

HAC Policies and Procedures

What is Continuing Review?

Continuing review is a report to the HAC on the progress of the study. Again, it is the responsibility of the investigator to request continuing review by the HAC.

Are All Studies Required To Undergo Continuing Review?

The request for continuing review applies to all studies (e.g., medical record reviews, sample processing or other) regardless of the initial review level. Please note that studies initially meeting the criteria for exempt and expedited review are eligible for expedited review for their continuation request. Although federal regulations don't require continuing review for those studies initially approved as exempt from full review, the HAC does require an annual submission for exempt studies in order to provide the maximum protection for human subjects and/or human derived materials.

It is the investigator's responsibility to seek continuing review. However, as a courtesy, the HAC Administrative Office will mail the HAC Form 107, Clinical Study Status Report, to the PI or designee approximately 60 days prior to the approval expiration date.

Which documents are required for continuing review submissions?

- Current Informed Consent Document in use at the site, if applicable
- Current Children's Assent Document in use at the site, if applicable
- Current Parent/Guardian Informed Consent Document in use at the site, if applicable
- New Clean Version of the Informed Consent Document, if applicable
- New Clean Version of the Children's Assent Document, if applicable
- New Clean Version of the Parent/Guardian Informed Consent Document, if applicable
- Current Advertisements/Recruitment Materials, if applicable
- New Clean Version of the Advertisements/Recruitment Materials, if applicable
- Current Description of Research Proposal
- Recent and Relevant Literature (by this research team or others)

Why Do We Have to Complete the HAC Form 107, Clinical Study Status Report?

FDA, DHHS OHRP and institutional policies require that all research be reviewed at least annually or more frequently depending on the risk assessment.

What Information is Provided to Me on the HAC Form 107 From the HAC?

HAC Policies and Procedures

The HAC uses the HAC Form 107, Clinical Study Status Report, to confirm the information submitted by the Principal Investigator or his designee during the course of the study with all actions related to the study. This report contains information about the:

- Research team members and their educational status, demographic information, ability to obtain informed consent
- Number of subjects approved for inclusion in the study
- If the PI submits Adverse Events or Serious Adverse Events and a summary of IND Safety Reports, to the HAC for review during the approval period, this information will be included in the report.
- If the PI submits protocol deviations/violations, to the HAC for review during the approval period, this information will be included in the report.
- If the PI submits amendments, to the HAC for review during the approval period, this information will be included in the report.

All of this information should be reviewed by the Investigator for accuracy. If any mistakes or omissions are discovered please report to the HAC office.

Do I Need To Submit The Yellow Copy Of The HAC Form 107, Clinical Study Status Report, Or Can I Print Out A Copy From The HAC Forms?

The HAC Administrative Office prefers that the original yellow HAC Form 107, Clinical Study Status Report, sent to the Investigator, be used when submitting the report. This report contains additional information that the Investigator is responsible for checking for accuracy before submitting the report. If you misplace the original you can print out a HAC Form 107, Clinical Study Status Report, from the HAC web site and submit it instead of the original.

What Are The Deadlines For Submission?

The Due Dates are noted on the HAC Form 107, Clinical Study Status Report.

My Approval Doesn't Expire Until The 25th Of Next Month. Why Do I Have To Turn In The Completed HAC Form 107, Clinical Study Status Report, So Early?

The HAC requires that the completed HAC Form 107, Clinical Study Status Report, must be approved at the monthly meeting for protocols that were initially reviewed as full review. Protocols that were initially reviewed as exempt from full review or expedited review must be reported to the full Committee at the next convened meeting. HAC requires that the completed HAC Form 107, Clinical Study Status Report, must be submitted by the due date noted on the form in an effort to avoid unnecessary termination.

What If I Can't Get The Completed HAC Form 107, Clinical Study Status Report, To the HAC Administrative Office, On Or Before The Due Date?

HAC Policies and Procedures

If the form is not returned to the HAC Administrative Office by the due date noted on the form, the protocol approval **terminates**. Data and/or samples collected after the approval expiration date may not be used. If the project is funded and the HAC approval expires, the funding may also be withheld. All study-related activities must cease after the expiration date. This includes recruitment, advertising screening, enrollment, obtaining research informed consent, interventions, interactions, and the collection of private identifiable information. If the HAC protocol approval lapses, then the protocol must be resubmitted in its entirety as if it were a new protocol. If the study has not been approved for continuation by the approval expiration date, all research activity must cease immediately. Subject accrual and data collection must be suspended pending re-approval of the research by the HAC. The protocol **must** be re-submitted as a new review.

What Happens if I Don't Submit the HAC Form 107, Clinical Study Status Report, by the Due Date and I Have Subjects Receiving Active Test Articles?

Research approval that expires because the HAC did not grant continuing review, either because the HAC did not receive the required materials from the investigator or because the HAC received the materials but did not grant continuing review requires additional procedures by the HAC, the sponsor and the investigator.

Subjects receiving test articles should be withdrawn in an orderly manner appropriate to the research medication. A plan for this procedure should be submitted in writing to the HAC for review as soon as possible per the Food and Drug Administration (FDA) regulations. The investigator must submit a list of research participants for whom stopping research procedures would cause harm. The HAC may allow continuation of the research intervention or interactions in already enrolled participants only when the convened HAC or HAC Chairperson finds an over-riding safety concern or ethical issue involved such that it is in the best interests of individual subjects. The investigator is required to submit a list of all subjects for whom stopping research activities would cause harm to the HAC immediately.

The Chief of Staff at the Augusta VAMC must be consulted for all protocols that list the Augusta VAMC as a performance site.

The HAC will also notify the sponsor of the termination.

The protocol should be re-submitted to the HAC for review. Follow the instructions for initial review and add the following information:

1. All information should be included based on the current status of the study. For example, if the initial submission approved in 1995 noted that there was not any current literature but now (ten years or so later) there is literature that supports the study, include that information.
2. The HAC Form 107 must be completed and submitted with the initial submission packet. 30 copies must be submitted.

HAC Policies and Procedures

3. A summary should be included of all items that were amended during the life of the study in addition to any risks that were discovered.

Can I Enroll New Subjects After the HAC Approval Expires?

No. Enrollment of new subjects cannot occur after HAC approval expires and the data collected on subjects after HAC approval expires cannot be included in the research analysis. Enrolling subjects after HAC approval expires is considered to be a protocol violation which requires the completion and submission of the HAC Form 120PDV, Protocol Violation, to the HAC.

What if I Don't Receive the HAC Form 107, Clinical Study Status Report, from the HAC Administrative Office?

If the PI does not receive the HAC Form 107, Clinical Study Status Report, it may be accessed on the HAC Forms web site or you may contact the HAC Administrative Office to obtain an additional form. **It is the investigator's responsibility to seek continuing review.**

What if I Am Out of the Country or On Leave?

These issues should be addressed with the HAC prior to extended leave. The form may be emailed to HAC@mcg.edu or faxed to the HAC Administrative Office at (706) 721-1479, if necessary.

What Am I Responsible for in Reviewing this Report?

It is the responsibility of the PI to review the HAC Form 107, Clinical Study Status Report, for accuracy, completeness, and study progress. The form must be completed in its entirety, **including a progress report regarding study activity and returned to the HAC by the requested due date.** In the case of multi-center studies, study progress occurring at the MCG or MCGHI site only is required. If a progress report is submitted to a granting agency, a copy of that report should be submitted with the continuation request. All information on the form should be typed or printed and correction fluid should not be used. The report should be a cumulative progress report beginning from the original approval date of the study.

What are the Directions for the Proper Completion of the HAC Form 107, Clinical Study Status Reports?

Page One

HAC Policies and Procedures

Confirm that all information regarding the PI and the SC is correct. If any information is incorrect, please submit a completed HAC Form 113, Amendment Submission Form, to modify the incorrect information. Do not make modifications on the HAC Form 107, Clinical Study Status Report.

Performance Sites:

Confirm that each site where the study is being conducted is included as a performance site. A copy of the approval letter from sites (other than MCGHI or the Augusta VAMC) and/or their IRB or equivalent is required. Please refer to the section on Performance Sites for additional guidance.

