

INSIDE PMB

NOVEMBER 2007

Management by Committee

So we had a contest last month, and readers were asked to suggest a motif for this issue in 50 words or less.

As these were health care people playing, most responses were considerably shorter than 50 words, like about 49 words shorter. So we did what we in the government excel at: we called together a committee to decide who should win. And we assigned points for following the directions, motif creativity and idea flexibility. The committee, however, tied in their selection and had to go into overtime. The result: the motif would be a combination of turkeys and football. Winners names appear on page 2.



In retrospect, the committee should have considered the editor's ability to understand and apply the motif (said editor, pictured to left, never having seen a football game in her entire life). AHA! So that's where the turkey comes in. The turkey is applying the motif to the newsletter.

Brace yourself. Enjoy!

Two Minute Warning!

PMB's customers use the Drug Accountability Record Form (DARF) to record receipt and document dispersal of investigational agents. The United States Office of Management and Budget (OMB) requires review and re-approval of the form every three years. Our team manager started this process in December 2006, but OMB has yet to approve the form. It looks like the earliest that the DARF will be renewed is January 2008. Until you receive official word, continue to use the existing form that has an 11/2007 expiration. We'll post the newly approved DARF on the CTEP web site as soon as it's available, and notify you via this newsletter.



Aloha? PMB calling! Is Bangor near San Diego?

Throughout the year, PMB does its best to stay apprised of national and global weather or unanticipated disasters that may impede agent shipments. Although individual sites have first-hand knowledge of how Mother Nature affects their surroundings, it is not always apparent to others. So, if we call to confirm delivery is possible because we aren't sure how close you are to San Diego or the World Trade Center, please don't think we are geographically challenged! We just want to be certain. We may also call to tell you delivery may be delayed when local or regional express courier service is disrupted. Yes, it does snow on occasion in Washington, D.C. (we PMB employees pray for "the big one"), so our local weather may affect distribution as well. Please be assured we make every effort to minimize impact on patients.

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Quick Kick Language

Slang	Football Meaning	PMB Analogy
Odds maker	One who establishes the odds for sports betting.	The pharmacist (and it is the PMB pharmacist; you can bet on it) who determines the exact likelihood that starter supplies will be available.
Piling On	An illegal play where several players jump on the player with the ball after he's been tackled.	An authorized ordering agent who "gets a feeling" that supplies of a certain drug are tight, and indicates he is treating 10 patients on his clinical drug request (and orders accordingly) when in actuality, he is treating only three.
Zone Defense	Coverage in which the secondary and linebacker's defensive players drop away from the line of scrimmage when defending a pass play to cover a certain area of the field (zone).	Addition of targeted therapies to the old workhorses to improve and extend response.
Tight End	An offensive player who serves as a receiver and also a blocker.	The few weeks before the next shipment of agent is expected and supplies are getting very low.
Necessary Line	A line the offense must cross to get a new first down. When a team gets a first down, the new necessary line is exactly ten yards away.	Eight weeks. That's it. We'll supply a maximum of an eight week supply per patient being treated on a protocol. And we simply cannot begin to address the "she's going on vacation to Europe for six months" request for more.
Foul	Any violation of a playing rule.	The source of several vaccines that require pox precautions.

Rookie's Corner

PMB/CTEP welcomes rookies into the clinical trial arena. We find, however, that not all Rookies took Clinical Trials 101—sometimes PMB throws the flag! Here are 10 common mistakes that prevent touchdowns:

1. Calling the drug's manufacturer for expiration dates or temperature excursion information. For CTEP-supplied agent, call PMB.
2. Forgetting to specify the date needed on the Clinical Drug Request Form (NIH 986). No first down if you don't specify the date you need the agent.
3. Omitting the protocol number, or investigator's name and/or NCI number, and the agent when requesting an investigators' brochure. Queue them up to speed the process.
4. Returning biohazardous substances to the Repository. Offsides Offense! Unless your facility is certified to ship dangerous goods, call PMB or E-mail pmbafterhours@mail.nih.gov for assistance.
5. Shipping investigational drug directly to patients. PMB policy does not permit repackaging and shipping our agents by mail or express courier. That's a passing penalty. Please use hand-to-hand transfer of investigational agents from clinical staff to patient.
6. Shipping investigational drug to another office or location located outside your institution. Please don't engage in secondary distribution by courier (e.g.; FedEx, UPS, US Postal). Another passing penalty.
7. Claiming ignorance of ordering or administration procedures. Look in the Pharmaceutical Information Section of the protocol.
8. Using commercial instead of investigational-supplied agent. E-mail pmbafterhours@mail.nih.gov and ask for our FAQ that explains how to "fix" this problem.
9. Assuming agents shipped on blue ice, should be stored refrigerated. Some investigational drugs are shipped in ice but stored at controlled room temperature. It's not a coin toss—always read the labels for appropriate storage condition.
10. Forgetting to provide your courier account number when you need the agent tomorrow! You'll be scrambling in the morning.



