Pharmaceutical Management Branch
Cancer Therapy Evaluation Program
Division of Cancer Treatment and Diagnosis
National Cancer Institute
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What's that again?

The protocol said administer it "T.B."
And Shirley said, "Good gracious, how must that be?"
Is that some novel way
To give agents, you say?
And PMB provided the answer for free!

Shirley uses E-mail to learn that "T.B." is a new topical administration technique: turkey baster! Have a question about agent availability, the best way to get agents fast, or if an order was even ever faxed?

E-mail pmbafterhours@mail.nih.gov.
Expect an answer on the next business day.

It's in here somewhere....

Often, working at PMB is like fishing around in the kitchen junk drawer. You need information, we have it, but it's a matter of putting our hands on it without being jabbed by something else. And sometimes, you need information, we should have it, but it's either not where it should be or it doesn't exist.

For the most part, the questions we field from you are pretty straightforward–so straightforward that most of us anticipate these questions when we start working with a new agent, and ask the company for information before you make your first call (because your refrigerator broke or the patient's line extravasated). But other times, you surprise us with your queries, and we initiate a fact-finding mission that delves through the dark and not-so-pretty places that constitute investigational drug development.

This issue of INSIDE PMB represents the start of our 7th year. You can find all previous issues on our web site (ctep.cancer.gov) on their own landing page at http://tinyurl.com/37wbyxs. As always in August, we've changed our format a lot and our focus a little. We welcome your feedback. Please e-mail us at pmbafterhours@mail.nih.gov.

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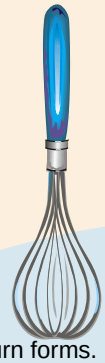

Kitchen Junk Drawer

When YOU Toss Stuff into OUR Junk Drawer

Each month the NCI Clinical Repository processes 400 to 500 Investigational Agent Return forms. That's 5000 to 6000 pieces of, well, junk—agents we sort, count, track, and document with the sole purpose of destroying them. This is, needless to say, time-consuming.

Lately, we've received (and that means you've submitted) some forms that didn't seem to have your full attention when you completed them. When you do that, you create audit compliance issues down the road—for yourself. When you return agent to the NCI, you are wholly and utterly responsible for making sure the form is complete and accurate (i.e., correct investigator name and number, correct NCI designated protocol number, correct lot dispensed by NCI, etc.). This is what appropriate documentation must have:

- The investigator name and number. The correct name and number, actually. If the name and number do not match, we don't play a guessing game as to which one is correct. Further, and this is a further as long as the piece of butcher's twine in your drawer, *we have to know exactly which institution is returning the investigator's agent supply.* Investigators move from site to site and sites even change their names, so don't scramble things up. Get the correct investigator and site!!!
- Only one investigator on each form. If you include multiple names, again we won't guess and the return will not be documented under any investigator's name.
- The NCI-designated protocol number on the return form. If this is not provided, again the return will not be properly captured and will not show-up on an audit report for the site.

If you mess up these items, we won't link the return to the correct protocol or investigator in our system. Consequently, it won't appear on an audit report for your site. The auditor will look at your drug accountability record, and be unable to find documentation that you returned the drug. They'll ask if you really returned the agent, and then you'll call here looking for documentation. And we'll start looking for the alleged return, but we won't be able to pull it up by the protocol number or investigator, so we'll start looking in other ways. It can take hours. Even if we find something that theoretically matches your return, it won't really verify the return.

When you dig around in your junk drawer, is a can opener generically equivalent to a screw driver? Nope! What we are saying here is, please don't use the Clinical Drug Request form for returns to the repository. The current return form is available on the CTEP web site (http://ctep.cancer.gov/forms/docs/return_form.pdf).

And double check this: Where did the agents really come from? (Look in the protocol if you aren't sure.) If you didn't get it from us, don't return it to the NCI Clinical Repository! The repository needs to document these returns for disposal purposes, but we will not send a return receipt for agents we didn't supply. Follow the protocol-specific return instructions for those non-PMB-supplied agents.

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Next issue:
November 2010

OAOP

PMB's Online Agent Order Processing (OAOP) shipment notification module went into production on Thursday, July 22, 2010. Ordering and Shipping Designees (and investigators if they enter orders into OAOP in the future or have no ordering or shipping designees who enter orders for them) will receive notification that an order has shipped. The e-mail will contain the order details and shipment date for U.S. Priority Mail shipments, and the order details, shipment date, tracking number and link to the express courier web site for express courier shipments.

Continue to fax Clinical Drug Requests to PMB for now, but you'll be able to submit online Clinical Drug Requests soon!

How is a Registration Packet like a Melon Baller?

PMB's staff is frequently asked, "Did you send me my registration packet?" PMB routinely mails renewal packets to investigators or their registration coordinators 60 days before their annual expiration date. We follow up with a warning letter 30 days prior. Before calling PMB, check the back of your paper junk drawer to see if your renewal packet went the way of the melon baller. (You might want to remind investigators that they cantaloupe with the manilla envelope that comes from PMB every year.) We will send another investigator specific registration packet if you need it (e-mail PMBRegPend@ctep.nci.nih.gov with your request) or you can download blank forms at http://tinyurl.com/8tz629.

