

Going Camping!

Welcome to Camp!

It's August, it's hot, air fares are higher than ever, so the NCI's Pharmaceutical Management Branch is taking you on a camping trip. Warning: It's a primitive campsite with a box privy, not the Hilton! So make a list, and pack your duffle then d-ra-a-a-g it to the car and lift...it...inside...the trunk! There! Success, and now you can squabble with your coworkers about who will be the "Oreo filling" in middle in the back seat. In a few short hours ("Are we there yet?") you can tug...the bag...out of...the trunk (is that sweat already?) and drag it to the campsite. Slap on some bug repellent and sunscreen, and we are off and running!



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INSIDE PMB



LOOK FOR INSIDE PMB QUARTERLY
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Be Prepared: Not Our Motto, But a Good One! ALERT! ALERT!

Always good to bring a Scout (or former Scout) with you if you're going camping because they live their motto, "Be Prepared." Someone once asked Scouting's founder, "Be prepared for what?" His response?: "Why, for any old thing."

Letters Home

Sometimes, camp is not so great and you get melancholy. It's kind of embarrassing because all your first letters home said camp was awesome, you loved your bunk, and you were making so many friends. Homesickness strikes and you write a stupid letter about how you want to go home, want your family to come visit, need to see your dog...And your family panics.

We get those missives from you, too, and we panic. And just like your darned homesickness-spewing letter, your communication with us leaves us worried. What do you want? When do you want it? How can we help you? The chances are you've moved on, gotten involved in leather crafts or horseback riding, and you're just fine. Regardless, some tricks can help you communicate your needs without putting us into a panic:

- Don't use "ASAP" for needed by date when ordering agent; use a real date.
- Set your fax machines so they display a banner with your institution's name and phone number at the receiving end (so we know who sent it if we can't read your handwriting).
- Treat yourself to a clean, bright form from our web site instead of re-using copies of copies of copies of faxed forms (especially order forms).

PMB is happy to announce that we now offer a training module so you can be prepared for any old thing related to investigational drug handling. This training is the Swiss knife of all training, and covers topics from investigator registration to ordering to returning investigational agent, and everything in between. And it has a touch of animation to keep you on your toes! To access the training, go to the CTEP camp site (<http://ctep.cancer.gov> -with no "www" in the address, by the way). Look at the yellow vertical banner on the right and scrooooooolllllllll down. You'll find a link called "Investigational Drug Handling Slide Show." Double click and you will find clear directions how to proceed.

Send your comments and questions to pmbafterhours@mail.nih.gov.

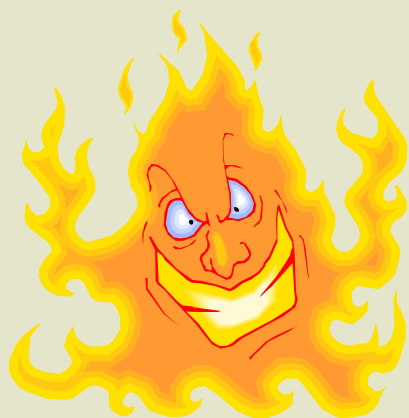
PMBafterhours

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.

Group Picture or Just a Snapshot?

Sometimes we get notes from you that ask, "Why do you keep sending agent stock recovery letters to individuals no longer working at our site? Can you change the name of the individual to whom the letters are sent?"

The simple answer to these questions, unfortunately, is "no." Stock recovery letters are generated and sent to two groups: 1) the responsible investigator to whom we shipped the agent and 2) the shipping designee at the address at the time of the shipment. We send one copy to the investigators' current FDA Form 1572 office addresses, as they are ultimately responsible for the agent; while the shipping designee and address is captured by a "snapshot" in time (i.e., at the time of the shipment). PMB cannot "erase" the shipping designees from the picture; it would make the historical information in our database inaccurate. By sending communication to multiple individuals, our expectation is that the information is received by or forwarded to those individuals that actually need to take some kind of action. Get the picture?



Although we never advocate playing with matches at camp, sometimes you have to fight fire with fire. We don't mean rubbing two sticks together until you see a wisp of smoke; we mean having a long, durable, multi-purpose butane lighter with a visible fuel supply window so you can light a fire under a person or process when necessary. At Camp PMB, Registration Coordinators (RC) are the counselors who light a fire under investigators. We received a HUGE response from our last article about Registration Coordinators, so we're sending out more information on how being an RC can help your site!

Who? RCs can be anyone who helps investigators process their annual paperwork, like administrators, clinical research personnel, pharmacists, and research nurses.

