Trends-in-Medicine

March 2007

by Lynne Peterson

SUMMARY

Pharma spending for 2007 is predicted to be flat but may be offset somewhat by increases in generic, CRO, small/medium-sized pharma, and biotech spending. ♦ The pricing environment is "pressured," and there is a lot of discounting and dealing going on but no price war. ♦ The mass spec market is healthy and picking up steam in the clinical lab setting. ♦ **Agilent**'s new high end triple quad (6410) is no serious threat to Waters high end triple quad, even with a 20% lower price, but it may lure single quad users up to a triple quad – if they don't opt for the **Applied Biosystems**' promotion, a lower-end triple quad for the price of a single quad, which underprices Agilent. But Agilent's strong base in GC and LC should help sales of its triple quad. ♦ Some sources are leery of **Waters**' Synapt, calling it a device in search of an application. ♦ Sales of **ThermoFisher**'s FTMS "plummeted" with the entry of the Orbitrap, and the Orbitrap market may be getting close to saturation. Customers are worried about Thermo's ability to integrate Fisher, and some are reporting service and delivery problems. ♦ The hottest new technology on the horizon is Agilent's LC-on-a-chip, but it is still a couple of years away from the breakthrough use that customers and the company envision. ♦ Millipore remains the gorilla in water purification.

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PITTSBURGH CONFERENCE (PITTCON) 2007

February 26-March 1, 2007
Chicago

Despite winter snowstorms, attendance at this year's PITTCON, a laboratory science conference and exposition, was slightly ahead of last year, but there were more exhibitors (10,440 from 1,086 companies) than attendees (9,477). Attendees and vendors repeatedly complained that attendance has been shrinking over the past five years. Traffic at the booths wasn't heavy, but most companies questioned were satisfied with the quality of the visitors and said they were getting sufficient sales leads. An official of one large company commented, "It seems more people are visiting the booth to try to sell to us or collaborate with us than buy."

PHARMA AND RELATED SPENDING

Senior officials of every major instrument company questioned at PITTCON agreed: big pharma spending will be flat in 2007 compared to 2006, which they described as a downturn since 2006 spending was higher than 2005 by low single digits. Pharma spending was strong in 4Q06, but sources warned against extrapolating that across 2007, saying it was a traditional end-of-year spending spree. Comments on pharma spending for 2007 included:

- *Agilent #1:* "If you take the top 30 accounts, there is no general pattern… Some are spending and upgrading; others are more in discovery. Some are outsourcing more of their research to biotech. In our first quarter, our business in the U.S. was stronger than we saw last year. I think moving forward in the U.S., growth will be in single digits, and the key growth will be in Asia and Europe…(But) even if the market is not growing, we will try to capture more share."
- *Agilent #2:* "Budgets for the top 15 pharmas are flat. Some are up, and some are down, but overall, budgets are flat. But pharmas have significant efforts in patient stratification and biomolecules, and you can grow in a flat market in those areas. We are new to high end MS (mass spectrometry), but we are deep in genomics, and that's what differentiates us from Waters…Pharma always has end-of-the-year spending. We didn't think there was anything unusual last year; it was typical seasonal spending. Spending on biomolecules and informatics can be extrapolated to 2007, but not other areas."
- *Waters #1:* "Generics are spending like the band. Big pharma spending is flat."
- *Waters #2:* "Last year, pharma business grew 8%. Outside pharma, business was up double digits."
- *Waters #3:* "CRO (contract research organization) and generic spending is growing, and we are going where the growth is."

- *ThermoFisher #1:* "You can't extrapolate from 4Q06 as the new run rate. 2007 pharma spending will be flat. Biotech and specialty pharma is driven by venture capital funding, and that is up. And large biopharmas have money to spend."
- *ThermoFisher #2:* "In general, though pharma spending has softened, it is still riding fairly high above the inflation rate. Most of it is on development, but discovery is still at the same level…No. 1 is consumables, which worldwide are about $500 million on QPCR consumables, and No. 2 is informatics…HPLC is about No. 5 on where pharmas spend R&D money…The RNA gene knockdown experiment we do is growing exponentially in pharma."
- *Contract research organization (CRO):* "Big pharma spending will be flat this year."

