Mother Nature: Friend, Foe

Seems like Mother Nature is having a go at us lately, and it is beginning to get old. This issue of INSIDE PMB is devoted to nature–how it affects the way we do business at a number of levels. For pharmacists, this means having good inclement weather plans, plans that are perhaps a bit more detailed than what was considered acceptable last year. For patients, it means understanding what to do and who to call if inclement weather shuts down your clinic. For PMB, it means monitoring weather patterns around the clock, checking with shippers to ensure deliveries are getting through, and replacing lost shipments tout suite!

Carved in Stone? OOPS! Sandstone!

We misspelled contest winner Dominic Solimando's name in the electronic version of the newsletter in August, and completely destroyed Yvonne Bossert's name. Our apologies! These errors were corrected in the paper version.

Clay Rouse of Mississippi caught a double negative, and won cookies for his vigilance, and Robert (Rupert) Hay, a former contest winner, of Huntington, West Virginia, sent a letter indicating he was disappointed that August's issue had no contest. See Page 2 for this issue's contest. Please take the time to complete it, or there will be no more!

PMB AFTER HOURS

A pharmacist looked in her crystal ball
Saw inclement weather often follows fall
Her work load may drift
Causing an awfully long shift
And difficulty completing anything at all!

So.....Have a question after 4:30 PM Eastern time or too busy to call during normal business hours? Try our after hours E-mail address, rain or shine, at any time of the day or night:
pmbafterhours@mail.nih.gov
Expect an answer within one business day.

New Fall Foliage, Snow Drifts:

ZD1839 250 mg will enter the autumn of its life as the last of the yellow tablets expire on November 30, 2005. After that, the 250 mg tablets will all be brown.....**Sunitinib malate** is an oh-so-turning-leaf-like Swedish orange/caramel, so much so that direct contact with the capsule causes yellow discoloration in the skin area that fades with soap and water. It may interact with CYP450-metabolized drugs and dysrhythmic drugs.....
All the rest of our new products are snow white unless otherwise noted. Metabolized by CYP 3A4 and known CYP 3A4 inhibitors, two new Src/Abl kinase inhibitors **AZD0530** (which is peonie pink) and **BMS-354825** are oral products. Food's effect on their absorption is unknown.....
GW-786034, an oral angiogenesis inhibitor, should be given on an empty stomach. Concurrent CYP 2C9 substrates are prohibited on GW-786034 trials. CYP 3A4 inducers or inhibitors should be used with caution.....
MLN518, a FLT3 antagonist, can prolong the QT_c interval. Time for you to visit http://torsades.org/ to brush up on what increases risk of sudden cardiac death.

Two-Four-Six-Eight! (The Octopus Rule of Ordering)

Maintaining PMB inventories is sort of like stuffing an octopus into a sock during a hurricane. By necessity (ours, not yours), PMB limits the amount of agent sent per patient per protocol per order. Generally PMB sends about an eight week supply of agent but actual guidelines depend on several tentacles, if you will:

- constraints placed on us by the agent manufacturer
- agent retest dates and likelihood of expiration
- the protocol's maturity (at a study's or several studies' onset, the initial strain on inventory can be great)
- specific treatment cycle length
- probable or actual duration of treatment
- the total amount of agent available
- the phase of each study
- the disease being studied
- your site's track record

Patient ineligibility after the drug ships, treatment discontinuation, or heavy-handed ordering may leave an excess supply of agent at sites. Using Quantity to Ship guidelines helps PMB maintain inventory, including expiration and forecasts for new studies, as well as offers the most efficient and expeditious shipping procedures.

International Shipments: Whistling In the Wind?

Whether you say, "J'ai besoin de le drougue investigational maintenant!" or ""¿Dónde diablos está esa medicina que ordene la semana pasada?" this article is for you, our international customer!

For each CTEP-sponsored trial, please (read as: you must) provide a letter from your country's National Ministry of Health or agency equivalent to the U.S. Food and Drug Administration. The letter must approve importation of the NCI-distributed agent for use in the NCI-sponsored protocol. Fax the documentation once, either before or with the first Clinical Drug Request Form (NIH Form 986). Then, subsequent orders are covered by the original form.

If the agent is classified as a dangerous good (DG), you may also need to send an additional import permit. Check with your country's National Ministry of Health for the requirements for importing DGs. How do you know if your agent is classified as a dangerous good–substances and articles that have properties that can injure people and damage the environment, property, and other goods unless handled correctly during transport? The United Nations maintains a list of all dangerous substances that are likely to be transported. Each substance is allocated a United Nations Substance Identification Number (U.N. S.I.N.), which is most commonly referred to as the UN number. This number is found in each agent's transportation section (section 14) of the MSDS.

Ciao!

Look for INSIDE PMB quarterly!
Next issue: February, 2006

Blinded by the Eclipse: So are we!

Even its title is blinding. The new protocol GOG-0218 is called "A Phase III Trial of Carboplatin and Paclitaxel plus Placebo versus Carboplatin and Paclitaxel plus Concurrent Bevacizumab (RHUMAB VEGF, NSC #704865, IND #7921) followed by Placebo versus Carboplatin and Paclitaxel plus Concurrent and Extended Bevacizumab in Women with Newly Diagnosed, Previously Untreated, Suboptimal Advanced Stage Epithelial Ovarian and Peritoneal Primary Cancer." (WHEW!) The first patient was accrued October 14th, 2005, and 1999 more patients are expected to follow. Because it is on the CTSU menu, a monumental number of clinical sites are eligible to participate.

