-----Original Message-----
From: Elizabeth Ness
Sent: Friday, March 07, 2003 10:54 AM
Subject: Treatment Assignment Instructions and Guidelines

In attempts to clarify the development and use of Treatment Assignment Codes for data submission via AdEERS and/or CDUS, CTEP has revised the original CDUS instructions for Treatment Assignment Codes. Attached are the new "Treatment Assignment Instructions and Guidelines". We hope that these new guidelines will assist you with your data submission. They will also be available on CTEP's web site.

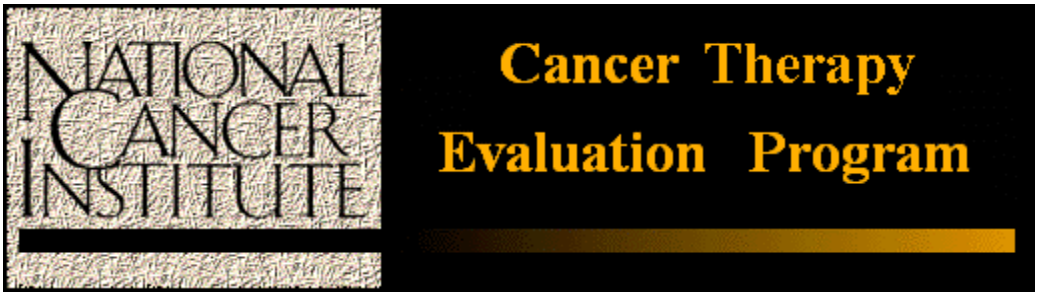
We would also like to take this opportunity to address some general coding related issues.

* Requests to change or create any code (treatment, subgroup or embedded correlative) or its descriptions should be sent directly to the Protocol and Information Office (PIO) at pio@ctep.nci.nih.gov.
* Please DO NOT submit data to an incorrect code either via AdEERS or CDUS. If a code or description is not available or incorrect, please contact the PIO immediately.

We request that you please distribute this email to all appropriate staff.

If you have any questions, please don't hesitate to contact me.

Thank you,
Liz Ness
BM__MailAutoSigElizabeth Ness, RN, MS
Deputy Program Manager
Protocol & Information Office
CTEP, DCTD, NCI
301-496-1367
Fax: 301-496-9384
 <mailto:pio@ctep.nci.nih.gov> pio@ctep.nci.nih.gov



TREATMENT ASSIGNMENT INSTRUCTIONS AND GUIDELINES

March 7, 2003

NCI CTEP Protocol and Information Office -
Telephone: (301) 496-1367
Fax: (301) 496-9384
E-mail: pio@ctep.nci.nih.gov

CONTENTS

Treatment Assignment Instructions and Guidelines

1 Overview

A Treatment Assignment Code (TAC) and a Treatment Assignment Description (TAD) must accompany each clinical trial where a unique treatment characteristic is utilized to uniformly group patients for separate analysis of adverse events and response data.

The TAC is a unique identification code (e.g., 'Level 1') assigned to each treatment assignment and is limited to ten alphanumeric characters. Patients on trials utilizing a single treatment assignment are entered on a TAC such as 'TA1.'

The TAD is a complete description of each treatment assignment (e.g., Cisplatin 100mg/m^2 IV over 1 hour on Day 1, every 21 days and Taxol 130mg/m^2 IV over 3 hours on Day 1, every 21 days). The agent name, dose (including units), route, and frequency/schedule for every agent within the treatment assignment must be included. A brief description of any non-pharmacologic treatment modality(s) (e.g., radiation, surgery) is also required.

CTEP develops TACs and TADs for all studies utilizing a CTEP-held IND (investigational) agent. Each arm or dose level is considered a distinct treatment assignment. Occasionally, TACs are developed for components of a regimen (e.g., induction phase, consolidation phase, maintenance phase) versus an arm or dose level. The protocol document serves as the guide for developing TACs and TADs.

1.1 TAC Availability

TACs are available for **all** dose levels as noted below.

1.1.2 Dose De-Escalation

A dose reduction that results when a patient experiences a Dose Limiting Toxicity (DLT) in a dose escalation/de-escalation (typically Phase 1) trial. The protocol indicates which adverse events and their associated grade are considered to be a DLT. This applies most frequently to Phase 1 trials.

1.1.3 Dose Escalation

A dose increase that occurs if a patient meets the appropriate criteria, as stated in the protocol, and they are able to receive the higher dose level of drug (e.g., intra-patient dose escalation). This applies most frequently to Phase 1 trials.

1.1.4 Crossover

A defined point where a patient switches from one treatment arm to another treatment arm. This most frequently applies to randomized trials when disease progression occurs.

1.2 TAC Unavailability

TACs will not be available for the following dose adjustments.

1.2.1 Dose Modification

A dose reduction or a dose increase that results when a patient experiences an adverse event that has not been defined in the protocol as a DLT, or has a low-grade adverse event, or meets the criteria to increase a dose. Dose modifications most frequently apply to Phase 2 and 3 trials.

1.2.2 Individual Patient Titration

An incremental dose increase or decrease of a specified agent to eventually achieve a point of tolerance or blood level. This will be stated in the TAC description.

1.3 Examples

The following are examples of TAC specification throughout patient enrollment on a protocol.

1.3.1 TAC Change Required

A TAC is selected for each course the patient receives. The enrollment TAC is used for subsequent courses **unless** one of the following occurs:

- **Dose De-Escalation** – If a patient in a dose finding trial develops a DLT and, per protocol, the dose level is reduced, then a new TAC should be selected (i.e., course 1 TAC is 'Level 1,' DLT occurs, course 2 TAC would become 'Level -1' [minus one], to denote a decrease).
- **Dose Escalation** – If the protocol is a dose finding study and allows for intra-patient dose escalation, a new TAC should be selected (i.e., course 1 TAC is 'Level 1,' patient's dose increases, course 2 TAC would become 'Level 2').
- **Crossover** – If a patient with a planned crossover changes to the crossover TAC (i.e., a patient is first randomized to either treatment 1 or treatment 2 and after disease progression on either treatment, is crossed over to either treatment 3 or treatment 4), then a new TAC should be selected. The crossover TACs will be clearly noted in the TAC description, even if the same dose is used.

1.3.2 TAC Change is NOT Required

A TAC is selected for each course the patient receives. The enrollment TAC will continue to be used even if the following criteria occur:

- **Dose Modification** – If a patient experiences an adverse event not considered to be a DLT based on the protocol, but does require a dose modification, or has a toxicity requiring dose reduction in a non-dose finding trial, then the patient's original TAC is used for data submission.
- **Individual Patient Titration** – If a patient has a dose changed because of their own outcome, whether planned or not (i.e., a patient who starts at a thalidomide dose of 200mg daily and is gradually increased to their own tolerance of 600mg), this will be stated in the TAC description and the original TAC is to be used for data submission.