Complete Final Version of the Form 7

(02-0898)

Dr. Kimberly Spence

Title: Precursor Preference in Surfactant Synthesis of Newborns

WUMC
WASHINGTON UNIVERSITY MEDICAL CENTER

Form #7 8/04
Human Studies Committee
Box 8089
(314)633-7400
Fax (314)367-3041

CONTINUING REVIEW REPORT

Use Form 7a for Expedited review of Minimal Risk research. Please refer to your last HSC approval letter for the research risk level.

All responses must be typed

Protocol Expiration Date 12/4/04

Date of Submission: **9/29/04**

HSC # **02-0898**

Principal Investigator (Last), (First), (Credentials)	**Spence, Kimberly, M.D.**
Study Title	**Precursor Preference in Surfactant Synthesis of Newborns**
HSC Designated Approval	[]3- Month [] Semi-Annual [X] Annual
	[] Minimal Risk [X] > Minimal Risk
Does this research involve cancer?	[X] No [ ] Yes If yes, the PRMC approval stamp is necessary through the treatment phase of the protocol. Those in follow-up only do not need PRMC approval. Otherwise, all cancer research must be approved by the PRMC prior to HSC submission. PRMC, Box 8100, 747-0374, **Consent Form Cancer Statement** Website:http://www.siteman.wustl.edu/physician/clinical_trials/PRMC_guidelines.shtml
Source of Funding:	**NIH**

[ ] Industry Sponsor* [X] Grant (**#F32 HL074601**)** [ ] Dept [ ] Cooperative Group [ ] None

* If this is industry sponsored, click here for fees charged for submission.

**Per OHRP Compliance Office, submit complete grant application with budget. Block out confidential salary information and dollar amount.

Signature of Department Chairperson Date

My signature confirms that the researcher has adequate resources and budget to conduct the research, and represents my approval of the research.
List of Departments

F. Sessions Cole, M.D.

Print Department Chairperson Name

Signature of Principal Investigator Date

My signature affirms that a) this research conforms with WUMC *Assurance of Compliance with HHS/FDA* (available in HSC office), and b) I have read and will comply with the Assurance of Commitment.

Signature of Faculty Sponsor Date
(Only needed if the PI is not WU, BJH, or SLCH)

For HSC Office Use Only

Committee # _____ Date of Committee _____ HSC _____

Data Sheet
Human Studies Committee
Box 8089
(314) 633-7400
Fax (314) 367-3041

INFORMATION SHEET

(Attach one copy with each Form 1 and Form 7submission. Submit with Form 5 when changing the PI.
Only fill out this form once and make copies to include with Form 1, Form 7, and Form 5. Cells will expand as needed)

Principal Investigator (Last, First, Credentials)	Spence, Kimberly, M.D.
PI Employer ("x" appropriately)	[X] WU [ ] BJH [ ] SLCH [ ] Other: (All non-WU staff must complete an "Unaffiliated Investigator Agreement." Contact the HSC office for more information.)
Division / Department	**Newborn Medicine/Pediatrics**
Department Billing #	**3163**
PI's Address (For Non-WU Staff)	
PI's Box #	**8116**
PI's Phone #	**(314) 454-4816**
PI's Fax #	**(314) 454-4633**
PI's e-mail address	**Spence_k@kids.wustl.edu**
Faculty Sponsor (if PI not WUSM, BJH, or SLCH)	**Aaron Hamvas, M.D.**
Person Responsible for Paperwork	**Marilyn Maksin**
Box #	**8208**
e-mail address	**Maksin_m@kids.wustl.edu**
Phone #	**(314) 286-2773**
Fax #	**(314) 286-2894**

A. CURRENT STATUS

[ ] Seeking funding; not yet activated	[ ] Study Closed to Accrual [subject(s) continue(s) to receive treatment, procedures, care] **Note**: Submit the most updated consent form if you plan to reconsent participants. Or, submit your last stamped and approved consent form if you do not plan to reconsent participants.*
[X] Enrolling subjects	Follow-up only – all treatment components are completed ***Please submit a Form 7c, category 8.***
	Data Analysis Only ***Please submit a Form 7c, category 8.***

* It is the responsibility of the PI to inform participants of any significant new findings developed during the course of the research which may affect the participants' willingness to continue in the study. Participants can be notified by signing an HSC approved information letter or an updated revised consent form.

