

# Molecular Spectroscopy Workbench

## Meeting Report: IFPAC 2004

The 18th International Forum for Process Analytical Chemistry saw increased participation by pharmaceutical companies and FDA, and the formation of a manufacturers' association that will address regulatory compliance issues.

**Emil W. Ciurczak**

**G**reetings, faithful followers. Some of you, who are long-time readers of this column, might remember that I once reviewed a number of conferences that I thought were important to spectroscopists. These conferences are covered by the full-time staff of this fine journal. However, occasionally a conference not attended by the *Spectroscopy* staff is worth noting. One such meeting was the 18th IFPAC (International Forum for Process Analytical Chemistry), held January 12–15, 2004, in Arlington, VA.

Because I do a fair amount of project management of pharmaceutical analysis method development, I will refer to IFPAC 2004 as the "Super Bowl of PAT (Process Analytical Technologies)." I was amazed at the number of pharmaceutical papers presented and pleasantly surprised at the percentage that showcased spectroscopy. The IFPAC conferences originally were aimed at the chemical and petroleum industries. Five or six years ago, one or two sessions of pharmaceutical papers were introduced. The director of the conference, Bob Zutkis, made the correct decision to involve Rick Cooley (Eli Lilly, Indianapolis, IN) as his point man for the pharmaceutical effort. This year, Rick and his co-chair, Lee McPeters (Rohm and Haas, Spring House, PA), put together a magnificent showcase of pharmaceutical process analysis. Instead of having one or two sessions as was the case a mere four years ago, this year there usually were three concurrent pharmaceutical sessions and the chemical portion was a single session.

In addition to the massive input of major pharma companies, FDA had a strong presence at the event. Representatives such as Ajaz Hussain (deputy director and major force behind PAT) and Ali Afnan (also CDER, FDA) gave several talks and were instrumental in many of the sessions.

Three individual parts of the conference are worth noting: the papers given at the conference, the formation of a new manufacturers' association, and a new American Society for Testing and Materials (ASTM) committee dedicated to PAT.

### Technical Papers

There were so many paper presentations this year, I had to make decisions as to which I could attend. Triage is unpleasant when there are at least two paper presentations at any given time worth seeing. True to my calling, I tried to attend any presentations involving spectroscopy, and there certainly were many of them.

As the old standby, near-infrared (NIR) spectroscopy was, of course, well represented. Fiona Clarke (Pfizer, Sandwich, UK), Mark Henson (Pfizer, Groton, CT), Robbe Lyon (FDA, CDER, Rockville, MD), and Neil Lewis and Linda Kidder (both from Spectral Dimensions, Olney, MD) all spoke about NIR chemical imaging. The advances in this technique during the past two or three years are amazing: both hardware and software have become incredibly sophisticated. NIR chemical imaging has moved from being a pure R&D, lab-based instrumental technique to the process line to aid granulating and mixing studies, essentially in real-time.

In fact, an entire half-day session was devoted to chemical imaging. Also speaking was Carl Anderson (Duquesne University, Pittsburgh, PA), who addressed the topic of pharmaceutical compacts. NIR chemical imaging can be used to show how each component is distributed within a mixture, amounts of each material, the particle sizes and agglomeration of materials, and, of course, physical changes such as the relative crystallinity and polymorph distribution.

Also in the imaging session were Andrew Kearsley (Oxford Lasers, Oxfordshire, UK), who spoke about imaging the size



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and shape of particles in the 1–1000  $\mu\text{m}$  size range; Brian Cole (TeraView Ltd., Cambridge, UK), who showed interesting data on terahertz spectroscopy and imaging; and S.G. Kazarian (Imperial College, London, UK), who shared data from a diamond attenuated total re-

each must be averaged over a number of scans (for example, from 32 to 64) to bring the signal-to-noise ratio to a usable level. He explained that diode arrays are becoming less expensive and narrower in range. These narrow-range arrays are excellent for specific

CT) provided several nice examples of how a Raman system can be used in a number of applications formerly reserved for NIR spectroscopy: raw material identification, process monitoring, blend uniformity, and polymorphism determination.

## THE “SUPER BOWL OF PAT” INCLUDED A LARGE NUMBER OF PHARMACEUTICAL PAPERS, WITH A PLEASANTLY SURPRISING PERCENTAGE THAT SHOWCASED SPECTROSCOPY.

flectance-infrared (ATR-IR) accessory. All these non-NIR papers were quite good and showed how imaging is expanding rapidly.

NIR spectroscopy also was seen in presentations about fluid-bed dryers, coating operations, and wireless blend uniformity studies. Of course, papers on chemical reaction monitoring were presented as well.

The important topic of calibration transfer was addressed by Katherine Bakeev (FOSS-NIRSystems, Silver Spring, MD) and was mentioned in passing in several other applications talks. With NIR spectroscopy becoming more of a PAT tool, calibration and validation, as per FDA’s definition, are being discussed more than the applications themselves. Jim Drennen (Duquesne University) presented a case study on calibration transfer; Ali Afnan (FDA, CDER, Rockville, MD) gave the FDA perspective on calibration transfer; and Barry Wise (Eigenvector Research) discussed the matter from a chemometric perspective.