Sponsor Information:

Confirm that the sponsor's name is correct. This should be the financial sponsor of the study. For example, a federal sponsor under the National Institutes of Health (NIH) may sponsor a study but the institution may serve as a sub-contract via a different university. For this case, the different university would be the sponsor.

PeopleSoft Account Number:

This number is required in order that study information may be shared with different areas within Research Administration. This information is also required for financial auditing purposes.

Section 1: Current Study Status

If the study was not funded and therefore not initiated, check the space next to "Completed" and note the reason(s) on page two under "Study Progress." If the study is finished, check "Completed". The HAC Form 107, Clinical Study Status Report, must be completed, especially the report section on page two. If the data is still being analyzed then, the study must remain active. If all data have been analyzed and publication is in process, the study may be completed and terminated.

What Should I Do If I Have Not Started the Study?

If a research study has not commenced (i.e., no subjects enrolled, no samples received, no data collected, etc.) and it has been three years since the original study approval date, the PI should submit a completed HAC Form 107, Clinical Study Status Report, or HAC Form 111, Final Report, to officially close the study.

If a study terminates before the HAC Form 107, Clinical Study Status Report, is received, the research team may submit a completed HAC Form 111, Final Report, to terminate the study.

SECTION 2: Subject Information

*HAC Policies and Procedures Section 3, Ongoing Research Activities
Version Date: 4/19/07, revised 4/10/08, 09/02/2008, 11/11/2008, 01/05/2009*

Page 5 of 14

HAC Policies and Procedures

What is meant by the Protocol Prior/New and Extension Prior/New?

If this is the first Clinical Study Status Report form completed for the study, leave the “Protocol Prior” section blank and enter the numbers on the “Subject Changes Since the Last Review” column. Leave the “New” section blank.

If an annual report was submitted to the HAC after 10/97, the Protocol Prior section will show the numbers previously submitted that were entered into the HAC database. Enter the numbers on the “Subject Changes Since the Last Review” column. Add the numbers from the “Prior” Section and “Subject Changes Since the Last Review” Section and place the cumulative number in the “New” Section.

If this is a multiple extension protocol and there is not enough room to include all of the information, attach a report with the numbers.

Cumulative Number of Subjects

The tables should indicate the cumulative number of subjects from the original approval date of the study.

Specified by protocol/contract: This is the maximum number of subjects approved by the HAC that the site can enroll. The protocol should state how many subjects were to be enrolled in the study. If the study receives external funding, then the grant or contract paperwork should state how many subjects would be enrolled. For example, if the study was initially approved to enroll 15 subjects, then the protocol prior column should indicate 15 under “Specified by Protocol/Contract”. If an amendment was submitted and approved to increase the number of subjects to 20, then indicate 20 under the “Specified by Protocol/Contract” for the new column.

We Often Conduct Studies That Don’t Have A Specified Number In The Protocol Or Contract, So What Should I Put In The Box?

Put an asterisk in the box and explain in the comments section on page two.

Screened: The number of subjects screened for inclusion/exclusion criteria. This number may exceed the number specified by the protocol/contract. If the number does exceed, then this information should be relayed to the Committee in the Brief Report section on page 2. This number should not exceed the number consented.

We Don’t Keep A Screening Log Of Patients. What Do We Enter in the Screened Section?

It is highly recommended that a screening log of subjects be used since the log can track whether a patient being screened may qualify or not qualify for the study, and can be used as documentation that subjects were actually screened, etc.

HAC Policies and Procedures

Consented: Enter the number of signed informed consent documents (ICD) and/or children assent documents (CAD).

Dropped/Withdrawn/Screen Failures: Enter the number of subjects who were dropped from the study by the PI, the number of subjects who withdrew from the study, and the number of subjects that were screening failures after signing the informed consent document. **NOTE: Each of these must be explained in the brief report section on page two for each year of the study.**

How Should Subjects That Are Lost To Follow-Up Be Reported On The HAC Form 107, Clinical Study Status Report?

