The Scientific Data Verification and Auditing System of the CALGB

Raymond B. Weiss, M.D.
Chair, CALGB Data Audit Committee

CALGB CRA Orientation, October 2005

Why Do Audits?
Chemotherapy Administration and Data Collection in an EORTC Collaborative Group---Can We Trust the Results?
W.P. Steward, K. Vantongelen, J. Verweij, D. Thomas and A.T. Van Oosterom


As part of a phase II study of the EORTC Soft Tissue and Bone Sarcoma Group, 15 centres took part in a programme to evaluate the quality of treatment delivered and data collected. The centres were visited and facilities for treatment and data management were reviewed. Source data in randomly selected patient hospital records were compared with information which had previously been completed on case record forms and returned to the EORTC Data Centre. The review included 71% of the patients entered into the study.

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

- 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

- One CRA reviews another’s data and discovers alterations on consent documents, performance status, and physical exams. A “for cause” audit found many problems.
- The CRA is disbarred.
- Two years later at the same institution another case of fraudulent data found in a routine audit. 25 cases of changed dates, writeovers, and questionable signatures.
Case Summary

• Through a routine audit an ineligible patient was found. The surgeon had asked the pathologist to revise the pathology report.
• 95 cases reviewed in a “for cause” audit.
• Sloppy data, poor quality data, and many deficiencies found.
• The surgeon admits to fraudulent data and resigns from the institution.

Case Summaries

• At one routine audit a physician’s signatures were not authentic on consents.
• During another routine audit it was noted exams had been added. When the audit was scheduled, the CRA had abruptly quit.
• During another audit notes in the chart stated the patient could not be contacted, yet a symptom checklist had been completed.
Newspaper Headlines

• 02/06/05: NY Times: “Abuses Endangered Veterans [at Albany VA] in Cancer Drug Experiments.”
• “Research violations were a way of life at Stratton [VA Hospital] for 10 years.”
• There was a “clear systems failure, permitting a research culture where rules weren’t followed, protocols weren’t applied, and supervision was nonexistent.”

- - - - Admits Cover-up, Loses Posts At Albert Einstein

------------------------- was removed from his posts as chairman of the oncology department and associate director of the cancer center of the Albert Einstein Medical Center after admitting that he had provided interleukin-2 to two neurosurgeons conducting unauthorized trials with brain tumor patients and subsequently covered up his actions.
Penn Researchers Sued In Gene Therapy Death
Teen’s Parents Also Name Ethicist as Defendant

CALGB Data Audit Committee
Motto

“In God We Trust
All Others We Audit”
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

Personnel

- Data Audit Committee (DAC): approx. 20 members, half are MDs and half CRAs.
- DAC Chair is the only paid member.
- A designated statistician (Jeff Johnson).
- A designated administrative assistant in the Central Office (Sally Scherer).
- Ad hoc auditors (CALGB MDs and CRAs who are not DAC members).

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
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 first patient.
• All institutions are subject to audit during any one year.

CALGB Data Audit System
Selection of Institution

• 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

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**

- The number audited depends on the number entered by the institution. Main institutions are at least 15%, and affiliates vary from 15% 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%.

**CALGB Data Audit System**

**Audit Preparations at Institution**

- Assemble all relevant IRB-review items (initial, annual, update, and SAE reviews) and assemble in chronologic order.
- Assemble all inpatient and outpatient records for the patients to be audited.
CALGB Data Audit System
Audit Preparations at Institution

- Inform the pharmacy staff of the impending audit and request they have all records (drug logs, NCI-shipping & return invoices, etc.) available and in chronologic order. A knowledgeable person must be available at the audit.
- Be prepared to locate the medical records for the unannounced patient(s).

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.
CALGB Data Audit System
Data Management Center Duties

• Make copies of all submitted data forms for use by auditors.
• After audit report is final & submitted to all concerned parties, any needed changes in the database are made.

CALGB Data Audit System
Administrative Elements Audited

IRB

• Were the protocols being audited fully approved prior to the first patient entry and were the annual reviews done annually (i.e., interval of <366 days).
• Were protocol Updates reviewed w/n 90 days & were consent revisions implemented
• Were local & broadcast Serious Adverse Events reviewed as required.
## CALGB Data Audit System
### Administrative Elements Audited

**Pharmacy**

- Are the NCI Drug Accountability Record Forms (DARFs) being used.
- Does drug income and dispensing match.
- Does the supply on the shelf match the log count.
- Is there any misuse of NCI-supplied drug for a non-study patient.

