

SMOKE AND MIRRORS

INSIDE PMB

May 2008

ABRA-CADABRA?

A loyal customer recently complained about receiving stock recovery letters from PMB addressed to an employee who left his institution's employ several years ago. He asked us to remove her name, and address all correspondence to him. Another dedicated customer asked us to change their organization's address ever-so-slightly.

Our stock recovery letters (SRL) are issued based on the discrete point in time when we sent the agent. The letter is sent to the shipping designee at the address to which the agent was shipped on that day in history. We cannot change it. We make the assumption (Oh, silly rabbits!) that official mail received at an institution bearing the name of an employee who has moved on will be opened by that employee's successor. After all, mail you receive at work in an official capacity and unrelated to human resources is official mail unless it is marked "To be opened by addressee only." It's the workplace's property.

Make your own magic: We also send the letter to the investigator at the address on their current 1572; ultimately, the investigator is responsible for the agent. You can do a little magic at your site—develop good relationships with your investigators, and ask them to send those SRLs to you as soon as they get them!

SIMPLE TRICK FOR YOU FROM PMB!

If you don't get anything else out of this newsletter, at least get this: Pretend you are preparing a Clinical Drug Request to submit to the NCI. In the "Date Needed" field you put "ASAP." Select your definition of ASAP in this context:

- A. Yesterday
- B. Today
- C. Tomorrow
- D. Next week
- E. Whenever PMB gets to it

We polled all the employees at PMB and asked what ASAP means to them. They pretty much agreed that ASAP is hocus pocus.



So here's the trick: You can make this problem disappear. If you have the abbreviation ASAP tucked up your sleeve, please ditch it. Instead of using ASAP, please write down the exact date (and time, if that's a concern) that you need the agent. Presto! We'll know exactly what to do without mind reading!



PULL THIS FROM THIN AIR:

We've used legerdemain and placed the updated Adobe pdf writeable Investigational Agent Accountability Record (DARF) on the CTEP web site; go to ctep.cancer.gov, then select the "CTEP Forms" link in the yellow bar on the right, and find it in the block of forms called "Requisition of Agents." This version expires 02/28/2011. Please update your forms! Let us know if you have questions.



LOOK FOR INSIDE PMB QUARTERLY
NEXT ISSUE: August 2008

IS LEVITATION REAL?

Marker	Standard interpretation of Elevated Levels	Other reasons for elevation
CEA	Malignant disease is present or recurrent.	About 5% of tests are false-positive levels, probably secondary to ovarian cysts, thyroid disorders, hepatitis, renal stones, sarcoidosis.
CA 19-9	Elevated primarily in patients with pancreatic and biliary tract cancers but also has been reported in patients with other malignancies	Patients with Lewis-null blood type do not produce CA 19-9. Thus, about 5 percent of persons are unable to produce this antigen.
IHC staining for EGFR	Early trials assumed that the presence of this receptor would quantitatively correlate with cetuximab activity.	Current techniques lack the sensitivity and predictability needed to make informed decisions as to the usefulness of cetuximab or other anti-EGFR therapies in the treatment of colorectal or other cancers.
b-hCG	Elevated b-hCG levels most commonly are associated with pregnancy, germ cell tumors, and gestational trophoblastic disease.	False-positive levels occur in hypogonadal states and with marijuana use.
PSA	PSA has become an indispensable marker for diagnosis and follow up of prostate cancer patients.	Despite remarkable performance, PSA is not cancer specific. High PSA levels are found in cancerous and healthy tissue, particularly in benign prostate disease, resulting in false positive readings.
CA 27.29	Highly associated with breast cancer, CA 27.29 levels are elevated in several other malignancies.	CA 27.29 can be found in patients with benign disorders of the breast, liver, and kidney, and in patients with ovarian cysts. But CA 27.29 levels higher than 100 units per mL are rare in benign conditions.

SIM-SALA-BIM!!!!!!!

Picture your typical hospital pharmacy and your typical hard working employees:
 Bob: "Joe, could you grab me a vial of epi?"
 Joe: "Sure, Bob!" Joe grabs a vial of epi.
 Bob: "Uhh... Joe. Where is my epirubicin?"
 Joe: "Oh, you need that, too? Sure thing Bob."
 Bob: "You bonehead! Joe, you completely ignored me when I asked you to grab the epi for me just a minute ago."
 Bob: "... hello....? You're the bonehead! You asked for epinephrine, not epirubicin."

Unfortunately, humans make mistakes. Even when we think we are paying paying attention closely, we may read and miss the repetition of one word in this sentence (Gotcha!). Jokes aside, the literature states that similar medication names accounted for about 15% of all reports to the United States Pharmacopoeia Medication Errors Reporting Program between 1996 and 2001. The Institute for Safe Medical Practices estimates that these mind tricks could be the culprit in up to half of all medication errors.

