

## Happy Anniversary to Inside PMB!

Time flies, and this is our fourth and anniversary issue of "Inside PMB"! This is a significant accomplishment, since the censors haven't shut us down (a real threat for yellow journalists like us), and our readership is growing. Wondering what has changed in a year?

\* Initially available only as the crumpled document stuffed into every order, we now send Inside PMB to approximately 150 people electronically. We call this our preferred customer list and invite you to join. Electronic subscribers can see all the colors that paper subscribers miss. HINT: If you contact PMBAfterhours and use the subject "Sign Me Up!" you can be on the preferred customer list.

\* Business at the PMBAfterhours E-mail address is brisk. Thanks to Dana Kelley and Beth Scully, leading the way in number of E-mails. Do you know each other?

\* The most covered topic has been carboxypeptidase, with bevacizumab running a close second.

What does the future hold?

\* We're hoping to put all issues on-line so you can find them when you need them.

\* We'd like to be more responsive to your needs. What is it that you need?

+ What would you like to see, esteemed reader?

## Homeless Squirrels Rejoice!

For a REALLY long time the NCI Repository has included blank Clinical Drug Request (CDR) and the Return Drug List (RDL) forms in every shipment. Before the web existed and while it was in it's infancy, this made good sense. However, it's time to move on. These forms are no longer included in shipments, and countless housing units for homeless squirrels will be available in the trees thus saved. Additionally, this ensures you are using the most current version of the form.



All CTEP forms (including the CDR and RDL) are available on CTEP's web page (<http://ctep.cancer.gov>).

### Speaking of forms.....

A pharmacist scooped us that the beloved Drug Accountability Record Form (DARF) has an expiration date of April, 2004. The Office of Management and Budget, which approves this form, is working on it, and we expect approval sometime soon. The updated form will be on the website as soon as we receive it.

## holidays-holidays-holidays

In the United States, we are approaching a few months that have what we at PMB consider an adequate number of Federal holidays (lots of them, meaning we are closed for business and can stay home eating cookies)! Labor Day (9/6), Columbus Day (10/11), Veterans Day (11/11), Thanksgiving (11/25), Christmas (closed 12/24 this year) and New Year's (closed 12/31 this year). Let's all be careful to order and ask for shipments with these holidays in mind.

For non-US sites, we ask folks specifically to U Make note of any holidays in your country that may delay delivery to you. Plan ahead.

AJ Note approaching holidays on your drug orders when you send them, like this, "Monday, October 11, is Thanksgiving Day here in Canada and we are closed" or "Monday the 24<sup>th</sup> of September is Heritage Day in South Africa; do not ship for delivery that day!"

U Send boxes of your traditional holiday cookies to us to sample!

Look for **INSIDE PMB** quarterly!

Next issue: chilly November 2004

## DMB AFTER HOURS

We close at 4:30. Our South African customers (Hello Dr. Slabber!) are contemplating whether a sedative-hypnotic or a pharmacy journal will induce sleep this evening.

So.....Need to reach us? Try our after hours E-mail address:

[pmbafterhours@mail.nih.gov](mailto:pmbafterhours@mail.nih.gov)

Expect a response on the next business day!

## Commercial Property

### 5-azacytidine Fast Facts

The FDA approved 5-AZA on 5/19/2004 as Vidaza™ for all types of MDS (FAB classification)

± Available from commercial distributors July 1, 2004

± Reimbursement issues? Call Pharmion's Reimbursement Hotline and Patient Assistance Program: at 1-866-742-7646

± NCI is out of the investigational 5-AZA business for MDS after July 30, 2004

± You may use your remaining supplies until exhausted

± You may transfer NCI-supplied 5-AZA from patients off of treatment to other NCI-supplied patients/studies

± Questions regarding end of study reports? Call 301-496-5725

## VOO DOO DOLLS?

There is no truth to the rumor that PMB will supply voodoo dolls resembling troublesome investigators. We are fully funded by the federal government and do not need to undertake such fund-raising projects \*yet\*.

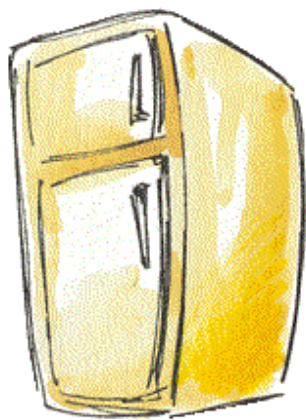
**When you call PMB, please have the investigator's NCI number ready!** This is the most frequent reason for callers to have to hang up and call us back.

## Question: Ship to ~~Shore~~ **STORE**

### “Why wasn’t my Herceptin shipped on ice?”

It’s summer. It’s hot. Everyone is cranky. And the be-all and end-all of a bad day? You’re poised between a breast cancer patient who is waiting for a treatment and the shipment of trastuzumab that just arrived... at room temperature! What in the world?

