. Indicate if the subject had a biopsy of skin ulcers, or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion.

D4. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours.

D5. Indicate if the subject had Beta-D-glucan detected in serum.

SECTION E: CLINICAL FACTORS

E1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to question E2.

E1a. Indicate if the subject has any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity.

E1b. Indicate if the subject has a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis.

E2. Indicate whether or not the subject has tracheobronchitis. If not, skip to question E3.

E2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

E3. Indicate if the subject has signs/symptoms of a sinonasal infection? If not, skip to question E4.

E3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer, black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

E4. Indicate if the subject has signs/symptoms of a CNS infection. If not, skip to question E5.

E4a. Indicate if the subject has focal lesions on imaging.

E4b. Indicate if there is meningeal enhancement on MRI or CT. If the subject has not had an MRI or CT answer No (2).

E5. Indicate if the subject has signs/symptoms of Disseminated candidiasis. If not, skip to question H1.

E5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen **AND** has had candidemia within the previous 2 weeks.

E5b. Indicate if the subject has progressive "cotton wool" exudates on ophthalmologic examination.

After completing Question E5b, Skip to Section G.

SECTION F: BACTEREMIA and INVASIVE BACTERIAL TISSUE INFECTION

F1. Indicate if the subject has typhlitis.

F2. Indicate if subject has a pure or predominant culture from normally sterile site or BAL. If so, document on G012.

F3. Indicate if the subject has a positive isolate from blood culture associated with type of infection (invasive tissue infection) or indicative or serious infection (bacteremia). If so, document on G012.

- For invasive tissue infections, the organism should be associated with the type of infection.
- For bacteremia, the organism must be indicative of serious infection.

F4. Indicate if the qualifying infection is an infection of the chest or sinuses.

F5. Indicate if the subject has radiographic evidence of disease. If so, document on Form G014.

F6. Indicate if the subject has ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention).

F7. Indicate if the subject has had a persistent fever for 48 hours and more than one positive culture from the same organism in spite of appropriate antimicrobial therapy.

- The second positive culture must be from a sample obtained at least 20 hours after results of initial culture were known; the last culture with known results prior to eligibility determination must be positive.

F8. Indicate if the subject has signs and symptoms compatible with disease.

F9. Indicate if the subject's signs and symptoms have been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours.

SECTION G: SIGNATURE

G1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

G2. Record the date the form was approved using mm/dd/yyyy.

		No evidence of an invasive bacterial tissue infection	Positive culture from normally sterile site or from BAL	Positive isolate from blood culture[1,2]	Clinical signs and symptoms compatible with disease[3]	Radiographic evidence of disease	Subject has ongoing hemodyna instability in opinion of attending physician[4]	Signs/symptoms unresponsive to appropriate clinical and antimicrobial management for more than 24 hours	Fever has persisted for at least 48 hours, and at least 2 positive cultures in spite of appropriate antimicrobia l therapy[5]
Invasive tissue infection	Typhlitis (neutropenic enterocolitis)				X	X			
	Invasive tissue infection (infection of chest or sinuses)		X		X	X			
				X	X	X			
	Invasive tissue infection (other than types listed above)		X		X				
				X	X				
Bactere mia		X		X			X		
		X		X	X			X	
		X		X					X

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G008 – Baseline Concomitant Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline..... GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __

A4. Initials of person filling out form: ___ ___ ___

Section B: CONCOMITANT INFECTION INFORMATION

B1. Does the subject have a concomitant baseline infection?	Yes 1	No..... 2 **(C1)**
B2. Cytomegalovirus (CMV)	Yes 1	No..... 2 **(B3)**
B2a. CMV Antigenemia/DNAemia (asymptomatic)	Yes 1	No..... 2
B2b. CMV Disease (specify site)	Yes 1	No..... 2 **(B3)**
B2b1. CMV Pneumonia	Yes 1	No..... 2
B2b2. CMV Colitis	Yes 1	No..... 2
B2b3. CMV Retinitis	Yes 1	No..... 2
B2b4. CMV Encephalitis	Yes 1	No..... 2
B2b5. CMV Hepatitis	Yes 1	No..... 2
B2b6. CMV Systemic / syndrome	Yes 1	No..... 2
B2b7. Other (specify)	Yes 1	No..... 2 **(B3)**
B2b7a. Specify other CMV disease: _____		
B3. Herpes Simplex Virus (HSV) disease	Yes 1	No..... 2
B4. Human Herpesvirus 6 (HHV-6) disease	Yes 1	No..... 2
B5. Varicella Zoster Virus (VZV) disease	Yes 1	No..... 2
B6. Epstein-Barr Virus (EBV) disease	Yes 1	No..... 2
B7. Polyoma (BK) Virus disease	Yes 1	No..... 2
B8. *M. tuberculosis* disease	Yes 1	No..... 2
B9. Mycobacterium other than *M. tuberculosis* (specify)	Yes 1	No..... 2 **(B10)**
B9a. Specify other mycobacterium:_____		
B10. Toxoplasmosis	Yes 1	No..... 2
B11. Nocardiosis	Yes 1	No..... 2
B12. Actinomycosis	Yes 1	No..... 2
B13. Parovirus B19	Yes 1	No..... 2
B14. Hepatitis B	Yes 1	No..... 2
B15. Hepatitis C	Yes 1	No..... 2
B16. Other symptomatic infection (specify)	Yes 1	No..... 2 **(C1)**
B16a. Specify other concomitant infection: _____		

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G008 – Baseline Concomitant Infection Documentation

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document a subject's concomitant infections (i.e. infections other than the study-qualifying infection) at baseline.

When to complete this form: This form must be completed for all subjects at baseline (Day 1).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: If there is no documentation that a subject has a listed infection, answer the question "No". If the subject is either diagnosed with a listed infection, or is being treated for a listed infection, select "Yes".

SECTION B: INFECTION INFORMATION

B1. Indicate whether or not the subject has a concomitant baseline infection. If not, skip to the end of the form.

B2. Indicate if the subject has cytomegalovirus (CMV) at baseline. If not, skip to question B3.

B2a. Indicate if the subject has asymptomatic CMV Antigenemia/DNAemia.

B2b. Indicate if the subject has CMV disease. If not, go to question B3. Otherwise, answer all questions B2b1 – B2b7 to specify the CMV disease.

B3 – B15. Indicate if the subject has any of the infections listed at baseline by answering each question. If the subject has Mycobacterium other than M. tuberculosis (question B9), specify the other mycobacterium in the space provided.

B16. If the subject has a symptomatic infection, other than the infections listed on the form, answer "Yes" and specify the infection in the space provided.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G009 – Granulocyte Administration Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -__ __ __ __ - __ __ __ - __

A2. Event: Granulocyte Transfusion ..... (GTRN)

A3. Date form filled out: ___ ___ / ___ ___ / ___ ___ ___ ___ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: ADMINISTRATION INFORMATION

B1. Unit ID number _____

B2. Was product volume reduced? Yes..... 1 No 2

B3. Was product aliquoted? Yes..... 1 No .....2 **(If B2 and B3 are answered "No", go to B7)**

B4. Volume of unit at issue: ___ ___ ___ mL

B5. Absolute neutrophil count at issue: ___ . ___ ___ ___ x 10^9 cells/L **(B7)** ☐ Not reported$_{-1}$ **(B6a)**

B6a. WBC at issue: ___ ___ ___.___ x 10^9/L B6b. % neutrophils at issue: ___ ___ ___%

B7. Transfusion status ____ ____ **(if = 2, 3 or 4 go to B8)**

B7a. If status = 1 or 99, specify reason: _____ **(if transfusion status = 1, go to H1)**

B8. Enter volume of unit **not** transfused: ___ ___ ___ B8a. Units: mL .....1 grams..... 2

B9a. Start date: __ __/__ __ /__ __ __ __ B9b. Start time: ___ ___ : ___ ___

B10a. Finish date: __ __/__ __ /__ __ __ __ B10b. Finish time: ___ ___ : ___ ___

B11. Was there a transfusion related event of grade ≥ 1? *If yes, please complete a Form G019 for this transfusion.* Yes..... 1 No 2

Transfusion Final Status Codes (Question B7)

1 = unit not given to subject (specify)
2 = transfusion of unit completed
3 = transfusion of unit discontinued due to transfusion reaction
4 = transfusion of unit discontinued due to failure to flow
99 = transfusion of unit discontinued due to other reason (specify)

__ __-__ __ __ __-__ __ __-__

Section C: LABORATORY

	a. Test done?	b. Date sample collected *(mm/dd/yyyy)*	c. Time sample collected *(24-hour clock)*	d. Value (x 10^9 cells/L)
C1. ANC within 4 hours prior to start of transfusion	Yes ..... 1 No..... 2 (**C2**)	__ __ / __ __ / __ __ __ __	___ ___ : ___ ___	__ . __ __ __
C2. ANC 30 minutes to 2 hours post transfusion	Yes ..... 1 No 2 (**D1**)	__ __ / __ __ / __ __ __ __	___ ___ : ___ ___	__ . __ __ __

Section D: MEDICATION

List all medications given specifically in preparation for pending transfusion:

D1. Medication	D2. Dose	D3. Dose Units	D4. Route	D5. Date administered	D6. Time administered
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __

Section E: VITAL SIGNS AND OXYGEN SATURATION

	a. Temp	b. Temp Unit	c. Temp Method	d. Respiration *(breaths/min)*	e. Pulse *(beats/min)*	f. Blood Pressure *(systolic/diastolic)*	g. O_2 Saturation	h. Date	i. Time
E1. 15 minutes prior to the start of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __
E2. 15 minutes after the start of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __
E3. 0:45 to 1:15 hours after the end of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __

Section H: SIGNATURE

H1. Approved by: Initials ____ ____ ____ H2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Purpose of this form: The purpose of this form is to document the administration of granulocytes during one transfusion episode.

When to complete this form: This form is completed for each granulocyte transfusion episode. A transfusion episode is defined as: all granulocyte products ordered by a subject's physician at one time (i.e. one order). ***Note***: this form must be completed for each granulocyte transfusion from a study donor that a subject receives while participating in the RING Study, even if the subject is not assigned to the granulocyte arm or if the granulocytes are not study (stimulated) granulocytes.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: ADMINISTRATION INFORMATION

B1. Record the Unit ID number. ***NOTE*: THIS NUMBER MUST MATCH THE NUMBER USED ON THE CORRESPONDING GD03**. During data entry, the form will have a status of pending edits if this number does not match a unit on the corresponding GD03.

B2. Indicate if the product was volume reduced.

B3. Indicate if the product was aliquoted. If the product was not volume reduced and not aliquoted, go to question B7. Otherwise, provide the volume and count of the product at issue in the following questions.

B4. Record the volume of the unit at issue.

B5. Enter the ANC count of the unit at issue using the units: $x10^9$/L, if available, and skip to question B7. If the ANC count was not reported, complete questions B6a and B6b.

B6a-b. Enter the WBC and the % neutrophils of the unit at issue.

B7. Record the transfusion status code.

Transfusion Final Status Codes	
1 = unit not given to subject (specify)	**4** = transfusion of unit discontinued due to failure to flow
2 = transfusion of unit completed	**99** = transfusion of unit discontinued due to other reason (specify)
3 = transfusion of unit discontinued due to transfusion reaction	

B7a. If the transfusion status code = "1 (unit not given to subject)" or "99 (transfusion discontinued due to other reason)," specify the reason why the unit was not given to the subject (e.g. the subject expired prior to the administration) or why the unit was discontinued.

B8. Record the volume that was **NOT** transfused and indicate if the unit of measurement is milliliters or grams. If the transfusion status = 1 (unit not given), skip to question H1.

B9a-b. Record the start date (mm/dd/yyyy) and time (24 hour clock) of the transfusion.

B10a-b. Record the finish date (mm/dd/yyyy) and time (24 hour clock) of the transfusion.

B11. Indicate if there was a transfusion-related event. ***Note***: the RING Study collects information on all transfusion-related events, regardless of grade. If a subject experiences any transfusion-related event during, or within 6 hours following the transfusion, form G019 and form G085 (if appropriate) must be completed and reported to the DCC.

SECTION C: LABORATORY

C1. This sample must be drawn within four hours prior to the start of a transfusion of granulocytes. If a subject has more than one sample drawn in the four hours preceding a granulocyte transfusion, record the sample drawn closest to the start time of the transfusion. Indicate if the test was done, and record the date and time a sample was collected and the ANC value (in units of 10^9 cells/L). An override reason must be entered if this test was not done.

C2. This sample must be drawn within 30 minutes to two hours after the end of a transfusion of granulocytes. If a subject has more than one sample drawn in the two hours after the end of a granulocyte transfusion, record the sample drawn closest to the end time of the transfusion. Indicate if the test was done, and record the date and time a sample was collected and the ANC value (in units of 10^9 cells/L). An override reason must be entered if this test was not done.

SECTION D: MEDICATION

In questions D1 through D6, record all medications given to a subject specifically in preparation for the granulocyte transfusion. Complete one row for each medication that was given. If more than one dose of a medication was given to a subject, record each dose on a separate line. If additional space is needed, attach additional copies of the form.

D1. Record the medication name. Note: this field will utilize a drop down feature for the following meds: acetaminophen, diphenhydramine, and hydrocortisone.

D2. Record the medication dose.

D3. Record the dose units (for example: mg, mL, units).

D4. Record the route of administration (for example, IM, po). Note: this field will utilize a drop down feature for the routes IV, IM, PO.

D5. Record the date the medication was given to the subject as mm/dd/yyyy.

D6. Record the time the medication was given to the subject using a 24-hour clock.

SECTION E: VITAL SIGNS AND OXYGEN SATURATION

E1 – E2. Record the measurements done closest to 15 minutes prior to the start (E1) or after the start (E2) of the transfusion.

E3. Record the measurements done closest to 1 hour after the end of the transfusion.

For each of the specified time periods, record each of the following measurements:

a-c. Record the subject's temperature, the unit of measurement (Celsius of Fahrenheit), and the method of measurement (see below). Note: this field will utilize a drop down feature for the method of measurement.

d. Record the respiration rate in breaths per minute

e. Record the pulse rate in beats per minute

f. Record the both systolic and diastolic blood pressures

g. Record O_2 saturation level

h. Record the date the measurements were taken as mm/dd/yyyy

i. Record the time the measurements were taken using a 24-hour clock

Temperature Method			
01 = oral	03 = tympanic	05 = esophageal probe	99 = other
02 = axillary	04 = rectal	-8 = unknown	

SECTION H: SIGNATURE

H1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

H2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G010 – Antimicrobial Therapy/G-CSF Log TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Measurement ......GMMT (circled)

***Record start and end times only for Amphotericin B, otherwise leave blank.**

B1. Medication Name	**B2. Dose**	**B3. Dose Units**	**B4. Route**	**B5. Freq**	**B6. Start date** *(mm/dd/yyyy)*	**B7. Start time*** *(24-hour clock)*	**B8. End date** *(mm/dd/yyyy)*	**B9. End time*** *(24-hour clock)*
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __
____________	______	_____	_____	______	__ __/__ __/__ __ __ __	__ __ : __ __	__ __/__ __/__ __ __ __	__ __ : __ __

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G010 – Antimicrobial Therapy/G-CSF Log

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document all antibiotic and antimicrobial therapies used to prevent and treat infections while a subject is in the hospital. These may include treatments the subject is on at the time of randomization in to the RING Study. This form will also capture any G-CSF given to a subject while they are in the RING Study. Therapies given after a subject has been discharged from the hospital will not be recorded.

When to complete this form: This worksheet must be completed when a subject's participation in the RING Study has ended. This CRF must be completed/data entered into ADEPT when a subject's participation in the RING Study has ended. You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, it is recommended that you wait until the subject is off study before data-entering this form. If you need more space to record therapy information, attach additional copies of this worksheet.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

SECTION B: ADMINISTRATION INFORMATION

B1. Record the name of the therapy given to a subject to treat an infection. ***Note***: granulocyte transfusions may not be recorded on this form. This field will utilize a drop down feature for the name of the medication

B2-3. Record the dose that was given to the subject, with the unit of measurement (for example: mg, mL, units). Note: this field will utilize a drop down feature for the unit of measurement.

B4. Record the route of administration (for example, IM, po). Note: this field will utilize a drop down feature.

B5. Record the frequency of the administration (for example: qd, qod, bid, tid). Note: this field will utilize a drop down feature.

B6-7. Record the date (in mm/dd/yyyy) and, if applicable*, time (using a 24-hour clock) the medication was started.

B8-9. Record the date (in mm/dd/yyyy) and, if applicable*, time (using a 24-hour clock) the medication was stopped.

***Note:** Each administration of Amphotericin B must be recorded on a separate line and include start and stop times. All other therapies only need start and stop dates recorded.

Example CRF completion:

Record start and end times only for Amphotericin B, otherwise leave blank.

B1. Medication Name	B2. Dose	B3. Dose Units	B4. Route	B5. Freq	B6. Start date *(mm/dd/yyyy)*	B7. Start time* *(24-hour clock)*	B8. End date *(mm/dd/yyyy)*	B9. End time* *(24-hour clock)*
Voriconazole	200	mg	IV	bid	05/02/2008	____	05/18/2008	____
Amphotericin B	0.6	mg/kg	IV	qd	05/04/2008	08:00	05/04/2008	10:25

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G011 – Vascular Access Form – Bloodstream Infections Only TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -__ __ __ __ - __ __ __ - __

A2. Event: Measurement.....(GMMT)

Section B: VASCULAR ACCESS

B0. Did the subject have a vascular access change while a subject on the RING Study? Yes.....1 No..... 2 **(C1)**

B1. Date of vascular access action:	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __
B2. Type of access:	☐1 Central line ☐2 Arterial line ☐3 Pulmonary artery catheter ☐4 PICC line ☐99 Other (specify)	☐1 Central line ☐2 Arterial line ☐3 Pulmonary artery catheter ☐4 PICC line ☐99 Other (specify)	☐1 Central line ☐2 Arterial line ☐3 Pulmonary artery catheter ☐4 PICC line ☐99 Other (specify)
B2a.Specify other:	_____	_____	_____
B3. Type of change:	☐1 New placement ☐2 Removal ☐3 Replacement	☐1 New placement ☐2 Removal ☐3 Replacement	☐1 New placement ☐2 Removal ☐3 Replacement
B3a. If replaced:	☐1 Same access type, same site ☐2 Same access type, new site ☐3 Different access type, new site	☐1 Same access type, same site ☐2 Same access type, new site ☐3 Different access type, new site	☐1 Same access type, same site ☐2 Same access type, new site ☐3 Different access type, new site
B4. Suspicion of infection at time of vascular access action?	☐1 Yes ☐2 No	☐1 Yes ☐2 No	☐1 Yes ☐2 No

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Purpose of this form: The purpose of this form is to document every vascular access a subject with a bloodstream infection has removed or placed during his or her participation in the RING Study.