Asked where pharma will spend money this year, a Waters official said, "Budgets this year are in flux. There is a lot of merger and acquisition activity (by pharmas)…There is restructuring in the industry in aggregate. Their budgets are not expanding at double digit levels. We expect that to be flat this year. But the companies are very focused on revitalizing their pipeline. There are a lot of drugs in development but a tremendous set of patent expirations over the next 3-5 years… There is a big focus on biotech, biopharma, and partnerships with universities and smaller companies. So, we see tremendous opportunities in libraries, and in focusing on efficiency and development." Another Waters official said, "We have had an opportunity to meet with a lot of (pharma) executives …and we met recently with pharma purchasing agents. They are looking for ways to change their business practices. They've determined the way they've been doing it is just not working as well as it needs to. Rather than looking for technology with 5%-10% efficiency gains, they are looking for ways to change business practices. Synapt and disruptive technologies are seeing more interest…Traditionally, all they want to do is push the price down…and initially we were concerned about that…but they also want to take technology back to their organization and change the overall lab process to result in a better investment in research…I think they recognize they have to change."

Asked what new paradigm pharma is likely to pursue after combinatorial chemistry, a Waters official said, "We spend a lot of time with these major accounts…With some new technologies we are seeing very senior level delegations coming to us to sit down and talk about their challenges. Big pharma recognizes that the paradigm of how they are developing has to change. Is there a particular singular direction today? No. Clearly, the whole trend to outsourcing and other models is a business trend, but does that get new drugs to market faster? Probably not. I think pharmas are putting their investments across a wider array…It is another period of transition for the pharma industry, but they know they have to continue to invest."

National Institutes of Health (NIH) and the National Science Foundation (NSF) budgets are relatively flat, and that is pressuring higher end products in particular, but generics and CROs still appear to be spending. A source said NIH and NSF like to fund leading edge technology, adding "Grants are more often given when they include leading-edge technology, like Thermo's Orbitrap." Another source said, "An NIH grant slowdown hurts academic researchers, and big pharma is flat…Small and mid-size pharmas and biotechs have to spend to bet on the future, and they are funded by venture capitalists, so they should be okay this year. And there appears to be an increase in nutraceuticals." A third source said, "Proteomics continues to be robust despite a flat NIH budget; Asia is good. Our technology will force people to rethink how they are doing proteomics." A fourth source said, "NIH is not a big driver for us; it's <1% of our business."

The market from ThermoFisher's view:

- Big biopharma is looking for more purchasing efficiency.
- Big biopharma increasingly is outsourcing non-core activities.
- There is a growing trend to do analysis outside the lab.
- There is a convergence of research and diagnostic tools.
- Scientists are demanding better integrated solutions to improve experimental accuracy and laboratory productivity.

PRICING ENVIRONMENT

Sources agreed that the pricing environment is feeling pressured, but list prices are holding. However, customers said there is a lot of backstage discounting and dealing. A Waters official said, "There is always price pressure. We recently had a meeting with procurement agents for our biotech and pharma customers, and we are really looking to build our supplier relationship. Pricing pressure is there, and they are hunting for value…But Acquity can replace two or three LCs." A CRO official said, "The pricing environment is flat. Budgets are tight, but companies are willing to spend."

Agilent and Applied Biosystems (ABI) are offering triple quads at discounted prices (*See details under each company*). An Agilent official said, "There is some price sensitivity, but price point/value is making it more affordable. It's a balance of throughput, data, and price. If a customer is only choosing throughput and data, then they are more likely to choose a triple quad than if price is an issue…We see people who would only buy a single quad before buying a triple because of price, and that is helping to shift all of MS…As any technology matures, it goes through a pricing curve. Then, you have to enhance the technology or optimize the manufacturing, and we are doing both."

Mass Spectrometry Market

Sources generally agreed the MS market will slow if pharma budgets are flat as projected, but that might be offset by an increase in spending by CROs. Comments on the MS market included:

- *Industry #1:* "When pharma spending on MS goes down, CRO spending usually goes up because pharma farms the work out, so sometimes a pharma spending decline is a positive for CROs, and they will buy a lot of equipment. If that happens, we will be okay. My CROs are growing …Smaller pharmas and biotech often use CROs, and that helps, too. But it depends on how many small-to-medium-sized pharmas/biotechs get bought (by large pharma). When that happens, MS sales go down because big pharma buys them for intellectual property (IP)."
- *Industry #2:* "The MS market is very healthy, especially in the focus on biomolecules."
- *Industry #3:* "We are seeing a tremendous number of bio drugs enter the pipeline. Ten years ago, 15% of development and discovery was biomolecules, and today it is ~26%. That and metabolomics are driving high end MS into therapeutic customers to accelerate trials."
- *Industry #4:* "Judging by the last year and the fourth quarter, our MS business grew robustly, and we think this will continue…We are confident of MS irrespective of pharma (budgets)."
- *CRO:* "The MS market just continues to grow because it is used for so many things."