Not to worry. Trastuzumab is stored in the refrigerator, but shipped at room temperature (RT). Our Repository uses guidelines provided by various manufacturers when creating their shipping protocol. These agents are stored in the refrigerator, but shipped at RT via FedEx next day delivery:



- o alfa interFERON
- o glucarpidase
- o interLEUKIN-4
- o trastuzumab
- o depsipeptide
- o rituximab
- o UCN-01
- o XL119

These drugs are shipped at room temperature via the US Postal Service:

- o azacitidine
- o bryostatin
- o KRN5500
- o O6-benzylguanine

There are a few others, too. During the summer months (end of May to beginning of September),

refrigerated agents that would normally be shipped Priority Mail are shipped via FedEx next day delivery. So chill out, but feel free to call if you are worried.

And PS-341 is stored at RT, but shipped on ice. Go figure.

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### CON-TACT! \* +

ÅNeed an Investigator Brochure for an agent for which NCI holds the IND? E-mail to [ibcoordinator@mail.nih.gov](mailto:ibcoordinator@mail.nih.gov) or call 301-496-5725 and ask for the IB Coordinator.

ÅHave investigator registration questions? E-mail [PMBregpend@mail.nci.nih.gov](mailto:PMBregpend@mail.nci.nih.gov) or call 301-496-5725 and ask for the Registration Coordinator.

ÅWant to request agent for non-human use? Send an E-mail to [PMBAfterhours@mail.nih.gov](mailto:PMBAfterhours@mail.nih.gov) and use the subject, “ATTN: NHU Coordinator.” Or call the NHU Coordinator here at PMB.

ÅHave issues with investigator-held INDs? Send an E-mail to [PMBAfterhours@mail.nih.gov](mailto:PMBAfterhours@mail.nih.gov) and use the subject, “ATTN: Investigator-Held IND Coordinator.”

ÅQuestions about a foreign shipment? We have a coordinator for those, too! Send E-mail to [PMBAfterhours@mail.nih.gov](mailto:PMBAfterhours@mail.nih.gov) and use the subject, “ATTN: Foreign Shipment Coordinator.”

## Hail and Farewell!

**Retiring soon:** The names carboxypeptidase G<sub>2</sub> and CPG<sub>2</sub> and the NSC 641273. This hard working enzyme has a new home and a new manufacturing process. So, **welcome** carboxypeptidase’s new generic name - glucarpidase - and new NSC -732443 - reflecting its new home with Protherics. No more risk of BSE!

**Welcome also** CC-5013, a thalidomide analog, AKA lenalidomide or Revlimid™. It will be available in 5 mg and 25 mg capsules in bottles of 21 or 28 capsules. Due to lack of stability data, dispense CC-5013 in its manufacturer’s original container only.

**Hello** to SB-715992, a new KSP inhibitor! Although manufactured in 4 mg, 5 mg, and 10 mg vials, PMB will only distribute the 5 mg vials initially.

**Last, but not least**, PXD 101 is a novel and potent histone deacetylase (HDAC) inhibitor. It influences chromatin accessibility and ultimately gene transcription. Additionally, HDAC inhibitors reduce the production of vascular endothelial growth factor (VEGF) and directly inhibit endothelial cell proliferation.

## WHO ARE WE?

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Diagnosis

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E-mail: [pmbafterhours@mail.nih.gov](mailto:pmbafterhours@mail.nih.gov)

## TEN THINGS you should know about angiogenesis inhibitors but were afraid to ask:

■ Antineoplastic angiogenesis inhibitors differ from conventional cytotoxic chemotherapy.

■ Targeting cells that support tumor growth is particularly promising because these cells are genetically stable and less likely to accumulate mutations that lead to rapid drug resistance.

■ Microvascular endothelial cells are a genetically stable target of antiangiogenic therapy.

■ Tumors respond to antiangiogenesis agents regardless of their vascularity (in other words, all tumors need vasculature).

■ Direct and indirect antiangiogenesis agents differ:

(1) Direct angiogenesis inhibitors target microvascular endothelial cells that are recruited to the tumor bed and prevent them from responding to various endothelial mitogens and motogens.

(2) Indirect angiogenesis inhibitors target proteins such as epidermal growth-factor tyrosine kinase and its products, bFGF, VEGF, and TGF- $\beta$ , or their receptors, on tumor cell endothelium.

■ Slowly growing tumors respond well to antiangiogenic therapy.

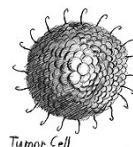
■ Rapidly growing tumors require higher angiogenesis inhibitor doses.

■ Angiogenesis inhibitors are most effective when administered on a dose-schedule that maintains a constant concentration in the circulation instead of a schedule in which therapy is periodically discontinued.

■ No surrogate markers for therapeutic efficacy have been identified.

■ Angiogenesis inhibitors might be added to chemotherapy, radiotherapy, immunotherapy, or vaccine therapy.

FROM: Kerbel R, Folkman J. Clinical translation of angiogenesis inhibitors. *Nat Rev Cancer* 2002 Oct;2(10):727-39.



Tumor Cell

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