# IN THE PIPELINE

Derek Lowe's commentary on drug discovery and the pharma industry. An editorially independent blog from the publishers of *Science Translational Medicine*.

By Derek Lowe

## Sticky Containers, Vanishing Drugs

By Derek Lowe | August 29, 2008

There's no end to the variables that can kick your data around in drug discovery. If you concentrate completely on all the things that could go wrong, though, you'll be too terrified to run any useful experiments. You have to push on, but stay alert. It's like medical practice: most of the time you don't have to worry about most of the possibilities, but you need to recognize the odd ones when they show up.

One particular effect gets rediscovered from time to time, and I've just recently had to take it into account myself: the material that your vials and wells are made out of. That's generally not a consideration for organic chemists, since we work mostly in glass, and on comparatively large scale. There are some cases where glass (specifically the free OH groups on its surface) can mess up really sensitive compounds, but in drug discovery we try not to work with things that are that temperamental.

But when you move to the chemistry/biology interface, things change. Material effects are pretty well-known among pharmacokinetics people, for example, although not all medicinal chemists are aware of them. The reason is that PK samples (blood, plasma, tissue) tend to have very small amounts of the desired analyte in them, inside a sea of proteins and other gunk. If you're going down to nanograms (or less) of the substance of interest, it doesn't take much to mess up your data.

And as it turns out, different sorts of plastics will bind various compounds to widely varying degrees. Taxol (OK, taxotere) is a **notorious** example, sticking to the sides of various containers like crazy. And you never know when you're going to run into one of those yourself. I know of a drug discovery project whose PK numbers were driving everyone crazy (weirdly variable, and mostly suggesting physically impossible levels of drug clearance) until they figured out that this was the problem. If you took a stock solution of the compound and ran it though a couple of dilutions while standing in the standard plastic vials, nothing was left. Wash the suckers out with methanol, though, and voila.

**Here's a paper** which suggests that polystyrene can be a real offender, and from past experience I can tell you to look out for polypropylene, especially the cheap stuff. You won't notice anything until you get way down there to the tiny amounts – but if that's where you're working, you'd better keep it in mind.

## 24 comments on "Sticky Containers, Vanishing Drugs"

**HelicalZz** says:
August 29, 2008 at 8:47 am

Two words – method validation.

Not full blown, but linearity and limit of detection just gotta be done. First.

**juniorprof** says: