

Meet Joe The Detective

Oxaliplatin: No More Red Herring

The secret is out: we have plenty of oxaliplatin, both sizes! We suspect that when placing drug orders, you'd like to base the number of 50 mg and 100 mg vials on the patient's BSA to avoid waste. For example, if you have a 1.72 m² patient and an 85 mg/m² dose, you want to order one 50 mg and one 100 mg vial per dose. Now, you can do that!

Sanofi is no longer manufacturing oxaliplatin powder (NSC 266046), so all sites will use oxaliplatin liquid for NCI-sponsored studies. E5202, our only study using NCI supplied commercial Eloxatin, will switch from oxaliplatin powder to liquid soon, and PMB will only supply 100 mg Eloxatin vials for that trial.

inside PMB

February 2009

Dummmmm-Dum-dump-DUMB!*

Agent Returns

Please remember to complete all information requested on NCI Investigational Agent Return Forms completely and accurately. Surveyors query the return database as they generate audit reports for site visits, and they expect accurate information. Sites often ask for documentation of a return (because they submitted incomplete and inaccurate paperwork, and the auditors are there), and sometimes we can't provide it, or it will take more time to find it than you like.

- The only documentation required to be provided with returns is the NCI Investigational Agent Return Form. Don't stuff anything else in there! Don't send copies of Drug Accountability Record Forms or copies of the PMB-issued stock recovery letter!
- If you're returning patient-specific supplies of NCI-supplied agents—please engage in cover-up activities: make sure no personal identifying information is on the agent label (i.e., "black-out" patient names).
- Double check the protocol for the source of the agent supplies. If the agent is supplied by somebody other than CTEP, please don't return it to the NCI Clinical Repository! Many cooperative group studies are now using agents supplied through other sources. Follow the protocol-specific return instructions for those non-NCI-supplied agents.

According to recent research, fingerprints can be recovered from difficult surfaces like paper using disulfur dinitride. We will be ordering this chemical, and tracking you down!

*Sing to the DRAGNET tune!

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Joe the Detective...At Your Service

Used to be you had to hire a detective to find information. The Internet and technology have changed that now, and detectives named "Joe" are now called "Google."

Technology has simplified the conduct of clinical trials in many ways; it has also accelerated their pace. For our customers, technology has made information retrieval easier, and we happily announce a newly designed web site that is even better than the old one. You can be your own detective in the following ways:

- The most current version of all CTEP forms are readily retrievable; see page 2 to see why you should update your forms.
- PMB's slide show and explanatory notes, "Investigational Drug Handling," are new and improved!
- We've added a Frequently Asked Question section.
- You can determine if the IB in your hand is the most recent available to PMB.
- You can check to see if your investigator's registration is current! All by yourself! From your desk!

Please visit <http://ctep.cancer.gov> today!

Please note that this motif is no accident; finding things on the new web site takes a little bit of looking. Can't find something? Please contact us and we'll help!

Stock Recovery Letters: Read the Fine Print

We've had a bunch of calls from folks who receive stock recovery letters from us, and cannot find the lot number on the agent's label.

Just so you know, blinded supplies are not labeled with a lot number; they have a Julian date. Letters referencing lot numbers apply only to open label stock.

No lot number!
It's blinded supply!

Cozy Mystery or Police Procedural: Correct Form, Current Process

Some private investigators specialize in white collar crime. One clue that something's amiss is finding information on an outdated form, or worse, one that was issued after the form was allegedly completed.

CTEP's Protocol and Information Office (PIO) is the central hub for all protocol-related information management for CTEP sponsored trials. The PIO's mission is to coordinate all administrative aspects of clinical trial development to assure that quality protocols are developed in the most expeditious and efficient manner possible. Towards that end, PIO collects, processes, tracks and monitors all protocol-related information between CTEP and its extramural collaborators (investigators, Cooperative Groups, Cancer Centers, FDA, pharmaceutical industry, other NCI programs, etc.).