When to complete this form: This worksheet is a running log of every vascular access a subject who has a bloodstream infection has removed or placed. This CRF must be completed/data entered into ADEPT when a subject's participation in the RING Study has ended. You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, it is recommended that you wait until the subject is off study before data-entering this form. If you need more space to record vascular access information, attach additional copies of this worksheet.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

SECTION B: VASCULAR ACCESS

B0. Indicate if the subject had a vascular access change while on the RING Study. If not, skip to question C1.

B1. Record the date the vascular access was removed, changed, or initially placed in mm/dd/yyyy.

B2. Record the type of access. If the type of access is not listed, select "Other (99)" and record the type of access in B2a.

B3. Record the type of change. If this is a replacement, indicate if the new type of access is the same type as the one that is being replaced and whether or not a new location on the subject's body will be used.

B4. Indicate if there is suspicion of infection at the time of the vascular access change.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Code	Name
001	Acinetobacter
002	Adenovirus
003	Agtrobacterium
004	Alcaligenes
005	Ambiasis
006	Anaerobic bacteria (except for Bacteroides and Clostridium)
007	Aspergillus flavus
008	Aspergillus fumigatus
009	Aspergillus niger
010	Aspergillus terreus
011	Aspergillus, not otherwise specified
012	Bacillus
013	Bacteria, Other
014	Bacteroides
015	Borrelia (Lyme disease)
016	Branhamella catarrhalis (also Moraxella catarrhalis, other genera for this species)
017	Burkholderia cepacia (also Pseudomonas cepacia)
018	Campyobacter
019	Candida albicans
020	Candida krusel
021	Candida lusitaniae
022	Candida or Torulopsis glabrata
023	Candida parapsilosis
024	Candida tropicalis
025	Candida, not otherwise specified
026	Capnocytophaga
027	Chlamydia
028	Citrobacter
029	Clostridium difficile
030	Corynebactedrium (all non-dephtheria species)
031	Coxiella
032	Cryptococcus (all species)
033	Cryptosporidium
034	Cytomegalovirus (CMV)
035	Echinococcalcyst
036	Enterobacter
037	Enterococcus (report vancomycin sensitivity)

Code	Name
038	Enterovirus (coxsackle, echo, polio)
039	Epstein Barr Virus (EBV)
040	Escherichia
041	Filamentous fungus, not otherwise specified (hyphae, hyphal fragment)
042	Flavimonas
043	Flavobacterium
044	Fungus, other
045	Fusarium (all species)
046	Fusobacterium
047	Giardia
048	Gram Negative diplococci
049	Gram negative Rod (bacillus, cocco bacillary, lactose fermenting, other species)
050	Gram positive bacillus
051	Gram positive cocci
052	Helicobacter pylori
053	Hemophilius (all species, including influenzae)
054	Hepatitis A (HAV)
055	Hepatitis B (HBS, Australian antigen)
056	Hepatitis C (includes non- A and non-B, HCV)
057	Herpes simplex (HSV1, HSV2)
058	Herpes Zoster (chicken pox, varicella)
059	HHV-6 (Human Herpes Virus)
060	HIV-1, HITLV-III
061	Influenza (flu)
062	Klebsiella
063	Lactobacillus
064	Legionella
065	Leptospira
066	Leptotrichia
067	Leuconostoc
068	Listeria
069	Measles (Rubella)
070	Methylobacterium
071	Micrococcus
072	Mucormycosis (zygomycotes, rhizopus)
073	Mumps
074	Mycobacteria (all species except tuberculosis)
075	Mycobacterium tuberculosis (TB, tuberculosis)
076	Mycobacterium, other
077	Mycoplasma
078	Neisseria (gonorrhea, meningitides, other species
079	Nocardia
080	Papovavirus
081	Parainfluenza

Code	Name
082	Pharyngeal/respiratory flora
083	Pneumocystis (PCP)
084	Polyomavirus
085	Propionlbacterium (acnes, avidum, granulosum, other species)
086	Protozoal, other (parasite)
087	Pseudomenas or stenotrophomonas or xanthomonas maltophilia
088	Pseudomonas (all species, except copacia and maltophilia)
089	Pseudomonas or burkholderia copacia
090	Respiratory syncytial virus (RSV)
091	Rhinovirus (common cold)
092	Rhodococcus
093	Rickettsia
094	Rotavirus
095	Rubella (German measles)
096	Salmonella (all species)
097	Serratia
098	Serratis marcescens
099	Shigelia
100	Staphylococcus (coag +)
101	Staphylococcus (coag-)
102	Staphylococcus (NOS)
103	Staphylococcus aureaus (coagulase positive) report sensitivity data)
104	Staphylococcus epidermidis (coagulase negative)
105	Stenotrophomonas maltophilia (also xanthmonas maltophilia, pseudomonas maltophila)
106	Stomatococcus mucilaginosis
107	Streptococcus (all species except enterococcus)
108	Streptococcus group D (enterococcus) (report sensitivity data)
109	Streptococcus pneumoniae (report sensitivity data)
110	Torulopsis galbrata (a busbspecies of candida)
111	Toxoplasma
112	Treponeum (syphilis)
113	Trichomonas (either vaginal or gingivitis)
114	Tuberculosis , (NOS) (SFB, acid fast bacillus, Koch Bacillus)
115	Typical Tuberculosis (TB)
116	Vibrio (any species)
117	Viral, Other
118	Yeast, (NOS) (pseudohyphae)
119	Zygomycetes (mucormycosis, rhizopus)
999	**Organism, other**

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G012 – Diagnostic Test Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Measurement..... GMMT

Section B: DIAGNOSTIC TESTS

	Test 1	Test 2	Test 3
B1. Collection date *(mm/dd/yyyy)*	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __
B2. Collection time *24-hour clock*	__ __ : __ __	__ __ : __ __	__ __ : __ __
B3. Source	__ __	__ __	__ __
B3a. If tissue or other, specify:	_____	_____	_____
B4. Diagnostic test	__ __	__ __	__ __
B4a. If other test, specify:	_____	_____	_____
B5. Result, if negative (C1)	__ __	__ __	__ __
B5a. If positive, specify result or etiology	_____	_____	_____
B6. If PCR result *(copies/mL)*	__ __ __ ☐Not Done-1	__ __ __ ☐Not Done-1	__ __ __ ☐Not Done-1
B7. Organism	__ __ __	__ __ __	__ __ __
B7a. If other (99), specify organism	_____	_____	_____

B3: Source code

Blood	01
Urine	02
Stool	03
Saliva	04
Sputum	05
CSF	06
Bronchoalveolar lavage	07
Tissue (specify)	08
Catheter Tip	09
Other (specify)	99
Unknown	-8

B4: Diagnostic Test

Bacteria Culture	01
Viral Culture	02
Fungal culture	03
Antigen	04
AFB Smear	05
Gram Stain	06
Other (specify)	99

B5: Result codes

Positive (specify)	01
Negative	02
Unknown	-8
Other	99

B7: See Organism Code List

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G012 – Diagnostic Test Form

Version A: 11/13/2008

Purpose of this form: The purpose of this form is to document all samples collected for diagnostic testing purposes, and to record the results of those tests.

When to complete this form: This worksheet is a running log of all diagnostic tests done while a subject is participating in the RING study. This CRF must be completed/data entered into ADEPT when a subject's participation in the RING Study has ended. You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, it is recommended that you wait until the subject is off study before data-entering this form. If you need more space for additional testing, attach additional copies of this worksheet.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

SECTION B: DIAGNOSTIC TESTS

For codes, refer to the table at the bottom of the page.

B1. Record the date the sample was collected in mm/dd/yyyy.

B2. Record the collection time using a 24-hour clock. If the time is not known, enter -8 ("don't know).

B3. Record the source code indicating the type of sample tested. If the source was tissue (08) or other (99), specify the source in the space provided in question B3a.

B4. Record the diagnostic test code indicating the suspected pathogen and type of sample. If the test was "other" (99), specify the test in the space provided in question B4a.

B5. Record the result code of the test. If the result is negative, skip to question C1.

B5a. If the test was positive (01), specify the result or etiology.

B6. If the test done was by PCR, indicate the result in copies per milliliter. If the test was not done by PCR, check 'Not Done'.

B7. Specify the organism using the Organism Code List (separate document). If the organism is not on the Code List, enter code (99) and specify the infection in the space provided in B7a.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form.

C2. Record the date the form was approved using mm/dd/yyyy. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G014 – Imaging Studies Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Measurement..... (GMMT)

SECTION B: RADIOLOGY STUDIES

B1. Test date:	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __	__ __ / __ __ / __ __ __ __
B2. Type of test: *Select ONE*	☐1 X-ray ☐2 CT Scan ☐3 MRI ☐4 Ultrasound ☐99 Other (specify)	☐1 X-ray ☐2 CT Scan ☐3 MRI ☐4 Ultrasound ☐99 Other (specify)	☐1 X-ray ☐2 CT Scan ☐3 MRI ☐4 Ultrasound ☐99 Other (specify)
B2a. Specify other test:	_____	_____	_____
B3. Site(s): *Check all that apply*	☐ Chest ☐ Liver ☐ Abdomen ☐ Head ☐ Pelvis ☐ Other (specify)	☐ Chest ☐ Liver ☐ Abdomen ☐ Head ☐ Pelvis ☐ Other (specify)	☐ Chest ☐ Liver ☐ Abdomen ☐ Head ☐ Pelvis ☐ Other (specify)
B3a. Specify other site:	_____	_____	_____
B4. Result	☐1 Normal **(B6)** ☐2 Abnormal	☐1 Normal **(B6)** ☐2 Abnormal	☐1 Normal **(B6)** ☐2 Abnormal
B5. Was there evidence of infection?	☐1 Yes ☐2 No	☐1 Yes ☐2 No	☐1 Yes ☐2 No
B6. Copy of report sent to DCC?	☐1 Yes ☐2 No	☐1 Yes ☐2 No	☐1 Yes ☐2 No

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G014 – Imaging Studies Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document all imaging studies done while a subject is a participant in the RING study.

When to complete this form: This worksheet is a running log of every imaging study a subject has done while participating in the RING study. This CRF must be completed/data entered into ADEPT when a subject's participation in the RING Study has ended. You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, it is recommended that you wait until the subject is off study before data-entering this form. If you need more space to record vascular access information, attach additional copies of this worksheet.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

SECTION B: RADIOLOGY STUDIES

B1. Record the date the test was done in mm/dd/yyyy format.

B2. Indicate the type of test that was done by selecting one item in the list provided. If the test is not listed, select "Other (99)" and record the type of test in B2a.

B3. Indicate the body site(s) that was(were) scanned by checking all that apply. If a test site is not listed, select "Other (99)" and record the site in B3a.

B4. Indicate the result of the test. If the results were "normal" skip to question B6.

B5. Indicate if there was evidence of infection.

B6. Indicate whether or not the test report was sent to the DCC. Note: all reports must be anonymized, labeled only with the subject ID number, and sent to the DCC.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G015 – Daily Measurement Log TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ - __ __ __ __ - __ __ __ - __

A2. Event: Measurement.......................GMMT (circled)

A3. Date randomized: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

A4. Date of discharge/end of study date: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

Section B: DAILY MEASUREMENT LOG

B1. **Date on Study**	**B2.** **T Max**	**B2a.** **T max unit**	**B2b.** **T max route code**	**B3.** **Gran transfusion on B1?**	**B3a.** **If no gran trans, reason**	**B4.** **Morning ANC count (cells x 10^9/mL) for B1**	**B4a.** **Date morning ANC drawn**	**B4b.** **Time morning ANC drawn**
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C...... 1 °F 2	__ __	Yes....... 1 No 2	__ __	__.__ __ __ Not Done -1 ☐	__ __/__ __/__ __ __ __	__ __:__ __

__ - __ __ __ - __ __ __ __ - __ __

Section B: DAILY MEASUREMENT LOG

B1. Date on Study	B2. T Max	B2a. T max unit	B2b. T max route code	B3. Gran transfusion on B1?	B3a. If no gran trans, reason	B4. Morning ANC count (cells x 10^9/mL) for B1	B4a. Date morning ANC drawn	B4b. Time morning ANC drawn
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
__ __/__ __/__ __ __ __	__ __ __ . __	°C ...... 1 °F 2	___ ___	Yes....... 1 No 2	___ ___	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G015 – Daily Measurement Log

TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ - __ __ __ __ - __ __ __ __ - __

A2. Event: Measurement .... GMMT

A3. Date randomized: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

A4. Date of discharge/end of study date: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

Section B: DAILY MEASUREMENT LOG

B1. Date on Study	**B2.** T Max	**B2a.** T max unit	**B2b.** T max route code	**B3.** Gran transfusion on B1?	**B3a.** If no gran trans, reason	**B4.** Morning ANC count (cells x 10^9/L) for B1	**B4a.** Date morning ANC drawn	**B4b.** Time morning ANC drawn
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			

__ - __ __ __ - __ __ __ __ - __ __

Section B: DAILY MEASUREMENT LOG

B1. Date on Study	B2. T Max	B2a. T max unit	B2b. T max route code	B3. Gran transfusion on B1?	B3a. If no gran trans, reason	B4. Morning ANC count (cells x 10^9/L) for B1	B4a. Date morning ANC drawn	B4b. Time morning ANC drawn
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______			

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G015 – Daily Measurement Log

TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ - __ __ __ __ - __ __ __ __ - __

A2. Event: Measurement .... (GMMT)

A3. Date randomized: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

A4. Date of discharge/end of study date: __ __ /__ __/__ __ __ __ *(mm/dd/yyyy)*

Section B: DAILY MEASUREMENT LOG

B1. Date on Study	**B2.** T Max	**B2a.** T max unit	**B2b.** T max route code	**B3.** Gran transfusion on B1?	**B3a.** If no gran trans, reason	**B4.** Morning ANC count (cells x 10^9/L) for B1	**B4a.** Date morning ANC drawn	**B4b.** Time morning ANC drawn
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	__ __	Yes .... 1 No......... 2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			

__ - __ __ __ - __ __ __ __ - __ __

Section B: DAILY MEASUREMENT LOG

B1. Date on Study	B2. T Max	B2a. T max unit	B2b. T max route code	B3. Gran transfusion on B1?	B3a. If no gran trans, reason	B4. Morning ANC count (cells x 10^9/L) for B1	B4a. Date morning ANC drawn	B4b. Time morning ANC drawn
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			
__ __/__ __/__ __ __ __	__ __ __ . __	°C ......1 °F.......2	___ ___	Yes ....1 No.........2	__ __ ↓	__.__ __ __ Not Done-1 ☐	__ __/__ __/__ __ __ __	__ __:__ __
					B3b. If B3a = 99, Specify ______________________			

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G015 – Daily Measurement Log

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document vital signs, transfusion status, and ANC counts for each day a subject participates in the RING Study while hospitalized.

When to complete this form: You may choose to update this form while a subject is on study, or wait until the subject finishes; however, the form is not data entered until the subject is off study. If you need more space to record daily measurements, attach additional copies of this form. The maximum daily temperature and granulocyte transfusion status must be recorded every day while the subject is in the RING study and hospitalized. The daily morning ANC count is required until 3 days after engraftment.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the subject was randomized by the data management system.

A4. Enter the date the subject is discharged, or is off of the study due to withdrawal or death.

SECTION B: DAILY MEASUREMENT LOG

B1. Record the date on study. The first date must be the date the subject was randomized.

B2-B2a. Record the subject's highest temperature reading for the date listed in question B1, and select the correct units (Fahrenheit or Celsius).

B2b. Record the method used to take the temperature (see below).

Temperature Method			
1 = oral	3 = tympanic	5 = esophageal probe	99 = other
2 = axillary	4 = rectal	-8 = unknown	

B3-B3a. Record whether or not the subject had a granulocyte transfusion on the calendar date listed in B1. If a transfusion was ordered, but not started until after midnight on the day on study (and no other granulocyte transfusion was given to the subject), circle "No (2)." If a granulocyte transfusion was given to a subject in the control arm, or if any subject receives a transfusion that is not stimulated, circle "Yes (1)." If a granulocyte transfusion was given, go to question B4; otherwise, indicate the reason in question B3a using the following codes:

Reason why granulocyte transfusion was not given		
1 = Subject randomized to control arm	5 = Collection failure	-8 = Unknown
2 = Patient engrafted	6 = Infection cleared	99 = Other
3 = Granulocytes not available	7 = Subject withdrew	
4 = No donor available	8 = Subject expired	

Morning Count Note: it is possible for a sample to be drawn on the day prior to which it will be used as a morning count. For example, a count may be drawn the evening prior to the day it is used as a "morning" count. To avoid potential confusion, we ask that you record both the day the count was drawn (B5) **AND** the day to which the count should be "applied" (B1)

B4. Record the ANC value used as the "Morning ANC Count" for the calendar date listed in B1 of the same row.

B4a. Record the date the sample for the ANC count used in B4 was drawn in mm/dd/yyyy format. (This may or may not be the same calendar day as B1.)

B4b. Record the time the sample for the ANC count used in B4 was drawn using to a 24-hour clock.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

RING Study

Form G015 – Daily Measurement Log

Version B: 02/11/2009

Purpose of this form: The purpose of this form is to document daily vital signs, transfusion status, and ANC counts for RING Study participants.