B. SUBJECT ACCRUAL STATISTICS

1. Accrual Progress

Notify the HSC when additional subjects are needed to obtain valid data.

	WUMC	Multicenter** *(if applicable)*
Total number of subjects currently approved by HSC	15-20	____
Subjects accrued since initial HSC approval	18	____

If subjects accrued exceeds the number of subjects currently approved, please explain: ____

If additional subjects (beyond what is approved) are required for valid statistical analysis, state how many subjects will be added? 10

**For multi-center studies, the number accrued can not exceed the total number being accrued for the entire study. However, HSC recognizes that the total number accrued at WUMC may exceed the number stated on the initial submission.

2. Time Frame

- Date first patient enrolled. 5/17/03
- Anticipated completion date as stated in original submission. January 2004

Justify keeping trial open and provide new completion date if accrual is not in keeping with time frame stated in original submission: **Please see Form 5 for our amendment. The results from our initial data indicate surfactant metabolism evolves with the age of infants. We plan on comparing surfactant metabolism at different ages in the first 6 weeks of life of preterm infants and comparing the results to intubated infants with normal lungs. This will require an additional 10 subjects. We plan on a new completion date of January 2007.**

C. CURRENT INCLUSION CRITERIA (List here or attach a copy of protocol section outlining criteria. Do not reference the protocol.)

Eligible infants include term intubated infants with normal lungs and premature infants whose gestational age is 28 weeks or less and require mechanical ventilation as part of the routine management of their illness.

D. CURRENT EXCLUSION CRITERIA (List here or attach a copy of protocol section outlining criteria. Do not reference the protocol.)

For studies excluding participants for drug abuse: If drug testing will be performed a Certificate of Confidentiality will be needed.

Infants for whom death appears imminent and those with known infection, congenital anomalies and pulmonary hemorrhage.

E. BREAKDOWN OF WU SUBJECT ACCRUAL

This information is REQUIRED for the HSC to ensure equitable selection of subjects under 46.111(a)(3).

Gender	Number Accrued	Ethnic/Racial	Number Accrued
Female	9	African American	10
Male	9	Asian	____
		Caucasian	8
Adult	____	Hispanic/Latino	____

Minor	____	Native American	____
		Pacific Islander	____
Prisoner	____	Other	

Please provide an explanation if there is a significant disparity in the gender or racial/ethnic numbers of participants accrued:

Note: Based on 2000 census data, 23% of the St. Louis County population report belonging to a racial/ethnic minority.

F. RENEWAL SUMMARY: ***Please write in lay language and define all acronyms at initial use.***

1. **Changes since last approval:**

a. Protocol: Briefly describe any amendments or modifications that have happened since your last HSC approval.

Please see attached amendment. We are expanding the study age of the patients up to 6 weeks of age based on preliminary data indicating kinetic parameters of surfactant metabolism evolve with infant's age. In order to decipher the impact of age vs. worsening chronic lung disease it is important to understand surfactant metabolism in infants without lung disease, normals. We thus will also be studying term infants without lung disease intubated for other reasons.

b. Science: Briefly describe any changes in the scientific knowledge base that might impact the merit or conduct of the study.

Please see attached amendment.