To target this problem, The Joint Commission considers sound alike-look alike medications a national patient safety goal. Accredited organizations must review a list of these deceptive medications at least annually, and make suggestions that will prevent optical or aural illusions. Individual institutions must also develop their own rules, regulations, and policies.



We're already familiar with most measures:

- TALL MAN lettering (vinCRIS^tine/vinBLAS^tine)
- stock label redesigns, and
- alternate or non-alphabetical storage of similarly labeled medications.

Most cancer pharmacies nationwide use a combination of double and triple checks and pre-printed order forms. Also, if prescribers hand-write all chemotherapy orders, they should avoid abbreviations to minimize confusion between regimens.

Unfortunately, this does not prevent all errors and this is where the effect of staff awareness and education can be Profonde. Take note of the many chemotherapeutic and biologic agents that look or sound like what they're not (Table 1)!

Oxaliplatin (NSC 266046): NCI will finally receive 50 mg oxaliplatin vials in May. Follow your usual ordering patterns for both 50 mg and 100 mg vials and our staff will adjust the orders based on availability.

TABLE I. SOUND ALIKE LOOK ALIKE (SALA) ONCOLOGY AGENTS

Agent Name	SALA
adriamycin	Aredia®, Idamycin®
aldesleukin	denileukin
capecitabine	gemcitabine
carboplatin	cisplatin
cyclophosphamide	Cycloserine, cyclosporine, ifosfamide
cytoxan	Cytosar®
darbepoetin	epoetin
melphalan	Myleran®
CeeNU	BCNU
temsirolimus	Sirolimus, tacrolimus
asparaginase	pegasparaginase
epirubicin	epinephrine
Neupogen®	Neulasta®
doxorubicin	daunorubicin, epirubicin, idarubicin
vincristine	vinblastine, vindesine, vinorelbine
docetaxol	"dose of taxol"
Filgrastim	Peg-filgrastim
G-CSF	GM-CSF
biologic agents	Agents ending with -inib, Agents ending with -mab
paclitaxel	Paxil®, docetaxel

FAQ: WHAT IF I USE COMMERCIAL DRUG FOR A STUDY PATIENT, OR VICE VERSA.....

Using commercial drug instead of investigational supply for a CTEP-sponsored trial is an audit compliance concern. What should you do?

- On the drug accountability log, clearly document that commercial supply was dispensed in error.

What about the opposite "oops"? You used a CTEP-supplied investigational agent on a patient not enrolled on a CTEP-sponsored trial.

- Clearly document on the drug accountability log, that an investigational agent was dispensed to a non-study patient.
- Notify PMB of the error by E-mail or snail mail. The letter should contain the investigator's name, the protocol number, agent name, NSC number, amount used, a short explanation of the error, and corrective action implemented to prevent future occurrences.

In both cases, certain actions are forbidden:

- Do not replace the pharmacy's supply of commercial agent with the NCI-supplied, investigationally labeled agent or vice versa.
- Do not charge the patient.

As you can see, these compliance violation are costly for your pharmacy. The folks here at the PMB suggest these preventive measures:

- Use pre-printed or computer generated, protocol-specific order sets.
- Educate your oncologists and/or cancer center clinical trials office to alert you of newly enrolled protocol patients and to include the protocol number on all orders.
- Generate a list of all patients enrolled in CTEP-sponsored trials using investigational agents and commit it to memory.

CCI-779 (NSC 683864) will transition to commercial Torisel in 25 mg/1 mL vials only; the 125 mg vials will be discontinued. Commercial Torisel and investigational CCI-779 are mixed differently. Get PMB approval before transferring CCI-779.

CTEP will close BMS-214662's IND (NSC 710086) soon.

DECEPTION IN THE PHARMACY:

PLACEBO

- The word placebo literally means “I will please” in Latin.
- Placebo effect refers to the propensity for people to improve after being given a placebo and being told it may relieve their symptoms.
- Nocebo is the mirror image of placebo, derived from the Latin word, nocere, meaning to inflict damage.
- The nocebo effect refers to a worsening of symptoms when a subject relates the specific treatment to a negative outcome.
- In 1955, Dr. Henry K. Beecher, a prominent anesthesiologist conducted a meta-analysis and suggested that 30% to 40% of people experience symptom relief after taking placebo.
- Beecher stressed—for the first time—the necessity of double-blind, placebo-controlled clinical trials.
- Positron emission tomography studies have recently shown that placebo effect in Parkinson's disease, pain, and depression is related to activation of the limbic circuitry. The observation that placebo administration induces the release of dopamine in the ventral striatum of patients with Parkinson's disease suggests a link between the placebo effect and reward mechanisms.
- Two placebo capsules generate a greater response than one.
- White tablets are perceived to be narcotics.
- Yellow tablets or capsules are frequently perceived to be stimulants or antidepressants.
- Large capsules are perceived to be stronger than small ones.
- Some effects associated with placebo persist after the drug is discontinued.