When to complete this form: You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, the CRF is not data entered until the subject is off study. If you need more space to record daily measurements, attach additional copies of this worksheet. The maximum daily temperature and granulocyte transfusion status must be recorded every day while the subject is in the RING study until the subject is discharged, reaches Day 42, or is off the study due to withdrawal or death. The daily morning ANC count is required until 3 days after engraftment.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the subject was randomized in the data management system.

A4. Enter the date the subject is discharged, reaches Day 42, or is off of the study due to withdrawal or death. Record the event that comes first.

SECTION B: DAILY MEASUREMENT LOG

B1. Record the date on study. The first date must be the date the subject was randomized.

B2-B2a. Record the subject's highest temperature reading for the date listed in question B1, and select the correct units (Fahrenheit or Celsius).

B2b. Record the method used to take the temperature (see below).

Temperature Method			
1 = oral	3 = tympanic	5 = esophageal probe	99 = other
2 = axillary	4 = rectal	-8 = unknown	

B3-B3b. Record whether or not the subject had a granulocyte transfusion on the calendar date listed in B1. If a transfusion was ordered, but not started until after midnight on the day on study (and no other granulocyte transfusion was given to the subject), circle "No (2)." If a granulocyte transfusion was given to a subject in the control arm, or if any subject receives a transfusion that is not stimulated, circle "Yes (1)." If a granulocyte transfusion was given, go to question B4; otherwise, indicate the reason no granulocyte transfusion was given in question B3a using the following codes:

Reason why granulocyte transfusion was not given		
1 = Subject randomized to control arm	5 = Collection failure	-8 = Unknown
2 = Patient engrafted	6 = Infection cleared	99 = Other
3 = Granulocytes not available	7 = Subject withdrew	
4 = No donor available	8 = Subject expired	

If B3a = "Other (99)," specify other reason in question B3b.

Morning Count Note: it is possible for a sample to be drawn on the day prior to which it will be used as a morning count. For example, a count may be drawn the evening prior to the day it is used as a "morning" count. To avoid potential confusion, we ask that you record both the day the count was drawn (B4a) **AND** the day to which the count should be "applied" (B1)

B4. Record the ANC value used as the "Morning ANC Count" for the calendar date listed in B1 of the same row.

B4a. Record the date the sample for the ANC count used in B4 was drawn in mm/dd/yyyy format. (This may or may not be the same calendar day as B1.)

B4b. Record the time the sample for the ANC count used in B4 was drawn using a 24-hour clock.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

RING Study

Form G015 – Daily Measurement Log

Version C: 06/02/2011

Purpose of this form: The purpose of this form is to document daily vital signs, transfusion status, and ANC counts for RING Study participants.

When to complete this form: You may choose to update this worksheet while a subject is on study, or wait until the subject finishes; however, the CRF is not data entered until the subject is off study. If you need more space to record daily measurements, attach additional copies of this worksheet. The maximum daily temperature and granulocyte transfusion status must be recorded every day while the subject is in the RING study until the subject is discharged, reaches Day 42, or is off the study due to withdrawal or death. The daily morning ANC count is required until 3 days after engraftment.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the subject was randomized in the data management system.

A4. Enter the date the subject is discharged, reaches Day 42, or is off of the study due to withdrawal or death. Record the event that comes first.

SECTION B: DAILY MEASUREMENT LOG

B1. Record the date on study. The first date must be the date the subject was randomized.

B2-B2a. Record the subject's highest temperature reading for the date listed in question B1, and select the correct units (Fahrenheit or Celsius).

B2b. Record the method used to take the temperature (see below).

Temperature Method			
1 = oral	3 = tympanic	5 = esophageal probe	99 = other
2 = axillary	4 = rectal	-8 = unknown	

B3-B3b. Record whether or not the subject had a granulocyte transfusion on the calendar date listed in B1. If a transfusion was ordered, but not started until after midnight on the day on study (and no other granulocyte transfusion was given to the subject), circle "No (2)." If a granulocyte transfusion was given to a subject in the control arm, or if any subject receives a transfusion that is not stimulated, circle "Yes (1)." If a granulocyte transfusion was given, go to question B4; otherwise, indicate the reason no granulocyte transfusion was given in question B3a using the following codes:

Reason why granulocyte transfusion was not given		
1 = Subject randomized to control arm	5 = Collection failure	9 = Adverse reaction to transfusion
2 = Patient engrafted	6 = Infection cleared	-8 = Unknown
3 = Granulocytes not available	7 = Subject withdrew	99 = Other
4 = No donor available	8 = Subject expired	

If B3a = "Other (99)," specify other reason in question B3b.

Morning Count Note: it is possible for a sample to be drawn on the day prior to which it will be used as a morning count. For example, a count may be drawn the evening prior to the day it is used as a "morning" count. To avoid potential confusion, we ask that you record both the day the count was drawn (B4a) **AND** the day to which the count should be "applied" (B1)

B4. Record the ANC value used as the "Morning ANC Count" for the calendar date listed in B1 of the same row.

B4a. Record the date the sample for the ANC count used in B4 was drawn in mm/dd/yyyy format. (This may or may not be the same calendar day as B1.)

B4b. Record the time the sample for the ANC count used in B4 was drawn using a 24-hour clock.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G016 – Leukocyte Compatibility Central Laboratory Sample Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Measurement..... GMMT

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: CENTRAL LAB BLOOD DRAW AND PROCESSING

B1. Time point: Baseline (Day 1) 1
Day 14 (± 2 days) 2
Day 42 (± 2 days) 3

B2. Date blood drawn: ___ ___ / ___ ___ / ___ ___ ___ ___ *(mm/dd/yyyy)*

	a. Aliquot ID Number	b. Volume	c. Is serum hemolyzed?	d. Variation from Lab MOP?
B3.	04--__ __ __ __ __ __ __ __ - __ 1	__ . __ __ml	Yes .....1 No 2	Yes .....1 No.....2
B4.	04--__ __ __ __ __ __ __ __ - __ 2	__ . __ __ml	Yes .....1 No 2	Yes .....1 No.....2
B5.	04--__ __ __ __ __ __ __ __ - __ 3	__ . __ __ml	Yes .....1 No 2	Yes .....1 No.....2
B6.	04--__ __ __ __ __ __ __ __ - __ 4	__ . __ __ml	Yes .....1 No 2	Yes .....1 No.....2

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G016 – Leukocyte Compatibility Sample Form

Version A: 04/01/2008

Purpose of this form: The purpose of this form is to document the sample collection and processing of a blood specimen for Leukocyte Compatibility testing.

When to complete this form: This form must be completed each time a sample is drawn for Leukocyte Compatibility testing: Day 1, Day 14 and Day 42.

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: CENTRAL LAB BLOOD DRAW AND PROCESSING

B1. Circle the corresponding time point for which the blood was drawn.

B2. Record the date the blood was drawn in MM/DD/YYYY format.

For each of the 4 aliquots created after processing the sample (B3-B6), complete the following:

a. Aliquot ID number: The ID number is 12 digits long. The first 10 digits are the subject ID number (beginning with 04). The next digit corresponds to the time point for the blood draw: A = Day 1, B = Day 14, and C = Day 42. The last digit indicates the aliquot number (1 to 4) and is pre-printed on the form.

b. Indicate if the serum is hemolyzed.

c. Indicate if the Central Lab Manual of Procedures (MOP) for the processing of the samples was followed. If the MOP was not followed, complete a Form G091 – Protocol Deviation and Unusual Event Form to provide details about the sample processing.

SECTION C: SIGNATURE

The Principal Investigator or designee must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G017 – Fungal Antigen Central Laboratory Sample Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Measurement..... GMMT

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: CENTRAL LAB BLOOD DRAW AND PROCESSING

B1. Does the subject have suspect or confirmed Aspergillosis? Yes.....1 No..... 2 **(End)**

B2. Time point:
Baseline (Day 1) 1
Day 7 (± 2 days) 2
Day 14 (± 2 days) 3
Day 42 (± 2 days) 4

B3a. Date blood drawn: ___ ___ / ___ ___ / ___ ___ ___ ___ *(mm/dd/yyyy)*

B3b. Time blood drawn: ___ ___ :___ ___ *(24 hour clock)*

B4. Aliquot ID: S-__ __ __ __ __ __ __

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G017 – Fungal Antigen Sample Form

Version A: 04/01/2008

Purpose of this form: The purpose of this form is to document the sample collection and processing of a blood specimen for Fungal Antigen testing.

When to complete this form: This form must be completed each time a sample is drawn for Fungal Antigen testing: Baseline (Day 1), Day 7, Day 14 and Day 42.

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: CENTRAL LAB BLOOD DRAW AND PROCESSING

B1. Indicate if the subject has a suspected or confirmed Aspergillosis infection. If not, skip to question C1 (do not collect fungal antigen samples).

B2. Circle the corresponding time point for which the blood was drawn.

B3a. Record the date the blood was drawn in MM/DD/YYYY format.

B3b. Record the time the blood was drawn in XX:XX format.

B4. Record the Fungal Antigen aliquot ID number. The ID number is 8 digits long, beginning with the letter S. The aliquot ID number is provided on the kits from the Fungal Antigen testing central lab.

SECTION C: SIGNATURE

The Principal Investigator or designee must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G019 – Granulocyte Transfusion Related Events TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -__ __ __ __ - __ __ __ - __

A2. Event: Granulocyte Transfusion ..... (GTRN)

A3. Date form filled out: ___ ___ / ___ ___ / ___ ___ ___ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: TRANSFUSION RELATED EVENTS

B1. Date of transfusion start: __ __ / __ __ / __ __ __ __

B1a. Time of transfusion start: ___ ___ : ___ ___ *(24 hour clock)*

B2. Date of transfusion finish: __ __ / __ __ / __ __ __ __

B2a. Time of transfusion finish: ___ ___ : ___ ___ *(24 hour clock)*

B3. Unit ID number: _____

	EVENT	GRADE 0	1	2	3	4
B4.	**Allergic reaction/ Hypersensitivity**	☐0 None	☐1 transient flushing or rash	☐2 rash, flushing, urticaria, dyspnea	☐3 symptomatic bronchospasm, with or without urticaria; parenteral medication(s), indicated; allergy-related edema/ angioedema, hypotension	☐4 anaphylaxis
B5.	**Sinus bradycardia**	☐0 None	☐1 asymptomatic, intervention not indicated	☐2 non-urgent medical intervention indicated	☐3 symptomatic and incompletely controlled medically, or controlled with device (e.g. pacemaker)	☐4 life-threatening (e.g. arrhythmia associated with CHF, hypotension syncope, shock)
B6.	**Sinus tachycardia**	☐0 None	☐1 asymptomatic, intervention not indicated	☐2 non-urgent medical intervention indicated	☐3 symptomatic and incompletely controlled medically, or controlled with device (e.g. pacemaker)	☐4 life-threatening (e.g. arrhythmia associated with CHF, hypotension syncope, shock)

__ __ - __ __ __ __ - __ __ __ - __

EVENT	GRADE 0	1	2	3	4
B7. **Hypertension**	☐0 None	☐1 asymptomatic, transient (<24hrs) increase by >20mmHg (diastolic) or to >150/100* if previously WNL; intervention not indicated	☐2 recurrent or persistent (>24hrs) symptomatic increase by >20mmHg (diastolic) or to >150/100* if previously WNL; monotherapy may be indicated	☐3 requiring more than one drug or more intensive therapy than previously	☐4 Life-threatening consequences (e.g. hypertensive crisis)
**Note: For pediatric patients, use age and sex appropriate normal values > 95th percentile ULN.*					
B8. **Hypotension**	☐0 None	☐1 changes, intervention not indicated	☐2 brief (<24hrs) fluid replacement or other therapy; no physiologic consequences	☐3 sustained (≥24hrs) therapy, resolves without persisting physiologic consequences	☐4 shock (acidemia; impairment of vital organ function)
B9. **Dyspnea** (shortness of breath)	☐0 Normal	☐1 dyspnea on exertion, but can walk 1 flight of stairs without stopping	☐2 dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping	☐3 dyspnea with ADL	☐4 dyspnea at rest; intubation/ventilator indicated
B10. **Hypoxia**	☐0 Normal	—	☐2 decreased O_2 saturation with exercise (e.g. pulse oximeter<88%); intermittent supplemental oxygen	☐3 decreased O_2 saturation at rest; continuous oxygen indicated	☐4 life-threatening; intubation or ventilation indicated
B11. **Wheezing**	☐0 None	☐1 asymptomatic	☐2 symptomatic not interfering with function	☐3 symptomatic interfering with function	☐4 life-threatening
B12. **Cough**	☐0 None	☐1 symptomatic, non-narcotic medication only indicated	☐2 symptomatic and narcotic medication indicated	☐3 Operative intervention indicated	☐4 life-threatening (e.g. hemodynamic instability or ventilatory support indicated)

__ __ - __ __ __ __ - __ __ __ - __

EVENT	GRADE 0	1	2	3	4
B13. **Hemolysis**	☐0 None	☐1 laboratory evidence of hemolysis only (direct antiglobulin test [DAT, Coombs'] schistocytes)	☐2 evidence of red cell destruction and ≥ 2gm decrease in hemoglobin, no transfusion	☐3 transfusion or medical intervention (e.g. steroids) indicated	☐4 catastrophic consequences of hemolysis (e.g. renal failure, hypotension, bronchospasm)
B14. **Rigors, chills**	☐0 None	☐1 mild requiring symptomatic treatment (e.g., blanket) or non-narcotic medication	☐2 severe and/or prolonged, requiring narcotic medication	☐3 not responsive to narcotic medication	—
B15. **Fever**	☐0 None	☐1 38.0 – 39.0°C (100.4 – 102.2°F)	☐2 >39.0 – 40.0°C (>102.2 – 104.0°F)	☐3 >40.0°C (>104.0°F) for ≤24 hours	☐4 >40.0°C (>104.0°F) for >24 hours

Note: The temperature measurements listed above are oral or tympanic

B16. Did the patient experience a Grade 4 transfusion-related event (questions B4-B15)? Yes ..... 1 No 2

If Yes (1) report the Grade 4 event on a Serious Adverse Event Form (Form G085)

B17. Comment:_____

_____

Section C: SIGNATURE

C1. Approved by PI or designee: Initials: ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Purpose of this form: The purpose of this form is to document the occurrence of granulocyte transfusion related events during and within 6 hours after a transfusion is completed or discontinued while a subject is in this study. The signs and symptoms identified on this form include most of the expected and common adverse events associated with granulocyte transfusions.

When to complete this form: This form is completed when a subject experiences a transfusion related event of Grade > 1 during or within 6 hours after a granulocyte transfusion the subject receives while on the study. The form must include all new or worsening transfusion related events that occur during, or within 6 hours after the transfusion episode is completed or discontinued.
Note: All Grade 4 events must also be reported on a Serious Adverse Event Form (G085).

Relationship to other study forms: There must be one Form G019 for each transfusion episode reported on G009 Form where it is indicated that the subject experienced a transfusion related event of Grade > 1. All Grade 4 events must also be reported on a Serious Adverse Event Form (G085).

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject number legibly.

A2. The response is pre-circled on the form, there is no need to circle anything.

A3. Record the date the form was filled out.

A4. Record the initials of the person filling out the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: TRANSFUSION RELATED EVENTS

B1- B1a. Enter the date and time the transfusion was started.

B2- B2a. Enter the date and time the transfusion was finished or discontinued.

B3. Enter the unit number of the product transfused.

For each question B4-B15 check the box that corresponds to the highest event grade that the subject experienced during or within 6 hours after the transfusion was completed or discontinued. If the subject did not experience a particular event, check the box marked Grade 0 (none or normal). Check only one box per item. **Data Entry**: enter the number to the right of the checked box.

B4. Allergeric Reaction / Hypersensitivity

B5. Sinus bradycardia

B6. Sinus tachycardia

For each question B4-B15 check the box that corresponds to the highest event grade that the subject experienced during or within 6 hours after the transfusion was completed or discontinued. If the subject did not experience a particular event, check the box marked Grade 0 (none or normal). Check only one box per item. **Data Entry**: enter the number to the right of the checked box.

Note: All Grade 4 events must also be reported on a Serious Adverse Event Form (G085).

B7. Hypertension WNL= within normal limits

Pediatric values:

Grade 1: Asymptomatic, transient (<24hrs) BP increase >Upper Limit of Normal (ULN); intervention not indicated
Grade 2: Recurrent or persistent (>24hrs) BP >ULN; monotherapy may be indicated
Grade 3: Same as adult
Grade 4: Same as adult

B8. Hypotension

B9. Dyspnea (difficulty breathing): ADL = activities of daily living

B10. Hypoxia

B11. Wheezing

B12. Cough

95th Percentiles of Blood Pressure for Girls and Boys Aged 1 to 17 Years at 95th Percentile of Height

	Boys		Girls	
Age, y	**SBP**	**DBP**	**SBP**	**DBP**
1	106	59	107	60
2	110	63	109	65
3	113	67	110	68
4	115	71	111	71
5	116	74	113	73
6	117	76	114	75
7	119	78	116	76
8	120	80	118	78
9	121	81	120	79
10	123	82	122	80
11	125	83	124	81
12	127	83	126	82
13	130	84	128	84
14	132	85	130	85
15	135	86	131	86
16	138	87	132	86
17	140	89	132	86

For each question B4-B15 check the box that corresponds to the highest event grade that the subject experienced during or within 6 hours after the transfusion was completed or discontinued. If the subject did not experience a particular event, check the box marked Grade 0 (none or normal). Check only one box per item. **Data Entry**: enter the number to the right of the checked box.

Note: All Grade 4 events must also be reported on a Serious Adverse Event Form (G085).

B13. Hemolysis

B14. Rigors, chills

B15. Fever. The temperature measurements listed on the form are oral or tympanic.

B16. Indicate if a Grade 4 transfusion-related event was reported on this form. If yes, the event must be reported to the DCC immediately, and a Serious Adverse Event form (G085) must be completed and sent to the DCC within 48 hours.