### CALGB Data Audit System
### Administrative Elements Audited

**Pharmacy**

- Were commercial supplies (if available) substituted for NCI-supplied drug and was NCI-supplied drug repaid to the commercial supply.
- Is drug storage secure with limited access.
- Were transfers of drug supplies approved by NCI & was excess drug handled correctly.
- 1-3 drugs will have unannounced reviews.
CALGB Data Audit System
Administrative Elements Audited

Consents

- Were the consents signed and dated on or before the date of registration.
- Were all local IRB requirements (witness, blanks, initials on pages, etc.) fulfilled.
- A sample of at least 3 consents are reviewed for completeness using the CALGB 28-item checklist (available on CALGB website).

CALGB Data Audit System
Protocol Elements Audited

- Were the pre-therapy baseline pathologic, radiologic, laboratory, and other required assessments properly performed and did they meet protocol minimums.
- Did the patient meet all eligibility requirements.
- Were stratification and randomization correct.
CALGB Data Audit System

Protocol Elements Audited

- Was the correct treatment given at the correct dose and schedule for all cycles.
- Was all treatment toxicity properly assessed, graded, and reported.
- Was the antitumor response (none, partial, complete) properly measured (often done with review of the relevant radiographs).

- Was the patient monitored after completion of therapy according to the requirements of the protocol.
- Were all required data forms submitted to the CALGB Data Management Center.
- Were all required ancillary submissions (pathology items, XRT data, blood/marrow samples, etc.) completed and on schedule.
CALGB Data Audit System
Audit Reports

- The 3 components are each rated as being Acceptable, Acceptable Needs FU, or Unacceptable.
- An Unacceptable rating requires a re-audit; an Acceptable Needs FU may require one, depending on the issues.
- An Unacceptable rating in IRB/consent category results in suspension of patient registration until the problem is corrected.

Avoidable Errors in IRB

- All Updates/Amendments must be reviewed by the IRB within 90 d. of implementation.
- All SAEs broadcast in the monthly mailing from the CO must be acknowledged by the IRB within 90 days of implementation.
- Annual renewals must be done within 365 days of the previous renewal.
- All closed studies with patients still in active FU must have annual renewals also.
- All “action letters” must be reviewed.
**Avoidable Errors in Pharmacies**

- Using a local version of the NCI DARF.
- Substituting commercial agents for INDs when the consent tells the patient the drug will be provided free by the NCI.
- Not returning unused drugs when a study closes or transferring to another open study with NCI authorization.
- Having vials of drug unaccounted for.
- Satellite pharmacies must use DARFs too.

**Avoidable Errors in Consents**

- Failure to include CALGB personnel (i.e., auditors) among those authorized to review records.
- Failure to include the Alternatives in exact same text as in the Model Consent.
- Failure to include all side effects present in the Model.
- Failure to include the new info present in the Updates.
Avoidable Errors, Consent Signing

- No consent available at all or only a copy.
- Boxes not filled in with information. The Yes/No responses for companion studies not completed.
- All IRB-required signatures not present and/or not dated.
- IRB-required initials on every page not present.

Avoidable Errors in Data Management

- Participants in cancer control studies are not patients, and thus source documents must be created for each patient contact.
- Keep a “tickler file” for sample collection time points and ancillary data such as XRT and blood/marrow specimens.
Avoidable Errors in Data Submission

• The pathology materials are not submitted at all or in proper fashion (check LabTrak).
• The pathology materials are submitted to the wrong place (one must pay attention to the requirements that apply to CALGB sites stated in the protocol).
• If the correct items cannot be submitted, the PCO, QARC, or LTB should be notified regarding the reason why.

Avoidable Errors in Data Submission

• For complex studies (e.g., 10105) with multiple required blood/marrow/serum sample submissions, it is useful to develop a one-page set of directions for local use.
• For participation in CALGB 8461 a local cytogeneticist must be approved by CALGB to participate before study activation and patient entry.
Avoidable Errors in Audit Follow-up

• Response must be submitted to CTMB within 45 days of submission of the Audit Report. It must be submitted to the CO within 30 days.
• Be sure to respond with specifics, not just “we’ll do better in the future.”
• When a re-audit is necessary, the corrective measures should have been put in place and improvements actually made.

CALGB Data Auditors

Nitpickers, Ad Nauseum
CALGB Data Audit Committee

Club Med for Type A Personalities

Nothing Can Fall Through The Cracks, If There Are No Cracks
Since When Is Obsessive-Compulsive Considered A Disorder?
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.
DAC Issues

• Please respond to messages about potential audit dates ASAP.
• We will be doing more and more CTSU case reviews, including more “endorsed” cases, with no additional funding.
• The audit site is now more of an issue than ever before.
• Notes on the “pink sheets” should be **legible** and written in fashion they can go in report.