2. **Renewal Summary Design Table** *Note that each box can only hold one page worth of information. Attach any information that is more than a page to the end of Form 7 documenting which box it addresses*

Diagnosis	**Respiratory Distress Syndrome (RDS) - a state of surfactant deficiency commonly but not exclusively found in premature neonates.**
Investigational Drug/Device/Procedure (Name & description) Does the drug/device continue to be investigational?	**Not applicable.** **[ ] Yes** **[ ] No**
Investigational Agent/Drug Preparation will be handled by For assistance, call Stephanie Porto, RPH, 454-7331. When investigational drug preparation is handled by PI, the HSC requires that the PI consult with Gerhard Bauer, 362-9011, and obtain documentation that the proposed investigational drug manufacturing meets Current Good Manufacturing Practices standards. In addition, the PI must attend a mandatory educational session focusing on the reporting and record-keeping responsibilities required in 21 CFR 312 and 21 CFR 314. Contact the HSC Office, 633-7400, to schedule the session.	**[ ] Pharmacist** **[ ] PI.** Submit documentation that proposed investigational drug manufacturing meets Current Good Manufacturing Practices standards. **[ ] Does not require preparation.** E.g. comes prepackaged and prepared. **[ ] Other.** Submit documentation that proposed investigational drug manufacturing meets Current Good Manufacturing Practices standards. **[ ] No investigational agent/drug being used.**

Drug Phase: (check one)	[ ] Pilot	[ ] I	[ ] II	[ ] III	[ ] IV	[ ] Not Phased
Device classification: *(check one)*		[ ] I	[ ] II	[ ] III		[ ] Not Classified

Investigational Device manufacturing will be handled by When investigational device manufacturing is handled by the PI, the HSC requires that the PI attend a mandatory educational session focusing on the reporting and record-keeping responsibilities required in 21 CFR 812 and 21 CFR 814. Contact the HSC Office, 633-7400 to schedule the session.	**[ ] Company sponsoring the research** **[ ] PI.** explain what arrangements and precautions have been taken to ensure proper manufacturing of the device and compliance with 21 CFR 812, 21 CFR 814, and Good Manufacturing Practices. [ ] NA
Data Monitoring	**Reference the page number and section of the Study Protocol that provides Data Monitoring information:** **Or, attach a copy of the committee or plan description.** Check the type of committee or plan the study has. **Committee - Phase III clinical interventions.** **[] Phase 3. Endpoints are mortality and/or major morbidity (21 CFR 312.32(c).** Submit a copy of the most recent data monitoring report for HSC review. None of the members are affiliated with the study. **[] Other studies requiring a Committee.** Submit a copy of the most recent data monitoring report for HSC review. The members are ordinarily independent of the study investigator(s). The DMC may or may not be external to the sponsor. The data monitoring committee may include Washington University or non-Washington University members. **[] Cooperative Group Studies.** Ordinarily the majority of members are external to the research team. **Plan - All other research submissions.** *(Based on size and risks of the study, the HSC may request: a) a plan where more than one individual monitors the study, b) a plan with an independent monitor, c) that the study have a Data Monitoring Committee.)* **[] Phase 1, 2, 4, or SAEs may be serious or life-threatening.** One member must be external to study team but the plan may otherwise include study team members. **[X] Phase 1, 2, 4, and All Other Studies.** All individuals involved in monitoring the study can be members of the study team.
Is this study monitored/audited by an outside entity (e.g., Clinical Research Organization, Sponsor, FDA, WU QA/QI)?	[ ] Yes [X] No If yes, submit a copy of the most recent audit/monitoring report.
Is this study part of a multi-center trial? If yes, does the coordinating center prepare and distribute multi-center trial reports?	[ ] Yes [X] No [ ] Yes [ ] No If yes, submit a copy of the most recent multi-center report.
Objectives (What are you hoping to learn?)	**To evaluate pulmonary surfactant metabolism and the effect of interventions on surfactant metabolism with stable, non-radioactive isotopes in preterm neonates with respiratory dysfunction.**

