

The Scientific Data
Verification and Auditing
System of the
Cancer & Leukemia Group B
(CALGB)

Why Do
Audits?

Stem-cell Transplant for Breast Cancer

- Bezwoda WR, et al: High-dose chemotherapy with hematopoietic rescue as primary treatment for metastatic breast cancer: A randomized trial. *J Clin Oncol* 1995;13:2483-9.
“[High-dose chemotherapy] ...results in a significant proportion of CRs and increased survival in patients with metastatic breast cancer.”
- Weiss RB, et al: An on-site audit of the South African trial of high-dose chemotherapy for metastatic breast cancer and associated publications. *J Clin Oncol* 2001;19:2771-7.
“The multiple publications of this study do not report verifiable data, and 9 other publications coauthored by the PI contain at least one major untrue statement.”

Cancer researcher admits falsifying trial results

Trial results presented at ASCO's annual meeting misrepresented treatment in the control group.

JOHANNESBURG--- The University of Witwatersrand Medical School is investigating Werner Bezwoda, MD, PhD, for scientific misconduct for allegedly lying about the results of a clinical trial on high-dose chemotherapy and stem cell support for breast cancer. In a document recently sent to his colleagues, Bezwoda acknowledged that he 'committed a serious breach of scientific honesty and integrity' by misrepresenting the results of that trial. Bezwoda has resigned his position at the university.

"ASCO regards these developments with the utmost seriousness."
Joseph S. Bailes, MD

Case Summary

- Event published in the Federal Register in March 2004.
- A CRA at Decatur Memorial Hospital was found guilty of falsifying the data in the study records of 35 patients on the SWOG SELECT Trial for prostate ca. prevention.
- The Clinical Trials Monitoring Branch and the Office of Research Integrity is currently investigating 11 other reports of scientific misconduct in the coop groups in past 20 m.

Case Summary

In a drug co. study of a toxicity protectant:

- The CRAs at 4 participating institutions falsified at least one QOL document to be completed by the patient.
- Three completed the form and signed the patient's signature.
- One used one form signed by the patient, changed the date with white-out, and submitted it as the form for a later date.

The Washington Post, Tuesday, September 19, 2000

Penn Researchers Sued In Gene Therapy Death

Teen's Parents Also Name Ethicist as Defendant

Reasons to Do Audits

- To discourage fraud & find its rare instances.
- To *educate & prod* investigators regarding protocol adherence & data collection.
- To find and correct errors.
- To assure all patient-protection measures and pharmacy procedures are followed.
- To help provide assurance the study results are valid.

Who Does Audits?

- Each cooperative group.
- NCI contractor (Theradex Corp.).
- Major cancer centers.
- NCI Intramural Program.
- Pharmaceutical companies.
- Others (General Accounting Office and Food & Drug Administration).

CALGB Data Audit System Selection of Institution

- All institutions entering at least one patient are subject to audit at a *maximum* interval of 36 months.
- New institutions are audited *by* 18 months after entry of the first patient.
- All institutions are subject to audit during any one year.

CALGB Data Audit System Selection of Institution (cont'd)

- Re-audits are done when patient accrual is sufficient to make them worthwhile, but in 12-18 months usually.
- Institutions leaving CALGB are still subject to audit of their entries since the previous audit.
- Geographical and weather considerations may affect scheduling.

CALGB Data Audit System Notification Lead Time for Audit

- Date is selected 3-4 months in advance & is arranged for mutual convenience of the Team Leader and the local staff.
- Patient list arrives 30 days in advance.

CALGB Data Audit System

Audit Teams

- 1-5 MDs and 1-5 CRAs make up teams and almost always work in pairs.
- Team Leader is always a DAC member.
- DAC members are those individuals with demonstrated audit interest and skill.
- Ad hoc auditors participate as an educational experience & always work with DAC member.
- Geographical and other considerations.

CALGB Data Audit System

Patient Selection

- Patients entered on 8-20 protocols representing a cross-section of diseases and stages, especially when there are special data submission requirements. 2-10 studies will involve NCI-supplied drugs.
- Patients at risk for audit are primarily, but not exclusively, those entered since the previous audit.
- At least one patient will be unannounced.

CALGB Data Audit System Patient Selection (cont'd)

- The number audited depends on the number entered by the institution. Main institutions are at least 15-20%, and affiliates vary from 20% to 100%.
- An attempt is made to select at least one entry from each participating MD.
- The percentage of entries to any one study audited within the whole Group varies from 5% to 40%.

New NCI Requirements for Audits

- There are no more new intergroup studies. CTSU now fulfills this role.
- CTSU studies will be audited just as if they were a CALGB study, but they will be segregated into “endorsed” and “non-endorsed” cases. Thus, samples from each category will be selected for review.
- If >3 CTSU cases are to reviewed, CTSU maybe will augment the Audit Team.

New NCI Requirements for Audits

- The CTSU cases will be included in the 24-hour Preliminary Report and the Final Audit Report along with the CALGB cases.
- Pieces of the audit reports now go to the lead group on a case-by-case basis for the non-CALGB studies action on the Patient Case Reviews.

Audit Preparations

- **PLEASE** read the Audit Announcement Letter and distribute it to all involved personnel including those at the relevant affiliate(s).
- **PLEASE** make sure all preparation directions in the letter are followed.
- Sending personnel to affiliates to assist with, and supervise, audits is **very** useful.
- CALGB Website has the Audit Preparation Workshop available for review.

CTMB Reminders for PIs

- The PI is responsible for ensuring all required IRB reviews are performed.
- The PI is responsible for pharmacy activities with INDs.
- The PI is responsible for all CRA activities.

Audit Preparation

We want it done correctly, accurately, exactly, absolutely, efficiently, precisely, reliably, expertly, proficiently, faithfully, perfectly, completely, totally, flawlessly, maturely, unequivocally, unmitigatedly, supremely, unsurpassedly, and certainly without any fault.

We want it unharmed, unbotched, untainted, and most of all....

Unscrewed up!