These subjects should be counted as dropped/withdrawn/screen failure. Please indicate lost to follow up in the comments section on page two.

Completed: The cumulative number of subjects who fulfilled their obligations as study participants and have completed all required visits.

Continuing: The cumulative number of subjects who are continuing their participation in the study because they have not completed all required visits.

Additional Examples:

Year One of the Protocol

	Prior	Subject Changes Since the Last Review	New Total
Specified by Protocol/Contract	15	0	15
Screened	0	20	20
Consented	0	20	20
Dropped/Withdrawn/Screen Failures	0	7	7
Completed	0	0	0
Continuing	0	13	13

Year Two of the Protocol

	Prior	Subject Changes Since the Last Review	New Total
Specified by Protocol/Contract	15	0	15

HAC Policies and Procedures

Screened	20	2	22
Consented	20	2	22
Dropped/Withdrawn/Screen Failures	7	0	7
Completed	0	0	0
Continuing	13	2	15

Only complete the extension column if the HAC approved a protocol extension. Continuing review of the protocol is not an extension of the original approval.

Section 3: Equitable Selection of Subjects

Why is the Gender and Minority Status Required?

The HAC is required to confirm that research is distributed fairly and equally across gender and minority lines, as appropriate. The VHA 1200.5 requires this information as well.

Section 4: Risks, Benefits, Conflicts of Interest and Required Reporting

Why are we required to answer these questions?

The questions in this section relate to activities that may have occurred since the last review. Answering them will assist the HAC in determining if there have been any changes that may have increased the degree of risks to subjects involved in the study.

What if I Have Not Enrolled on the Study After Three Years?

The HAC will not approve the renewal of a project that lacks the appropriate resources if subjects have not been enrolled after three years. The only exceptions are oncology cooperative studies.

SECTION 5: Additional Reports

Adverse Events, Serious Adverse Events, and IND Safety Reports

A listing of all received reports will be included with the HAC Form 107, Clinical Study Status Report, if adverse events (AE), serious adverse events (SAE) or a summary of investigational new drug (IND) safety reports were submitted. Please review the listing carefully to determine if all reports were submitted to the HAC. It is the investigator's responsibility to compare this listing with all documents located at the study site. If a discrepancy is found, it must be promptly addressed with the HAC via the HAC Form 113, Amendment Submission Form, and indicate by marking the box labeled "Other". Additional forms may be required.

HAC Policies and Procedures

Amendments

A listing of all received amendments will be included with the HAC Form 107, Clinical Study Status Report, if amendments were requested. Please review the listing carefully to determine if all amendments were submitted to the HAC. It is the investigator's responsibility to compare this listing with all documents located at the study site. If a discrepancy is found, it must be promptly addressed with the HAC via the HAC Form 113, Amendment Submission Form, and indicate by marking the box labeled "Other". Additional forms may be required.

Protocol Deviations/Violations

A listing of protocol deviations/violations will be included with the HAC Form 107, Clinical Study Status Report, if protocol deviations/violations were reported. Please review the listing carefully to determine if all protocol deviations/violations were submitted to the HAC. It is the investigator's responsibility to compare this listing with all documents located at the study site. If a discrepancy is found, it must be promptly addressed with the HAC via the HAC Form 113, Amendment Submission Form, and indicate by marking the box labeled "Other". Additional forms may be required.

The Principal Investigator is responsible for ensuring that they have reviewed all applicable logs attached to the HAC Form 107. The PI must certify that all the information contained in the logs is accurate. The HAC should be notified about any discrepancies via the HAC Form 113.

Brief Report on Study Progress

Please note that the statement **"Study is proceeding as planned" is *not* an adequate report regarding the study progress.** If there were any unanticipated problems with recruitment, retention, lab tests, supplies, the protocol itself or if there were unanticipated benefits, this information must be provided. If a progress report was made to the sponsoring agency, a copy should be submitted with this HAC Form 107, Clinical Study Status Report. If an article was published on data collected, a copy should be submitted with this HAC Form 107, Clinical Study Status Report. Reasons for subject withdrawal and/or termination should be stated. **The HAC Form 107, Clinical Study Status Report, will be returned to the PI and may be allowed to expire if a brief study report is not completed as requested.**

Are There Any Examples of Guidance Statements for the Brief Report Section?