Literature Summary Provide a summary of recent (within the last year) relevant literature. (If the most recent literature summary is found in the protocol, reference it below. If not, provide a narrative literature summary. For studies that sent in a literature summary with the initial submission or the most recent renewal, an update of relevant literature within the last year is sufficient. For assistance, contact the Research Desk at Becker Medical Library, 362-4734.)	**One other group is using stable isotopes to study surfactant metabolism in infants. Recent studies using stable isotope labeled exogenous surfactant preparations suggest that premature infants with evolving chronic lung disease have more rapid catabolism of surfactant. For this reason, we would like to assess older infants to determine if this is the case for endogenous surfactant metabolism.** **1) Cogo PE, Carnielli VP, Bunt JEH, Badon T, Giordano G, Zacchello F, Sauer PJJ, Zimmermann LJI. Endogenous surfactant metabolism in critically ill infants measured with stable isotope labeled fatty acids. Pediatr Res 45:242-246, 1999.** **2) Cogo PE, Zimmermann LJ, Pesavento R, Sacchetto E, Burighe A, Rosso Rederica, Badon T, Verlato G, Carnielli V. Sufactant kinetics in preterm infants on mechanical ventilation who did and did not develop bronchopulmonary dysplasia. Crit Care Med 2003; 31(5): 1532-38.**
Rationale/Justification for study (What is the scientific reason for this study?)	**Dysfunction of surfactant metabolism may contribute to respiratory dysfunction. Understanding the mechanisms of these metabolic disruptions will permit development of specific therapeutic interventions.**
Methodology (check all applicable) see Suggested Language for HSC standard statements pertaining to the underlined Methods: * See applicable HSC Guideline on web, http://medicine.wustl.edu/~hsc/guidelines/ ** This includes skin tests/biopsies, lab results, and physical findings.	[ ] approved drug [ ] approved device [X] blood drawing [ ] data collection regarding family members [ ] diagnostic imaging [ ] diagnostic procedure [ ] diet and/or exercise [ ] experimental drug* [ ] experimental device* [ ] existing data** [ ] existing specimen** [ ] genetic testing* [ ] gene therapy * [ ] interview/questionnaire [ ] observation [ ] placebo* [X] prospectively obtained data** [X] prospectively obtained specimens** [ ] radioactive isotopes [ ] x-rays/examinations (for research only) [ ] teaching / focus group [X] treatment [ ] videotaping/audiotaping/photographs * [ ] substance, device, procedure exempt from FDA approval [X] other (specify) **stable isotope infusions**
Describe subjects' participation (For example, use of investigational drugs, randomization, placebos, questionnaires, videotaping). Explain what will be expected of the study population.	**Infants of a gestational age of 28 weeks or less or term intubated infants with normal lungs will receive a 24-hour continuous infusion of the stable isotopes [1-$^{13}C_1$] acetate and [1,2,3,4-$^{13}C_4$] palmitate.**
Specify which procedures are for research.	**The research interventions include administration of a 24-hour infusion of stable isotopes and drawing 2.5 ml of blood (0.5 ml of blood at five different times in the first 27 hour period from indwelling catheter or at clinically indicated times if no indwelling access available).**
Specify which procedures are part of standard clinical care.	**Blood samples and tracheal aspirates (obtained with routine airway suctioning that is standard practice for intubated infants) will be**

	obtained before the start of the infusion and at selected intervals over the next two weeks.
Duration of Individual Subject Treatment (in weeks, months or years)	**The intravenous infusion of stable isotopes will occur over 24 hours, tracheal aspirate samples will be obtained for the next 14 days or as long as the infant is intubated.**
Duration of Individual Subject Follow-Up	**The infants will be followed for the duration of their hospitalization.**
Anticipated duration of entire research activity (in weeks, months, or years) • What is the time frame from the time the study opens until the last participant is enrolled? • What is the time frame for the "active intervention" of the protocol? • How long will each participant be followed after the intervention has taken place?	**4 years including:** **• beginning of data collection January 2003** **• end of data collection January 2007** **Participant will be followed for the duration of their hospitalization.**
Criteria for Evaluation (end points)	**Previous work with stable isotope techniques to evaluate surfactant metabolism has suggested that 15-20 patients should be sufficient to detect differences in specific aspects of surfactant metabolism at a single time point. However, preliminary data indicate surfactant metabolism evolves with time. In order to investigate the impact of age on kinetic parameters of surfactant metabolism we plan to compare infants at different ages over approximately a 6 week period. In order to decipher the impact of age vs. worsening chronic lung disease it is important to understand surfactant metabolism in infants without lung disease, normals. We anticipate 10 patients will provide adequate numbers for statistical analysis.**