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Who's Responsible for This Mess?

We needed a theme, and the fans responded. We appreciate all of your remarkable, creative, and sometimes edgy suggestions. But, only three groups or individuals can win. And those winners are...

Most Valuable Players (for the football motif)

Donald L. Chalupa, Pharm.D.
The Ohio State University Medical Center
Columbus, OH

Debbie Kahler, PharmD
Shands Hospital
Gainesville, FL

Heisman Trophy (for the turkey motif)

Robert "Rupert" Hay, R.Ph.
St. Mary's Medical Center
Huntington, WV 25702

For the effort, they received chocolate chip cookies, and a couple of rum balls that we hope they didn't eat before operating heavy equipment. New contest--page 3!

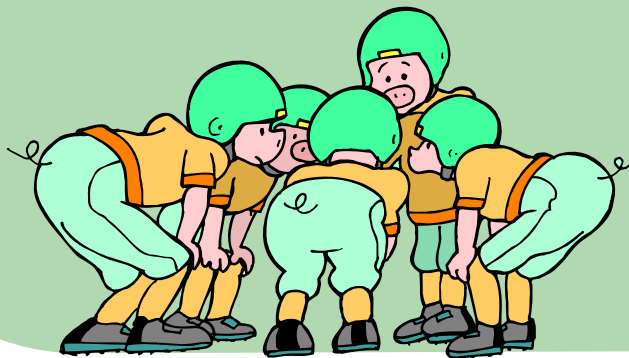
A Touch Down or Just a Field Goal?

When it comes to renal cell cancer (RCC), the NCI has been in a wishbone formation for years. Finally, our efforts might be paying off. RCC is relatively uncommon, with 51,190 cases expected to be diagnosed in 2007. Localized disease is curable by surgery; locally advanced or metastatic disease is incurable in most cases and, until recently, had a limited response to drug treatment. Since the middle to late 1980's, treatment for advanced RCC has generally consisted of high dose interleukin-2 and interferon alpha. During the last 5 years, however, researchers have made excellent progress. Understanding RCC biology better has led to development and approval of several novel agents. Sorafenib was approved in December 2005, sunitinib in January 2006, and temsirolimus in May 2007. In addition, Genentech is planning to submit a supplemental BLA to the Food and Drug Administration for bevacizumab based on the positive interim results of Roche's AVOREN study in first-line metastatic RCC.

Do these drugs wear the same jersey? Absolutely—each targets the angiogenesis pathway. Sorafenib and sunitinib are multikinase inhibitor; temsirolimus targets mTOR; and bevacizumab acts against VEGF. Although not all affect overall survival, all promote disease stabilization and increase progression-free survival.

According to the National Comprehensive Cancer Network, sorafenib and sunitinib are now considered first- and second-line treatment options for patients with advanced RCC. Temsirolimus is considered first line treatment in clear cell RCC patients who have poor prognostic risk factors and first-line therapy in patients with non clear cell histology. Although not yet FDA-approved for RCC, bevacizumab should be considered as first line therapy in combination with interferon in patients with clear cell histology (as opposed to papillary, oncocytoma, collecting duct or chromophobe) regardless of prognostic risk factors. Bevacizumab alone is also recommended as second line therapy in clear cell RCC.

Catching RCC early in the game is still the best strategy. Future and ongoing trials are studying combinations of these targeted agents and research is directed towards their optimal use.



Get It In Writing!

A tech was running back in motion
To find an investigational potion
A hot dog was he
A free agent to be
His failure to order caused quite a commotion!

Have a question about agent availability, the best way to get agents fast, or if an order was even ever faxed, and want the answer in writing? E-mail pmbafterhour@mail.nih.gov. Expect an answer within the next business day.

Wait a darn minute!

We need an instant replay!

Several protocols using dasatinib (BMS-354825, NSC 732517) indicate a 70 mg tablet is available. The Company did, at one point, say that they would provide it. Then they said they wouldn't. Then they said they would. Now we are at, "Maybe."

The long and the short of it is, PMB doesn't have any 70 mg tablets. Please use one 50 mg tablet and one 20 mg tablet for each 70 mg dose.

And, please note that the 20 mg and 50 mg dasatinib tablets will look different in the future. They will be the same size and shape as the investigational dasatinib, but be marked with "BMS" instead of "20" or "50." Just remember, the 20 mg is round, and the 50 mg is football shaped (oval). Audible groan here.