An eclipse occurs when one celestial body obscures another. This study's complex design requires re-registration after completion of Phase A's chemotherapy and maintenance. Will Phase A's requirements obscure Phase B's? We are a little worried. Remember the following:

•PMB will send sufficient clinical supplies to complete Phase A automatically when and only when the patient is registered. We will use the body weight you provide for the patient during registration to determine the required number of vials.

•When preparing doses of bevacizumab/placebo, be certain that the protocol number and the patient ID on the order from the physician match those on the clinical supplies of bevacizumab/placebo.

•Once the patient completes cycle 6 of chemotherapy, you must re-register the patient with GOG; we will send clinical supplies to start Phase B automatically once this registration takes place.

•No starter supplies will be allowed for Phase A or B. No reorders for Phase A will be allowed. Reorders for Phase B will be allowed if they include the protocol number, the patient ID, the patient initials, and the patient's body weight in "kg."

•Ophthalmologists can sometimes determine which phase of an eclipse a patient with solar damage was watching by noting the "sickle" on each retina--that is, the arc of retinal swelling that corresponds to crescent-shaped portions of the sun left uncovered at various points. You can find clues about the study phase that can prevent errors in this study, too. Patients receiving concurrent chemotherapy (i.e., carboplatin and paclitaxel), should also receive bevacizumab/placebo from Phase A clinical supplies. Patients who have completed chemotherapy should be receiving bevacizumab/placebo from Phase B clinical supplies.

Natural Knack CONTEST

If you have a natural knack for science, this contest is for you. Match the antineoplastic to its source:

1. XL119 (rebeccamycin analogue)
2. Paclitaxel
3. E7389 (Halichondrin B Analog)
4. Topotecan
5. PV701
6. Doxorubicin
7. Bryostatin
8. Teniposide
9. Dolastatin-10
10. Vincristine
11. Mitomycin-C
12. Homoharringtonine

a. Camptotheca acuminate (Chinese xi shu tree)
b. Streptomyces peucetius
c. Podophyllotoxin
d. Bugula neritina (marine invertebrae)
e Catharanthus roseus (Madagascar periwinkle)
f. Dolabella auratium (sea hare)
g. Cephalotaxus harringtonia (evergreen plant)
h. Saccharothrix aerocolonigens
i. Newcastle disease virus (an avian paramyxovirus)
j. Streptomyces caespitosus
k. Halichondria okadai (marine sponge)
l. Taxus brevifola (Pacific yew)

Here's a hint if you think this is too hard: type the Latin name into your search engine and see what pops up. Please send your answers to pmbafterhours@mail.nih.gov. We will enter correct entries into a drawing on November 15, and three winners will (again) be able to select homemade cookies or dog biscuits as prizes.

Get It In Writing AND Save a Tree

Every disaster, natural or manmade, shares a curious number of similarities with those that have happened before. That's why we receive so many questions that are...well, slightly reminiscent of other questions. In order to improve our services and ensure consistent responses, PMB developed an electronic file of FAQs. Some of our most popular:

- Why do this agent's shipping and storage temperatures differ?
- How should I document trastuzumab–by mg, by mL, or what?
- What is a satellite?
- Why was my courier charged for this shipment?
- Where can we find NCI-sponsored and other clinical trials?

For a list of all available FAQs or a pdf of one of those listed above, E-mail pmbafterhours@mail.nih.gov.

Are You A Symbiont?

Symbiosis–the close association of two dissimilar organisms–is a necessity in the clinical trials environment. Your symbiotic relationships may be

mutual like that of a crocodile bird (a bird that enters the crocodile's open mouth in pursuit of flies; the bird gets nutrients and the crocodile gets clean teeth) or pollinating like that of a dung beetle and a skunk cabbage (the skunk cabbage's putrid scent attracts dung beetles that carry pollen; the flower is pollinated and the beetle gets warm). Queasy readers can delete the skunk cabbage/dung beetle example and use the large earth bumblebee and foxglove/digitalis example instead (foxglove needs a bee of a certain size for pollination; the bee gets honey and the plant spreads). Where are we going with this?

Often, people who work on clinical trials call PMB for their symbiont–another person who works with them. Sadly, we cannot help them on the first call, because they only have a portion of the information they need. If you are such a symbiont, check out these tips to improve our ability to help you:

Have any identifying numbers available (investigator number, protocol number, etc)

Check http//:ctep.cancer.gov (No www, please!) to see if you can find the information.

Pharmaceutical Management Branch ☆ Cancer Therapy Evaluation Program ☆ Division of Cancer Treatment and Diagnosis ☆ National Cancer Institute
6130 Executive Blvd ☆ Suite 7149 ☆ Rockville, Maryland 20852 ☆ Phone: (301) 496-5725 ☆ Order fax: (301) 480-4612 ☆ Other fax: (301) 402-0429 ☆ E-mail pmbafterhours@mail.nih.gov