3. **Interim Findings**: Describe your significant preliminary observations/interim findings since the last full board review.

Preliminary data suggests that palmitate is the preferred substrate for surfactant synthesis in preterm infants at different ages. The rate of new surfactant synthesis increases with age of the infants studied. Apparently the contribution of recycled surfactant to overall surfactant production decreases with the age.

4. **New Information:** Provide any new information about risks and potential benefits that might affect the risk/benefit ratio and the willingness of current study subjects to participate or to continue to participate in the research.

Not applicable.

5. **Revisions/ Amendments**: Are any revisions or amendments being requested with this submission? Yes [X] No []
If research includes a revised questionnaire or interview, **highlight the questions that are being added or revised**. (Changes to the research design or questionnaire must receive HSC approval prior to implementation.)

If yes, describe below.

Please see attached amendment. We are expanding the study age of the patients up to 6 weeks of age based on preliminary data indicating kinetic parameters of surfactant metabolism evolve with infant's age. Also in order to provide a comparison it is necessary to have infants with normal lungs studied.

Does this change affect how the materials are being collected, used or shared? Yes [ ] No [X]
If yes, complete a HIPAA Compliance Form and submit with your Form 7. If you are uncertain, call the HIPAA Compliance Manager at 314-633-7475.

G. UNANTICIPATED PROBLEMS

1. Please provide a summary of all adverse events that occurred since the last continuing review (or initial review).
[X] Not applicable (No adverse events were reported during the last approval period)
[] Adverse events are consistent with the severity and frequency experienced in comparable non-research participant population.
[] Other (explain below)

2. If unanticipated, life-threatening, or fatal adverse events have occurred, do you have documentation of HSC receipt of reports?
   [ ]Yes
   [ ] at WU
   [ ] other site
   [ ] No (Contact the HSC office)
   [X] No SAEs have occurred

3. Have there been any unanticipated problems involving risks to subjects or others during the last approval period? (Unanticipated problems involving risks to subjects or others are events that are serious, unexpected, and possibly related to the research.)
   [X] No
   [] Yes (Provide a summary below)

   If yes, submit the cumulative electronic Unanticipated Problem Report listing all adverse events/problems that have occurred at WU and any Form 6 cumulative reports you may have. For multi-center studies, also submit the sponsor's cumulative report.

4. Withdrawals

   Total Individuals invited to participate._44 invited to participate, 25 consented, 18 infused (studied)

   Indicate the number of withdrawals (not including screen failures) for each of the following reasons.
   - Participant Withdrawal: Dissatisfaction ___ Relocation ___ Other (specify) _____
   - PI Withdrawal __7 were withdrawn prior to the infusion secondary to extubation or deteriorating clinical status._____

5. Have there been any complaints about the research since the last review?
   [X] No
   [] Yes (Provide a summary below)

6. Have any protocol deviations occurred during the last approval period, including all protocol deviations pre-approved by the study sponsor?
   [X] No
   [] Yes (Provide a summary below)

H. INFORMED CONSENT/AUTHORIZATION (Must be documented in subject's research file)

1. **Number and Type** (Indicate the type of consent with an "X"):
   [X] Written. [2] Indicate number of consent forms to be reviewed.
   [ ] Modified **guidelines**. [ ] Indicate number of questionnaires, telephone/verbal scripts, etc.
   [ ] Waiver of consent, submit **Form K1**
   [ ] Alteration of the eight required elements of consent, submit **Form K2**
   [ ] Waiver of written consent (i.e. verbal consent, implied consent), submit **Form K3**
   [ ] Short form written consent, submit **Form K4**
   [ ] **Non-English speaking**. [ ] Indicate number of consent forms to be reviewed.
   [ ] Third Party, submit **Form D**. [ ] Indicate number of consent forms to be reviewed.