Unlucky enough to have your registration suspended? Please allow time for PMB to receive and process the renewal. The time varies depending on how you sent it to us: approximately 10 days for USPS and two to five days for express courier. An easy way to check the expiration date for a specific investigator is to query our database at http://tiny.cc/dsuse.

If sufficient time has passed and your registration is still not renewed, call PMB at (301) 496-5725. Some key points to bear in mind when sending your renewal:

- Keep copies of all documents
- Keep tracking information for all important packages
- Remember to sign and date the 1572, the IDF, and the FDF
- Don't leave any fields on the 1572 blank (NA for IRB or LAB does not make the FDA happy)
- Do not send your registration packet to the FDA (guaranteed to end up in someone's junk drawer with the melon baller!)

And skewer this to your bulletin board: the FDA-1572 form and FDF form require an original signature, not a copied one.

Cooperative Groups:

Since 1955 when Congress approved increased support for studies designed to identify chemotherapy to fight cancer, the NCI has sponsored the Clinical Trials Cooperative Group Program. This program

- promotes and supports clinical trials of new cancer treatments
- explores methods of cancer prevention and early detection, and
- examines quality-of-life issues and rehabilitation during and after treatment.

More than 8,400 institutions and 14,000 individual investigators enroll about 25,000 patients on group-conducted clinical trials each year. Although the groups all develop and conduct large-scale trials in multi-institutional settings, their structures and research focus differ. They may focus on a medical specialty (e.g., pediatrics), a specific type of cancer therapy (e.g. radiation) or a group of related cancers (e.g. gynecologic or leukemia). This means that their administrative and clinical issues also differ.

Some cooperative groups have pharmacy committees. These committees identify and discuss problems related to the use of investigational agents, and plan corrective action. If you want to become involved with a cooperative group pharmacy committee, refer a problem, or simply learn about the topics they discuss, consider contacting a pharmacy committee chairs and co-chairs, listed here:

ECOG: Eastern Cooperative Oncology Group
Virna Alumuete, Pharm.D., BCOP
E-mail: valmuet1@jhmi.edu

George Carro, RPh, MS, BCOP
GCarro@northshore.org

Stu Guenther, RPh
guenther.stu@marshfieldclinic.org

SWOG: Southwest Oncology Group
Siu-Fun Wong, PharmD, FASHP, FCSHP
E-mail: sfwong@llu.edu

Gerry Migaki, RPh
E-mail: Gerald.Migaki@providence.org

CALGB: Cancer and Leukemia Group B
Christine M Berard-Collins, MBA, RPh
E-mail: ccollins2@lifespan.org

COG: Children of Oncology
Mark K. Sorenson
E-mail: mark-sorenson@uiowa.edu

Michael Kellick, MS, PharmD
E-mail: kellickm@mskcc.org

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Old Condiments Packets are Junk, and Other Lessons

In the mishmash of a kitchen junk drawer, you'll often find unit dose packets of condiments. If it's a common condiment like ketchup or mustard, and the plastic is still shiny and intact, it may be OK to use it in a pinch. If it's tartar sauce in Nebraska or wasabi in Maine, and the package is dull and dirty, you'll prudently decide it's reached the end of its useful life, and destroy it according to your local destruction policy.

Sites often have a mishmash of inventory for clinical trials despite their best efforts to be organized. Be sure to check your inventory routinely for expired agents or agents left over from completed trials. (More than the usual number of protocols have been completed in the last six months.) If anything looks fishy or seems too hot to handle, check to see if you still need it.

Please return expired and unneeded supplies to the NCI within 90 days of expiration or study closure

QUESTION: Yesterday, you dispensed an eight week supply of investigational agent to a patient who lives a few hours away. Today, you received a stock recovery letter from PMB indicating that the agent's shelf life date is the end of the current month. Do you need to retrieve the investigational agent and replace it with better-dated stock? What's the cookie cutter answer?

ANSWER: You do not. Our stock recovery program is for inventory that remains in the pharmacy only. There is sufficient wiggle room in the shelf life date so that patients can continue to take the agent for up to 2 to 3 months.

This is not the case if the agent is recalled for stability or sterility reasons.

Peeling the Layers: CAEPRs, RAs, and RRAs

Susan Westcott, R.Ph., MBA, of the Mayo Clinic, Rochester, MN asked that we explain recent changes related to Action Letters*, and the required use of the Comprehensive Adverse Event and Potential Risks (CAEPR) in CTEP-supported studies. We've pulled out our potato peeler, and will work down through the layers.

The outside peel is this: If CTEP has a CAEPR for an agent, protocol authors must include it in any protocol that CTEP reviews regardless of the source of the agent (CTEP, commercial, company, etc). When the CAEPR is used in protocols that have no CTEP IND agent, you may remove the Agent-Specific Adverse Event List (ASAEL) column of the CAEPR if it makes you happy!