The PIO is making a concerted effort to ensure its collaborators have access to the most recent forms and processes.

PIO happily announces that you can find updates to CTEP processes and forms on the recently redesigned CTEP web site.

You'll detect them at the PIO Landing Page (<http://ctep.cancer.gov/branches/pio/default.htm>). At the bottom of the page under "Process and Forms Update," you'll find lists of updated forms and/or processes by date. En-trench the habit of using the web site regularly to obtain information regarding processes and/or revised forms. Always use the most current version available.

Please continue to e-mail PIO at pio@ctep.nci.nih.gov with specific questions and concerns.



Short-Dated Stock: Accent on Action

Recently, we've had some issues with short-dated supply. Our inventory approaches expiration, but the company cannot resupply until close to the expiry date. This situation troubles us, and it probably annoys you, too! When this happens, this is what we do:

- ▶ We limit the amount of drug we send if you order.
- ▶ We type a note on the shipping receipt telling you all of our inventory is short-dated.
- ▶ We nag at the company!

If you are replacing investigational agent simply because it is expiring, always

- ▶ Put a note in the "comments" section saying when all your stock is due to expire, and you need better dated stock.
- ▶ Continue to use your inventory right up to its expiry date!

The Job: Not Finished until the Paperwork is Done....And Maybe Not Then

Recently, HHS finished its annual sleuthing—watching, observing, and quietly following cancer statistics. The result: its Annual Report to the Nation announced that mortality and incidence rates in all cancers have declined in men and women of most races and ethnic groups but American Indian/Alaska Native.

This is the first time they've included incidence rates (new cases). Overall incidence rates decreased by 0.8% per year from 1999 through 2005 for all cancers combined. In men, the rates declined by 1.8% per year from 2001-2005 and by 0.6% per year from 1998-2005 in women. The authors consider this decline dramatic in the three cancers (prostate, lung, and colorectal) most common in men and the two (breast and colorectal) most common in women.

Mortality rates for all cancers increased 0.5% per year from 1975-1990. Then from 1990-1993 and from 1993-2002, the cancer death rates decreased 0.3 percent per year and 1.1% per year, respectively. Men lead the death rate decline (2% per year, from 2001-2005) whereas the rate in women was only 1.6% per year from 2002-2005. This significant progress is believed to be the result from advances in cancer control: early detection, prevention, and better treatment regimens.

Screening and diagnostic practices might be responsible. For instance, in colorectal cancer, the decline correlated with increased screening and precancerous adenomatous polyps removal. Colonoscopy increased by 20% from 2000-2005 in adults aged 50 years and older, while fecal occult blood testing decreased 5%. Improved mammography use has markedly improved breast cancer's statistics; although breast cancer incidence increased 1.7% per year from 1994-1999, it decreased by 2.2% per year from 1999-2005.

A twist in the plot: prostate-specific antigen (PSA) screening has not significantly influenced prostate cancer's picture. PSA testing frequency increased during visits for a general medical examination from 1995-2002, then leveled off until 2004. The recent decline in prostate cancer may be due to a decline in detection, or decreased number of undiagnosed men.

Smoking is still a major smoking gun. The trends in lung cancer, tobacco control and tobacco use vary across geography and by age. In 13 states, lung cancer death rates for women are rising. It was in these states that butts left in ashtrays were more likely to have lipstick on them, if you know what we mean. These states also have low excise taxes, and local economies dependent on tobacco farming and production. While tobacco use has declined in adults, our youth haven't quite gotten the message yet—they still light up. Sadly, cigarette smoking is responsible for 30% of all cancer deaths in the United States, despite reduction in smoking prevalence. Other cancers associated with cigarette smoking are pancreas, liver, pharynx, larynx, esophagus, stomach, bladder, kidneys, and cervix.

