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Interacting With the Pharmaceutical Industry

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understanding and keeping “the enemy” close, this may lead to a new standard of partnership that will result in benefits for our patients.

**Note:** Dr. Hayden has no relationships with any pharmaceutical or biomedical companies, has received no research funding from industry sources, and does not participate in any industry sponsored speakers bureau.

## **Upcoming CAL/AAEM Officers & Board of Directors Elections Call for Nominations**

Elections for the Cal/AAEM officers and board will be held this January 2003.

- 1) Open Positions will include: President, Vice President, Secretary-Treasurer**
- 2) An additional five positions on the CAL/AAEM Board will be made available.**
- 3) Submit your nomination(s) by email to [Calaaem@aaem.org](mailto:Calaaem@aaem.org)**

- Simply state your name, the full name of your nominee(s).
- Self-nominations are welcomed and encouraged.. We also would appreciate a brief statement stating why you wish to nominate the candidate.

### **Deadline for nominations: December 15, 2003**

- Ballots will be mailed to all CAL/AAEM members in early January 2003. Deadline for ballot return is February 1st, 2003.
- Results will be announced prior to the February 2004 CAL/AAEM Board meeting at the Annual AAEM Scientific Assembly in Miami, Florida.

Assume leadership in your own CAL/AAEM. Our patients and clinicians strongly need you!

Antoine Kazzi, MD, FAAEM  
CAL/AAEM Executive Director

## **INTERACTING WITH THE PHARMACEUTICAL INDUSTRY**

**Stephen R. Hayden, MD** Associate Professor of Clinical Medicine, Program Director Emergency Medicine Residency Program, UCSD Medical Center San Diego, CA

It is time to stop hiding our heads in the sand when it comes to interactions with the pharmaceutical industry! This is an issue of reality, not ideology. In an ideal world there would be no industry sponsored research and no potential for tainted research. In an ideal world there would be no need for marketing of new drugs to physicians or to the public and all the savings would be passed on to consumers. In an ideal world there would also be no crime, no disease (and no doctors), and no war; everyone would look like they just walked off the set of *Baywatch*, and no one would have to work unless they wanted to! The reality is that there is not enough money in all the governments or independent organizations in the world to fund the all research that is necessary, and so some funding must also come from the pharmaceutical industry. It is also reality that marketing campaigns work, whether it be to physicians or to the lay public. It is time to stop the rhetoric about conspiracy theory (what I sometimes hear people say would make a good episode for the *X-Files*) and get down to the business of creating a framework that will in every possible manner limit bias and maximize objectivity in conducting, reporting, and using the results of clinical trials. Whether as investigators or educators in emergency medicine, interaction with the pharmaceutical industry is inevitable. Rather than attempting to naively avoid it, we can use such interactions to enforce ethical conduct and scientific

rigor in research, as well as to teach EM residents and students the principles of critical appraisal and critical thinking.

At present, more than 70% of funding for clinical trials comes from the pharmaceutical industry.<sup>1</sup> Even if vast increases in government and foundation funding sources were possible, elimination of industry funding of research entirely would mean that a great deal of very worthy research would not be completed; patients would ultimately suffer from lack of progress in treating many disease conditions. Realizing that at least a portion of funding for important research must come from the pharmaceutical industry, the Society for Academic Emergency Medicine (SAEM) published a set of guidelines in 1995<sup>2</sup> in an attempt to set ethical, scientific, and professional standards for academic EM investigator involvement in clinical trials sponsored by industry. This was a rational approach to the issues, providing a framework for research that essentially promotes unrestricted collection and interpretation of data, open sharing of data from research studies, and unrestricted publication of sponsored clinical trials. These guidelines will not eliminate potential influence on research, but rather they will offer a practical solution that encourages the highest scientific integrity. In a recent article Reed and Camargo<sup>3</sup> suggest going even further than the original guidelines and distinguishing between industry initiated research and investigator initiated research with industry support. The latter would be the preferred option, when possible, because it can optimize the unrestricted use of financial support and independence of the study investigators. Reed and Camargo suggest the following methods can be employed to minimize industry influence:

1. Development of independent study review

panels to assess the scientific merit of the design and implementation of the study.

2. Creation of independent data centers to house study databases and an independent monitoring committee that will have the discretion to continue enrolling patients until preplanned parameters are met, or stop a study before data collection is complete for safety reasons. In this manner, trials cannot be stopped by either pharmaceutical companies or investigators if interim analyses show results that may not favor the specific interests of industry or investigators.