Is MS picking up steam in the clinical lab setting? Yes, sources agreed. One said, "There is a big push to do more lab work without more expense, and the biggest expense is people, and MS is automatable."

One area that sources at several companies cited is immunosuppressant drugs, where a chemistry kit costs $12 to run a blood level test but MS can run it for ~$1-$2 – and in significantly less time – after the $200,000 initial cost. ABI's MS is not FDA-approved, so for clinical lab use it is sold to laboratories with a CLIA license. An ABI source said, "We'd have a bigger market (for MS) with FDA approval, but the time and cost of that is not justified – and there is always the risk of an FDA turn-down." Another said, "MS is picking up somewhat. It is a potential growth market in a few years." A Waters official said, "LC-MS is getting a lot of sales to clinical labs for monitoring drug therapy, for drugs-of-abuse testing, and for neo-natal screening." An Agilent official said, "Clinical lab use is real, and it is now. It is due to metabolomics." Another Waters official said, "Ten years from now, I don't think there will be an MS market. (But) MS is picking up steam in the clinical lab setting, particularly neo-natal screening and immunosuppressant drug monitoring."

How is the low-end MS market faring? An Agilent official said its QTOF is selling "above expectations," adding, "We thought everyone would go to large molecule applications and ~25% to small molecule applications."

Food Safety Testing

Asked how food safety testing in Europe and the U.S. compare, a Waters official said, "We have experience working with Europe, Asia, and U.S. testing labs…It is fair to say, in most situations, in Europe and now in Japan the regulations are more stringent than what we've seen in the U.S. As we see more and more issues (like spinach and peanut butter) in the U.S., there will be pressure to put more regulations in place. And we work with large food companies that need to bring the standards up so the product can go anywhere in the world." He indicated that it is likely to be food producers who will really lead the testing business because they want to assure quality of the product for exportation, "When you look to Europe and Japan, regulations drive the industry. When you look to the U.S., food producers are more taking the lead to be sure of their legal and financial risk and to be sure they can move product around the world."

Individual Companies

Sources generally agreed that there is little that is very exciting at this year's PITTCON. The hottest new technology may be Agilent's LC-on-a-chip. An Agilent source said, "Today, this is very specific to applications and a component, and it still requires an LC or pump or some mechanism that goes into the chip. But in the future, it may be able to be utilized as a type of chromatograph. How far away that is is uncertain. But it is very unique IP." Another Agilent official said, "LC-on-a-chip is two years away. We have prototypes running with gradients on a chip. It is breakthrough technology. When it is ready, it will sell as a fully-integrated workflow solution."

India and China are key markets for the large instrument companies right now. Waters and ThermoFisher manufacture in Singapore, and Agilent manufactures in Shanghai. An Agilent official said, "We have a strong position in China, and we are expanding in India. Japan has been a key focus." A Waters official said, "India and China are exploding, in the high double digits. We are manufacturing now in Singapore. It is not as inexpensive as China, but it is safe, stable, had a lack of corruption, and a respect for IP." Another Waters official said, "The Chinese government is very interested in technology, very interested in high end technology, but our China business is only about as big as our business in New England, so we are very early in the adoption curve." A third Waters official said, "The Indian generic market is the fastest growing market for us. Agilent has been in China longer than us. China exceeded Waters' expectations, but generics in India is the primary opportunity." A Thermo official said, "The highest growth is occurring in India and China…It is unbelievable what is going on there, especially in China."

In a 2006 ASMS survey, Thermo was ranked No. 1 in instrument reliability, customer service, ease of use, technical specifications, and software and data handling. Agilent took No. 1 in price/value. An instrument sales rep said, "Agilent is more in smaller, applied markets. ABI is more in pharma than Agilent or Waters…Agilent is the gorilla in GC-MS; Agilent and Waters are both good in LC-MS…In MS, Agilent is gaining share, and we think it is from Waters. Waters seems to want to be more in HPLC than MS. It's interesting that Waters licensed control of the Acquity HPLC to Thermo and Applied Biosystems for the front-end, so any of the big three MS companies can have an Acquity front-end, which weakens Waters' MS position tremendously. However, Acquity is starting to find its place. It was over-marketed at first, and everyone wanted it…The HPLC market is settling out."