B17. Space is provided for a comment or additional explanation of any transfusion-related event. If there is no comment, write **–1** (not applicable).

SECTION C: SIGNATURE

The Principal Investigator or their designee must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G025 – Hospital Discharge Worksheet TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

Section B: DISCHARGE INFORMATION

B1. Was the subject discharged from the hospital on or prior to day 42 Yes.....1 No.....2 **(End)**

B2. Date of discharge: ___ ___ / ___ ___ / ___ ___ ___ ___ *(mm/dd/yyyy)*

B3. What was the location the subject was discharged to?

Home 1
Another hospital 2
Rehabilitation facility.....3
Hospice 4
Other 5

B3a. Discharge Location: Specify other: _____

Section C: COMMENTS

C1. Comments: _____

RING Study

Form G025 QxQ – Hospital Discharge Worksheet

Version A: 01/08/2010

Purpose of this form: The purpose of this form is to document subject's discharge prior to Day 42.

When to complete this form: This form must be completed for each subject that is discharged from the hospital prior to Day 42

SECTION A: GENERAL INFORMATION

A1. Enter the subject's ID number.

SECTION B: DISCHARGE INFORMATION

B1. Indicate if the subject was discharged prior to day 42.

B2. If the subject was discharged prior to day 42, record the date of discharge.

B3. Indicate the location subject was discharged to using options provided.

B3a. If indicated other on B3, specify location.

SECTION C: COMMENTS

C1. If applicable, provide additional comments.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G026 – Vital Status/End of Study Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ - __ __ __ __ - __ __ __ - __

A2: Event: Measurement ..... GMMT

A3. Date form filled out: __ __/__ __/__ __ __ __

A4. Initials of person filling out form: ___ ___ ___

Section B: END OF STUDY REPORT

B1. Primary reason for end of study ***(circle one)***

Subject completed study through 3 month follow-up ..... 1 *(Complete Section C)*

Subject (or guardian) decision to withdraw..... 2

Physician decision to withdraw subject 3

Study terminated at site 4

Entire study terminated..... 5

Death..... 6 **(C2)**

Other ..... 99 **(B1a)**

B1a. Specify other _____

B2. End of study date __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section C: VITAL STATUS

C1. Was subject alive 3 months after randomization? Yes ..... 1 **(C3)**

No..... 2 **(C2)**

Unknown -8 **(C3)**

C2. Date of death __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C3. Date of last known contact __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C4. Comment: _____

_____

_____

_____

Section D: SIGNATURE

D1. Approved by PI or designee: Initials: ___ ___ ___ D2. Date approved: __ __ / __ __ / __ __ __ __

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G026 – Vital Status/End of Study Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ - __ __ __ __ - __ __ __ - __

A2: Event: Measurement ..... (GMMT)

A3. Date form filled out: __ __/__ __/__ __ __ __

A4. Initials of person filling out form: ___ ___ ___

Section B: END OF STUDY REPORT

B1. Primary reason for end of study ***(circle one)***

Subject completed study ..... 1 *(Complete Section C)*

- Subject alive through Day 90
- Subject died on or prior to Day 90

Subject (or guardian) decision to withdraw 2

Physician decision to withdraw subject 3

Study terminated at site 4

Entire study terminated 5

B2. End of study date/Date withdrawn __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section C: VITAL STATUS

C1. Was subject alive 3 months after randomization? Yes ..... 1 **(C3)**

No ..... 2 **(C2)**

Unknown -8 **(C3)**

C2. Date of death __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C3. Date of last known contact __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C4. Comment: _____

_____

_____

_____

Section D: SIGNATURE

D1. Approved by PI or designee: Initials: ___ ___ ___ D2. Date approved: __ __ / __ __ / __ __ __ __

RING Study

Form G026 QxQ – Vital Status/End of Study Form

Version A: 11/13/2008

Purpose of this form: The purpose of this form is to document that a subject has reached the end of the study, to identify the primary reason for the end of study, and to document the subject's vital status at Day 90.

When to complete this form: This form is completed when the subject reaches the end of study for one of the reasons listed in section B. This form is to be completed for every subject who is determined to be eligible on Form G002 – Subject Consent, Eligibility and Randomization Form.

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out in MM/DD/YYYY format.

A4. Enter the initials of the person filling out the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: END OF STUDY REPORT

B1. Indicate the primary reason the subject's participation in the study has ended by circling one number:

- **01:** Subject completed study through 3 month follow-up (complete section C)
- **02:** Subject (or guardian) decision to withdraw
- **03:** Physician decision to withdraw subject
- **04:** Study terminated at site
- **05:** Entire study terminated
- **06:** Death (skip to Question C2)
- **99:** Subject has reached the end of study for an "other" reason. Specify reason in Question B1a.

B1a. If subject has reached the end of study for an "other" reason, specify reason.

B2. Record the date of the last day the subject was in the study in MM/DD/YYYY format.

SECTION C: VITAL STATUS

C1. Was subject alive 3 months after randomization? Indicate Yes (1), No (2) or Unknown (-8). If Yes (1), skip to question C3. If No (2), go to question C2. If Unknown (-8), skip to question C3.

C2. Record the date that the subject died in MM/DD/YYYY format.

C3. Record the date of the last known contact with the subject in MM/DD/YYYY format. This can be contact with the subject, family member or physician.

C4. Include comments in this section applicable. If there are no comments, enter -1 (N/A).

SECTION D: SIGNATURE - The Principal Investigator or designee must approve the form.

D1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

D2. Record the date the form was approved in MM/DD/YYYY format.

RING Study

Form G026 QxQ – Vital Status/End of Study Form

Version B: 03/23/2011

Purpose of this form: The purpose of this form is to document that a subject has reached the end of the study, to identify the primary reason for the end of study, and to document the subject's vital status at Day 90.

When to complete this form: This form is completed when the subject reaches the end of study for one of the reasons listed in section B. This form is to be completed for every subject who is determined to be eligible and randomized on Form G006 – Eligibility, Study Qualifying Infection Documentation and Randomization form.

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject ID number legibly.
A2. The response is pre-circled on the form; there is no need to circle anything.
A3. Enter the date the form was filled out in MM/DD/YYYY format.
A4. Enter the initials of the person filling out the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: END OF STUDY REPORT

B1. Indicate the primary reason the subject's participation in the study has ended by circling one number:

01: Subject completed study through 3 month follow-up (complete section C)
02: Subject (or guardian) decision to withdraw
03: Physician decision to withdraw subject
04: Study terminated at site
05: Entire study terminated

B2. Record the date of the last day the subject was in the study in MM/DD/YYYY format.

SECTION C: VITAL STATUS

C1. Was subject alive 3 months after randomization? Indicate Yes (1), No (2) or Unknown (-8). If Yes (1), skip to question C3. If No (2), go to question C2. If Unknown (-8), skip to question C3.

C2. Record the date that the subject died in MM/DD/YYYY format.

C3. Record the date of the last known contact with the subject in MM/DD/YYYY format. This can be contact with the subject, family member or physician.

C4. Include comments in this section applicable. If there are no comments, enter -1 (N/A).

SECTION D: SIGNATURE - The Principal Investigator or designee must approve the form.

D1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

D2. Record the date the form was approved in MM/DD/YYYY format.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G027 –Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

NOTE: Complete this form for all remaining infections (other than the study qualifying infection) that were present at the time of study entry.

Section B: INFECTION INFORMATION

B1. Site of infection: Bloodstream.....1
Pulmonary 2
Facial/sinus.....3
Localized skin or soft tissue 4
CNS.....5
Disseminated (more than one site) ....6➔Specify sites:_____
Other.....99➔Specify: _____

B2. Type of infection: Proven invasive fungal infection.....1
Probable invasive fungal infection .....2 **(Go to Section C)**
Bacteremia .....3 **(Go to Section F)**
Invasive bacterial tissue infection.....4 **(Go to Section G)**

For ***proven invasive fungal infections***, is the causative agent:

B3. Mold Yes.....1 No.....2 (B4)

B3a. Identify the specific agent:
Aspergillus 1
Zygomycetes..... 2
Fusarium..... 3
Scedosporium 4
Mold not otherwise specified 5
Other ..... 99 ➔➔ B3a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B3b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen showing hyphal or melanized yeast-like forms with evidence of associated tissue damage (either microscopically or as an infiltrate or lesion by imaging)	Yes..... 1	No 2
B3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine.	Yes..... 1	No 2
B3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes..... 1 **(H1)**	No ..... 2 **(H1)**

B4. Yeast Yes .....1 No 2 (B5)

B4a. Identify the specific agent:

Candida 1

Non-Candida .....99 ➔➔ B4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

B4b. Histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site (mucous membranes excluded) showing yeast cells e.g. Cryptococcus species indicated by encapsulated budding yeasts, Candida species showing pseudohyphae or true hyphae	Yes..... 1	No 2
B4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly (<24h) placed drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes..... 1	No 2
B4d. Blood culture that yields yeast (e.g. Cryptococcus species, Candida species), or yeast-like fungi (e.g. Trichosporon spp.)	Yes..... 1	No 2
B4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes..... 1 **(H1)**	No ..... 2 **(H1)**

B5. Dimorphic Fungal Infection Yes..... 1 No 2 (H1)

B5a. Identify the specific agent:

histoplasmosis 1

coccidioidomycosis 2

Other .....99 ➔➔ B5a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms (if culture is sterile or not obtained)	Yes..... 1	No 2
B5c. Proven by recovery in culture from a specimen obtained from the affected site, and the host must at the same time have an illness consistent with a fungal infectious disease	Yes..... 1	No 2

B5d. Blood culture that yields an agent of endemic mycosis	Yes..... 1	No 2
B5e. Histoplasmosis: diagnosis of disseminated disease can be established by means of a positive Histoplasma antigen EIA test on CSF, urine or serum, or by showing the presence of characteristic intracellular yeast forms in a peripheral blood smear or in bone marrow. OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise in the coccidioidal antibody titer measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process.	Yes..... 1 **(H1)**	No ..... 2 **(H1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion

Section C: HOST FACTORS		
Identify the criteria that apply to the infection by answering yes or no to each question		
C1. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease?	Yes.....1	No.....2
C2. Has the subject received an allogeneic stem cell transplant?	Yes.....1	No.....2
C3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes.....1	No.....2
C4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, nucleoside analogues) during the past 90 days?	Yes.....1	No.....2
C5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes.....1	No.....2

Section D: MICROBIOLOGICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
D1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes.....1	No.....2
D2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples?	Yes.....1	No.....2
D3. Did the subject have a biopsy of skin ulcers or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion?	Yes.....1	No.....2
D4. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours?	Yes.....1	No.....2
D5. Does the subject have Beta-D-glucan detected in serum?	Yes.....1	No.....2

__ __ - __ __ __ __ - __ __ __ - __

Section E: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
E1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes.....1	No.....2 **(E2)**
E1a. Are any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity?	Yes.....1	No.....2
E1b. Is a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis?	Yes.....1	No.....2
E2. Does the subject have ***tracheobronchitis***?	Yes.....1	No.....2 **(E3)**
E2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes.....1	No.....2
E3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes.....1	No.....2 **(E4)**
E3a. Is there imaging showing sinusitis **AND** one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer, black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes.....1	No.....2
E4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes.....1	No.....2 **(E5)**
E4a. Are there focal lesions on imaging?	Yes.....1	No.....2
E4b. Is there meningeal enhancement on MRI or CT?	Yes.....1	No.....2
E5. Does the subject have signs/symptoms of ***Disseminated candidiasis?***	Yes.....1	No.....2 **(H1)**
E5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen and has the patient had candidemia within the previous 2 weeks?	Yes.....1	No.....2
E5b. Does the subject have progressive "cotton wool" exudates on ophthalmologic examination?	Yes...1**(H1)**	No.....2 **(H1)**

Section F: BACTEREMIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
F1. Does the subject have a positive isolate from bacterial blood cultures indicative of serious infection (e.g., gram negative bacteremia, S. aureus bacteremia)?	Yes...1	No...2 **(H1)**
F2. Does the subject have bacteremia with hemodynamic instability?	Yes...1	No...2 **(F4)**
F3. Has the subject been unresponsive to appropriate clinical and antimicrobial management for > 24 hours?	Yes...1(**H1)**	No...2 **(H1)**
F4. Does the subject have bacteremia that has persisted for 72 hours in spite of appropriate antimicrobial therapy?	Yes...1(**H1)**	No...2 **(H1)**

__ __ - __ __ __ __ - __ __ __ - __

Section G: INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
G1. Does the subject have clinical signs and symptoms compatible with disease (e.g., sinusitis, pneumonia, intra-abdominal abscess)?	Yes.....1	No.....2
G2. Is there radiographic evidence of disease?	Yes.....1	No.....2
G3. Does the subject have a pure or predominant culture from sterile site biopsy or bronchoalveolar lavage (BAL)?	Yes.....1	No.....2
G4. Does the subject have a positive blood culture with an organism that is a plausible cause of infection (e.g. isolation of Streptococcus pneumoniae from blood in a subject with pneumonia)?	Yes.....1	No.....2
G5. Does the subject have typhlitis (neutropenic enterocolitis) with signs and symptoms compatible with disease and typical radiographic evidence of disease (with or without culture confirmation)?	Yes.....1	No.....2

Section H: SIGNATURE

H1. Approved by: Initials ____ ____ ____ H2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G027 –Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline ..... (GBSL)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: INFECTION INFORMATION

B1. Site of infection:
- Bloodstream 1
- Pulmonary 2
- Facial/sinus 3
- Localized skin or soft tissue 4
- CNS 5
- Disseminated (more than one site) .... 6➔Specify sites: _____
- Other ..... 99➔Specify: _____

B2. Type of infection:
- Proven invasive fungal infection..... 1
- Probable invasive fungal infection ..... 2 **(Go to Section C)**
- Bacteremia ..... 3 **(Go to Section F)**
- Invasive bacterial tissue infection..... 4 **(Go to Section F)**

For ***proven invasive fungal infections***, is the causative agent:

B3. Mold **Yes ..... 1** **No ..... 2 (B4)**

B3a. Identify the specific agent:
- Aspergillus 1
- Zygomycetes..... 2
- Fusarium 3
- Scedosporium 4
- Mold not otherwise specified..... 5
- Other ..... 99 ➔➔ B3a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B3b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen showing hyphal or melanized yeast-like forms with evidence of associated tissue damage (either microscopically or as an infiltrate or lesion by imaging)	Yes..... 1	No..... 2
B3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine.	Yes..... 1	No..... 2
B3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes..... 1 **(G1)**	No..... 2 **(G1)**

B4. Yeast Yes .....1 No 2 (B5)

B4a. Identify the specific agent:

Candida..... 1

Non-Candida ..... 99 ➔➔ B4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

B4b. Histopathologic or cytopathologic examination of a needle aspiration or biopsy specimen from a normally sterile site (mucous membranes excluded) showing yeast cells e.g. Cryptococcus species indicated by encapsulated budding yeasts, Candida species showing pseudohyphae or true hyphae	Yes..... 1	No..... 2
B4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly (<24h) placed drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes..... 1	No..... 2
B4d. Blood culture that yields yeast (e.g. Cryptococcus species, Candida species), or yeast-like fungi (e.g. Trichosporon spp.)	Yes..... 1	No..... 2
B4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes..... 1 **(G1)**	No..... 2 **(G1)**

B5. Dimorphic Fungal Infection Yes ..... 1 No 2 (G1)

B5a. Identify the specific agent:

histoplasmosis 1

coccidioidomycosis 2

Other ..... 99 ➔➔ B5a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms (if culture is sterile or not obtained)	Yes..... 1	No..... 2
B5c. Proven by recovery in culture from a specimen obtained from the affected site, and the host must at the same time have an illness consistent with a fungal infectious disease	Yes..... 1	No..... 2

B5d. Blood culture that yields an agent of endemic mycosis	Yes..... 1	No..... 2
B5e. Histoplasmosis: diagnosis of disseminated disease can be established by means of a positive Histoplasma antigen EIA test on CSF, urine or serum, or by showing the presence of characteristic intracellular yeast forms in a peripheral blood smear or in bone marrow. OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise in the coccidioidal antibody titer measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process.	Yes..... 1 **(G1)**	No..... 2 **(G1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion

Section C: HOST FACTORS		
Identify the criteria that apply to the infection by answering yes or no to each question		
C1. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease?	Yes..... 1	No 2
C2. Has the subject received an allogeneic stem cell transplant?	Yes..... 1	No 2
C3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes..... 1	No 2
C4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, nucleoside analogues) during the past 90 days?	Yes..... 1	No 2
C5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes..... 1	No 2

Section D: MICROBIOLOGICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
D1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes..... 1	No 2
D2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples?	Yes..... 1	No 2
D3. Did the subject have a biopsy of skin ulcers or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion?	Yes..... 1	No 2
D4. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours?	Yes..... 1	No 2
D5. Does the subject have Beta-D-glucan detected in serum?	Yes..... 1	No 2

__ __ - __ __ __ __ - __ __ __ - __

Section E: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
E1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes..... 1	No .... 2 **(E2)**
E1a. Are any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity?	Yes..... 1	No 2
E1b. Is a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis?	Yes..... 1	No 2
E2. Does the subject have ***tracheobronchitis***?	Yes..... 1	No .... 2 **(E3)**
E2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes..... 1	No 2
E3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes..... 1	No .... 2 **(E4)**
E3a. Is there imaging showing sinusitis **AND** one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer, black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes..... 1	No 2
E4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes..... 1	No .... 2 **(E5)**
E4a. Are there focal lesions on imaging?	Yes..... 1	No 2
E4b. Is there meningeal enhancement on MRI or CT?	Yes..... 1	No 2
E5. Does the subject have signs/symptoms of ***Disseminated candidiasis?***	Yes..... 1	No .... 2 **(G1)**
E5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen and has the patient had candidemia within the previous 2 weeks?	Yes..... 1	No 2
E5b. Does the subject have progressive "cotton wool" exudates on ophthalmologic examination?	Yes... 1**(G1)**	No .... 2 **(G1)**