We've reduced the mortality and incidence rates of breast, prostate, lung, and colorectal cancers, but more research is needed in these cancers, and in leukemia, NHL, myeloma, kidney, brain, testicular, and female thyroid cancers—their incidence has increased. You don't need to be a private eye to see that we must supplement our focus in cancer research—identifying cancer early and developing personalized/targeted therapies—with public health initiatives. In particular, large state and regional differences in lung cancer trends among women underscore the need to strengthen state tobacco control programs.

Prudent Use of PMB Web Site: It's a Lifesaver!

Pharmacist Plum is found dead in a dark stairwell. Next to him is an empty cup of coffee and a hand gun. What happened?

Suspects: motive, opportunity, and means

- Mr. Green, R.Ph., is pursuing a PharmD degree and completing his hospital clerkship. Mr. Green repeatedly used commercial agent instead of investigational supply for an NCI-sponsored study. (To see the correct way to deal with this problem, find the FAQ at <http://tinyurl.com/bhohns>.) Plum recently told Mr. Green that he was failing his hospital pharmacy clerkship.
- Patient Peacock is a widow on a limited income. She was recently overheard telling Dr. Plum that he needed to order a 16 week supply of investigational AZD6244 for her so she could take it on her round-the-world cruise. He refused.
- Mrs. White is a pharmacy technician who works the night shift. She was the last person to see Plum alive—she found Pharmacist Plum dead and called 911.
- Colonel Mustard works at a different hospital and forgot to order study medication from PMB. His patient was scheduled for treatment the morning after Dr. Plum's death. When he heard about the murder, he called Mrs. White and said that Plum had agreed to loan him investigational study agent the evening before. (Borrowing? See <http://tinyurl.com/afd33c> on transferring investigational agent.)
- Miss Scarlet is a nurse practitioner. She recently argued with Dr. Plum over a study order that she'd written. (Is she authorized to write an order? See the FAQ at <http://tinyurl.com/ahwqzh>.)

Clues:

An ECOG auditor discovered that:

- Mr. Green had been falsifying records.
- Mrs. Peacock was neither poor, nor a cancer patient. The actual patient was her now deceased 4th husband and somehow the staff had not realized that Mr. and Mrs. Peacock's first name's were similar: Carmen/Carmin.
- Mrs. White was having an affair.
- The site had illegally transferred study medication to an unaffiliated site. Several times, even. Colonel Mustard wasn't lying!
- Many orders at the site had been written by nurse practitioners or physician's assistants without a co-signature.

Who killed Dr. Plum?

Although Mr. Green was upset because failing this rotation would put him on academic probation and had wanted to kill Dr. Plum, true to his habit, he carelessly grabbed NaCl instead of KCl. He also didn't realize that KCl has to be injected to be fatal and he put it in Dr. Plum's coffee. Plum had actually spit his coffee out before he died, thinking a prankster had filled the sugar dispenser with salt.

Mrs. Peacock (a retired veterinarian) was angry enough to kill because Plum refused to give her the 16 week supply. She was using the AZD6244 to treat her beloved but dying beagle, Poopsie. She didn't kill Plum but was later arrested for the murder of her previous 4 husbands. Plum should have realized something was amiss; poor widows don't take cruises!

Colonel Mustard just wanted his study medication to treat his study patient.

Miss Scarlet, a notorious gossip, initially appeared to have killed Plum because she began spreading stories about the White/Plum affair. The stories ultimately proved true; the ECOG auditor just happened to be Mrs. White's husband and had walked in on the nefarious pair during the audit.

Mr. White accidentally killed Plum...but not because of the affair. (Mr. White was actually in love with Colonel Mustard.) Mr. White met Plum at the top of the stairwell. They argued about the abysmal pharmacy audit results. White told Plum he was finished and that he was going to lose his pharmacy license. Plum pulled out his handgun to kill White, there was a struggle and Plum lost his balanced and fell down the stairwell to his death.

Whodunnit?

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Revised Web Site! Please Update Your Links!