Why? RCs receive the annual investigator registration (IR) forms directly, so they don't have to wait for the doctors to pass them along, which saves valuable time. RCs help prevent registration delays by ensuring forms are complete, and if we have questions during processing, we contact them directly—not the doctor. They ensure that files are complete by keeping copies of submitted documents. Registration is the gateway to protocol approval, patient registration, and drug shipment, and RCs keep the process running smoothly!

What should I expect? You won't receive drug or protocol status information—only the investigator will. But, you'll get the registration forms automatically two months before the registration expires. There's no confirmation of re-registration from PMB, but you can email the IR Team at pmbregpend@ctep.nci.nih.gov to find out your investigators' statuses. To add new doctors at your site to your list, just include a cover letter when you send their registration forms.

If you want to be an RC, email the CTEP Registration Help Desk at ctepreghelp@mail.nih.gov with the subject line "Make me an RC," or call the CTEP Registration Help desk at (703) 738-9171 with questions.

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Upgraded Amenities

Oxaliplatin (NSC 266046): 50 mg vials are back!!! If you need s'more, send an order!

AZD6244 (NSC 741078): A new 25 mg capsule formulation will be used for some NCI protocols. Canoe imagine that the new capsules and current "mix and drink" formulation have markedly different pharmacokinetic profiles? For example, the capsules' maximum tolerated dose (MTD) is 75 mg twice daily whereas the "mix and drink" MTD is 100 mg twice daily. Each protocol will use only one formulation. Please be careful! Request PMB approval before transferring AZD6244 from one protocol to another.

Temsirolimus (CCI-779, Torisel®, NSC 683864): Soon, all NCI trials will use 25 mg commercial Torisel, which is mixed differently than investigational CCI-779. Note that neither the drugs nor supplied diluents are interchangeable. Again, be careful and request PMB approval before transferring this agent from one protocol to another. Also, when your protocol is amended to use commercial Torisel®, remember to return the investigational CCI-779 to PMB to avoid confusion.

Kumbaya: Love a Snake Today

Since we're visiting Camp PMB in a warmer month, we'll surely see one of the more than 2,700 snake species in the world. Not to worry, your PMB guides love and respect snakes. Some are more poisonous than others. There is a chance that if you are bitten, you'll need some attention. Snakes usually bite people as self defense, and the most common snake bites are from pit vipers or rattlesnakes. Although they are venomous, fatality is rare. Be on the lookout for coral snakes, too. Their venom activates more slowly than rattlesnake venom because they have small teeth and must hang on longer to get the venom out of their fangs. Common signs and symptoms are numbness, local pain, swelling, scaring, bruising or skin discoloration at the bite site.

If you are bitten, pull out your first-aid kit (You did pack a first aid kit, didn't you?) Wash the bite with soap and water, immobilize the bitten area and keep it lower than your heart, and get medical help. We need to tell you two other things: (1) if it hurts, consider taking an ASP-rin, and (2) *INSIDE PMB* is not intended to be medical advice.

Snake venom need not to be wasted, so if you are bitten, consider vialing the venom. Contortrostatin (CN), a protein extracted from various snake species, has been used in cancer research. Its chemical properties offer many opportunities in the treatment of breast, prostate, bladder, melanoma, and glioma. CN is a homodimer disintegrin containing disulfide-rich protein of Arg-Gly-Asp. It binds to integrins on the surface of the tumor cells and inhibits mediated cell-cell, extracellular matrix interactions, and platelet aggregation at receptor GPIIb/IIIa, preventing tumor growth and metastasis. Disintegrins are very small, stable proteins used as encapsulated liposomal infusion in breast cancer research. Compared to unencapsulated CN, encapsulated CN minimizes potential immunological reaction, provides longer circulatory half-life, and accumulates passively in the tumor. This new class of molecules that also inhibits angiogenesis makes us squirm with excitement! Its potential benefit in the clinical research arena is endless.



Playing Blind Man's Bluff

We look forward to playing blind man's bluff at camp, don't you? You know: one person ("It") is blindfolded and fumbles about attempting to tag others while they scatter—sneaking up close, or teasing from a few feet away—and try to avoid "It." The PMB version is called "Blinded Protocol Bluff," and it seems like PMB is "It" more than its fair share of the time. Can you help us change trends?