In the HPLC market the three competiting instruments are: Thermo's Accela UHPLC, Waters' Acquity UPLC, and Agilent's 1200. Thermo has a very clever two-speed system with Accela, Waters' UPLC is not really fully ready, and both are slightly ahead of Agilent's 1200. However, even Thermo sources predicted that Agilent will do well with the 1200 because of its installed base of LC and GC customers.

Support and service are very important to most customers. Both Waters and Agilent were claiming to have the best service. Waters officials pointed out that all of their technicians are employees of Waters, that service is not contracted out as it is at Agilent. One said, "We rejected third party management of instruments. We've seen people here at PITTCON who've come back to us (for service) after a fling with a third party…Large pharma is looking to cut cost in service, and we don't think that is sustainable in the long term. They left for a lower price, but downtime cost is enormous, and they can't afford that."

Agilent countered that 55%-60% of its service is done with Agilent employees, and the rest is with well-trained adjunct service providers (ASPs). In fact, Agilent was touting its Intelligent Services, broad service contracts for customers who are out of the one-year warranty on Agilent equipment or want other companies' products covered. In Europe, more than in the U.S., Agilent is doing multi-vendor service, but Agilent is not doing any multi-vendor service in Asia. An Agilent official said, "Pharma wants to lower costs in non-core areas and do it in the most efficient manner with maximum uptime. Some pharmas do service in-house…I see strategy shifts as pharmas experiment…We support not only Agilent products but other companies' equipment." Another Agilent official said most of the ASPs are in applied materials, much less in pharma, but he noted, "Pharma and big biotech contracts for lab-wide support are growth, with ASPs sometimes."

He added that Agilent doesn't segment customer services customers by industry but by:

- **Risk.** High risk customers (those willing to accept high risk, where they generally aren't running 24/7) or low risk, where downtime is critical.
- **Compliance vs. non-compliance.** Compliance customers include pharmas and food plus some QA and QC.

Both ABI and Agilent are trying to lure single quadrupole users up to triple quadrupoles.

- **Agilent's** strategy is to offer its new, high end triple quad at a 20% discount to Waters triple quad, but an official admitted that this is likely to lure more single quad users to upgrade than to wrest higher end business from Waters, though, of course, they hope to do that, too.

- **Applied Biosystems** (ABI) doesn't sell a single quad, but it is offering its lowest sensitivity triple quad (API 2000) for the price of a single quad – $99,000 – in a special promotion running in 2007 called Triple Play. The API 2000 used to be sold for ~$165,000; it is now touted as the least expensive triple quad on the market. An ABI source said, "Competitors say Triple Play is because we plan to discontinue the API 2000, and we are ***not***. We will send a letter to customers that we aren't discontinuing it…We have been the gorilla at the high end, and we want to reach down into the Waters and Agilent areas…We like finding a new market for this product instead of discontinuing it." The API 2000 is not as sophisticated or sensitive as Agilent's high end triple quad, which is more comparable to the API 3200 or API 4000, according to ABI.

The ABI triple quad has a very different look to the triple quads by Waters or Agilent. An ABI source explained, "There are a lot of people comfortable with HPLC and not MS, so Agilent and Waters packaged their box more like a UV detector. Ours looks like an MS."

ABI MS Systems

Model	Sensitivity	Approximate price	Typical customers
API 2000	1x	$99,000	Applied markets, food, environment
API 3200	10x the API 2000	$185,000	Applied markets, food, environment
API 4000	10x the API 3200	$295,000	Pharma, CROs
API 5000	3-6x the API 4000	$375,000	Pharma, CROs

AGILENT TECHNOLOGIES

Agilent is predicting growth in its life sciences (pharma, academic labs, and diagnostics) business of 12%-15%, vs. a market growth rate of 7%-9%. An official said, "Diagnostics is a new market space. It is an opportunity. We are only focused on heart disease and really in that cholesterol testing. Many pharmas are looking at the next generation of cholesterol lowering drugs. They need more information than they can get today…They want to look at subfractions of HDL and LDL." Another official said, "We see pharma growing in the high single digits worldwide, and we expect to outgrow the market by a couple percent, so we are at the high end of single digits, and that is mostly LC…The academic market is pretty good size double-digit growth for us, but the segment itself is

soft with 6%-7% growth…We expect to outpace the market and take share."