3. Avoiding or renegotiating contracts to eliminate “gag” clauses or the ability to suppress any of the results. Furthermore, publication of all results must be guaranteed even if the results of the study are negative.

4. Exclusivity contracts should be avoided in large multicenter investigations (such contracts would attempt to limit enrollment of eligible patients into the sponsored study only, thereby restrict patients from receiving benefit from other trials being simultaneously conducted at that site).

5. Emergency medicine researchers should be on the steering committee from the outset in any large trial sponsored or initiated by industry.

6. Require independent IRB approval for all clinical trials.

7. Require full disclosure of funding sources during all phases of the study including publication.

As Rothman<sup>4</sup> put it, “open, rational criticism and an

evaluation based on the study's merit is the only fair way to proceed." While the pharmaceutical industry often gets bashed for undue influence, in reality most representatives in the industry are concerned about these issues as well, and in fact, the industry recently published a set of guidelines on the subject.<sup>5</sup>

Perhaps the strongest argument in favor of continuing involvement of academic researchers in industry research is the growing number of private, for profit Contract Research Organizations (CROs), and Site Management Organizations (SMOs). The pharmaceutical industry is increasingly utilizing such entities instead of academic institutions/investigators because of lower costs and often greater productivity that stems from less red tape. In the last 10 years the amount of industry money going to academic medical centers for research has dropped from 80% to 40% in favor of CROs and SMOs.<sup>6</sup> There is great concern that industry has even greater potential to influence the conduct of such trials than trials with academic medical centers. Academic investigators must maintain a prominent role in industry research to ensure that clinical trials are conducted with the highest degree of scientific merit and ethics.

Researchers in emergency medicine are not alone in their interactions with the pharmaceutical industry. As educators in emergency medicine, instead of disappearing when drug reps come around or barring them from coming within 100 feet of our residents, we can use interactions and materials provided by drug companies to teach residents and students the principles of critical appraisal. The issue, of course, is one of *conflict of interest*. The dictionary defines conflict of interest as the circumstance of an individual whose personal interests might benefit from his or her official actions or influence. It is certainly possible,

and in fact the literature supports the notion that interactions with pharmaceutical representatives can influence physician behavior. However, I believe we should teach our residents *conflict resolution*, not complete *conflict avoidance*! It does our residents little good to for us to be overprotective. Someday, they will graduate and have to deal with promotional materials and individuals from pharmaceutical companies or perform industry-sponsored research. Arming both researchers and end users of the results of clinical trials with the skills necessary to separate marketing from evidence will allow them to make up their own minds, avoid potential conflict of interest, and become educated consumers/investigators.

Let us take a few examples of how to make interactions or advertisements into teaching moments. Anyone who has seen the back cover of the *Annals of Emergency Medicine* lately will recognize the familiar "Shock N Load" ad campaign for Amiodarone; "Now Instead of Lidocaine". One of the ads states "29 percent more people in cardiac arrest reached the hospital alive thanks to Cordarone IV". After seeing a copy of the *Annals* lying on top of one of my residents' mail piles, I asked her what she knew about the ARREST Trial.<sup>7</sup> After it became clear that she was only familiar with the results as stated in the ad, we proceeded to briefly analyze the original article. In this randomized placebo controlled trial of Amiodarone in prehospital victims of ventricular fibrillation (V Fib), 44% in the Amiodarone group, compared to 34% in the placebo group made it to hospital admission with vital signs. By simple division (44%/34%), the relative risk difference is 29%; however, the absolute risk difference between the two groups is only 10%. Ten victims of prehospital V Fib arrest need to be treated with Amiodarone compared to placebo in order for one additional patient to be admitted to the hospital