Section F: BACTEREMIA AND INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
F1. Does the subject have typhlitis (neutropenic enterocolitis)?	Yes……1	No .. ….2
F2. Does the subject have a pure or predominant culture from normally sterile site or BAL (bronchoalveolar lavage)?	Yes……1	No .. ….2
F3. Does the subject have a positive isolate from blood cultures associated with type of infection (invasive tissue infection) or indicative of serious infection (bacteremia)?	Yes……1	No……2
F4. Is study qualifying infection an infection of the chest or sinuses?	Yes……1	No……2
F5. Is there radiographic evidence of disease? (document on G014)	Yes……1	No……2

__ __ - __ __ __ __ - __ __ __ - __

F6. Does the subject have ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention)?	Yes……1	No……2
F7. Has subject had persistent fever for 48 hours and more then one positive culture from the same organism in spite of appropriate antimicrobial therapy?	Yes……1	No .. …2
F8. Does the subject have clinical signs and symptoms compatible with disease?	Yes……1	No .. …2
F9. Have the subject's signs and symptoms been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours?	Yes……1	No……2

Section G: SIGNATURE

G1. Approved by: Initials ____ ____ ____ G2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G027 –Infection Documentation Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __-- __ __ __ __ -- __ __ __ -- __

A2. Event: Baseline.....GBSL

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section D: INFECTION INFORMATION

B1. Type of infection:

Proven invasive fungal infection..... 1**(Complete Section B)**

Probable invasive fungal infection..... 2 **(Complete Sections C, D, E)**

B1a. Is this infection a mold? Yes….1 No….2

Presumptive invasive fungal infection..... 3 **(Complete Section C & E)**

Probable Endemic Mycosis..... 4 **(Complete Section C & Question E6)**

Typhlitis..... 5 **(Complete Section F)**

Proven Invasive Bacterial Tissue Infection of Chest and/or Sinuses..... 6 **(Complete Section G)**

Proven Invasive Bacterial Tissue Infection of Other Location..... 7 **(Complete Section G)**

Presumptive Invasive Bacterial Tissue Infection of Chest and Sinuses.... 8 **(Complete Section G)**

Presumptive Invasive Bacterial Tissue Infection of Other Location..... 9 **(Complete Section G)**

Bacteremia..... 10 **(Complete Section H)**

B2. Site of infection: Bloodstream.....1

Pulmonary/Chest 2

Facial.....3

Sinus.....4

Localized skin or soft tissue 5

CNS.....6

Disseminated (more than one site) ....7➔Specify sites:_____

Other.....99➔Specify: _____

For ***proven invasive fungal infections***, is the causative agent:

B3. Mold Yes.....1 No.....2 (B4)

B3a. Identify the specific agent:

Aspergillus 1
Zygomycetes..... 2
Fusarium..... 3
Scedosporium..... 4
Mold not otherwise specified.... 5
Other ..... 99 ➔➔ B3a1: Specify Other: _____

Indicate whether the following EORTC/MSG criteria apply:

B3b. Histopathologic, cytopathologic, or direct microscopic examination of a specimen obtained by a needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage	Yes..... 1	No 2
B3c. Recovery of a Mold or 'black yeast' by culture from a sample obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL, cranial sinus cavity, and urine	Yes..... 1	No 2
B3d. Blood culture that yields a Mold, e.g. *Fusarium* spp. in the context of a compatible infectious disease process	Yes..... 1 **(I1)**	No ..... 2 **(I1)**

B4. Yeast Yes .....1 No 2 (B5)

B4a. Identify the specific agent:

Candida 1
Non-Candida ..... 99 ➔➔ B4a1: Specify: _____

Indicate whether the following EORTC/MSG criteria apply:

B4b. Histopathologic, cytopathologic, or direct microscopic examination of a needle aspiration or biopsy specimen from a normally sterile site (other than mucous membranes) showing yeast cells e.g. *Cryptococcus* species indicated by encapsulated budding yeasts, *Candida* species showing pseudohyphae or true hyphae	Yes..... 1	No 2
B4c. Recovery of a yeast by culture from a sample obtained by a sterile procedure (including a freshly placed, <24 hours ago, drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process	Yes..... 1	No 2
B4d. Blood culture that yields yeast (e.g. *Cryptococcus* species, *Candida* species), or yeast-like fungi (e.g. *Trichosporon* spp.)	Yes..... 1	No 2
B4e. Disseminated cryptococcosis: cryptococcal antigen in CSF	Yes..... 1 **(I1)**	No ..... 2 **(I1)**

B5. Endemic Fungal Infection Yes..... 1 No 2 (I1)

B5a. Identify the specific agent:

Paracoccidioidomycosis..... 1
Coccidioidomycosis..... 2
Other ..... 99 ➔➔ B5a1: Specify Other: _____

__ __ - __ __ __ __ - __ __ __ - __

Indicate whether the following EORTC/MSG criteria apply in a host with an illness consistent with endemic mycosis:		
B5b. Histopathologic or direct microscopic demonstration of appropriate morphologic forms with a truly distinctive appearance characteristic of dimorphic fungi, such as *Coccidioides* species spherules, *Blastomyces dermatitidis* thick-walled broad-based budding yeasts, *Paracoccidioides brasiliensis* multiple budding yeast cells, and, in the case of histoplasmosis, the presence of characteristic intracellular yeast forms in a phagocyte in a peripheral blood smear or in tissue macrophages	Yes..... 1	No 2
B5c. Recovery in culture from a specimen obtained from the affected site	Yes..... 1	No 2
B5d. Recovery in culture from a specimen obtained from the blood	Yes..... 1	No 2
B5e. Paracoccidioidomycosis: demonstration in 2 consecutive serum samples of a precipitin band to paracoccidioidin concurrently in the setting of an ongoing infection disease process OR Coccidioidomycosis: demonstration of coccidioidal antibody in CSF, or a 2-dilution rise measured in two consecutive blood samples tested concurrently in the setting of an ongoing infectious disease process	Yes..... 1 **(I1)**	No ..... 2 **(I1)**

For *probable invasive fungal infections*, subjects must have at least one host factor, one microbiologic criterion and one clinical criterion. For *presumptive invasive fungal infection,* subjects must have at least one host factor and one clinical criterion. For *probable endemic mycoses infection,* subjects must have at least one host factor criterion and a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive *Histoplama* antigen test result from urine, blood or CSF.

Section C: HOST FACTORS

Identify the criteria that apply to the infection by answering yes or no to each question

C1. C1a. Does the subject have relapsed or refractory acute leukemia or MDS and a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease? (presumptive invasive fungal infection)	Yes ..... 1 **(C2)**	No 2
C1b. Does the subject have a recent history of neutropenia (ANC<500/mm^3 or <0.5x10^9/L for >10 days) temporally related to the onset of fungal disease? (probable invasive fungal infection)	Yes 1	No 2
C2. Has the subject received an allogeneic stem cell transplant?	Yes 1	No 2
C3. Does the subject have prolonged use of corticosteroids (excluding patients with allergic bronchopulmonary aspergillosis) at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks?	Yes 1	No 2
C4. Has the subject received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues) during the past 90 days?	Yes 1	No 2

__ __ - __ __ __ __ - __ __ __ - __

C5. Does the subject have inherited severe immunodeficiency (e.g., chronic granulomatous disease, severe combined immunodeficiency)?	Yes 1	No 2

Section D: MICROBIOLOGICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
D1. Does the subject have sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold?	Yes.....1	No 2
D2. Was there recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid, bronchial brush, or sinus aspirate samples? D2a. Specify organism identified: _____	Yes...1 **D2a)**	No 2
D3. Does the subject have a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF?	Yes.....1	No 2
D4. Does the subject have Beta-D-glucan detected in serum?	Yes.....1	No 2

Section E: CLINICAL CRITERIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
E1. Does the subject have signs/symptoms of ***lower respiratory tract fungal disease***?	Yes.....1	No.....2 **(E2)**
E1a. Is there presence of one of the following imaging signs on CT: • dense, well defined nodule(s) with or without a halo sign; • air crescent sign; • cavity	Yes.....1	No.....2
E2. Does the subject have ***tracheobronchitis***?	Yes.....1	No.....2 **(E3)**
E2a. Were any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar?	Yes.....1	No.....2
E3. Does the subject have signs/symptoms of a ***sinonasal infection***?	Yes.....1	No.....2 **(E4)**
E3a. Is there imaging showing sinusitis **AND** at least one of the following: • acute localized pain (including pain radiating to eye); • nasal ulcer with black eschar; • extension from the paranasal sinus across bony barriers, including into the orbit	Yes.....1	No.....2
E4. Does the subject have signs/symptoms of a ***CNS infection***?	Yes.....1	No.....2 **(E5)**
E4a. Are there focal lesions on imaging?	Yes.....1	No.....2
E4b. Is there meningeal enhancement on MRI or CT?	Yes.....1	No.....2
E5. Does the subject have signs/symptoms of ***Disseminated candidiasis?*** *(At least one of the following after an episode of candidemia within the previous 2 weeks):*	Yes.....1	No.....2 **(I1)**
E5a. Does the subject have small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen?	Yes.....1	No.....2
E5b. Does the subject have progressive retinal exudates on ophthalmologic examination?	Yes...1	No.....2

E6. Does the subject have a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive *Histoplasma* antigen test result from urine, blood or CSF?	Yes...1 **(I1)**	No.....2 **(I1)**

Section F: TYPHLITIS		
Identify the criteria that apply to the infection by answering yes or no to each question		
F1. Is there evidence compatible with disease by imaging techniques? (document on G014)	Yes…...1	No……2
F2. Does the subject have clinical signs and symptoms compatible with disease?	Yes...1 **(I1)**	No…2 **(I1)**

Section G: INVASIVE BACTERIAL TISSUE INFECTION		
Identify the criteria that apply to the infection by answering yes or no to each question		
G1. Does the subject have a pure or predominant culture from normally sterile site **or** BAL (bronchoalveolar lavage) **or** a blood culture of an organism that is a plausible cause of the infection (for example, isolation of Streptococcus pneumoniae from blood in a subject with pneumonia)? G1a. Specify organism identified: _____	Yes..1**(G1a)**	No... ….2
G2. Is there evidence compatible with disease by imaging techniques? (document on G014)	Yes…...1	No……2
G3. Does the subject have clinical signs and symptoms compatible with localized bacterial infection (e.g. sinusitis, pneumonia, intra-abdominal abscess, perirectal cellulitis/ecthyma/abscess, lesions with crepitation or blebs, multiple skin lesions with bacteremia)?	Yes...1 **(I1)**	No…2 **(I1)**

Section H: BACTEREMIA		
Identify the criteria that apply to the infection by answering yes or no to each question		
H1. Does the subject have a positive isolate from bacterial blood cultures indicative of serious infection (e.g. gram negative Bacteremia or S. aureus Bacteremia) [coagulase-negative staphylococcal bacteremias are excluded])? H1a. Specify organism identified: _____	Yes..1 **(H1a)**	No……2
H2. Does the subject have ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention)?	Yes….1	No….2
H3. Has subject had persistent fever for 48 hours and more than one positive culture from the same organism, in spite of appropriate antimicrobial therapy? The second positive culture must be from a sample obtained at least 20 hours after the sample for the initial culture was drawn. The most recent culture results available at the time eligibility is determined must be positive.	Yes....1	No….2
H4. Have the subject's signs and symptoms been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours?	Yes….1	No….2

Section I: SIGNATURE	
I1. Approved by: Initials ____ ____ ____	I2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G027 – Infection Documentation Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document an invasive fungal, bacteremia, or invasive bacterial infections (other than the subject's study-qualifying infection) that is present at the time of study entry. If there are multiple infections present (in addition to the study-qualifying infection), complete one Form G027 for each infection.

When to complete this form: This form must be completed at baseline (Day 1).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: When answering the questions on this form, select "No" if a particular test was not done to prove the subject's infection.

SECTION B: INFECTION INFORMATION

B1. Indicate the site of the subject's infection to be documented on this form. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

B2. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section B
- Probable invasive fungal infection, complete Sections C, D and E
- Bacteremia, complete Section F
- Invasive bacterial tissue infection, complete Section G

B3. Indicate if the subject's infection is a mold infection. If it is not, skip to question B4.

B3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

SECTION B: INFECTION INFORMATION, cont.

B3b-d. Answer yes or no to each question B3b, B3c, and B3d to indicate which of the EORTC/MSG criteria apply to the subject's infection.

After completing question B3d, skip to question H1.

B4. Indicate if the subject's infection is a yeast infection. If it is not, skip to question B5.

B4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

B4b-e. Answer yes or no to each question B4b, B4c, B4d, and B4e to indicate which of the EORTC/MSG criteria apply to the subject's infection.

After completing question B4e, skip to question H1.

B5. Indicate if the subject's infection is a dimorphic fungal infection. If it is not, skip to question H1.

B5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

B5b-e. Answer yes or no to each question B5b, B5c, B5d, and B5e to indicate which of the EORTC/MSG criteria apply to the subject's infection.

After completing question B5e, skip to question H1.

SECTION C: HOST FACTORS

C1. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease. Neutropenia in this case is defined as an ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days.

C2. Indicate if the subject has received an allogeneic stem cell transplant.

C3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks. Subjects with allergic bronchopulmonary aspergillosis are excluded from this criterion.

C4. Indicate if, in the past 90 days, the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues).

C5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION D: MICROBIOLOGICAL FACTORS

D1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

D2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples.

D3. Indicate if the subject had a biopsy of skin ulcers, or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion.

D4. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours.

D5. Indicate if the subject had Beta-D-glucan detected in serum.

SECTION E: CLINICAL FACTORS

E1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to question E2.

E1a. Indicate if the subject has any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity.

E1b. Indicate if the subject has a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis.

E2. Indicate whether or no the subject has tracheobronchitis. If not, skip to question E3.

E2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

E3. Indicate if the subject has signs/symptoms of a sinonasal infection. If not, skip to question E4.

E3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer, black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

E4. Indicate if the subject has signs/symptoms of a CNS infection. if not, skip to question E5.

E4a. Indicate if the subject has focal lesions on imaging.

E4b. Indicate if there is meningeal enhancement on MRI or CT. If the subject has not had an MRI or CT answer No (2).

E5. Indicate if the subject has signs/symptoms of Disseminated candidiasis. If not, skip to question H1.

E5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen **AND** has had candidemia within the previous 2 weeks.

E5b. Indicate if the subject has progressive "cotton wool" exudates on ophthalmologic examination.

After completing Question E5b, Skip to Section H.

SECTION F: BACTEREMIA

F1. Indicate if the subject has a positive isolate from bacterial blood cultures indicative of serious infection (for example, gram negative bacteremia, S. aureus bacteremia).

F2. Indicate if subject has bacteremia with hemodynamic instability. If not, skip to question F4.

F3. Indicate if the subject has been unresponsive to appropriate clinical and antimicrobial management for > 24 hours.

F4. Indicate if the subject has bacteremia that has persisted for 72 hours in spite of appropriate antimicrobial therapy.

SECTION G: INVASIVE BACTERIAL TISSUE INFECTION

G1. Indicate if the subject has clinical signs and symptoms compatible with disease (e.g., sinusitis, pneumonia, intra-abdominal abscess). If not, skip to question H1.

G2. Indicate if there is radiographic evidence of disease. If not, skip to question H1.

G3. Indicate if the subject have a pure or predominant culture from sterile site biopsy or bronchoalveolar lavage (BAL).

G4. Indicate if the subject has a positive blood culture with an organism that is a plausible cause of infection (e.g. isolation of Streptococcus pneumoniae from blood in a subject with pneumonia).

G5. Indicate if the subject has typhlitis (neutropenic enterocolitis) with signs and symptoms compatible with disease and typical radiographic evidence of disease (with or without culture confirmation).

SECTION H: SIGNATURE

H1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

H2. Record the date the form was approved using mm/dd/yyyy.

Form G027 –Infection Documentation

Purpose of this form: The purpose of this form is to document the subject's study-qualifying infection.

When to complete this form: This form must be completed and data entered at baseline (Day 1), prior to randomization.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: When answering the questions on this form, select "No" if a particular test was not done to prove the subject's study qualifying infection.

SECTION B: INFECTION INFORMATION

B1. Indicate the site of the subject's study-qualifying infection. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

B2. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section B
- Probable invasive fungal infection, complete Sections C, D and E
- Bacteremia, complete Section F
- Invasive bacterial tissue infection, complete Section F

B3. Indicate if the subject's study-qualifying infection is a mold infection. If it is not, skip to question B4.

B3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

SECTION B: INFECTION INFORMATION, cont.

B3b-d. Answer yes or no to each question B3b, B3c, and B3d to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B3b-d must be answered yes.

After completing question B3d, skip to question G1.

B4. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question B5.

B4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

B4b-e. Answer yes or no to each question B4b, B4c, B4d, and B4e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B4b-e must be answered yes.

After completing question B4e, skip to question G1.

B5. Indicate if the subject's study-qualifying infection is a dimorphic fungal infection. If it is not, skip to question H1 – the subject is not eligible for the RING Study.

B5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

B5b-e. Answer yes or no to each question B5b, B5c, B5d, and B5e to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B5b-e must be answered yes.

After completing question B5e, skip to question G1.

To qualify for the RING Study based on a "probable invasive fungal infection" subjects must have at least one host factor (i.e. at least one question in Section C must be answered "yes"), one microbiologic criterion (i.e. at least one question in Section D must be answered "yes"), and one clinical criterion (i.e. at least one question in Section E must be answered "yes").

SECTION C: HOST FACTORS

C1. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease. Neutropenia in this case is defined as an ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days.

C2. Indicate if the subject has received an allogeneic stem cell transplant.

C3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks. Subjects with allergic bronchopulmonary aspergillosis are excluded from this criterion.

C4. Indicate if, in the past 90 days, the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues).

C5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION D: MICROBIOLOGICAL FACTORS

D1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

D2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples.