Hat Production

A traditional Hat Production was not the production of hats, but a bizarre production of an almost endless number of items from a hat. Today, a hat seems more like a prop rather than an ordinary object because men eschew hats, and Hat Productions are rare. Except at NCI's Clinical Repository. Here's a sample of items our A-rated team of investigational agent handlers have pulled out of boxes you've sent: anastrozole, bevacizumab, calcium, cetuximab, clodronate, filgrastim, gemcitabine, letrozole, and selenium.



Why is this a hat production? (Answer below)

ANSWER: These items were returned on studies on which PIMB was not the distributor! Please return only items you received from us to us!

CARD TRICKERY: UP IN SMOKE!

“Lite” is not a word to be taken lightly! Added to cigarette brand, smokers read “less tar and less nicotine” and think “less addiction and less health risk.” Only a deuce should believe such an illusion!



Epidemiologic studies found an increase in smoking-related cancer prevalence in the 1950s; this raised questions about the level of tar in cigarettes. In 1960s, public health authorities concluded that low tar cigarettes would reduce cancer risks and thus endorsed the production of light cigarettes. Cigarette manufacturers began to advertise “Light” or “Ultra-Light” cigarettes as healthy alternatives to regular cigarettes, revolutionizing the US market. Smokers began to select these cigarettes for better health, or as the first step toward smoking cessation. Engaging in this illusory behavior not only contributes to an underestimation of health risks with light cigarettes, but perpetuates misperception among adult and teen smokers.

Bridge-Sized Deck

Magicians frequently use bridge-size cards to get an advantage in certain tricks, capitalizing on the cards' smaller width. Are light cigarettes the equivalent of a bridge-sized deck? In fear of losing smoking customers, the tobacco industry began designing delivery “elasticity” into low tar yield cigarettes by putting vents—tiny pinholes—on the filters. They also used porous cigarettes, and altered the tobacco content in an effort to comply with FTC protocol. When their machine models of smoking puffed on these cigarettes, artificially low tar and nicotine levels were recorded. In humans, however, these cigarettes deliver a larger amount of nicotine. Why? Without realizing it, many smokers block the tiny vent holes with their fingers or lips—it's unavoidable. This turns the light cigarette into a regular cigarette.

In addition, people, unlike machines, inhale more deeply, more rapidly, or more frequently to satisfy their craving. They may smoke extra cigarettes as well. By “compensating,” smokers inhale more tar, nicotine, and other harmful chemicals than the machine-based numbers suggest.

An NCI report indicates that tobacco industry strategies used to advertise and promote light cigarettes were intended to reassure smokers and to prevent them from quitting, and to lead consumers to perceive filtered and light cigarettes as safer alternatives to regular cigarettes.

