

## Interview with Ray McCain, Manager of Discovery Research at Merck's West Point, PA

# Current trends and the future of SFC

Ray McCain has 15 years of experience in the pharmaceutical industry and has a wide knowledge of analytical and preparative chromatography. He has held positions of increasing responsibility, working in Merck's Manufacturing Division for the first half of his career before transitioning to Merck Research Laboratories. Ray has spent the past five years managing the chiral and achiral separations lab in Discovery Research at Merck's West Point, Pa. facility. In addition, he is a member of the Board of the Green Chemistry Group.

### Phenomenex:

Do you see the SFC market increasing this year... 5 years? Do you see other purification techniques increasing as well or decreasing due to SFC?

### RM:

I think the SFC market will increase over the next 12 months and will continue to increase in the next five years as the benefits of SFC are experienced by an increasing number of people in the chromatography community. SFC is the preferred choice for many purification laboratories handling chiral molecules and it appears that achiral applications are growing at a rapid rate as users want to experience the same benefits from achiral purification as they do with their chiral separations. Some of the drivers that will lead to increased SFC exposure in the achiral world are the development of more robust instrumentation and the recent delivery of numerous novel achiral stationary phases to market.

I think SFC will continue to replace semi-preparative and preparative HPLC systems used for chiral applications. I don't feel that HPLC will be completely replaced by SFC for chiral applications but in labs I am familiar with, once SFC is embraced for chiral purification, 90% or more of the work is routed from HPLC to SFC. On the achiral front, I consider SFC as an orthogonal technique to HPLC, with considerable overlap. There have been numerous papers out over the past 2-3 years showing how achiral SFC and HPLC are complimentary techniques. Most of the studies reveal that separation is possible by SFC when it is not possible by HPLC and vice versa. As a result I feel the two techniques will continue to coexist for years to come.

### Phenomenex:

What is the biggest challenge that SFC needs to overcome to make it a widely used technique?

### RM:

The cost of the instrumentation as well as the perceived difficulty in performing system validation are two of the barriers for labs entering the SFC market. I think the introduction of some of the newer analytical SFC systems that are reported to be able to be validated for GxP applications will help the technique enter numerous regulated markets where it will be in the hands of a much wider, and larger, audience. This increased market presence should give us the confidence that the technique does in fact deserve its own space in the appropriate laboratories and should diminish some of the anxiety associated with experimenting with a new technique.

### Phenomenex:

How important is the "Green Chemistry" concept and what impact does it have on the overall chromatography market?

### RM:

The Green Chemistry concept is being embraced by many separa-

tions lab for several reasons. First, the "greener" chromatographic processes are economically more efficient than the alternatives. Many of the traditional co-solvents used in SFC, methanol and ethanol, are cheaper, renewable, and less toxic, than the solvents they replace in both normal phase and reversed-phase chromatography. The decreased waste disposal stemming from an SFC separation compared to the alternative 100% liquid separation is also favorable from a cost standpoint. Second, it improves public relations companies develop with their neighbors, communities, and government(s) by showing them that they are conducting business in an environmentally friendly fashion.

### Phenomenex:

Which applications benefit the most from the advantages of SFC separations?

### RM:

The most beneficial applications for SFC in my opinion are chiral separations, due to the historical extensive use of normal phase conditions in this area. Supercritical/subcritical CO<sub>2</sub> has similar properties to hexane which often provides similar chromatographic selectivity when comparing chiral SFC with normal phase chiral HPLC. This similarity allows for a relatively easy transition to SFC while immediately experiencing the benefits of SFC. In contrast, achiral SFC often requires a switch from reversed-phase to normal phase thus often demanding a multiple column screening protocol to find an appropriate separation. At this point there is no direct correlation in chromatographic selectivity between SFC and RP-HPLC which is why the screening is performed.

### Phenomenex:

Today, SFC is used primarily in the lab and smaller scale environment, do you think that this technology will become a production scale technology one day?

### RM:

I consider some of the SFE work currently being performed as production scale. The decaffeinating of coffee is a prime example.

### Phenomenex:

What is one change or improvement you hope to see in the SFC separations industry over the next few years?

### RM:

I continually hope for an achiral stationary phase to be developed for SFC, a phase that has wide applicability, similar to the quasi-universal C18 phase in RP-HPLC. The delivery of such a phase would minimize screening and in combination with a validated and robust SFC system, could propel the technique into much wider acceptance.