An Agilent official said the company keeps adding more automation because "that is what customers are asking for." He said the growth initiatives are in life sciences and informatics, adding, "We intend to regain the market leadership we had in SW and informatics." He said LCMS sales have been strong "across the portfolio" but insisted, "We are not done yet …Worldwide the portfolio is healthy, and we've refreshed it and keep expanding it."

Agilent is trying very hard to take business from Waters, but sources did not think it is displacing ABI or Waters at the high end, and with ABI targeting single quadrupole users, ABI could feel pressure on both ends. An Agilent sales source said, "Overall sales are 45% in life sciences and 55% clinical…I think we are taking share from smaller companies. But no one is growing by leaps and bounds…We are a broader separations company than Waters. We know chromatography very well. We have a broader technical footprint." A Thermo official commented, "Agilent's LC is doing well. Waters UPLC is doing well. Agilent and Waters are more than ever going head-to-head. In single quad, Waters and Agilent are comparable, so Agilent wins on price. In triple quad, Waters has better performance. In bioanalysis, quality trumps price."

The new technology that Agilent brings to the table was described as:

- **Capillary flow technology** to solve challenging application problems easily with simplified flow control.
- **Trace ion detection** for better detection of trace level residues in complex matrices.
- **Lab monitoring and diagnostic software** to maximize instrument uptime with real-time monitoring and alert notification. Every 7890 has this.

The Agilent value proposition was described as:

- Products – a broad portfolio of reliable workflow solutions.
- Optimizing customer applications and lab operations – customers reportedly increasingly are asking for this.
- Software – easy to use, open systems to maximize lab productivity.
- Services – good support and high uptime.

Asked if Agilent's high end triple quadrupole is ready for use in clinical trials or delayed for more data, an official said, "We are selling it today to customers using it in clinical trials. We have not completed the validation software…We will have more update on that timing at ASMS (American Society for Mass Spectrometry in Indianapolis, June 3-7, 2007)."

Asked about Agilent's goal of becoming No. 1 in HPLC consumables, an official said, "Currently, we are No. 3. It will be a focus through product development, collaborations, and acquisitions. The time horizon is three years."

Asked about the micro-array business, an official said it grew 56% last quarter but is still just breaking even. He said, "The micro-array space has been stuck…All the players in the space suffer on profitability. The general market, gene expression, is really not a very good market. It is growing in the number of tests, but the price per test is dropping. It is a difficult equation to balance…Our main focus in emerging areas is…pushing into chip-on-chip and human genomics. That is what we see driving the fundamentals, and if we can get that, we can continue to serve profitably the gene expression market."

Later, attendees were asked about this comment, and they all agreed that the gene expression market is as tough as the Agilent official indicated. Everyone believes it will eventually find applications, but they don't expect that to happen in the near-term. An academic source said, "We get a lot of information from gene array testing, but what question does it answer? It is just a piece of the puzzle. Gene expression still has a long way to go." Another academic source said, "Protein studies are still looking for an application."

Agilent products include:

- **6410 Triple Quadrupole LC-MS.** This high end triple quad lists for $220,000 or about $280,000 with HPLC. Sales have been about one-third to pharma. A state police forensics lab was looking at this. As mentioned above, though, Agilent is selling it for 20% below the price for a Waters triple quad. A customer said, "Agilent will sell it at that price."

  Does Agilent have a problem with the 6410 triple quad? A source said, "There have been some negative field reports on Agilent's triple quad – mainly software issues." However, Agilent sources denied any software problems with their triple quad.

- **6510 QTOF LC-MS.** This device was new in the last six months. It costs $450,000, but an Agilent source said there are a lot of discounts, generally 10%-20%. About 75% of sales are to pharmas and 25% to forensics, environmental, and food customers. Pharma uses it half for large molecules/peptides and half for small molecules. In drug discovery it is used to identify and characterize new molecule entities (NMEs), screening impurities, and metabolite identification. An Agilent sales rep called it "fabulous," adding, "LC-MS is growing and expanding, though sales have slowed to low to high single digits… We are taking sales from ABI and Waters, which owns the segment today, but we are making huge inroads. We have 10% share now…Our LC-GC footprint with pharma is a foot in the door for this."