2. Is consent form, identical to that previously approved by the HSC?
   [X] Yes (Enclose unstamped copy of consent) [ ] No* [ ] NA (Follow-up or waiver)
   *If no, please explain. **Highlight any changes to the consent document in yellow.**
   * WU HSC approved consent form must be used unless a different process has been approved by HSC.

3. Has the informed consent process been properly utilized with ALL subjects? Yes [X] No [ ]
   If no, explain.

4. Do you have signed consent forms from ALL subjects and are they on file for inspection? Yes [X] No [ ]
   If no, please explain.

I. Performance Site(s)

1. Please list only those sites that WU coordinates with.

- [ ] WU facility (e.g. pediatric/adult GCRCs)
- [ ] BJH
- [X] SLCH
- [ ] WU is the coordinating center for the multi-center project
- [ ] Other

Site(s) that have an IRB: submit IRB approval from other sites.

Site(s) that do not have an IRB: Submit **Form B**

2. Is WUMC acting as the coordinating center for other study sites? [X] No [ ] Yes
   If yes, it is the responsibility of the WUMC PI to ensure that all collaborating sites have obtained IRB approval and that procedures are in place to ensure that protocol information is managed and disseminated to all participating sites. Please describe the method for management and communication of protocol information (e.g. unanticipated problems, serious adverse events, protocol modifications, interim findings).

J. Collaborators: Each Collaborator named has reviewed the protocol and has consented to his or her inclusion.
List all Collaborators, including any listed in study budget.

Name (Expand table as needed.)	Credentials	Department	Box
Aaron Hamvas	**M.D.**	**Pediatrics**	**8116**
Bruce Patterson	**Ph.D.**	**Internal Medicine**	**8031**
Tami Garmany	**M.D.**	**Pediatrics**	**8116**

K. CONFLICT OF INTEREST *Institutional policy states that a "Conflict of interest exists if an employee's position or authority may be used to influence or make decisions that lead to any form of financial or personal gain for that employee or for his or her family which includes spouse or dependent children.*

Check one of the boxes below to indicate whether you* or any investigator* participating in the study has, or anticipates having, any income from or financial interest in:

- the sponsor of the protocol,
- the supporting organization, or
- the company that owns/licenses the technology being studied.

If applicable, describe the extent of the involvement in the space provided.

*includes spouse and dependent children

[X] No Financial Interest	[ ]Financial Interest Under $10,000 in aggregate	[ ] Financial Interest Over $10,000 in aggregate
	Check all those that apply: [ ] Consulting [ ] Speaking Fees [ ] Honoraria [ ] Gifts [ ] Licensing agreement or royalty income [ ] Equity interests: including stock, stock options, warrants, partnership or equitable ownership interests) [ ] Serving on a scientific advisory board or board of directors [ ] Other fees/compensation	**Check all that apply:** [ ] Consulting [ ] Speaking Fees [ ] Honoraria [ ] Gifts [ ] Licensing agreement or royalty income [ ] Equity interests, including stock, stock options, warrants, partnership or equitable ownership interests) [ ]serving on a scientific advisory board or board of directors [ ] Other fees/compensation

	Describe the extent of the involvement:	**Describe the extent of the involvement:**
	A current, up-to-date Financial Disclosure Statement must on file with the DRC that describes the above financial relationship. Contact the DRC Office at 747-4152 or DRC@msnotes.wustl. be edu.	A current, up-to-date Financial Disclosure Statement must be on file with the DRC that describes the above financial relationship. Contact the DRC Office at 747-4152 or DRC@msnotes.wustl.edu.
	Incorporate the Financial Disclosure statement into the consent form**	Incorporate the Financial Disclosure statement into the consent form**

