

Date: 2008-SEP-22

To: Principal Investigators  
Principal Clinical Research Associates  
Ethics Clinical Research Associates

From: Elizabeth Eisenhauer, Director, NCIC CTG Investigational New Drug Program

**RE: FOLLOW-UP REQUIREMENTS FOR CLOSED IND STUDIES**

Dear Participants,

We are aware that the need to submit a final report at the time of death on all patients entered on phase I or II NCIC CTG IND studies represents a significant work-load for participating centres, both in terms of patient follow-up, and the requirement for REB annual re-approval. Accordingly, a review of closed IND studies was undertaken recently, and the requirement for continued follow-up on these studies, and on IND studies in general, was discussed.

It is acknowledged that for the majority of phase I and II studies, where survival is not a primary (or an important secondary) endpoint, follow-up until death is not necessary. Therefore for *most* IND studies, follow-up beyond the 4 week post-treatment assessment (Form 5P), is required only for patients in two circumstances:

- 1) ***For patients with response or SD ongoing, follow-up is required only until progression or relapse, or until the patient goes on to subsequent therapy (at which point duration of response/SD is no longer evaluable).***
- 2) ***Patients with ongoing, protocol-related adverse events must be followed until toxicities have resolved to  $\leq$  grade 2.*** Late onset adverse events, including second malignancies, which are thought to be related to protocol therapy, must also be reported for all studies. Indeed, this is in keeping with the language in almost all of the current and closed IND protocols at present.

Patients should be followed until both (1) and (2) above are met. Protocols for all new IND studies will be written to explicitly reflect these follow-up requirements unless there are clear reasons why follow-up for prolonged periods is needed.

For completed IND studies, the need for continued follow-up and annual approval has been evaluated on a trial by trial basis. For those studies where survival is an endpoint as described in protocol objectives, Form 6 is required. For those studies where survival is not an endpoint, Form 6 is not required. Please see next page for detailed instructions regarding follow-up requirements on these trials.

***The following CLOSED studies have survival as an endpoint. Follow-up until death (Form 6) is therefore required:***

IND.165, 173

We have enclosed with this letter a list of patients registered on the above trials for whom we have not yet received a Form 6 (Appendix A).

*If patients on this list have died, please submit Form 6 now.*

*If there are no patients on this list from your centre, follow-up from NCIC CTG perspective is complete, and annual ethics approval is no longer required.*

***The following CLOSED studies do NOT have survival as an endpoint. Follow-up until death (Form 6) is therefore NOT required.***

***Follow-up is required only until progression or relapse to protocol therapy has been documented, and protocol related toxicities have resolved to  $\leq$  grade 2.***

IND.48, 49, 51, 51A, 54, 56, 57, 58, 60, 61, 62, 65, 66, 67, 69, 71, 73, 74, 75, 78, 79, 80, 82, 86, 87, 88, 89, 90, 91, 93, 94, 95, 96, 97, 98, 100, 103, 104, 105, 106, 106B, 109, 110, 111, 112, 113, 116, 119, 120, 121, 122, 123, 124, 125, 126, 127, 129, 130, 131, 132, 134, 135, 136, 138, 139, 140, 141, 142, 143, 144, 145, 146, 147, 148, 149, 150, 152, 153, 154, 155, 160, 161, 163, 164, 166, 166B, 167, 168, 169, 170, 171, 175

We have enclosed with this letter a list of patients registered on the above trials for whom we do not have a date of relapse/progression in our database (Appendix B).

*(Note that for some of these studies, the follow-up period is defined in the protocol as one or two years post treatment, regardless of response status. For those studies, follow-up may not be required even if relapse/progression has not been documented, and this has been taken into account in generating the listing.)*

*If patients on this list have relapsed/progressed, please submit date of relapse/progression (Form 5S) now.*

*If there are no patients on this list from your centre, follow-up from NCIC CTG perspective is complete, and annual ethics approval is no longer required.*

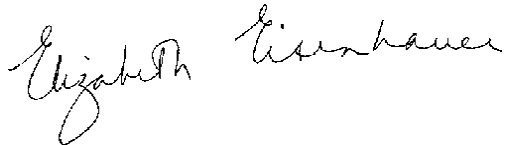
***For studies where follow-up is not yet complete, please note the following requirements for REB annual approvals:***

*Non NCI US affiliated studies must continue to receive annual ethics approval until patients have completed protocol treatment and all protocol mandated interventions. Ethics approval may be either expedited or full board, depending on local REB policy.*

Studies which are *NCI US affiliated* require Full Board annual renewal until all patients have completed protocol mandated interventions. Annual re-approval must then continue until no more data is being submitted on patients from the site and may be expedited.

This letter has been submitted to Health Canada and to the NCI US. ***This Notification must also be submitted to your REB. A copy of this Notification must also be kept on file at your centre and made available if/when requested by NCIC CTG for each trial.***

Sincerely,

A handwritten signature in cursive script that reads "Elizabeth Eisenhauer". The signature is written in black ink on a white background.

Elizabeth Eisenhauer, Director  
NCIC CTG Investigational New Drug Program

Cc Health Canada  
NCI US Contacts