CTEP Home page	http://ctep.cancer.gov/
PMB's Main web page	http://ctep.cancer.gov/branches/pmb/default.htm
Investigator Registration (forms)	http://ctep.cancer.gov/investigatorResources/investigat_or_registration.htm
Investigator Registration Expiration Date <i>NEW!</i>	http://ctep.cancer.gov/branches/pmb/expiration_date.htm
CTEP Forms (CDR; DARF; Return Agent form; Transfer form; and policies)	CLICK on "Protocol Development" on the task bar on the CTEP home page; then on the drop down select "Agent / Drugs"

CONTEST: You Be The Detective!

Find this information on the web site, and copy the web site link into an e-mail. Fax your answers to (301) 402-0429, and you'll be eligible for our drawing to win homemade cookies or dog biscuits!



Provide the link for

1. CTCAE v 3.0.
2. PMB's Policy and Guidelines for Investigational Agent Distribution.
3. A cytochrome P450 drug interaction table.
4. The NCI Clinical Trials Cooperative Group Program Guidelines for Development, Conduct, and Analysis of Clinical Trials with International Collaborating Institutions.
5. A description of the NCI's Clinical Trials Cooperative Group Program.

Mystery Solving: Ongoing Suspense

Several investigators have renewed their registration paperwork, only to find that their NCI numbers are still suspended. We hired Joe the Detective to determine why. He ferreted out the explanation:



A number of investigators still have pending Special Exceptions (SPEX) paperwork with CTEP. Once PMB approves an investigator for a SPEX protocol, he or she must submit the following information:

- A signed protocol
 - A patient summary report (Report of Independent Investigator)
 - If applicable, an AdEERS adverse event report
- If any of this information is missing, your NCI number may still be suspended. To get the suspension lifted, please call PMB and ask to speak with the Special Exceptions Coordinator for further assistance.

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Yo Joe! Figure it Out!

Detectives use unusual mental acumen to unravel a mystery—sometimes. Sometimes, they just use experience. Strictly speaking, a detective is a policeman or private detective, but anyone who possesses analytic ability or imaginative ratiocination (Look it up! It's a real skill!) can sort out puzzling investigational agent quandaries.

Detective's Dilemma	Description	PMB Equivalent
Suspected Infidelity	Joe the Detective is hired to determine if a blonde's spouse is cheating. His photographs show the investigation's target consorting with a red head!	PMB suspects that a site's DARF balance is incorrect because they used commercial agent instead of NCI-supplied agent. It happens so often, we have an FAQ about this!
Possible Embezzlement	A company asks Joe to review their financial records to determine why it looks like money is missing. Reviewing all of their documentation, he finds that the comptroller has absconded with millions!	A site calls and says that the balance on their DARF is wrong, and they think it's because PMB shipped the wrong quantity of investigational agent. PMB's slide show, "Investigational Drug Handling," available on the web site, explains how to receive and track agents correctly.
Probable Malingering	Wearing dark glasses, a nondescript hat, and binoculars, Joe shadows a fellow who's on disability to see if what the insurer suspects—his back is bad when he needs to work, but he plays tennis daily—is true.	Jane the IDS person is busy. Regardless, she acts on every stock recovery letter by pulling the expiring agent. But she misses the part about returning the agent to NCI within 90 days. Auditors will call you on this; see page 1 re: returns!
Illegal Dumping	Emerald City is having trouble with illegal dumping, probably because their dump fees are high. Joe is hired to stake out a dark stretch of road littered with dead refrigerators, old sofas, lumpy mattresses, and broken lawn machines.	A site destroys NCI-supplied agent without permission. Always return unused DCTD-supplied investigational agent to the NCI Clinical Repository when studies end and the agent cannot be transferred to another protocol, or the agent is outdated, damaged or unfit for use. For the exact procedure and an FAQ, see the web site.

PMBAfterhours

Do you have a question and need an answer soon, but not necessarily right this minute?
E-mail pmbafterhours@mail.nih.gov, any time day or night!
Expect an answer on the next business day.

LOOK FOR INSIDE PMB QUARTERLY
NEXT ISSUE: May 2008