"The study was not begun at the desired start date. Therefore, our enrollment goals were not met. We enrolled 12 of the projected 50. One subject was dropped from the study since the subject relocated to another area. Ten subjects have completed the study and one subject is nearing completion. There have been no unexpected adverse events or problems with this study."

HAC Policies and Procedures

Or:

"Twelve medical records were reviewed. The data were gathered and protected per the Description of Research Proposal. The poster presentation was made at the July meeting of National Principal Investigators. The study is now complete."

NOTE: The above examples are suggestions to assist the investigators. Please be as informative as possible when completing the report section. Use of these guides does **not** guarantee that the HAC will approve the continuation request.

Are Other Approvals Required?

If the study involves the use of MCGHI resources (equipment, personnel, patients, space, supplies and/or records) and has a new impact on the budget that was originally approved by MCGHI via the OCIS HSRO, the HAC Form 107, Clinical Study Status Report, and all supporting documentation must be submitted to the OCIS HSRO for their review prior to HAC approval.

What About the Education Program?

Members of the research team who have not successfully completed the appropriate tiers of the required web-based education program or the recertification program must complete the program prior to the HAC Form 107 due date or the continuation request will not be processed. Individuals who fail to cooperate with the education program requirements must be removed from the study via the HAC Form 113, Amendment Submission Form, and may not conduct any research-related procedures after that time.

Are There Any Other Documents That Should Be Submitted with the Completed HAC Form 107, Clinical Study Status Report?

Informed Consent Document (ICD)/Children's Assent Document (CAD)

A "clean" unstamped version of the ICD and/or CAD must be submitted with the HAC Form 107, Clinical Study Status Report, for those studies that are still actively enrolling subjects. A "clean" version means without the HAC approval stamp. This clean copy is required so that the HAC can stamp it approved. The HAC Administrative Office will maintain the original and a copy will be returned to the PI or designee if approved for continuation. In compliance with federal regulations, each ICD and/or CAD will be reviewed and stamped approved as necessary. The version date of the ICD and/or CAD should not be revised unless the content of the document has been revised.

Advertisements/Recruitment Plans

If a study has an approved advertisement and will continue to recruit subjects, then a "clean" unstamped copy of the advertisement must be submitted with the HAC Form 107, Clinical Study Status Report. A "clean" version means without the HAC approval

HAC Policies and Procedures

stamp. This clean copy is required so that the HAC can stamp it approved. The HAC Administrative Office will maintain the original and a copy will be returned to the PI or designee if approved for continuation. In compliance with federal regulations, each advertisement will be reviewed and stamped approved as necessary. This includes brochures and pamphlets that may be given to the study subjects.

What Should I Do if Research Team Members Are No Longer on this Protocol?

Submit a completed HAC Form 113, Amendment Submission Form, to remove the research team members from the study. Please follow all policies and note that other forms or documentation may be necessary.

What Should I Do to Add New Research Team Members to the Protocol?

Submit a completed HAC Form 113, Amendment Submission Form to add new research team members to the study. Please follow all policies. Other forms may be necessary.

CVs/Résumés

Submit a currently dated and preferably signed CV or résumé must also be on file with the HAC Form 107, Clinical Study Status Report, if one is not on file with the HAC for all approved members of the research team. **Please note:** CVs must be submitted annually.

We Are Conducting a Study That Will Use Investigators Off-Site (that is, not MCG or MCGHI, etc). Do we need to submit a copy of their CV to the HAC?

No. Only those investigators with MCG or MCGHI affiliations must submit their dated and preferably signed CV or résumé.

I Submitted A Protocol Last Month For My Investigator With Five Copies Of the CV/ Résumés. Do I Have To Submit This Again This Month?

No. One copy of the dated and preferably signed CV or résumé should be submitted on an annual basis.

Should I Keep Copies of this Submission Packet to the HAC?