D3. Indicate if the subject had a biopsy of skin ulcers, or a swab of draining soft tissue lesions or fistulas with detection of yeast by microscopy **AND** recovery of *Candida* species by culture of the lesion.

D4. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF, **AND** the subject has not been treated with pipercillin/tazobactam within the last 48 hours.

D5. Indicate if the subject had Beta-D-glucan detected in serum.

SECTION E: CLINICAL FACTORS

E1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to question E2.

E1a. Indicate if the subject has any of the following "specific" imaging signs on CT: well defined nodule(s) with or without a halo sign, wedge-shaped infiltrate, air crescent sign, or cavity.

E1b. Indicate if the subject has a new non-specific focal infiltrate present with pleural rub, pleural pain or hemoptysis.

E2. Indicate whether or not the subject has tracheobronchitis. If not, skip to question E3.

E2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

E3. Indicate if the subject has signs/symptoms of a sinonasal infection? If not, skip to question E4.

E3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer, black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

E4. Indicate if the subject has signs/symptoms of a CNS infection. If not, skip to question E5.

E4a. Indicate if the subject has focal lesions on imaging.

E4b. Indicate if there is meningeal enhancement on MRI or CT. If the subject has not had an MRI or CT answer No (2).

E5. Indicate if the subject has signs/symptoms of Disseminated candidiasis. If not, skip to question H1.

E5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen **AND** has had candidemia within the previous 2 weeks.

E5b. Indicate if the subject has progressive "cotton wool" exudates on ophthalmologic examination.

After completing Question E5b, Skip to Section G.

SECTION F: BACTEREMIA and INVASIVE BACTERIAL TISSUE INFECTION

F1. Indicate if the subject has typhlitis.

F2. Indicate if subject has a pure or predominant culture from normally sterile site or BAL. If so, document on G012.

F3. Indicate if the subject has a positive isolate from blood culture associated with type of infection (invasive tissue infection) or indicative or serious infection (bacteremia). If so, document on G012.

- For invasive tissue infections, the organism should be associated with the type of infection.
- For bacteremia, the organism must be indicative of serious infection.

F4. Indicate if the qualifying infection is an infection of the chest or sinuses.

F5. Indicate if the subject has radiographic evidence of disease. If so, document on Form G014.

F6. Indicate if the subject has ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention)

F7. Indicate if the subject has had a persistent fever for 48 hours and more than one positive culture from the same organism in spite of appropriate antimicrobial therapy

- The second positive culture must be from a sample obtained at least 20 hours after results of initial culture were known; the last culture with known results prior to eligibility determination must be positive.

F8. Indicate if the subject has signs and symptoms compatible with disease.

F9. Indicate if the subject's signs and symptoms have been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours.

SECTION G: SIGNATURE

G1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

G2. Record the date the form was approved using mm/dd/yyyy.

Form G027 – Infection Documentation Form

Version C: 03/23/2011

Purpose of this form: The purpose of this form is to document other qualifying infections if more than one.

When to complete this form: If subject has more than one infection, this form must be completed and data entered at baseline (Day 1).

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

Form completion note: When answering the questions on this form, select "No" if a particular test was not done to prove the subject's study qualifying infection.

SECTION B: INFECTION INFORMATION

B1. Indicate the type of infection to be documented on this form. If the infection is a:

- Proven invasive fungal infection, complete Section B
- Probable invasive fungal infection, complete Sections C, D, E
  B1a. Indicate if above infection is mold
- Presumptive invasive fungal infection, complete Section C, E
- Probable endemic mycosis, complete Section C & Question E6
- Typhlitis, complete Section F
- Proven invasive bacterial tissue infection of chest and/or sinuses, complete Section G
- Proven invasive bacterial tissue infection, other location, complete Section G
- Presumptive invasive bacterial tissue infection of chest and/or sinuses, complete Section G
- Presumptive invasive bacterial tissue infection other location, complete Section G
- Bacteremia, complete Section H

B2. Indicate the site of the subject's qualifying infection. If the subject's infection is disseminated (more than one site), specify the sites of infection in the space provided. If the site is not listed, choose "other" and write in the site of infection in the space provided.

B3. Indicate if the subject's infection is a mold infection. If it is not, skip to question B4.

B3a. Identify the specific agent of infection. If the agent is not on the list provided, choose other and write the agent in the space provided.

B3b-d. Answer yes or no to each question B3b, B3c, and B3d to indicate which of the EORTC/MSG criteria apply to the subject's infection. To be eligible for the RING Study, at least one question B3b-d must be answered yes.

After completing question B3d, skip to question I1.

B4. Indicate if the subject's study-qualifying infection is a yeast infection. If it is not, skip to question B5.

B4a. Identify the specific agent of infection. If the agent is non-candida, specify the agent in the space provided.

B4b-e. Answer yes or no to each question B4b, B4c, B4d, and B4e to indicate which of the EORTC/MSG criteria apply to the subject's infection.

After completing question B4e, skip to question I1.

B5. Indicate if the subject's study-qualifying infection is endemic fungal infection. If it is not, skip to question I1.

B5a. Identify the specific agent of infection. If the agent is not listed, choose other and write in the agent in the space provided.

B5b-e. Answer yes or no to each question B5b, B5c, B5d, and B5e to indicate which of the EORTC/MSG criteria apply to the subject's infection.

After completing question B5e, skip to question I1.

SECTION C: HOST FACTORS.

C1a. Indicate if the subject has had a recent history of relapsed or refractory acute leukemia or MDS and a recent history of neutropenia (neutropenia in this case is defined as ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days) temporarily related to the onset of fungal disease (presumptive invasive fungal infection). If no, then answer C1b.

C1b. Indicate if the subject has a recent history of neutropenia temporally related to the onset of fungal disease (probable invasive fungal infection). Neutropenia in this case is defined as an ANC < 500/mm^3 (0.5 x 10^9 cells/L) for >10 days.

C2. Indicate if the subject has received an allogeneic stem cell transplant.

C3. Indicate if the subject has had a prolonged use of corticosteroids at an average minimum dose of 0.3 mg/kg/day prednisone equivalent for > 3 weeks. Subjects with allergic bronchopulmonary aspergillosis are excluded from this criterion.

C4. Indicate if the subject has received treatment with other recognized T-cell immune suppressants (such as cyclosporine, TNF-α blockers, specific monoclonal antibodies such as alemtuzumab, or nucleoside analogues) during the past 90 days.

C5. Indicate if the subject has an inherited severe immunodeficiency (such as chronic granulomatous disease, or severe combined immunodeficiency).

SECTION D: MICROBIOLOGICAL CRITERIA

D1. Indicate if the subject has sputum, BAL fluid, bronchial brush or sinus aspirate samples with the presence of fungal elements indicating a mold.

D2. Indicate if there was recovery by culture of a mold (e.g. Aspergillus spp., Fusarium spp., Zygomycetes, Scedosporium spp.) from sputum, BAL fluid or bronchial brush samples. If yes answer D2a.

D2a. Specify organism identified.

D3. Indicate if the subject had a positive Galactomannan antigen detected in plasma, serum, BAL fluid or CSF.

D4. Indicate if the subject had Beta-D-glucan detected in serum.

SECTION E: CLINICAL CRITERIA

E1. Indicate if the subject has signs/symptoms of lower respiratory tract fungal disease. If not, skip to questionG2.

E1a. Indicate if the subject has any of the following "specific" imaging signs on CT: dense, well defined nodule(s) with or without a halo sign, air crescent sign or cavity.

E2. Indicate whether or not the subject has tracheobronchitis. If not, skip to question E4.

E2a. Indicate if any of the following seen on bronchoscopy: tracheobronchial ulceration, nodule, pseudomembrane, plaque or eschar.

E3. Indicate if the subject has signs/symptoms of a sinonasal infection? If not, skip to question E4.

E3a. Indicate if the subject has imaging showing sinusitis **AND** at least one of the following:

- acute localized pain (including pain radiating to eye);
- nasal ulcer with black eschar;
- extension from the paranasal sinus across bony barriers, including into the orbit

E4. Indicate if the subject has signs/symptoms of a CNS infection. If not, skip to question E5.

E4a. Indicate if the subject has focal lesions on imaging.

E4b. Indicate if there is meningeal enhancement on MRI or CT. If the subject has not had an MRI or CT answer No (2).

E5. Indicate if the subject has signs/symptoms of Disseminated candidiasis. If not, skip to question K1.

E5a. Indicate if the subject has small, target-like abscesses (new nodular filling defects, bull's-eye lesions) in liver or spleen.

E5b. Indicate if the subject has progressive retinal exudates on ophthalmologic examination.

E6. Indicate if the subject has a clinical picture consistent with endemic mycosis and mycological evidence, such as a positive histoplasm antigen test result from urine, blood or CSF.

After completing Question E6, Skip to Question I1.

SECTION F: TYPHLITIS

F1. Indicate if the subject has evidence compatible with disease by imaging techniques. If yes, document on form G014.

F2. Indicate if subject has clinical signs and symptoms compatible with disease.

After completing Question F2, Skip to Question I1.

SECTION G: INVASIVE BACTERIAL TISSUE INFECTION

G1. Indicate if subject has a pure or predominant culture from normally sterile site or BAL or blood culture of an organism that is a plausible cause of the infection (for example, isolation of Streptococcus pneumonia from blood in subject with pneumonia). If yes, answer questions G1a.

G1a. Specify organism identified.

G2. Indicate if the subject has evidence compatible with disease by imaging techniques. If so, document on Form G014

G3. Does the subject have clinical signs and symptoms compatible with localized bacterial infection (e.g., sinusitis, pneumonia, intra-abdominal abscess, perirectal cellulitis/ecthyma/abscess, lesions with crepitation or blebs, multiple skin lesions with bacteremia.

After completing Question G3, Skip to Question I1.

SECTION H: BACTEREMIA

H1. Indicate if the subject has a positive isolate from bacterial blood culture indicative of serious infection (e.g. gram negative bacteremia or S. aureus bacteremia) [coagulase-negative staphylococcal bacteremias are excluded]. If yes, answer questions H1a and document on G012.

H1a. Specify organism identified.

H2. Indicate if the subject has ongoing hemodynamic instability in opinion of attending physician (e.g., need for pressors, fluid boluses, or other intervention).

H3. Indicate if the subject has had a persistent fever for 48 hours and more than one positive culture from the same organism in spite of appropriate antimicrobial therapy.

- The second positive culture must be from a sample obtained at least 20 hours after results of initial culture were known; the last culture with known results prior to eligibility determination must be positive.

H4. Indicate if the subject's signs and symptoms have been unresponsive to appropriate clinical and antimicrobial management for more than 24 hours.

SECTION I: SIGNATURE

I1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

I2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form G029 – Non-Study Donor Granulocyte Product Administration Form TMH-04

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -__ __ __ __ - __ __ __ - __

A2. Event: Granulocyte Transfusion ..... (GTRN)

A3. Date form filled out: ___ ___ / ___ ___ / ___ ___ ___ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

Section B: ADMINISTRATION INFORMATION

B1. Unit ID number _____

B2. Was donor stimulated with G-CSF? Yes..... 1 No 2

B3. Volume of product: ___ ___ ___ mL

B4. Absolute neutrophil count: ___ ___. ___ ___ ___ x 10^9 cells/L **(B5)** ☐ Not reported$_{-1}$ **(B4a)**

B4a. WBC: ___ ___ ___.___ x 10^9/L B4b. % neutrophils: ___ ___ ___%

B5. Was product volume reduced? Yes..... 1 No 2

B6. Was product aliquoted? Yes..... 1 No .....2 **(If B5 and B6 are answered "No", go to B9)**

B7. Volume of unit at issue: ___ ___ ___ mL

B8. Absolute neutrophil count at issue: ___ . ___ ___ ___ x 10^9 cells/L **(B9)** ☐ Not reported$_{-1}$ **(B8a)**

B8a. WBC at issue: ___ ___ ___.___ x 10^9/L B8b. % neutrophils at issue: ___ ___ ___%

B9. Transfusion status ____ ____ **(if = 2, 3 or 4 go to B10)**

B9a. If status = 1 or 99, specify reason: _____ **(if transfusion status = 1, go to H1)**

Transfusion Final Status Codes (Question B9)

1 = unit not given to subject (specify)
2 = transfusion of unit completed
3 = transfusion of unit discontinued due to transfusion reaction
4 = transfusion of unit discontinued due to failure to flow
99 = transfusion of unit discontinued due to other reason (specify)

__ __-__ __ __ __-__ __ __ __-__

Section B: ADMINISTRATION INFORMATION cont.

B10. Enter volume of unit **not** transfused: ___ ___ ___ B10a. Units: mL..... 1 grams 2

B11a. Start date: __ __/__ __ /__ __ __ __ B11b. Start time: ___ ___ : ___ ___

B12a. Finish date: __ __/__ __ /__ __ __ __ B12b. Finish time: ___ ___ : ___ ___

B13. Was there a transfusion related event of grade ≥ 1? *If yes, please complete a Form G019 for this transfusion.* Yes..... 1 No 2

Section C: LABORATORY

	a. Test done?	**b. Date sample collected** *(mm/dd/yyyy)*	**c. Time sample collected** *(24-hour clock)*	**d. Value** (x 10^9 cells/L)
C1. ANC within 4 hours prior to start of transfusion	Yes ..... 1 No..... 2 (**C2**)	__ __ / __ __ / __ __ __ __	___ ___ : ___ ___	__ . __ __ __
C2. ANC 30 minutes to 2 hours post transfusion	Yes ..... 1 No 2 (**D1**)	__ __ / __ __ / __ __ __ __	___ ___ : ___ ___	__ . __ __ __

Section D: MEDICATION

List all medications given specifically in preparation for pending transfusion:

D1. Medication	**D2. Dose**	**D3. Dose Units**	**D4. Route**	**D5. Date administered**	**D6. Time administered**
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __
_____	_____	_____	_____	__ __ / __ __ / __ __ __ __	__ __:__ __

__ __-__ __ __ __-__ __ __-__

Section E: VITAL SIGNS AND OXYGEN SATURATION

	a. Temp	b. Temp Unit	c. Temp Method	d. Respiration *(breaths/min)*	e. Pulse *(beats/min)*	f. Blood Pressure *(systolic/diastolic)*	g. O_2 Saturation	h. Date	i. Time
E1. 15 minutes prior to the start of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __
E2. 15 minutes after the start of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __
E3. 0:45 to 1:15 hours after the end of the transfusion	__ __ __ . __	°C .....1 °F 2	__ __	__ __	__ __ __	__ __ __ / __ __ __	__ __ __ %	__ __/__ __/__ __ __ __	__ __:__ __

Section H: SIGNATURE

H1. Approved by: Initials ____ ____ ____ H2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Form G029 – Non-Study Donor Granulocyte Product Administration Form

Purpose of this form: The purpose of this form is to document the administration of granulocyte products obtained from non-study donors during one transfusion episode.

When to complete this form: This form is completed for each granulocyte transfusion episode where the granulocyte product was obtained from a non-study donor. A transfusion episode is defined as: all granulocyte products ordered by a subject's physician at one time (i.e. one order). ***Note***: this form must be completed for each granulocyte transfusion of a product from a non-study donor that a subject receives while participating in the RING Study, even if the subject is not assigned to the granulocyte arm.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the subject's Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: ADMINISTRATION INFORMATION

B1. Record the Unit ID number.

B2. Indicate if the donor was stimulated with G-CSF.

B3. Enter the volume of the collected product in milliliters.

B4. Enter the ANC count of the collected product, using the units: $x10^9$/L, if available. If the ANC count was not reported, complete questions B4a and B4b.

B4a-b. Enter the WBC and the % neutrophils of the collected product.

B5. Indicate if the product was volume reduced.

B6. Indicate if the product was aliquoted. If the product was not volume reduced and not aliquoted, go to question B9. Otherwise, provide the volume and count of the product at issue in the following questions.

B7. Record the volume of the unit at issue.

B8. Enter the ANC count of the unit at issue using the units: $x10^9$/L, if available, and skip to question B9. If the ANC count was not reported, complete questions B8a and B8b.

B8a-b. Enter the WBC and the % neutrophils of the unit at issue.

B9. Record the transfusion status code.

Transfusion Final Status Codes	
1 = unit not given to subject (specify)	**4** = transfusion of unit discontinued due to failure to flow
2 = transfusion of unit completed	**99** = transfusion of unit discontinued due to other reason (specify)
3 = transfusion of unit discontinued due to transfusion reaction	

B9a. If the transfusion status code = "1" (unit not given to subject) or "99" (transfusion discontinued due to other reason), specify the reason why the unit was not given to the patient (e.g. the subject expired prior to the administration) or why the unit was discontinued. If the transfusion status code = "1", go to H1.

B10-10a. Record the volume that was **NOT** transfused and indicate if the unit of measurement is milliliters or grams.

B11a-b. Record the start date (mm/dd/yyyy) and time (24 hour clock) of the transfusion.

B12a-b. Record the finish date (mm/dd/yyyy) and time (24 hour clock) of the transfusion.

B13. Indicate if there was a transfusion-related event. ***Note***: the RING Study collects information on all transfusion-related events, regardless of grade. If a subject experiences any transfusion-related event during, or within 6 hours following the transfusion, form G019 and form G085 (if appropriate) must be completed and reported to the DCC.

SECTION C: LABORATORY

C1. This sample must be drawn within four hours prior to the start of a transfusion of granulocytes. If a subject has more than one sample drawn in the four hours preceding a granulocyte transfusion, record the sample drawn closest to the start time of the transfusion. Indicate if the test was done, and record the date and time a sample was collected and the ANC value (in units of 10^9 cells/L). An override reason must be entered if this test was not done.

C2. This sample must be drawn within 30 minutes to two hours after the end of a transfusion of granulocytes. If a subject has more than one sample drawn in the two hours after the end of a granulocyte transfusion, record the sample drawn closest to the end time of the transfusion. Indicate if the test was done, and record the date and time a sample was collected and the ANC value (in units of 10^9 cells/L). An override reason must be entered if this test was not done.