Avoidable Errors in Eligibility

• Auditors will declare a patient ineligible **only** when a specific protocol criterion is not followed.
• Close attention to the details of the path. report is essential.
DAC Issues

• When doing pharmacy review, the DARF should reflect only the drug that can be dispensed to the patient; i.e., no pt. returns.
• Excess or expired drugs should be returned to NCI only when they came from NCI.
• All expired, unused, or “damaged” NCI drug should be returned.
• Drugs coming from pharm co. can be destroyed on site with co. authorization.

DAC Issues

• Unannounced pharmacy reviews of drugs will usually involve only the patients already being audited. One may not. Thus, please be sure you do compare patient records to the on-site pharmacy records.
DAC Issues

- Unannounced protocols for IRB oversight should have all items since last audit reviewed, not just the annual renewals.
- Be sure to identify these studies as being “closed and audited prev.” in the report.
- CTMB reminds us that not only should all side effects listed in the Model Consent be present in the local consent version, the “Alternatives” section must be essentially identical to the Model.

DAC Issues

- When writing the reports, please use complete sentences and only recognized abbreviations.
- The companion studies should be so designated in the IRB section, and the number of patients reviewed is “zero.”
- In the Pharmacy section, anytime the “N/A” is used, a comment why is required.
- Please fax me legible and interpretable comments for the pathology and sample submission appendices for revision.
DAC Issues

• For affiliates, the lead physician is the Local Responsible Investigator.
• “Old” delinquencies that were corrected long prior to the audit are not cited. Only those that exist as of the date the Patient List is generated are counted.

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.
CALGB Data Audit System

Instances of Inaccurate Data

• An MD at an affiliate institution entered 26 patients and provided inaccurate data for all of them (1977-1982).
• An MD at a main institution entered 50 ineligible patients on his own CALGB study (1981-83).
• A cytogeneticist at an affiliate institution provided inaccurate data on 9 patients (1989-93).

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.
Avoidable Errors in Stratification

• When registering the patient, please be sure that the stratification is correct. Example of 2 most common errors: # of nodes involved for the adjuvant breast cancer studies and the ER status.

US government suspends clinical research at another university

The US government has ordered a halt to all federally funded human research at the University of Oklahoma College of Medicine in Tulsa, Oklahoma, charging that university researchers carrying out a melanoma vaccine trial had breached numerous safety regulations and that the university's institutional review board (IRB) failed to provide adequate oversight.

Last March, independent auditors looking into the conduct of the trial found that personnel producing the vaccine were unqualified and as a result study participants received vaccines that had not been properly tested for viral and bacterial contaminants. The auditors recommended that the trial be terminated immediately and all the existing lots of the vaccine be either destroyed or labelled: "For research use only-Not for use in humans."

In a letter ordering the halt of federally funded clinical trials at the university, investigators for the US Department of Health and Human Services' Office of Human Research Protections (OHRP) concluded that those statements were misrepresentations. The OHRP also found that the trial's informed-consent documents were also misleading, overstating the possible benefits of participation in the trial, which was a phase I safety study.

But the OHRP investigators also found that university officials and the IRB had not monitored the trial as required by US regulations. They noted that as the trial progressed, numerous changes to the trial's protocol were allowed without IRB approval and "that the IRB failed to conduct substantive and meaningful continuing review of this research since the time of the initial IRB review".

The OHRP said that if the university wants to resume conducting federally supported clinical trials, it must restructure its system for protecting human participants, adding "such restructuring would necessarily include changes in leadership and an enhanced institutional commitment to human subject protections."

THE LANCET - Vol 356 - July 22, 2000
Jury convicts
-------------, MD
of 5 fraud counts

Dr. -------------, the University of Minnesota's
top child psychiatrist, was convicted in federal court
Thursday of falsifying data in a $250,000 drug study.
CALGB Data Audit System

Members Discontinued

• Audit Cycle #1 (1982-84): 33 affiliates
• Audit Cycle #2 (1985-86): 14 affiliates
  1 main
• Audit Cycle #3 (1987-89): 26 affiliates
  1 main
• Audit Cycle #4 (1990-92): 23 affiliates
  1 main
• Total: 99 institutions in 11 years