1. Please use the correct patient specific supplies. Please don't select supplies blindly if you are "it." You'll need to examine the label carefully. All investigational agents for double-blinded studies are patient-specific and labeled with the patient's ID. Unlike most open label supplies, blinded supplies are not interchangeable, are assigned to one specific patient, and must only be used for one patient. Some studies generate patient ID numbers that are similar. Take extra care to read the entire patient ID prior to preparing or dispensing.
2. Please order early enough. Blinded shipments require additional patient-specific labeling and quality checks to insure that each patient receives the correct supplies. The protocol's drug information section indicates how often/early you can order your next shipment.
3. Never cheat! Some agents employed on double-blinded studies are also available commercially. Ooops! Forgot to order? There's no way for you to know if the patient is on active treatment or placebo. If you use commercial supplies to treat a patient prescribed blinded treatment, you're "It!", but it's the patient who may get thrown out of the game.
4. Weigh in on dose modifications! Most protocols only require a dose adjustment if the patient's weight changes more than 10%. Changing doses based on smaller changes is a protocol variance, and confuses the heck out of the folks who must prepare the drug here at NCI. Check each blinded protocol for specifics.
5. Play in an area free of dangerous obstructions. NCI is sponsoring an increasing number of protocols that assign patients to a designated treatment during one phase (this could be open, active, or placebo) and then randomized to a second, different open, active, or placebo treatment. Is this not an invitation for errors? To prevent errors:
 - Never mix leftover first phase supplies with supplies sent for the second.
 - Review your protocol to determine how to handle supplies left at the end of each treatment phase of treatment--and do it promptly.
 - Post prominent reminders about the study's complex design and treatment.



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ASCO Pow-wow Results

At the 2008 American Society of Clinical Oncology (ASCO) Annual Meeting, researchers presented evidence that patients' KRAS genes predict cetuximab (Erbix) efficacy as first-line therapy in metastatic colorectal cancer patients. Patients whose tumors express normal (wild type) KRAS genes show significantly improved progression-free survival and overall objective responses when cetuximab is added to first-line FOLFIRI regimen (irinotecan, fluorouracil and leucovorin). Adding cetuximab offers no clinical benefit in patients whose tumors express KRAS mutations. CTEP is amending their protocol to screen patients for KRAS mutation, reflecting this advancement.

Annoying Little Problems...

Camping is just loaded with little problems...mosquitoes, bees, sand in your bathing suit, and cold showers. That makes it similar to maintaining investigational agent records. One necessary evil: sites should download the most recent CDR from CTEP's web site periodically. The correct version is dated 02/2007, is a fillable form, and has a very important change: It asks for your e-mail address.

A random sample of orders sent as this newsletter was going to press revealed that 50% of our customers are using old, and sometimes very old, CDRs. Campers, please update your forms! And once you do that, please check out your Return Drug Form....



Everybody Out of the Pool! Surprise inspection!

Seems like everybody loves a "Top 5" list lately, so here are the Top 5 finding when campers and sites that participate in NCI-sponsored studies are surveyed. Remember: if you accrue enough demerits, you won't be able to participate anymore!



RANK	Camping Concern	NCI Audit Finding
1	Camper did not obtain all the the items listed on the pre-camp supply list (e.g. Sunscreen, DEET, bed roll) and is unprepared for emergencies or planned trips.	No DARF used, or a creative camper "modified" the form and the local version lacks some required elements. Or, the DARF is not completely filled out, and errors are corrected poorly if at all. (No correction fluid please!)
2	Camper does not have required footwear; plans to wear flip-flops while hiking or has obvious athlete's foot and no shower shoes to protect other campers.	The DARF isn't protocol and drug-specific, e.g. Site maintains one DARF for a multi-agent protocol; or one DARF for all patients on a blinded study; or has tracked commercial agent on the NCI DARF.
3	Evidence that unauthorized campers have been living in the room.	Satellite and control DARFS are not maintained or are maintained incorrectly.
4	Camper "borrows" another camper's camp-issued supplies, as evidenced by more than her fair share of pillows, pool towels, or sleeping bags.	The DARF is not the primary and complete record of an investigational agents history at the site; shelf counts and DARF balance do not match; transaction (receipts, transfers) not logged; DARF indicates agent was "borrowed."
5	Camper has contraband [cell phones (apparently an extra in case the first was found and confiscated), candy bars, etc]	NCI-supplied agent not returned to NCI or transferred to an appropriate NCI protocol within 90 days of study closure or last use. Send unneeded supplies back promptly!

Differential Diagnosis: icky Hands and Feet

Hands and feet receive special attention when you go camping—scouting troops are taught to always keep their extremities warm and dry; wear shower shoes to avoid fungal infections; and to stand on cardboard while changing if the ground is cold or damp. So suppose a camper comes to you and her palms and soles are red, scaly, tight, tingling, and swollen? She reports two things of interest: (1) She picked a bouquet of a vine that had glossy, compound leaves consisting of three pointed leaflets yesterday, and (2) she was treated for breast cancer five days ago. So what's up with her hands?