SECTION D: MEDICATION

In questions D1 through D6, record all medications given to a subject specifically in preparation for the granulocyte transfusion. Complete one row for each medication that was given. If more than one dose of a medication was given to a subject, record each dose on a separate line. If additional space is needed, attach additional copies of the form.

D1. Record the medication name. Note: this field will utilize a drop down feature for the following meds: acetaminophen, diphenhydramine, and hydrocortisone.

D2. Record the medication dose.

D3. Record the dose units (for example: mg, mL, units).

D4. Record the route of administration (for example, IM, po). Note: this field will utilize a drop down feature for the routes IV, IM, PO.

D5. Record the date the medication was given to the subject as mm/dd/yyyy.

D6. Record the time the medication was given to the subject using a 24-hour clock.

SECTION E: VITAL SIGNS AND OXYGEN SATURATION

E1 – E2. Record the measurements done closest to 15 minutes prior to the start (E1) or after the start (E2) of the transfusion.

E3. Record the measurements done closest to 1 hour after the end of the transfusion.

For each of the specified time periods, record each of the following measurements:

a-c. Record the subject's temperature, the unit of measurement (Celsius of Fahrenheit), and the method of measurement (see below). Note: this field will utilize a drop down/pre-fill feature for the method of measurement.

d. Record the respiration rate in breaths per minute

e. Record the pulse rate in beats per minute

f. Record the both systolic and diastolic blood pressures

g. Record O_2 saturation level

h. Record the date the measurements were taken as mm/dd/yyyy

i. Record the time the measurements were taken using a 24-hour clock

Temperature Method			
01 = oral	03 = tympanic	05 = esophageal probe	99 = other
02 = axillary	04 = rectal	-8 = unknown	

SECTION G: SIGNATURE

G1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

G2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

RING Study

TMH-04

Form G085 – Serious Adverse Event and Unexpected Adverse Event Form

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -- __ __ __ __ -- __ __ __ -- __

A2. Event: Adverse Event ..... (GADV)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ (M M D D Y Y Y Y)

A4. Initials of person filling out form: __ __ __

REPORTING INSTRUCTIONS: *All serious adverse events and unexpected adverse events must be documented using this form. The Principal Investigator (or designee in their absence) must notify the DCC of the event by telephone or e-mail within 24 hours and fax the form to the DCC within 48 hours. A separate form must be used to report each serious adverse event or unexpected adverse event.*

Section B: ADVERSE EVENT DESCRIPTION

B1. Event number: ___ ___ ___

B2. Type of Report:

Initial 1

Follow-up 2

B3. Adverse Event : _____

B4. Body system: (**circle one**):

Body as a whole	01	Musculoskeletal system	07
Cardiovascular system	02	Nervous system	08
Digestive system	03	Respiratory system	09
Endocrine system	04	Skin and appendages	10
Hemic and lymphatic system	05	Special senses	11
Metabolic and nutritional disorders	06	Urogenital system	12

B5a. Date of onset: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)* B5b. Time of onset: ___ ___:___ ___

B6. SAE / UAE category: *(**answer all questions**)*

a. Unexpected adverse event possibly, probably or definitely related to granulocyte transfusion	Yes 1	No..... 2
b. Death	Yes 1	No..... 2
c. Life-threatening event	Yes 1	No..... 2
d. Hospitalization or prolongation of existing hospitalization	Yes 1	No..... 2
e. Congenital anomaly/birth defect	Yes 1	No..... 2
f. Persistent significant disability/incapacity	Yes 1	No..... 2
g. Important medical event	Yes 1	No..... 2

Continued on Next Page

__ __ -- __ __ __ __ -- __ __ __ -- __

Section B: ADVERSE EVENT DESCRIPTION (cont.)

B7. Relationship of adverse event to:

	Unrelated	Unlikely	Possible	Probable	Definite
a. Granulocyte Transfusion	1	2	3	4	5
b. Study-qualifying infection	1	2	3	4	5
c. Other infection	1	2	3	4	5
d. Underlying condition and/or treatments	1	2	3	4	5

B8. Event Status:

Resolved, no sequelae 1

Resolved with sequelae..... 2

Ongoing..... 3 **(B10)**

Death..... 4

Unknown at this time 5

B9. Date of resolution or death: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy*)

B10. Action Taken:

a. None	Yes ..... 1 **(B11)**	No.....2
b. Medical	Yes 1	No.....2
c. Surgical	Yes 1	No.....2
d. Other (specify in B11)	Yes 1	No.....2

B11. Brief description of clinical presentation, treatment and evolution of event, and any other assessments (e.g. laboratory data) which help explain the event and have not been recorded elsewhere on this form. If the outcome of the SAE / UAE was death, write cause of death.

_____

_____

_____

_____

_____

Principal Investigator (or designated Co-Investigator) must approve form.

Section C: SIGNATURE

C1. Approved by PI or Co-Investigator: Signature: _____ Initials: ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy*)

Form G085 QxQ – Serious Adverse Event and Unexpected Adverse Event Form

Version A: 08/26/2008

Purpose of this form: The Serious Adverse Event (SAE) and Unexpected Adverse Event (UAE) Form is used to record information on all Serious Adverse Events and Unexpected Adverse Events that occur while the patient is in the RING Study (i.e. from the time the consent form is signed until an end-of-study point is reached).

Reporting Procedures / When to complete this form: A copy of this form must be completed for each SAE/UAE that occurs while the patient is part of the RING Study. **A SAE/UAE must be reported to the Data Coordinating Center (DCC) via telephone or email within 24 hours and this form must be completed and faxed to the DCC within 48 hours of learning of the event** using whatever information is available at the time.

The first time information about the event is reported, question B2 must be coded as 1 (Initial). Complete information about the SAE/UAE may not be available for some time. Each time an update to the SAE/UAE is submitted, question B2 must be coded as 2 (Follow-up). Only submit data for events or consequences that occur while the patient is on study.

Definitions: Adverse Event: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure regardless of whether or not it is considered related to the medical treatment or procedure (attribution of unrelated, unlikely, possible, probable, or definite).

A **serious adverse event** is any untoward medical occurrence for which at least one of the following applies:

- Results in death,
- Is life-threatening (there is a risk of death at the time of the event),
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity, OR
- Results in a congenital anomaly / birth defect.

SECTION A: GENERAL INFORMATION

A1. Affix the patient ID label in the space provided. If the label is not available, record the patient number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person completing the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: SERIOUS ADVERSE EVENT (SAE) DESCRIPTION

B1. Record the event number: Number each **new** SAE/UAE the patient experiences sequentially.

B2. Circle 1 if this is the initial reporting of the SAE/UAE. Circle 2 if this is a follow up report (i.e. an initial report has already been filed).

B3. Describe the primary SAE/UAE in the space provided.

B4. Circle one of the body system codes from the list provided to indicate the affected area of the subject. Refer to the RING Study Manual of Procedures for a description of each body system.

B5a-b. Record the date (in MM/DD/YYYY format) and time (using a 24 hour clock) of the SAE/UAE onset.

B6a-g. Circle 1 (yes) or 2 (no) to indicate the category/result of the SAE/UAE: (B6a) unexpected adverse event possibly, probably, or definitely related to granulocyte transfusion, (B6b) death, (B6c) life threatening event, (B6d) hospitalization or prolongation of existing hospitalization, (B6e) congenital anomaly/birth defect, (B6f) persistent significant disability/incapacity and (B6g) important medical event. Answer all questions.

B7a-d. Circle the code describing the relationship of the adverse event to the **Granulocyte transfusion** (B7a), **Study-qualifying infection** (B7b), **Other infection** (B7c), and **underlying condition and/or treatments** (B7d) according to the Adverse Event Relationship Definitions listed below.

Adverse Event Relationship Definitions

1. **Unrelated:** The adverse event is **clearly NOT related** to the study drug/device/treatment(s).
2. **Unlikely:** The adverse event is **doubtfully related** to the study drug/device/treatment(s).
3. **Possible:** The adverse event **may be related** to the study drug/device/treatment(s).
4. **Probable:** The adverse event is **likely related** to the study drug/device/treatment(s).
5. **Definite:** The adverse event is **clearly related** to the study drug/device/treatment(s).

B8. Using the Adverse Event Outcome Definitions below, choose one event status for this adverse event. If status is "ongoing," skip to question **B10.**

Adverse Event Outcome Definitions

1. **Resolved, no sequelae:** After the adverse event ends, the patient returns to pre-adverse event status.
2. **Resolved with sequelae:** After the adverse event ends, the patient does not return to pre-adverse event status.
3. **Ongoing:** The adverse event is still ongoing at the time of the report.
4. **Death:** The patient dies as a result of the adverse event, or the event was death.
5. **Unknown at this time:** Sufficient information is not available to determine a final event status.

B9. Record the date the SAE/UAE was resolved or resulted in death in MM/DD/YYYY format.

B10a-d. Indicate the action taken by answering Yes (1) or No (2) to each Question a through d. If Question B10a (none) is answered Yes (1), specify reason for no action taken in Question B11. If Question B10d (other) is answered Yes (1), specify the action taken in Question B11.

B11. Provide a brief description of the clinical presentation, treatment (including medications and other therapies or procedures that were initiated to treat this condition), evolution of the event and any other assessments that help explain the event. If the outcome of the SAE/UAE was death, include cause of death.

SECTION C: SIGNATURE

The Principal Investigator or designated Co-Investigator must approve the form.

C1. PI or Co-Investigator must sign the form and include their initials. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.

SOURCE DOCUMENTS AND MAILING INFORMATION:

If this is the first time that the SAE/UAE is being reported (B2 = 1), then this form must be completed and faxed to the DCC within 48 hours. Send copies of all relevant source documents as soon as they become available. Black out all identifying patient information, such as name and medical record number, and replace with the RING Study ID number.

When additional source documents and information about this SAE/UAE are obtained, complete a new Form G085, indicate in question B2 that it is a follow-up report, and submit it to the DCC with the additional relevant source documents.

Transfusion Medicine/Hemostasis Clinical Trials Network

RING Study

TMH-04

Form G089 – Serious Adverse Event and Unexpected Adverse Event Review

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -- __ __ __ __ -- __ __ __ -- __

A2. Event: Adverse Event ..... GADV

A3. Date form filled out: __ __ / __ __ / __ __ __ __ (M M D D Y Y Y Y)

A4. Initials of person filling out form: __ __ __

Section B: SERIOUS ADVERSE EVENT REVIEW

B1. Event number: ___ ___

B2. Type of Report:

Initial 1

Follow-up 2

B3. Adverse Event as reported on G085: _____

B4. Date Form G085 completed: __ __ / __ __ / __ __ __ __

B5. Did SAE meet criteria for review by second Medical Monitor? Yes .....1 No 2

B5a. Did second Medical Monitor review this SAE? Yes .....1 No 2

B5b. Was SAE reported to NHLBI promptly? Yes .....1 No ..... 2 **(B6)**

B5c. Date SAE reported to NHLBI: __ __ / __ __ / __ __ __ __

B6. Do you agree with site's designation of relationship of SAE to transfusion, underlying disease and bleeding? Yes .....1**(B8)** No 2

B7. If you do not agree, indicate relationship of adverse event to:

	Unrelated	Unlikely	Possible	Probable	Definite
a. Granulocyte Transfusion	1	2	3	4	5
b. Study-qualifying infection	1	2	3	4	5
c. Other infection	1	2	3	4	5
d. Underlying condition and/or treatments	1	2	3	4	5

B8. Comment:

_____

_____

Section C: SIGNATURE

C1. Medical Monitor: Initials: ____ ____ ____

C2. Date signed: __ __ / __ __ / __ __ __ __

Transfusion Medicine/Hemostasis Clinical Trials Network

RING Study

TMH-04

Form G091 – Protocol Deviation/Unusual Event Form

Section A: GENERAL INFORMATION

A1. Subject ID: __ __--__ __ __ __ -- __ __ __ -- __

A2. Event: Miscellaneous .....(GMSC)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ____ ____ ____

Section B: PROTOCOL DEVIATION/ UNUSUAL EVENT

B1. Date of protocol deviation/unusual event: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

B2. Time of protocol deviation/unusual event: ___ ___ : ___ ___ *(24-hour clock)*

B3. Describe unusual event or protocol deviation and any action taken:

_____

_____

_____

_____

_____

_____

_____

_____

B3a. Code ____ ____ ____ ***DCC use only***

B3b. Code ____ ____ ____ ***DCC use only***

B3c. Code ____ ____ ____ ***DCC use only***

Section C: SIGNATURE

C1. Approved by PI or designee: Initials: ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form G091 QxQ – Protocol Deviation / Unusual Event Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document any protocol deviation or unusual event.

When to complete this form: This form may be completed anytime during the study. It must be completed as soon as study staff is made aware that a protocol deviation or unusual event has occurred.

SECTION A: GENERAL INFORMATION

A1. Affix the subject ID label in the space provided. If the label is not available, record the subject number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person completing the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: PROTOCOL DEVIATION / UNUAUAL EVENT

B1. Record the date of the protocol deviation / unusual event in MM/DD/YYYY format.

B2. Record the time of the protocol deviation / unusual event using a 24-hour clock.

B3. Describe any unusual events or protocol deviations as well as any action taken in regard to the events reported on the form. Please provide as much detail as possible, and include the unit ID number if applicable.

SECTION C: SIGNATURE

The Principal Investigator or designee must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form GD01 – Pre-Donation Form TMH-04

Section A: GENERAL INFORMATION

A1. Study ID: __ __ -- __ __ __-- __ __ __ __ -- __

A2. Event: Study Data.....GDDT

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ___ ___ ___

A5. Planned collection date: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section B: CONSENT

B1. Has the donor signed a consent form? Yes.....1

B2. Date consent signed: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section C: DONOR INFORMATION

C1. Date eligibility assessed: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

C2. Donor status:
Biological relative of the recipient.....1 **(D2)**
Other family or friend of the recipient .....2 **(D2)**
Community donor.....3

Section D: INCLUSION CRITERIA

D1. (For community donors only) Has it been at least 72 hours since the end of the donor's last G-CSF/dexamethasone-stimulated donation?	Yes .....1 *(eligible)* No.....2 *(ineligible)*
D2. Has the donor made 7 or fewer previous G-CSF/dexamethasone-stimulated granulocyte donations within the past 12 months?	Yes .....1 *(eligible)* No.....2 *(ineligible)*
D3. Does the donor meet the standard blood donor criteria established by the local blood center where the donation will be made, the American Association of Blood Banks (AABB), and the FDA?	Yes .....1 *(eligible)* No.....2 *(ineligible)*

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Section E: EXCLUSION CRITERIA	
E1. Does the donor have a personal or family history of severe sickle cell disease or variant?	Yes..... 1 No ..... 2 *(eligible)* **(E2)**
E1a. Has the donor had a test for sickle cell disease or variant?	Yes..... 1 No ..... 2 *(ineligible)* **(E2)**
E1b. Did the donor test positive?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E2. Does the donor have a known positive test result for any infectious diseases test dictated by local blood bank's SOP?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E3. Does the donor have current uncontrolled hypertension?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E4. Does the donor have diabetes mellitus?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E5. Does the donor have active peptic ulcer disease?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E6. Is the donor pregnant or breastfeeding?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E7. Is the donor currently taking lithium?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E8. Does the donor have a current medical history of autoimmune disease for which he/she is receiving medication?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E9. Does the donor have a history of coronary disease?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E10. Does the donor have a history of deep vein thrombosis or venous thromboembolism?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*
E11. Does the donor have a history of iritis or episcleritis?	Yes..... 1 *(ineligible)* No ..... 2 *(eligible)*

Note: If any question in Sections D or E is answered with "ineligible," the donor is not eligible to participate in the RING Study.

Section F: SIGNATURE

F1. Approved by: Initials ____ ____ ____ F2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form GD01 QxQ – Pre-Donation Form

Version A: 05/15/2007

Purpose of this form:

1) To confirm that a donor (or the donor's legal guardian, if applicable) and the Site Investigator have signed an Informed Consent document indicating that the donor has agreed to participate in the RING Study
2) To document the eligibility status of the donor based on all inclusion and exclusion criteria. This form must be completed for every donor who signs an Informed Consent document.

When to complete this form: This form is completed during the eligibility assessment of the donor, only after the donor (or the donor's legal guardian) and the Site Investigator have signed an Informed Consent document.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

A5. Enter the planned collection date for this donation. This date must match the planned collection date recorded on the corresponding Form GD02 and the pheresis start date on the corresponding Form GD03.

SECTION B: CONSENT

B1. Indicate that the donor (or the donor's legal guardian) signed an Informed Consent document. Case Report Forms should only be completed for donors who sign an Informed Consent document.

B2. Record the date the donor (or the donor's legal guardian) signed the Informed Consent document.

SECTION C: DONOR INFORMATION

C1. Enter the date the donor's eligibility status was assessed.

C2. Indicate the donor's relationship to the recipient of the granulocytes:

- Circle 1 if the donor is genetically related to (blood relative of) the recipient. Skip to question D2.
- Circle 2 if the donor is not genetically related to the recipient, but knows the recipient because they are a family member or friend. Skip to question D2.
- Circle 3 if the donor does not know the recipient.

SECTION D: INCLUSION CRITERIA

Note: all applicable questions in Section D must be answered "Yes" in order for the donor to be eligible to make a donation for the RING Study. If an answer to a question makes a donor ineligible, please continue to complete the remainder of the form as this will capture complete information about the donor's eligibility status.

D1. If the donor is a community donor (i.e., you answered question C2 with "3"), indicate if it has been at least 72 hours since the end of the donor's last G-CSF/dexamethasone-stimulated donation.

D2. Indicate if the donor has made 7 or fewer previous G-CSF/dexamethasone-stimulated granulocyte donations within the past 12 months. Note: non-G-CSF and dexamethasone-stimulated granulocyte transfusions do not count as part of this total.

D3. Indicate if the donor meets the standard blood donor criteria established by the local blood center where the donation will be made, the American Association of Blood Banks (AABB), and the FDA.

Note: the Study ID must be recorded at the top of this page. Affix the label in the space provided. If the label is not available, record the Study ID number legibly.

