interview

Steve Carney talks to Vincent Lee on the pharma industry, the FDA and public education with respect to drugs and their development

Interviewed by Steve Carney

Vincent H.L. Lee
Associate Director FDA/CDER/OPS

Vincent H.L. Lee joined the Office of Pharmaceutical Science, US FDA in March 2004, after serving on the faculty of the University of Southern California (USC) in Los Angeles for 24 years. While at USC, Lee and his research team were recognized for their research contributions in three interrelated areas. These are: defining the biochemical barriers to peptide and protein drug delivery; elucidating the structure–function of drug transporters, notably the oligopeptide transporter PepT1; and characterizing the pharmacokinetic barriers to drug delivery in treating retinal degenerative diseases, including macular degeneration. His research has been recognized by several international honors and awards, including the Young Investigator Award of the Controlled Release Society, Research Achievement Award in Pharmaceutics and Drug Delivery of the American Association of Pharmaceutical Scientists, and Pharmaceutical Scientist of the Year award sponsored by the FIP Board of Pharmaceutical Sciences. In 2003, he was awarded an Honorary Doctor of Science degree from the University of London, United Kingdom. Lee served as Past President of the American Association of Pharmaceutical Scientists (1996) and of the Controlled Release Society (1993). He is presently editor-in-chief of *Pharmaceutical Research* and of *Advanced Drug Delivery Reviews*. He is a member on the editorial advisory boards of several journals, including *Drug Discovery Today*.

How do you think that publication of clinical trial data will affect public perception in the drug industry?

For the record, I am here to express my own opinion on your well-thought-out questions. Furthermore, my opinion is not necessarily reflective of the FDA's thinking or opinion.

Public disclosure, certainly, and, upon peer-review, publication of clinical data by sponsors are long overdue. This is a powerful statement of transparency in all aspects of conducting a clinical trial. It will not only inspire confidence in the public but, I hope, it might set the stage for disclosing all relevant data, including non clinical data, in the development of a drug product. A major hurdle to progress in research is access to the entire knowledge base, of which negative data is a part. As a member of the scientific community, I feel obligated to inform other members of every dead-end I encountered, so as to increase the probability of zeroing in on the critical path to target. But in reality, no peer-reviewed publications today or tomorrow would encourage the publication of negative results. So, finding a way to authenticate and then archive negative results is what the scientific community must grapple with. I hope we can learn from the human genome project the merit of depositing the data in the public domain. It is essential that all users of the knowledge space fulfill their obligation to add to the knowledge base as well.

Do you think that the information should be universally accessible or do you think it is of little value to the general public?

Yes, in principle, the information should be available to the scientific community at large. The question is how can we be assured of the integrity of the data? As for the general public, I am not so sure of the value of the information, given its technical nature.

'A major hurdle to progress in research is access to the entire knowledge base'

In view of the recent issues related to various COX-2 inhibitors, how do you feel the issues of drug safety will affect the process of drug discovery?

Balancing safety versus efficacy is always in the consciousness of the pharmaceutical

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interview

community in the development and regulatory approval of drug products. But as a society, we tend to accentuate the positives while downplaying the negatives. The time has come to address the side effects of drug products as well, but in a 'personalized' way. As you already knew, there is usually a laundry list of side effects in every package insert. But pharmacists should put that information in the context of the genetic profile and life style of the patients to identify only those side effects that are relevant. As to whether drug development time would increase due to the concern of drug safety, it would depend on how we look at it. Personally I don't think drug development time will increase dramatically, provided we are willing to build innovative thinking into the design and conduct of clinical trials.

Is there a reliable means to estimate the 'gestation period' of a drug product? Should pharmaceutical companies working on the same therapeutic target for the first time be motivated to form a consortium? Do you see what I am trying to drive at?

To pool data and find out adverse effects?
That's correct. We must realize that if one member of a therapeutic class fails, all members of that class may also be at risk. Also, if we truly embrace that science drives drug product development and regulatory approval, then we should acknowledge the reality that progress in science is highly dependent on our access to prior knowledge. Hopefully, the path of a second drug product in a class would benefit from what was learned in the first drug product in the class. I am not sure whether the current business model does encourage this type of scientific exchange. If not, then we need to find a way to make it happen.

Related to that, the relative lack of serious drug issues is perhaps a testament to the success of agencies such as the FDA. Maybe the public thinks that there is such a thing as a totally safe drug. Do you think it's time to educate the public with respect to the risk: benefits issues, and there should be an element of informed consent at the point of care?
Those are very good points. Your second point of informed consent is intriguing and merits further study. As for your first point, let's assume consumers of the future will be very much in tune with managing their own health, lifestyle and everything else by accessing the internet. But who on the health care team should be charged with assisting the consumers to interpret the deluge of information? Perhaps the time has come for a major restructuring of health care delivery as well. As I alluded to earlier, the pharmacist is that health care professional who should step forward, but she must have access to the consumer's genetics and lifestyle profiles in order to map a 'personalized' side-effect profile and engage the consumer to be on the alert for those side effects.

'Perhaps the time has come for a major restructuring of health care delivery'

On the basis that for very serious diseases, people are prepared to put up with significant side effects it is perhaps a case of what they are prepared to tolerate for the condition that they have?
I agree. To add to that, future drug development may opt for relatively homogeneous targeted populations with respect to drug pharmacokinetic and pharmacodynamics rather than the current heterogeneous population model, the so-called blockbuster model. I am optimistic that this more focused approach would be able to shorten drug product development time, allowing timelier introduction into the therapeutic space without sacrificing product quality.

How avidly do you think pharmaceutical companies will take up the invitation to submit pharmacogenomic data?
Well, amazingly enough, the trend is encouraging. But I don't have the exact numbers to date at my finger tips.

But do you envisage a time perhaps when such information will be mandatory rather than encouraged?
Let me put it this way. If that information is essential for the industrial scientists to render a decision on the drug products' safety and efficacy, then reviewer scientists should be granted access to it as well. Today, even though we are living in a knowledge society, sadly we are still operating as if we were in the bygone industrial era. That can't go on for much longer. What we are finding now is that the sponsors have access to the public database, their in-house database, but not their competitors' database. Won't our resources for drug product development be better utilized if we can learn from the experience of our peers?

'Pharmacists must be more proactive in educating both the consumers and the physicians'

What do you think about the trend to direct to consumer advertising? Do you think there needs to be some more legislation here or, in your opinion, would you ban it all together?
Well, the pharmaceutical companies are already addressing this very issue on their own. It is not so much about the overarching principle of direct to consumer advertising, it is more about the way advertising is done on television. A spot on TV in prime time has to be succinct because of the associated cost. Consequently, the context surrounding that claim may not be highlighted. But what about the internet, which is a marvelous tool to lead the user down a critical path. At the same time, pharmacists must be more proactive in educating both the consumers and the physicians of the context of whatever claims made.

Do you think that pharmacists could prove to be the point of information for patients more than they are at the moment?
Absolutely. Please allow me to speculate on the future of how consumers would prefer to have their prescriptions filled. So long as drug products are viewed as a commodity of commerce, consumers of the future may not hesitate to fill their prescriptions on line from the so-called 'internet pharmacies'. As a consumer, I am apprehensive about doing that right now because I am not sure of the quality of the drug product. But once that is done, I won't be surprised that I will order the drug product directly from the manufacturer, bypassing the pharmacy. What prompted that thought was my recent experience of ordering an iPod from Apple. I was amazed to notice my order was shipped directly from