Gentle Reminder

PMB rarely closes and makes every attempt to provide reliable service. That said, mother nature doesn't always cooperate, especially in the winter, and the next few months are full of holidays.

Please plan ahead.

Remember five of the US's 11 Federal holidays fall in the next three months (see sidebar)!

No next day shipment on November 21, or December 24, or December 31!

Allow lots of time for shipping.

Order sufficient quantities.

Send homemade cookies to PMB.

Have enjoyable holidays!

Veteran's Day (11/12), Thanksgiving (11/22), Christmas (12/25)
New Year's Day (1/1), MLK's Birthday (1/21)

Contest: Place and Show

OK, so that's horse racing. Regardless, send your predictions of the two teams going to the National Championship Game on January 7, 2008 to pmbafterhours@mail.nih.gov before November 17, 2007. Three winners (drawn by lottery if more than three people are correct) will win cookies or dog biscuits. And maybe a rum ball. Maybe.



Fantasy Football: PMB Turkeys vs. ???

It's never off-season for the PMB Research Turkeys and the Clinical Site Rats (AKA the Whitecoats); both teams have been collecting and cultivating a nucleus of gifted offensive and defensive playmakers. Through repeated games, a popular play has been for the Whitecoats to call the Turkeys, alleging they need a drug shipped immediately for delivery tomorrow morning. Their excuse for failing to complete the play earlier (as in before 2 PM) have been myriad: injuries across the offensive line have stunted the group, their Whitecoat pharmacist quarterback is a rookie, they've had dormant off-seasons because of hamstring injuries, or the Turkey's front seven have returned a previous Clinical Drug Request (CDR) because the investigator wasn't registered.

How the Whitecoats underestimate the Turkeys is glaring to the crowd: the Turkeys will always use a conservative game plan—fake passes and stellar running backs will not budge them. They will not promise anything, repeating over and over, "Please fax a Clinical Drug Request." Meanwhile, the offensive players will start making calls to individual Turkey team members. The Whitecoat's tech will approach LaToya Townson, Drug Authorizer, and want to know if the order will arrive tomorrow. The Whitecoat's pharmacist-quarterback will call the responsible Turkey pharmacist and try to improve their rushing yards. Other Whitecoats will join the scrimmage randomly but with zeal. The lack of breakout performances will remain glaring, however, with each Turkey team member saying, "Please fax a CDR!" Soon the crowd will take up the chant, "We want C D R! We. Want. Cee Dee RRRR!"

The Whitecoats will be minutes from the end of the final quarter and the score will be perilously tied when they realize how to produce the bulk of yards. They'll pass the CDR to their fastest tailback, flank her with offensive players, and use their confluence of personnel, coaching acumen and scheme to rush to the fax machine and fax the @#%&*&# CDR! The Turkey's defensive backs will be poised to intercept and pass it to their quarterback, who will average 15 yards per carry, ensuring that CDR gets to aforementioned Townson, the game-breaking ref. She will enter it into the automated system, checking to make sure that all parts are properly executed and there are no fouls. The order will go to the referees at the NCI Repository (which is located at a distance from PMB—if we passed some of the people who work there on our way to get a hot dog, we wouldn't know them unless they spoke and we recognized the voice!), and the Repository will work the crowd into a frenzy as they find, pack, and label the shipment. They'll station zone coverage at the loading dock, and physically detain the FedEx man if necessary.

And, once the package enters that truck and the Repository blows the whistle, a member of the PMB Turkeys will call or e-mail an anticlimactic message to the Whitecoat's ordering personnel. "Your order has been shipped for delivery before 10 AM tomorrow. The tracking number is @#%&*&#."

And the crowd will go wild.

Moral of the story: If you need it tomorrow and it's after 2 PM, make sure you fax the CDR before you begin calling. PMB will not promise delivery until the order has been successfully delivered and we have a tracking number.

Skills, Drills and Coaching: Kicking Stuff Back to Us

Some great football players are born. Some are made. Some sites seem to know how to return investigational agents accurately. Others flub up. For football and agent returns, a little coaching can

- produce consistent power and control using proven mechanics/skills
- create muscle memory with established practice routines
- help you think and act like a player

According to FDA regulations, the NCI Clinical Repository must ensure proper, safe disposal of approximately 4000 return units that arrive with more than 300 Investigational Agent Return forms monthly. Needless to say, it's very time-consuming.

Here's the drill. Sites are entirely responsible for completing return forms COMPLETELY and ACCURATELY (i.e., correct investigator, NCI designated protocol number, actual lot dispensed by NCI, etc.). Repository staff will only change information on the form that they can verify visually and physically (i.e., lot number, quantity).