John Gethner (Adaptive Analyzer Technologies, New York, NY) presented an interesting paper that showed the benefits of real-time mixing measurements with a wireless diode-array instrument. The ability to monitor processes more quickly also was emphasized by Martin Warman (Pfizer, Sandwich, UK). He declared that grating-, interferometer-, and even acoustic-optic tunable filter (AOTF)-based instruments were too slow for many process measurements. Although individual scans with each might be rapid (from  $<1$  s to  $\sim 1$  s),

analyses. The two most used spectral regions for water in the NIR, for instance, are well documented: 1420 and 1940 nm. Narrow-range diode arrays over one of these regions could provide resolution approaching the best Fourier-transform (FT) instrument, with the natural speed of the diode-array instrument.

There were more Raman papers than in recent meetings. In one of the best presentations, Stuart Farquharson (Real-Time Analyzers, East Hartford,

### A New Manufacturers’ Association

A major initiative also was announced at this year’s conference: a manufacturers’ association established through IFPAC. One purpose is to attempt to standardize criteria used to judge whether a company is in compliance with FDA standards. Instead of a steady stream of QA personnel from pharmaceutical companies performing audits of instrument companies (interrupting business and tying up personnel), a single audit, agreed upon by a majority of

companies, could be performed once and the results disseminated among pharma manufacturers.

While the concept is in its infancy, the idea is quite noble. At the moment, there are so many standards in use that a company, long doing business with major pharmaceutical manufacturers, could be deemed unworthy by another company.

Members will meet and form a constitution, list goals, elect officers, and begin to do business. In an effort supported by FDA, the mission of the organization would be to make the lives of both FDA and pharmaceutical QA groups a lot easier. If the IFPAC-MA is successful, time and money will be saved in the approval of equipment for PAT use. Because the purpose of PAT is to streamline manufacturing and encourage innovative applications of technology, speeding up approvals is a good thing.

The ability to ensure that instruments meet minimum specifications certainly is a worthy goal, as is the desire to minimize the amount of validation needed for installation qualification and operational qualification (IQ, OQ). This certification, similar to ISO 9000, would cover most concerns held by companies. If there were a few smaller concerns expressed by some departments of pharma companies, these mini-audits could be performed as extensions of the IFPAC-MA documentation. The effect would be a shorter, less-intrusive audit process, and the instrument manufacturer and pharmaceutical customer ultimately would benefit.

### ASTM Committee E-55

The ASTM has long been a mainstay of analytical chemistry. The organization, through careful, deliberate study, has given the industry a large number of definitions and procedures. The range of topics covered is huge, but includes all branches of spectroscopy and

chemometrics. Committee E-55 will specialize in PAT. The sub-branches will be:

- E55.01 PAT Systems Management
- E55.02 PAT Systems Implementation and Practice
- E55.90 PAT Executive Subcommittee
- E55.91 PAT Terminology

By using consensus standards for PAT, FDA will be able to assess any manufacturer's systems more rapidly and, more importantly, all will be judged against a common standard. This will take much of the subjective nature of an inspection out of the process.

Early last year, FDA approached ASTM and proposed the formation of a



PAT committee. In October 2003, there was a PAT Committee planning meeting at ASTM, with an organizational meeting on December 1, 2003. In January 2004, officers were nominated and elected, and, on February 11–12, 2004, the committee held its first meeting. The committee members are: Chairman, Don Marlowe, US FDA; Vice Chairman, Ray Scherzer, GSK; Membership Secretary, James Drennen, Duquesne University; and Recording Secretary, Gawayne Mahboubian-Jones, Optimal Industrial Automation.

The question, "why ASTM?" was asked. The answers were specific. The

organization has been setting standards for more than 100 years, is accredited by the American National Standards Institute (ANSI), is recognized worldwide, and is not aligned with any for-profit organization. The members of the E-55 committee, like all ASTM committees, are from government, industry, and academia, thus assuring a balanced approach to the problem. This committee, yet to officially meet, could well prove a boon to PAT. Despite the importance of PAT to industry, the measured pace of *any* ASTM committee might be a bit slow for industry. There will be a time between the formation of E55 and any useful standards. In the meantime, industry and FDA will work together to make PAT work. . . I am sure. For further information about the E-55 committee, contact Pat Picariello (e-mail: [ppicarie@astm.org](mailto:ppicarie@astm.org)) or check the ASTM Web site at [www.astm.org](http://www.astm.org).

### Some Observations

Considering all the happenings at a single three-day conference, you can see why I was excited to be there. During the past five years, I have seen the pharmaceutical sessions grow from 10 to 15 papers, in total, to three days of concurrent sessions. The PAT initiative has invigorated the analytical instrument business and spectroscopy is alive and well in the 21st century. Almost as a side-effect, drug product consumers will get lower cost products at an increased rate of production. This sounds like the win-win-win scenario Ajaz Hussain (FDA) keeps talking about. I'm anxious to see where we go from here. ■

### Next month in Molecular Spectroscopy Workbench ...

Near-infrared chemical imaging is an important tool in the PAT initiative for pharmaceutical manufacturing. Neil Lewis and co-authors explain what NIR-CI is and what its role in PAT will be.