SECTION E: EXCLUSION CRITERIA

Note: if an answer to a question makes a donor ineligible, please continue to complete the remainder of the form as this will capture complete information about the donor's eligibility status.

E1. Indicate if the donor has a personal or family history of severe sickle cell disease or variant. If "No (2)," skip to question E2.

E1a. If the donor **does** have a personal or family history of sickle cell disease or variant, has the donor had a test for sickle cell disease or variant? If "No (2)," skip to question E2.

E1b. If the donor did have a test for sickle cell disease or variant, was the test positive?

Note: if the donor has a family or personal history of severe sickle cell disease or variant, but does not have a negative test result for sickle cell disease, the donor is not eligible to donate.

E2. Indicate if the donor has a known positive test result for any infectious diseases test dictated by local blood bank's SOP.

E3. Indicate if the donor has current uncontrolled hypertension, defined as per local donor center policy.

E4. Indicate if the donor has diabetes mellitus.

E5. Indicate if the donor has active peptic ulcer disease.

E6. Indicate if the donor is pregnant or breastfeeding.

E7. Indicate if the donor is currently taking lithium.

E8. Indicate if the donor has a current medical history of autoimmune disease for which they are receiving medication such as corticosteroids.

E9. Indicate if the donor has a history of coronary disease.

E10. Indicate if the donor has a history of deep vein thrombosis or venous thromboembolism.

E11. Indicate if the donor has a history of iritis or episcleritis.

DONOR ELIGIBILITY CHECK

If any question in Sections D or E is answered with "ineligible," the donor is not eligible to participate in this study.

SECTION F: SIGNATURE

F1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

F2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form GD02 – G-CSF and Dexamethasone Administration Form TMH-04

Section A: GENERAL INFORMATION

A1. Study ID: __ __ -- __ __ __-- __ __ __ __ -- __

A2. Event: Study Data .....GDDT

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ____ ____ ____

A5. Planned collection date: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section B: G-CSF AND DEXAMETHASONE ADMINISTRATION

B1. G-CSF dose: ___ ___ ___ µg

B2. Injection date: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

B3. Injection time: ___ ___ : ___ ___ *(24 hour clock)*

B4. Dexamethasone dose: ___ ___ mg

B5. Date dexamethasone administered: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

B6. Time dexamethasone administered: ___ ___ : ___ ___ *(24-hour clock)*

B7. Instructions for Adverse Events given to Donor: Yes..... 1

No 2

Section C: SIGNATURE

C1. Approved by: Initials ____ ____ ____ C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form GD02 QxQ – G-CSF and Dexamethasone Administration Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document the administration of G-CSF and dexamethasone to the donor.

When to complete this form: This form is completed whenever a donor receives G-CSF and dexamethasone.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

A5. Enter the planned collection date for this donation. This date must match the planned collection date recorded on the corresponding Form GD01 and the pheresis start date on the corresponding Form GD03.

SECTION B: G-CSF AND DEXAMETHASONE ADMINISTRATION

B1. Indicate the amount of G-CSF given to the donor in micrograms. If no G-CSF was given to the donor, enter “0”.

B2. Indicate the date the G-CSF injection took place in mm/dd/yyyy format.

B3. Indicate the time the G-CSF injection took place according to a 24-hour clock.

B4. Indicate the amount of dexamethasone given to the donor in milligrams. If no dexamethasone was given to the donor, enter “0”.

B5. Indicate the date the dexamethasone was administered to the donor in mm/dd/yyyy format.

B6. Indicate the time the dexamethasone was administered to the donor according to a 24-hour clock.

B7. Indicate if the donor was given instructions for what to do if he or she experiences an Adverse Event within 1 week after the donation is made.

SECTION C: SIGNATURE

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

The RING Study

Form GD03 – Data on Granulocyte Product Form TMH-04

Section A: GENERAL INFORMATION

A1. Study ID: __ __ -- __ __ __-- __ __ __ __ -- __

A2. Event: Study Data..... (GDDT)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ A4. Initials of person filling out form: ___ ___ ___

Section B: DONATION INFORMATION

B1. Did the donor make a donation after being stimulated with G-CSF? Yes.....1 **(B2)** No.....2

If no, indicate the reason(s) why the donor did not make a donation:	**Yes**	**No**
B1a. Cancelled by recipient's physician	1	2
B1b. Positive screening test	1	2
B1c. Other reason (specify)	1	2 **(E1)**
B1c1. Specify other reason: _____		

B2. Pre-leukopheresis ANC count: __ __ . __ __ __ x 10^9cells/L **(B3)** ☐ Not reported$_{-1}$ **(B2a)**

B2a. Pre-leukopheresis WBC: __ __ __.__ x 10^9/L B2b. Pre-leukopheresis % neutrophils: ___ ___ ___%

B3. Date pheresis started: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy)*

B4. Time pheresis started: ___ ___ : ___ ___ *(24-hour clock)*

B5. Date pheresis ended: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy)*

B6. Time pheresis ended: ___ ___ : ___ ___ *(24-hour clock)*

B7. Volume of blood processed: ___ ___ ___ ___ ___ mL

Section C: CMV TEST RESULTS

C1. Recipient CMV status: Positive.....1 **(D1)** Negative.....2 Unknown..... -8

C2. Donor CMV test result: Positive.....1 Negative.....2

C3. Date of CMV test: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

Section D: PRODUCT INFORMATION

D1. Unit ID: _____

D2. Volume: ___ ___ ___ mL

D3. Absolute neutrophil count: ___ ___. ___ ___ ___ x 10^9 cells/L **(E1)** ☐ Not reported$_{-1}$ **(D4a)**

D4a. WBC: ___ ___ ___.___ x 10^9/L D4b. % neutrophils: ___ ___ ___%

Section E: SIGNATURE

E1. Approved by: Initials ____ ____ ____ E2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form GD03 QxQ – Data on Granulocyte Product Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to collect information about an intended donation of granulocytes.

When to complete this form: This form is completed each time a donor receives G-CSF and dexamethasone, even if the donor does not make a donation. Complete this form either after a donation is made or if the donor does not make a donation.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was filled out.

A4. Enter the initials of the person filling out the form. If the person filling out the form does not use a middle initial, enter a dash (-) in the middle space.

SECTION B: DONATION INFORMATION

B1. Indicate if the donor made a donation after being stimulated with G-CSF and dexamethasone. If the answer is "Yes (1)," skip to question B2.

B1a. through B1c. If the donor did not make a donation after being stimulated, answer each question with "Yes (1)" or "No (2)". If the donor did not make the donation for any other reason, specify the reason in the space provided. After answering B1c (and B1c1 if applicable), skip to question E1.

B2. Enter the donor's immediately pre-leukopheresis ANC count using the units: $x10^9$/L, if available. If the ANC count was not reported, complete questions B2a and B2b.

B2a-b. Enter the donor's pre-leukopheresis WBC and the % neutrophils.

B3. Enter the date the pheresis started in mm/dd/yyyy.

B4. Enter the time the pheresis started according to a 24-hour clock.

B5. Enter the date the pheresis ended in mm/dd/yyyy.

B6. Enter the time the pheresis ended according to a 24-hour clock.

B7. Enter the volume of blood processed in milliliters.

SECTION C: CMV Test Results

C1. Indicate the CMV status of the recipient. If the recipient is CMV positive, go to question D1.

C2. If the recipient is CMV negative, indicate CMV results for the donor obtained at the time of the collection.

C3. Enter the date of the donor's CMV test.

SECTION D: PRODUCT INFORMATION

D1. Enter the Unit ID of the collected product.

D2. Enter the volume of the collected product in milliliters.

D3. Enter the ANC count of the collected product, using the units: $x10^9$/L, if available. If the ANC count was not reported, complete questions D4a and D4b.

D4a-b. Enter the WBC and the % neutrophils of the collected product.

SECTION E: SIGNATURE

E1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

E2. Record the date the form was approved using mm/dd/yyyy.

Transfusion Medicine/Hemostasis Clinical Trials Network

RING Study

TMH-04

Form GD85 – Serious Adverse Event Form

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -- __ __ __-- __ __ __ __ -- __

A2. Event: Adverse Event ..... (GDAE)

A3. Date form filled out: __ __ / __ __ / __ __ __ __

A4. Initials of person filling out form: __ __ __

A5. Date of Collection: __ __ / __ __ / __ __ __ __

REPORTING INSTRUCTIONS: *All serious adverse events and unexpected adverse events must be documented using this form. The Principal Investigator (or designee in their absence) must notify the DCC of the event by telephone or e-mail within 24 hours and fax the form to the DCC within 48 hours. A separate form must be used to report each serious adverse event or unexpected adverse event.*

Section B: ADVERSE EVENT DESCRIPTION

B1. Event number: ___ ___ ___

B2. Type of Report:

Initial 1

Follow-up 2

B3. Adverse Event : _____

B4. Body system: (**circle one**):

Body as a whole.....01	Musculoskeletal system 07
Cardiovascular system.....02	Nervous system 08
Digestive system.....03	Respiratory system 09
Endocrine system 04	Skin and appendages 10
Hemic and lymphatic system.....05	Special senses..... 11
Metabolic and nutritional disorders.....06	Urogenital system 12

B5a. Date of onset: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)* B5b. Time of onset: ___ ___:___ ___

B6. SAE category: *(***answer all questions***)*

a. Death	Yes 1	No..... 2
b. Life-threatening event	Yes 1	No..... 2
c. Hospitalization or prolongation of existing hospitalization	Yes 1	No..... 2
d. Congenital anomaly/birth defect	Yes 1	No..... 2
e. Persistent significant disability/incapacity	Yes 1	No..... 2
f. Important medical event	Yes 1	No..... 2

Continued on Next Page

__ __ -- __ __ __ -- __ __ __ __ -- __

Section B: ADVERSE EVENT DESCRIPTION (cont.)

B7. Relationship of adverse event to:

	Unrelated	Unlikely	Possible	Probable	Definite
a. G-CSF	1	2	3	4	5
b. Dexamethasone	1	2	3	4	5
c. Granulocyte collection procedure	1	2	3	4	5

B8. Event Status:

Resolved, no sequelae 1

Resolved with sequelae..... 2

Ongoing..... 3 **(B10)**

Death..... 4

Unknown at this time 5

B9. Date of resolution or death: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy*)

B10. Action Taken:

a. None	Yes ..... 1 **(B11)**	No.....2
b. Medical	Yes 1	No.....2
c. Surgical	Yes 1	No.....2
d. Other (specify in B11)	Yes 1	No.....2

B11. Brief description of clinical presentation, treatment and evolution of event, and any other assessments (e.g. laboratory data) which help explain the event and have not been recorded elsewhere on this form. If the outcome of the SAE was death, write cause of death.

_____

_____

_____

_____

_____

_____

Principal Investigator (or designated Co-Investigator) must approve form.

Section C: SIGNATURE

C1. Approved by PI or Co-Investigator: Signature: _____ Initials: ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ (*mm/dd/yyyy*)

RING Study

Form GD85 QxQ – Serious Adverse Event Report

Version B: 08/26/2008

Purpose of this form: The Serious Adverse Event form is used to record information on Serious Adverse Events that occur while a donor is in the RING Study and for one week following their donation (i.e. from the time of the G-CSF administration until one week following the granulocyte donation).

Reporting Procedures / When to complete this form: A copy of this form must be completed for each serious adverse event that occurs from the time of the G-CSF administration until one week following the granulocyte donation. **A serious adverse event must be reported to the Data Coordinating Center (DCC) via telephone or email within 24 hours and this form must be completed and faxed to the DCC within 48 hours of learning of the event** using whatever information is available at the time.

The first time information about the event is reported, question B2 must be coded as 1 (Initial). Complete information about the serious adverse event may not be available for some time. Each time an update to the serious adverse event is submitted, question B2 must be coded as 2 (Follow-up). Only submit data for events or consequences that occur while the donor is on study.

Definitions: Adverse Event: Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom or disease temporally associated with the use of a medical treatment or procedure regardless of whether or not it is considered related to the medical treatment or procedure (attribution of unrelated, unlikely, possible, probable, or definite).

A **serious adverse event** is any untoward medical occurrence for which at least one of the following applies:

- Results in death,
- Is life-threatening (there is a risk of death at the time of the event),
- Requires inpatient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity, OR
- Results in a congenital anomaly / birth defect.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Record the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person completing the form.

SECTION B: SERIOUS ADVERSE EVENT (SAE) DESCRIPTION

B1. Record the event number: Number each **new** SAE the donor experiences sequentially.

B2. Circle 1 if this is the initial reporting of the adverse event. Circle 2 if this is a follow up report (i.e. an initial report has already been filed).

B3. Describe the primary adverse event in the space provided.

B4. Circle one of the body system codes from the list provided to indicate the affected area of the subject. Refer to the RING Study Manual of Procedures for a description of each body system.

B5a-b. Record the date (in MM/DD/YYYY format) and time (using a 24 hour clock) of the SAE onset.

B6a-f. Circle 1 (yes) or 2 (no) to indicate the result of the adverse event in relation to death (B6a), life-threatening event (B2b), hospitalization or prolongation of existing hospitalization (B6c), congenital anomaly/birth defect (B6d), persistent significant disability/incapacity (B6e), and important medical event (B6f). Be sure to answer all questions.

B7a-c. Circle the code describing the relationship of the adverse event to the **G-CSF** (B7a), **Dexamethasone** (B7b), and **granulocyte collection procedure** (B7c) according to the Adverse Event Relationship Definitions listed below.

Adverse Event Relationship Definitions

1. **Unrelated:** The adverse event is **clearly NOT related** to the study drug/device/treatment(s).
2. **Unlikely:** The adverse event is **doubtfully related** to the study drug/device/treatment(s).
3. **Possible:** The adverse event **may be related** to the study drug/device/treatment(s).
4. **Probable:** The adverse event is **likely related** to the study drug/device/treatment(s).
5. **Definite:** The adverse event is **clearly related** to the study drug/device/treatment(s).

B8. Using the Adverse Event Outcome Definitions below, choose one event status for this adverse event. If status is "ongoing," skip to question **B10.**

Adverse Event Outcome Definitions

1. **Resolved, no sequelae:** After the adverse event ends, the donor returns to pre-adverse event status.
2. **Resolved with sequelae:** After the adverse event ends, the donor does not return to pre-adverse event status.
3. **Ongoing:** The adverse event is still ongoing at the time of the report.
4. **Death:** The donor dies as a result of the adverse event, or the event was death.
5. **Unknown at this time:** Sufficient information is not available to determine a final event status.

B9. Record the date the serious adverse event was resolved or resulted in death in MM/DD/YYYY format.

B10a-d. Indicate the action taken by answering Yes (1) or No (2) to each question a through d. If question B10d (other) is answered Yes (1), specify the action taken in Question B11.

B11. Provide a brief description of the clinical presentation, treatment (including medications and other therapies or procedures that were initiated to treat this condition), evolution of the event and any other assessments that help explain the event. If the outcome of the SAE was death, include cause of death.

SECTION C: SIGNATURE

The Principal Investigator or designated Co-Investigator must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.

SOURCE DOCUMENTS AND MAILING INFORMATION:

If this is the first time that the SAE is being reported (B2 = 1), then this form must be completed and faxed to the DCC within 48 hours. Send copies of all relevant source documents as soon as they become available. Black out all identifying donor information, such as name and donor ID number, and replace with the RING Study ID number.

When additional source documents and information about this SAE are obtained, complete a new Form GD85, indicate in question B2 that it is a follow-up report, and submit it to the DCC with the additional relevant source documents.

Transfusion Medicine/Hemostasis Clinical Trials Network

RING Study

TMH-04

Form GD91 – Protocol Deviation/Unusual Event Form

Section A: GENERAL INFORMATION

A1. Subject ID: __ __ -- __ __ __-- __ __ __ __ -- __

A2. Event: Miscellaneous .....(GDMS)

A3. Date form filled out: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

A4. Initials of person filling out form: ____ ____ ____

Section B: PROTOCOL DEVIATION/ UNUSUAL EVENT

B1. Date of protocol deviation/unusual event: __ __ / __ __ / __ __ __ __ (mm/dd/yyyy)

B2. Time of protocol deviation/unusual event: ___ ___ : ___ ___ *(24-hour clock)*

B3. Describe unusual event or protocol deviation and any action taken:

_____

_____

_____

_____

_____

_____

_____

_____

B3a. Code ____ ____ ____ ***DCC use only***

B3b. Code ____ ____ ____ ***DCC use only***

B3c. Code ____ ____ ____ ***DCC use only***

Section C: SIGNATURE

C1. Approved by PI or designee: Initials: ____ ____ ____

C2. Date approved: __ __ / __ __ / __ __ __ __ *(mm/dd/yyyy)*

RING Study

Form GD91 QxQ – Protocol Deviation / Unusual Event Form

Version A: 05/15/2007

Purpose of this form: The purpose of this form is to document any protocol deviation or unusual event.

When to complete this form: This form may be completed anytime during the study. It must be completed as soon as study staff is made aware that a protocol deviation or unusual event has occurred.

SECTION A: GENERAL INFORMATION

A1. Affix the Study ID label in the space provided. If the label is not available, record the Study ID number legibly.

A2. The response is pre-circled on the form; there is no need to circle anything.

A3. Enter the date the form was completed in MM/DD/YYYY format.

A4. Enter the initials of the person completing the form.

SECTION B: PROTOCOL DEVIATION / UNUSUAL EVENT

B1. Record the date of the protocol deviation / unusual event in MM/DD/YYYY format.

B2. Record the time of the protocol deviation / unusual event using a 24-hour clock.

B3. Describe any unusual events or protocol deviations as well as any action taken in regard to the events reported on the form. Please provide as much detail as possible, and include the (planned) collection date and unit ID number if applicable.

SECTION C: SIGNATURE

The Principal Investigator or designee must approve the form.

C1. Enter the initials of the person approving the form. If the person approving the form does not use a middle initial, enter a dash (-) in the middle space.

C2. Record the date the form was approved in MM/DD/YYYY format.