Often, sites contact us after the fact for documentation of a return they sent earlier—they may have forgotten to keep a copy of the form or failed to indicate they wanted a receipt. Finding the information can be challenging because the forms they sent may have been incomplete or inaccurate. Information available in our database is only as good as the information the site provided in the first place. Some common errors include:

- Omitting the return form from the shipment
- Returning non-NCI-supplied agents, non-CTEP-supplied agents

or returning agent lots never distributed by the NCI

- Indicating lot numbers or quantities on the form that do not match the lots or quantities in the shipment
- Referencing the wrong NCI-designated protocol number
- Forgetting to include investigator names/number
- Not using the correct return form

Coaches never ask players to go on the field and collide with another player at full speed without good equipment. Colors help them look good and feel proud. NCI provides sites with some "protective equipment," too--the protocol and the shipping receipt! Please double check protocols for agent's source. Many cooperative group studies now use agents supplied through other sources. Not from the Cancer Therapy Evaluation Program, Pharmaceutical Management Branch? Please don't return it to the NCI Clinical Repository! Although the repository documents these rogue returns, they will not send a return receipt. Next, look at the shipping record receipt—it contains all the information needed to complete the return form accurately (unless you have received approval to transfer the agent to another NCI-sponsored protocol or investigator). Here's a real skill: put the complete (no truncating), correct NCI-designated protocol number on the form (especially for group studies with multi-groups participation).

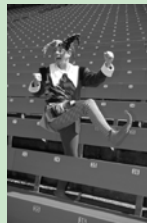


We receive many questions about partial containers. Never return used or partially used injectables, unless the protocol specifically directs you to. Your institution should have procedures for destruction of partially used injectable containers—we call that your "local destruction policy." For oral agents, do not return full or partial bottles that were dispensed to and returned from patients. Document the patient return according to institutional policy for open-label studies (not on the DARF!) and on the patient-specific DARF for blinded studies, then follow your local destruction policy. Return partial bottles of oral agents that have never been dispensed to the NCI Clinical Repository—note that this is a change.

Be a player: practice makes perfect, so try to get it right every time! Create a drill sheet and ask someone to spot-check your returns!

Do not send returns to PMB! PMB is NOT located with or near the Repository! Use the address on the form!

PMB Cheerleaders Present Frequently Asked Questions



Here at PMB, we hear certain questions pretty often. Some of us have had trouble memorizing the cheers, so we wrote them down. Want a copy? E-mail pmbafterhours@mail.nih.gov, and we'll send you a pdf!

- A1. What's the best way to account for oral agents?
- B2. How do I ask for and receive an IB?
- C3. What are Canadian no-objection-letters or fax-back forms?
- D4. How do I document discrepancies on the drug accountability record form (DARF)?
- E5. How do I find other names for investigational agents?
- F6. How do I order investigational agent?
- G7. Can two patients who receive the same injectable agent on the same NCI-sponsored trial share a vial?
- H8. Why is my IRB asking all these questions? (Includes Special Exceptions information)
- I9. How can I find a list of clinical trials for an investigational agent, a disease or condition, or a geographic location?
- J10. We know that our shipment of PMB-distributed agent was delivered, but we think that the housekeepers thought it was trash and took it. What should we do? (Lost shipments)
- K11. How should we handle and dispose of monoclonal antibodies?
- L12. Can our nurse practitioners, physician assistants, or fellows who are listed as co-investigators on the protocol write orders for the investigational agents?
- M13. How do I obtain an NCI investigational agent for preclinical use (non-human use)?
- N14. I have several questions about a multidose vial? If so, should I designate one vial per patient, or can patients share? Is there any overfill and can I use the overfill? If they can share, how do I document the vials on the Drug Accountability Record Form (DARF)?
- O15. How do I return investigational agent that I don't need anymore?
- P16. I have drug leftover and the study closed. What do I do? (Transferring agent)
- Q17. Why does PMB use "retest" dates?
- R18. Why are an agent's shipping conditions different than the storage conditions?
- S19. I need agent urgently. How can I get it faster? Or: Why did you charge my courier account?
- T20. What if I use commercial drug for a study patient, or investigational drug for a commercial patient?
- U21. How do I know if an investigational agent (or any drug) is a "dangerous good"?
- V22. Can we vaccinate a cancer patient who is undergoing treatment?
- W23. What is the definition of a "satellite"?
- X24. What is an NSC?
- Y25. What should I do when a patient returns NCI-supplied clinical supplies?
- Z26. What does it mean when a protocol refers to P-glycoprotein drug interactions?