CALGB Data Audit System

Ancillary Data Submission Deficiencies

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<th>Years</th>
<th>Pathology</th>
<th>XRT data</th>
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<td>1985-86</td>
<td>24%</td>
<td>31%</td>
</tr>
<tr>
<td>1987-89</td>
<td>17%</td>
<td>33%</td>
</tr>
<tr>
<td>1990-92</td>
<td>9%</td>
<td>21%</td>
</tr>
</tbody>
</table>
Original Contributions
A Successful System of Scientific Data Audits for Clinical Trials
A Report from the Cancer and Leukemia Group B
Raymond B. Weiss, MD; Nicholas J. Vogelzang, MD; Bruce A. Peterson, MD; Lawrence C. Panasci, MD; John T. Carpenter, MD; Molly Gavigan, RN, BSN; Karen Sartell; Emil Frei III, MD; O. Ross McIntyre, MD
JAMA 270:459-464, 1993

CALGB Data Audit System
Preparations by DAC Chair

- Assembles audit team and coordinates all travel arrangements, even when not attending the audit himself.
- Works with statistician for patient selection.
- Coordinates provision of feedback for special submissions for central review.
- Usually attends all re-audits.
### CALGB Data Audit System

#### Additional Duties of Chair

- In conjunction with Central Office staff, monitors who is due for audit.
- Works with the Central Office staff to review and edit draft reports before final NCI submission.
- Assists in adjudication of PI responses and complaints and NCI requests.

### CALGB Data Audit System

#### Statistician Duties

- Generates patient lists for initial logistical planning.
- Assists in generation of final patient list.
CALGB Data Audit System

Workload Accomplished

• Most patients on list are fully reviewed in all categories of protocol compliance.
• One pair of auditors can usually review 8-10 patients in one work day.
• If there are 25 records to review, 6 auditors will travel on that audit.
• Experienced CRAs sometimes will do the administrative & prevention-study reviews by themselves.

CALGB Data Audit System

Categories of Deviations

• **Trivial**: A protocol variance so minor it would have no bearing on the study outcome. These are ignored at the audit.
• **Lesser**: The protocol is not followed exactly, but the data are usable and valid.
• **Major**: A protocol variance of sufficient magnitude as to make the data from that patient questionable.
**CALGB Data Audit System**

**Examples of Major Deviations**

**IRB**
- Annual review not performed or performed at interval of >365 days.
- Protocol Updates not submitted for review as required or submitted very late.
- Serious Adverse Events not reported to IRB as required.

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**Consents**
- No signed consent available.
- Consent not properly signed and dated.
- Consent signed after patient was registered on study.
- Patient is non-English speaking, and there is no documentation of consent translation.
CALGB Data Audit System
Examples of Major Deviations

Eligibility

• Wrong diagnosis or wrong stage.
• Prior treatment exceeds protocol limits.
• Pre-therapy tests assessing eligibility were not performed.
• Performance status exceeds protocol limits.
• Concurrent or past diseases exceed protocol limits.

CALGB Data Audit System
Examples of Major Deviations

Randomization

• Wrong stratification.
• Wrong regimen administered.
CALGB Data Audit System
Examples of Major Deviations
Treatment

• Wrong drug is used or a component of a combination regimen is omitted.
• A “significant” number of treatment cycles are omitted.
• A drug dose deviation of >10% that is more than an isolated event or an XRT deviation.
• “Significant” dose modifications made or not done in accordance with the protocol.

CALGB Data Audit System
Examples of Major Deviations
Response and Toxicity

• Failure to record “significant” tumor sites.
• Incorrect assessment of response.
• Major toxicity observed but not recorded.
• An unexpected Serious Adverse Event not reported as required.
• More than an isolated event of drug dose adjustment made but no toxicity.
Examples of Major Deviations

Data Submission

• “Significant” failure to submit required data forms.
• Patient follow-up delinquent >6 months.
• Required submission of ancillary data (XRT, etc.), pathology materials, and blood samples for central review not fulfilled or deficient in quality.

Audit Reports (cont’d)

• Copies are sent to chairs of Membership & Institutional Performance Evaluation committees and DAC members.
• NCI staff in the Clinical Trials Monitoring Branch (CTMB) review all reports.
• CTMB staff may request clarifications, answers to questions, and even require changes in ratings.
CALGB Data Audit System
Audit Report Actions

• PI may rebut or request review by the full DAC at the next meeting.
• PI may warn or drop unsatisfactory affiliates, or the affiliate may withdraw voluntarily.
• The Group Chair or the Board of Directors may warn or drop members.