Hand-foot syndrome (HFS or palmar-plantar erythrodysesthesia) is a cutaneous drug reaction. Its painful bullae (large blisters) can impede walking and picking up objects. It may progress to desquamation and ulceration of fingers, toes, palms, and soles. (Hey! That sounds like getting poison ivy on your instep or palm!) Dark-skinned patients may present with skin hyperpigmentation and thickening. Many drugs are associated with HFS: cytarabine, conventional and pegylated doxorubicin, methotrexate, fluorouracil, capecitabine, docetaxel, and most recently, multikinase inhibitors, such as sorafenib and sunitinib. It has also been reported following total body irradiation and high-dose chemotherapy prior to allogeneic bone marrow transplantation. HFS generally occurs as early as 3-5 days after starting therapy, is usually self-limiting, and resolves within a few weeks even without medical intervention. It can, however, be dose-limiting.

Common therapeutic interventions include dose reduction, lengthening the dosing interval, or drug discontinuation. There is no proven treatment. Supportive care, such as wound care, elevation to reduce edema, cold compresses, emollient creams, topical and systemic corticosteroids, and pain medications are approaches often helpful in the management of HFS. Premedication with oral corticosteroids starting 24 hours before chemotherapy and continued for up to 3 to 5 days and tapered over the following 48 hours may prevent the appearance of HFS and permit administration of an adequate chemotherapy dose. Pyridoxine use is not well supported but doses of up to 800 mg daily (usual dose 100 to 300 mg per day) have been used to help alleviate HFS-associated pain.

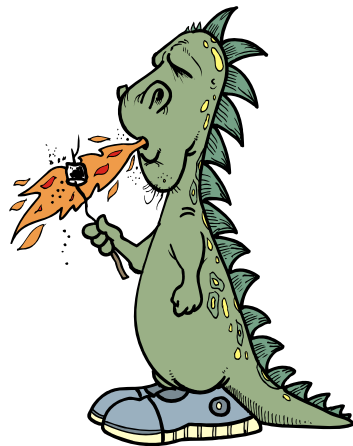
Patient education and monitoring can reduce the incidence and severity of HFS. Educate patients before they start therapy. Tell them HFS's early signs and symptoms, and emphasize the importance of early intervention. Instruct patients to avoid hot bath or showers, tight clothing, skin irritants, adhesive bandage use, repetitive activity or staying in one position for long periods of time, vigorous skin rubbing, and extreme temperature, pressure and friction. Encourage them to wear loose fitting clothing to minimize rubbing or perspiration, and rubber gloves while doing dishes. Other recommendations include sitting or lying on padded surfaces, and avoiding jogging or vigorous exercise.

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Happy Campers Get Cookies!

Find the following words in this puzzle, and fax your results to (301) 402-4870. Include your name, address, and e-mail, and we will enter you into a drawing to win cookies!

- blinded
- borrowing
- cetuximab
- chocolate
- contortrostatin
- DARF
- folfiri
- ForgetASAP
- grahamcracker
- KRAS
- kumbaya
- marshmallow
- poisonivy
- pyridoxine
- registration
- stockrecovery
- temsirolimus



V	K	R	Z	C	A	S	C	E	I	Z	L	T	P	C
D	F	O	R	G	E	T	A	S	A	P	J	Z	O	E
C	F	E	N	I	X	O	D	I	R	Y	P	N	I	T
D	E	T	A	L	O	C	O	H	C	A	T	O	S	U
A	Y	A	B	M	U	K	X	E	V	O	S	I	O	X
R	I	S	X	S	Z	R	Y	U	R	O	V	T	N	I
F	B	L	I	N	D	E	D	T	K	X	D	A	I	M
G	R	A	H	A	M	C	R	A	C	K	E	R	V	A
W	S	U	M	I	L	O	R	I	S	M	E	T	Y	B
F	Y	U	O	H	S	V	D	Y	K	R	A	S	F	G
Y	X	P	Y	T	Q	E	R	F	O	L	F	I	R	I
Y	Y	S	A	B	O	R	R	O	W	I	N	G	N	G
R	X	T	H	P	F	Y	Z	D	V	C	K	E	S	T
O	I	R	I	W	O	L	L	A	M	H	S	R	A	M
N	B	T	F	K	V	P	N	K	K	L	J	R	E	M

May's Contest Winners

Joan Ollie, R.N., B.S.N., CCRP, Integrated Community Oncology Network, Orange Park, FL
Nancy Meuler, RN, BSN, OCN, Rockwood Cancer Treatment Center, Spokane, WA
Cyndi Rup, Investigational Pharmacy Technician, UMass Memorial Health Care, Worcester MA