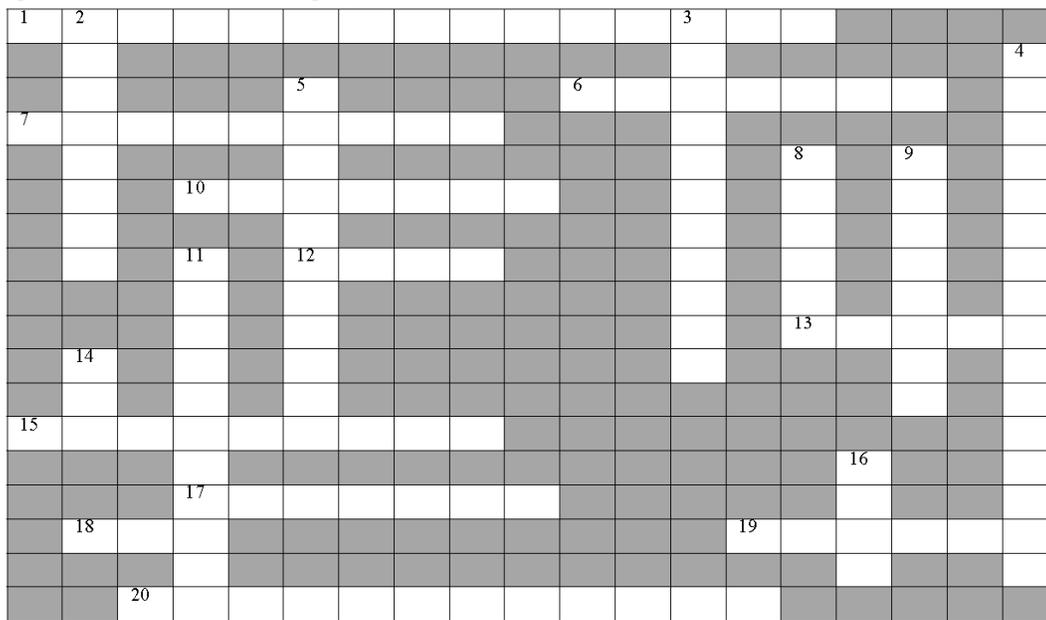
False Shuffle

A false shuffle leaves the deck in the same order as it was before the shuffle; light cigarettes leave the risks of smoking the same as they were before light cigarettes were invented. Thus, cigarette smoking remains a critical issue in public health. Each year, the disease burden attributed to cigarette smoking is stunning: about 440,000 people die prematurely from smoking or exposure to secondhand smoke in the US, and an estimated 9 million have serious illness attributed to smoking. Despite this health risk, 45 million adults smoke cigarettes. Among adolescents, the smoking rate decreased between 2000 to 2003, but stabilized during 2003 to 2006.



Many adults and adolescents still believe that long term use of light cigarettes poses less health risk and is less likely to result in nicotine addiction. Some use lights as a stepping stone to smoking cessation. This manipulation from tobacco companies (promoting low-tar brand as a better choice for health) gathers momentum. It not only supports the use of light cigarettes, but also promotes smoking among nonsmokers. Unless the public is educated about the consequences of light or regular cigarettes, no program will achieve the goal of eradicating smoking and reducing its disease burden nationally and globally.

CROSSWORD CONJURER



ACROSS

1. A three word metaphor for a deceptive, fraudulent or insubstantial explanation or description
6. Latin for "I will please"
7. Proven to be highly addictive, as well as a cause of multiple types of cancer
10. An anesthesiologist who stressed the necessity of double-blind, placebo-controlled clinical trials
12. Investigational Agent Accountability Form
13. This color tablet is usually perceived to be a narcotic
15. Medical term used to describe a severe and progressively worsening disease; not benign
17. An agricultural product processed from the fresh leaves of plants in the genus Nicotiana
18. Abbreviation for National Cancer Institute
19. The mirror image of a placebo
20. An mTOR inhibitor for renal cancer, soon to be PMB-distributed in commercial packaging

DOWN

2. Person skilled in the mysterious and hidden art of magic
3. The NCI will have 50 mg size vials of this drug in May
4. The number of adults in the US that smoke
5. French for "lightness of hand"
8. This color tablet is usually perceived to be a stimulant
9. A distortion of the senses, revealing how the brain normally organizes and interprets sensory stimulation; an unreal image
11. Vinca alkaloid
14. An indispensable marker for diagnosis and follow up of prostate cancer
16. False positive levels of this marker occur with marijuana use

PRESTIDIGITATION IN ACTION

The protocol was written by NABTT
 And Greta had happened to grab it
 Was her agent in date?
 She queried its fate!
 And PMB answered as quick as a rabbit.



Greta uses E-mail to get answers to her questions! Wondering if anyone ordered more agent, or if we've shipped it yet? 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.

CALORIE FREE COOKIES

Three lucky ladies will receive enchanted cookies with no calories (heh,heh,heh). February's cookies winners are

Kristin Henderson, CCRP
Great Falls MT

Yvonne D. Bossert
Clinical Research Coordinator
Stockton, CA

Cynthia L. Rup
Pharmacy Technician
Worcester, MA

This quarter's quiz tests your ability to read and interpret the important information in this issue. Except that really, the person who did this just took words from the newsletter and looked up their definitions.

Fill out the crossword puzzle, and then list your answers in numerical order and E-mail them to pmbafterhours@mail.nih.gov. Put "CONTEST" in the subject line. You, too, could win cookies.



NO MAGIC NECESSARY

- Need an **Investigator Brochure** for an agent for which NCI holds the IND? E-mail to ibcoordinator@mail.nih.gov or call 301-496-5725 and ask for the IB Coordinator.
- Have **investigator registration questions**? E-mail PMBregpend@ctep.nci.nih.gov or call 301-496-5725 and ask for the Registration Coordinator.
- Want to **request agent for non-human use**? Send an E-mail to PMBafterhours@mail.nih.gov and use the subject, "ATTN: NHU Coordinator." Or call the NHU Coordinator here at PMB.
- Have issues with **investigator-held INDs**? Send an E-mail to PMBafterhours@mail.nih.gov and use the subject, "ATTN: Investigator-Held IND Coordinator."
- Questions about a **foreign shipment**? We have a coordinator for those, too! Send E-mail to PMBafterhours@mail.nih.gov and use the subject, "ATTN: Foreign Shipment Coordinator."
- For **Associate Registration (non-physicians)** questions E-mail ctepreghelp@ctep.nci.nih.gov.
 Unsure where to send your query? We will forward your E-mail to PMBafterhours@mail.nih.gov to the appropriate box.