The next layer: We've just finished updating all CAEPRs from CTCAE v3.0 language to CTCAE v4.0 language.

- Some of those updates involved only a language change–we swapped out a lot of adverse event (AE) terminology. For example, v3.0 "peripheral neuropathy" is either "peripheral motor neuropathy" or "peripheral sensory neuropathy" in v4.0. If the only change is language, we sent a Request for Amendment (RA) and no Action Letter**.
- In some CAEPRs, there were language changes plus AE changes, and we sent an Request for Rapid Amendment (RRA) and an Action Letter.

To prevent any further gouging out of eyes: Since all CAEPRs are now in CTCAE v4.0 language, CAEPR updates should go back to the more normal once/year (if that–we won't update if we have no substantive change), and most of them will be RRAs and have an Action Letter.

PIO sends the CAEPR along with LOI/Concept approval letters for all investigational agents listed on studies if we have one. Sites can always request a CAEPR from PIO. As we do with investigator brochure (IB) requests, PIO will check to see if the investigator requesting the CAEPR has a legitimate need for it–an approved LOI, a protocol in the works, etc. Unlike IB requests, however, PIO will only release CAEPRs to the lead organization.

CTEP launched the first phase of a secure web site on Monday, July 26. Eventually, we hope to offer different libraries that folks with appropriate roles can access. One library will be CAEPRs. We'll eventually make PDSs and IBs available in similar libraries.

Susan, who appears to be razor-sharp, will receive a bag of cookies (closed with at twist-tie from PMB's junk drawer) for suggesting this article. And, yes, that is a hint.

**CTEP issues an Action Letter when new risks are added or the risk/benefit ratio to participants increases significantly. Sites must send Action Letters to their IRB immediately upon receipt. CTEP suspends accrual (and in rare situations, treatment) until a site submits an amendment and sample informed consent incorporating the new safety information.*

***An RA is not followed by an Action Letter, patient notification is unnecessary, and accrual may continue.*

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New Patient Page

For the next four issues of INSIDE PMB, we'll provide information you can use to help patients. Below, find our first attempt to help address one of the more common problems patients face when taking an investigational agent. Cancer patients often have comorbidities and complications of their cancer treatment. When they seek care from regular prescribers or at the emergency department, they often cannot answer the health care teams' reasonable questions about their study agent. You can fill out this template so all stakeholders will know what the patient is taking, and if there are any significant interaction concerns. Find the scissors and clip here:

Information for Patients and Their Caregivers and Non-Study Health Care Team

The patient _____ is enrolled on a clinical trial using the experimental agent _____. This clinical trial is sponsored by the National Cancer Institute. This form is addressed to the patient, but includes important information for others who care for this patient.

Many health care prescribers can write prescriptions. You must tell your other prescribers (doctors, physicians' assistants or nurse practitioners) and your regular pharmacist that you are taking part in a clinical trial. **Bring this paper with you to all appointments and emergency visits**. Because investigational agents have only been tried in few patients, we sometimes don't know about possible side effects or drug interactions. This table lists possible problems. We've "checked" to indicate if these common concerns are a problem while you are taking _____.

YES	NO	Don't know	POTENTIAL CONCERN
			_____ is drug called a CYP(circle those that apply) strong/moderate/weak enzyme inducer/inhibitor or substrate. CYP enzymes are present in your liver. _____ must be used very carefully with other medicines that need certain liver enzymes to be effective or to be cleared from your system. • The specific enzymes are (circle those that apply; cross out those that do not) CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, and CYP3A4/5/7. • Before you started the study, your study doctors worked with your regular prescriber to switch any medicines that use the enzyme(s) listed above. • You and healthcare providers must be careful about adding or removing any drug in this category. • Your regular prescribers should look at this web site http://medicine.iupui.edu/clinpharm/ddis/table.asp to see if any medicine they want to prescribe is on a list of drugs to avoid.
			If you take acetaminophen (Tylenol) regularly, you should not take more than 4 grams a day if you are an adult or 2.4 grams a day if you are older than 65 years of age. Read labels carefully! Acetaminophen is an ingredient in many medicines for pain, flu, and cold.
			If you drink grapefruit juice or eat grapefruit, avoid them until the study is over.
			If you take herbal medicine regularly, tell your doctor.
			_____ has been know to prolong the QTc interval. The QTc interval is the length of an electrical cycle in your heart. The faster the heart rate, the shorter the QT interval. A prolonged QT interval is a risk factor for irregular heart beat and sudden death. Your regular prescribers should look at this web site http://www.azcert.org/ to be sure they do not add a drug that prolongs the QTc interval to your regular drugs.
			If you are taking an anticoagulant, your regular prescriber should not change your dose without notifying your study doctor.
			Your regular prescriber should check a medical reference or call your study doctor before prescribing any new medicine for you. Your study doctor's name is _____ and he or she can be contacted at _____.

This patient information sheet was completed by _____ on this date _____.

I am a nurse/pharmacist/doctor, and you can reach me at _____.

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