with vital signs. This is the first teaching point you can make to your residents; drug company advertisements often will present results as a *relative* risk difference instead of the more clinically relevant *absolute* risk difference in order to make the results look better. I then asked my resident if this result is important and she told me yes, but not as important as whether these patients survive to hospital discharge. In the ARREST Trial, survival to hospital discharge in the placebo group was 13.2% and in the Amiodarone group 13.4% (p=NS). Even if the study was large enough that this difference was statistically significant, the absolute benefit difference is 0.2%, which means that 500 victims of prehospital V Fib arrest need to be treated with Amiodarone in order for one additional patient to survive to hospital discharge! Interesting that the advertisement in the Annals did not present the results in this manner. This is essentially the critical appraisal issue of choosing the right outcome to measure and report. We then proceeded to have a debate over whether it is better to first have patients make it to hospital admission so that they may have some increased chance of surviving to hospital discharge, or whether using Amiodarone in the field may actually result in increased utilization of critical care resources for no significant improvement in the most important outcome. It became obvious in this case that the evidence alone does not make the clinical decision for you; rather it must be taken in consideration along with physician and patient values and clinical circumstances. That is a lot of teaching points from one advertisement. What a wonderful learning experience came from simply using literature supplied by a pharmaceutical company to teach critical appraisal skills!

Good clinical teachers look for every opportunity to exploit a teaching moment. As educators in EM it is

our responsibility to seek these for our residents and model the ethical and professional behavior that we want them to develop. If our residents never have the opportunity to see a seasoned clinician use such circumstances for teaching or modeling behavior, then an important facet of their education is lost. Recently, in my own ED, a police and paramedics brought in a combative young male who required immediate chemical sedation in order to protect the patient and staff. My senior EM resident was busy with a cardiac patient at that moment so I ordered the customary 5 mg intramuscular Haloperidol and 2 mg of Lorazepam. Almost before I hit the enter key on the computer, the nurses came to me and said "Steve, you are killing us! The Geodon drug rep is in the nurses' lounge right now with lunch and she told us that there is an article that says Geodon is better than Haldol for acute agitation, so we have to give this patient Geodon." My senior EM resident had just come up at this point to see what was going on with this new patient and looked at me with a sly smile when the nurse made this statement.

Some educators in EM would say that the drug rep should never have been allowed in the ED in the first place, so that these kinds of situations do not disrupt our clinical practice. I believe, however, that this is an opportunity to be seized for teaching. Rather than going ballistic (which was very tempting), I calmly explained to the nurses and EM residents in earshot that I had just reviewed the article they referred to with one of our toxicologists and that the patients entered into the Brook study<sup>8</sup> were patients *admitted* to a psychiatric unit. The relevant endpoints were measured at the end of three days of treatment, not after the first dose or two, and therefore we did not know from this study how well Geodon compared to traditional treatment for *acute* uncontrolled behavior

in the ED. I then asked the nurses to look at the patient we were currently taking care of and note that it was taking three police officers to restrain him with a spit rag on his face. I asked the nurses if he was in a state where they would be able to do an appropriate informed consent for a research study and they all laughed. I then pointed out to them that every patient entering into the Brook study was in a condition in which they were able to give informed consent before receiving medications. This really made a big impression, as I pointed out to them the results of the Brook study may not apply to our patients in the ED. Lastly, I informed the nurses that the study also excluded patients suspected of being under the influence of alcohol or any drug of abuse and patients who had a history of substance abuse in the past couple of months. The nurses laughed again and noted that that would exclude virtually every ED patient who requires acute chemical sedation. I told my senior resident that this was an issue of applicability, and that while the Geodon study was nicely designed, the patient population was just too dissimilar to directly apply the results to our patients in the ED. Furthermore, I had no objection and in fact would be interested in using Geodon for acutely combative patients in the ED, but that it had not been studied well enough to date. My resident suggested that this might make an interesting research project. At that point, the nurse taking care of the patient smiled and said she had better go draw up the Haloperidol and Lorazepam so the police officers could take a break from restraining the patient. Before she left, she said that she would be interested in helping out in such a study, and a couple of the other nurses nodded their heads in agreement. What a terrible shame it would have been to lose a teaching moment like this by avoiding all contact with pharmaceutical representatives.

My resident and the nurses all learned a lot that day. It was an opportunity to model behavior skills to my resident in handling the nurses in the ED, deal with issues of conflict of interest, and ultimately lead to the development of collaborative research in the ED between our nurses and EM residents. That is a lot for a five minute teaching moment stimulated by an encounter with a pharmaceutical representative!

Lee Goldman has been quoted as saying, “companies translate biologic advances into usable products for patients. They do it for a profit motive, but they do it and it needs to be done.”<sup>9</sup> This is reality, and instead of avoiding all exchanges, it is up to the academic community in EM to develop strategies to interact ethically, professionally and to promote the highest ideals of education and scientific merit in interactions with the pharmaceutical industry.

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