**See model consent for suggested language.

Please note: The Disclosure Review Committee (DRC) must review the financial relationship prior to the IRB review. When a potential financial conflict of interest is indicated, the financial interest will need to be reviewed, and, if necessary, managed by the DRC. A summary of the DRC findings and recommended management strategy will be provided to IRB members for review and discussion at a full board meeting. DRC review of the potential financial conflict of interest is required in order for the HSC to approve the protocol.

University Conflict of Interest and Clinical Research Policy

L. Questions regarding Appendix Forms and Special Approvals—answer all

1. Is your research a multi-center trial funded by DHHS (i.e. NIH cooperative group)? Yes [ ] No [X]
   If yes, submit a Form A

2. Does this research involve minors? Yes [X] No [ ]
   If yes, submit Form E.

3. Does this research involve collection of any type of tissue to be used for genetic research? Yes [ ] No [X]
   If yes, submit a Form H along with renewal submission.

4. Does this research involve a placebo? If yes, submit Form S. Yes [ ] No [X]

5. Will this Research utilize the outpatient or inpatient resources of the Washington University **pediatric/adult General Clinical Research Center (GCRC)?** Yes [ ] No [X]
   If yes, please include the attached language in your consent form. GCRC consent language.
   Please forward a copy of this completed Form 7 in its entirety to Michelle Jenkerson RSA, GCRC, Box 8071, or email to: jenkerson_m@gcrc.wustl.edu, for compliance with the GCRC DSMP. A copy of the newly stamped consent form from the IRB must also be forwarded. (Questions call: 362-5626)

6. Will this research take place at **Barnes-Jewish West County Hospital (BJWCH)**? Yes [ ] No [X]
   If yes, please provide a letter of support from BJWCH. For information, contact Mary Mantese, (314) 996-8567.

7. **Center for Clinical Studies** only: Is this a Multicenter Academic Clinical Research Organization (MACRO) Submission? Yes [ ] No [ ]

8. Has this protocol ever been rejected by the HSC? Yes [ ] No [X]
   If yes and the HSC number differed, please provide that number: _____

M. CHECKLIST Any application that does not meet the following standards will be sent back to the PI without being reviewed. Check all items *relevant to your research* and **enclose three (3) copies** of all designated materials:

Every submission is required to have the following:

[X] A completed Form 7 with all signatures, spell checked, and typed.
[X] All appendix forms that are relevant to your study.
[X] Most **current version of the protocol** that includes: background information, objectives, inclusion/exclusion criteria, treatment plan, a description of the data monitoring committee or plan and follow-up procedures. Note: Protocols must be submitted with each application regardless of whether any changes have occurred to the

protocol.
[X] For grant funded studies: progress report or cumulative cooperative group progress report

If applicable, please submit:
[ ] Certificate of Confidentiality unless covered by a blanket COC
[ ] Copies of any publication(s) to date that have resulted from the research and were not previously submitted.
[ ] PRMC Approval stamp on front page of Form 7
[ ] Copy of the relevant literature (Question F2)
[ ] Cumulative Unanticipated Problem Report
[ ] Data Monitoring Progress Report (if separate from your study progress report)
[ ] Most recent Outside Audit/Monitoring Report
[ ] Most recent Multi-Center Trial Report
[ ] Revised Questionnaires (highlight changes in yellow and only submit those pages that have been revised)
[ ] Recruitment Materials (if being revised at the time of renewal, highlight changes in yellow.)
[X] Unstamped consent: written consent, verbal script, materials for implied consent or waiver application, Form K1.Copy of Consent Form(s) on the most current version of the HSC form in a 12 pt font (Note: Not necessary if in follow-up)