CALGB Data Audit System
Protocol Compliance Follow-Up

• Deviations and other information learned at the audit that warrant a change in the database are reported to DMC for action.
• Manuscripts for studies where >15% of the total patients entered were audited include this information in the Methods section.
CALGB Data Audit System
Statement for Publications

As part of the quality assurance program of the CALGB, members of the Data Audit Committee visit all participating institutions at least once every three years. The auditors verify compliance with Federal regulations and protocol requirements, including those pertaining to eligibility, treatment, toxic effects, tumor response, and outcome in a sample of protocols at each institution. Such on-site review of medical records was performed for a randomly-selected subgroup of xx (xx%) of the patients treated under this study.

THE LANCET, July 1997

Edinburgh doctor struck off because of clinical-trial fraud
CALGB Data Audit System

NCI Oversight

• Clinical Trials Monitoring Branch: a 7-member staff to oversee clinical trial audits.
• CTMB (or Theradex) staff attend a random 10-15% of regular audits and most all re-audits.
• All audit reports are reviewed by CTMB staff and changes in the results may be requested.

CALGB Data Audit System

Some people use paper clips, others prefer staples. We don’t care which you use, as long as they are polished.
U. S. restores Duke’s medical research funds
Some projects still face review board scrutiny
  U. S. officials, who on Monday halted clinical research at the Duke University Medical Center, lifted the suspension on Friday, in response

CALGB Data Audit System Audit Reports
• A one-page Preliminary Report must be faxed to CTMB within 24 hours of audit.
• Within 70 calendar days the Final Report must be submitted electronically to CTMB.
• Within 45 calendar days any required PI responses must be submitted to CTMB (with a cover note from the Central Office).
CALGB Data Audit System
Audit Reports

• Are generated using an NCI-provided program. Are typed in the Central Office.
• 3 components (IRB/consent, pharmacy, and protocol compliance) are assessed.
• Protocol compliance is rated for each patient in 6 categories as being OK, Lesser Deviation, or Major Deviation.

Clinical Trials:
Data Falsified In Two Studies; NCI Says Results Not Affected

The HHS Office of Research Integrity said it has found that a former data manager for Rush Presbyterian-St. Luke's Medical Center committed scientific misconduct by falsifying research data collected at the center on several participants in two NCI-funded studies.
ORI Says Study Coordinator
Committed Misconduct

The HHS Office of Research Integrity has made final findings of scientific misconduct in the following case:
-------------------, R.N., Northwestern University: Based on an investigation conducted by its Division of Research Investigations, ORI found that ----------------, while serving as clinical coordinator for the Collaborative Ocular Melanoma Study (COMS) at Northwestern University, committed scientific misconduct by falsifying clinical trial data.

The Lancet, August 1997

Karolinska Institute rocked by research misconduct
University acknowledges violations in 3-year cancer study
Review: Chief researcher and oversight official broke patient-safety regulations. University seeks new dean after vaccine scandal. U president announces changes

Research Integrity
ORI Finds Student Of Collins Falsified Research Data

The HHS Office of Research Integrity said it has made a final finding of scientific misconduct in the case of a former research trainee who worked in the lab of Francis Collins, director of the National Center for Human Genome Research at NIH.
DISQUALIFIED/RESTRICTED/ASSURANCE LIST FOR CLINICAL INVESTIGATORS

FDA regulates scientific studies in human or animal subjects that are designed to develop evidence of the safety and effectiveness of investigational human or animal drugs, biological products, or medical devices. The data from these studies may form the basis of an application to FDA for marketing approval of the tested products. These studies are conducted by physicians and other health care professionals who are required to conduct these studies in accordance with FDA and other applicable regulations and rules.
NIH Orders Duke Medical Center To Stop Enrollment In Human Research Studies

The NIH Office of Protection from Research Risks earlier this week ordered Duke University Medical Center to suspend enrollment in all of its 2,000 research studies that involve human subjects.

OPRR officials said the agency took this drastic action May 10 because Duke was slow to improve its human subjects protection procedures, despite being directed to do so five months ago. The issue of Duke's compliance with federal regulations arose following a random site visit last December, officials said.

Problems listed by OPRR included failure of the medical center's Institutional Review Board to oversee studies after they began, failure to......

The Cancer Letter, 14 May 1999

N. Y. Research Centers Faulted in Child Study
Patient Protection Is Found Lacking

The Washington Post; June 12, 1999

The federal Office for Protection from Research Risks (OPRR) said the Mount Sinai School of Medicine and the City University of New York breached federal regulations meant to protect human subjects in a study several years ago of elementary school children with attention deficit hyperactivity disorder.
The CALGB Data Audit Committee Dictum

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

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

**Unscrewed up!**

To All You Demanding, Hypercritical People Out There---

You Are Not Alone
Exposure of Surgeon’s 13-Year Deception Has Heavy Public Impact

Washington Post, April 13, 1994