Retain a copy of the completed HAC Form 107, Clinical Study Status Report, and any support documentation (e.g., such as informed consent documents, children's assent documents, publications, study reports to funding agency, etc.) with the regulatory files or binders as maintained by the PI.

Who Reviews the HAC Form 107, Clinical Study Status Report?

HAC Policies and Procedures

The HAC Administrative Office performs the initial review of the HAC Form 107 and the investigator will be contacted if the form is incomplete.

If the form is complete, the HAC Administrative office will forward the HAC Form 107 to the Chairperson or his designee to review.

Can Continuing Review Fall Under the Expedited Criterion?

Yes. If the protocol was originally reviewed as exempt or expedited and continues to qualify as such, then the Chairperson or designee will review the HAC Form 107 and/or attachments (e.g., advertisement, informed consent document, etc.). If approved, these results are reported to the full Committee at the next HAC meeting via the agenda.

If the protocol was originally reviewed as full review and may now be reviewed via the expedited method, the Chairperson or designee will review the submission. If approved, these results are reported to the full Committee at the next HAC meeting via the agenda.

8. Continuing review of research previously approved by the convened IRB as follows where:
 - (i) The research is permanently closed to the enrollment of new subjects;
 - (ii) All subjects have completed all research-related interventions; and
 - (iii) The research remains active only for long-term follow-up of subjects; or
 - (iv) Where no subjects have been enrolled and no additional risks have been identified; or
 - (v) Where the remaining research activities are limited to data analysis.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

¹ *Children are defined in the DHHS regulations as "persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted." 45 CFR 46.402(a).*

What Will Determine if the Continuing Review Should be Conducted as a Full Review?

HAC Policies and Procedures

If the protocol was originally reviewed as full review and continues to require full review, the Chairperson and an additional HAC member will review the submission and will then forward the HAC Form 107 and/or attachments to the full Committee for review.

What if the HAC Needs Additional Information After Reviewing My Completed HAC Form 107?

The HAC will approve the protocol for continuing review on contingent basis pending the satisfactory response by the investigator. The approval will be held until the requested items are received. This approval will be for a defined time period and may be extended upon receipt of the requested items. If the requested items are not received in a timely manner, the convened HAC may disapprove the protocol.

When Can I Expect the HAC Determination Letter For The Continuation?

The HAC meetings are held on the fourth Monday of each month, unless otherwise designated. Therefore, the letters should go out via campus mail, no later than the Monday following the meeting.

Why Do We Have To Have The Informed Consent Document And/Or Children's Assent Document Reviewed And Approved During The Continuing Review Time?

If the protocol is still recruiting subjects, then the ICD and/or CAD must be reviewed and approved. As part of the continuing review each protocol must be reviewed and approved by the IRB as outlined by the Food and Drug Administration and the Office for Human Research Protections. Each informed consent document (ICD) and/or children's assent document (CAD) will be reviewed and stamped approved, as appropriate.

What If The HAC Requires Changes To The Protocol As A Result Of Continuing Review?

The investigator must ensure that the sponsor and/or the FDA and the NIH are informed of actions, if any, taken by the HAC as a result of its continuing review. The HAC may set conditions under which a protocol can be approved for continuing review. If the conditions are substantive regarding the protocol or informed consent process/documents then the approval must be deferred until the next convened HAC meeting. If the conditions are not substantive

Are There Any General Tips And Hints For The Continuing Review Process And HAC Form 107?

- Start the process early and ask questions!
- Prepare a reminder on your calendar indicating the HAC approval expiration date.
- Keep a copy of the submitted materials.
- Request a list of studies from the HAC Administrative Office, if needed.

HAC Policies and Procedures

Who Do I Contact if I Have Any Questions?

Contact the HAC Administrative Office at HAC@mcg.edu or call the following extensions:

(706) 721-8397 for PIs whose last names begin with A-G

(706) 721-3110 for PIs whose last names begin with H-P

(706) 721-1482 for PIs whose last names begin with Q-Z

Although the above listing indicates the staff's primary PI assignments, all HAC Administrative Office staff can answer your questions. There may be situations when your questions may require consultation with the HAC or OHRP leadership.