- **6100 series Q LC-MS.** There are four models, ranging in price from $80,000-$125,000. A single quad is about $100,000. An Agilent source said the company is the market share leader, with ~35%-40% share, with pharmas the biggest customers (about 75% of sales). What's Agilent's advantage? An official said, "Better spectral quad data, faster scan speed, broader molecular weight range, and compatibility with the Agilent 1200 series (HPLC)."

What's new at PITTCON 2007 for Agilent:

- **GC and GC/MS: 7890A GC and 5975C GC/MS.** An official said the 7890 will be orderable on March 1, 2007, and it will be priced "very similar to the 6890…Where we have added capability, we will value price for that." Another official said this platform has been refreshed and expanded, "We have an installed base of more than 200,000 GC and 50,000 GC/MS systems."

The 6890 is being discontinued, but an official said it will stay around "for at least 6 more months," and Agilent "will be very tuned in to customer ability, through channel partners and competitors to connect to our boxes, to be sure they do all the work they need to do in that 6 months so we can discontinue the 6890…There is no method change between the 6890 and the 7890. The user will see new software tools, but no method changes."

Capillary flow technology is an add-on to the 7890 that costs $2,500.

Agilent also was touting the time savings in pesticide detection with the 7890. An official said that in the detection of pesticides in milk extract, for example, the 7890 saved 27 minutes.

- **LC/MS:** An official said this portfolio has been expanded, with new HPLC chip capability for triple quad and QTOF.

- **Services:** Expanded lab-wide services. An official said, "What we've learned is that mid-sized labs typically are much better targets. They are focused on optimizing the operations of the lab. The rest is just squeezing margins…Some deals are doing very well, but we are walking away from some deals, too."

- **Applications:** Expanded applications, particularly MS-based metabolomics solutions.

Coming later this year:

- **March:** expanding intelligent services portfolio.
- **April:** miRNA micro-arrays and new ICP/MS platform.
- **June:** new LC/MS System at ASMS.

Applied Biosystems

No new products were launched at PITTCON, but the company was showcasing the prototype of its autonomous autosampler, which was announced last year but has not been formally introduced yet. A sales rep said the key advantages of this are that the syringes are autonomous from the robot arm, so a customer can do multiple operations simultaneously. He commented, "LC has gotten faster, but autosamplers haven't kept up – until this." This should be particularly useful for pharmas and CROs. Key autosampler competitors are: Leap, Shimadzu, Agilent, and Waters. A standard auto-sampler costs $15,000-$30,000, but this will cost more than $30,000, though the final price has not been announced.

Millipore

The company's key product is water purification, and the key competitors for that are Thermo/Barnstead, U.S. Filter, and Elga. Pall may consider itself a competitor in water purification, but a Millipore official said Pall isn't in their Top 10 competitor list for water, adding that Pall is more a competitor in the bioprocessing space than in water.

Pharma and lab sources who were questioned about their water purification use praised Millipore. One said, "We did extensive research on water purification recently and decided to stay with Millipore. There are competitors, but none are a real threat to Millipore." However, another former customer decided to stop purifying its own water and buy bottled water.

There was nothing new in water purification at PITTCON – the system on display was introduced in September 2006 – but Millipore has a new water system coming out in the fall that will be shown at PITTCON 2008.

Millipore had no new product introductions at PITTCON, but the company was showcasing two things:

1. **Point-of-use water filters** – EDS-Pak, BioPak, and Millipak. These are sold to everyone from academic labs to pharmas, CROs, pulp and paper companies, cosmetic firms, and more, but a Millipore official would not say what percent of sales are to pharmas.
2. **Millex 33 mm nylon syringe filters.** This does compete directly with Pall filters. Millipore was demonstrating head-to-head comparisons of a Pall and an HPF Millex Millipore filter (with a pre-filter). The filters were matched as to surface area and size (33 mm), pore size (0.45), and membrane (PNDF). The Millipore filter demonstrated greater throughput and did it faster. The Pall filter clogged more quickly. A Millipore staffer also claimed there is less back pressure on the operator's thumb with the Millipore filter. The point goes to Millipore on this challenge.

Asked about the market for water purification systems, an official noted, "All new labs need a new water purification system, other labs are undergoing renovations, and there are a lot of new grants that require a water purification system…A slowdown in big pharma spending and a slowdown in the drug pipeline may mean a slowdown in sales, but support and service should continue to boom." Another official said, "Big pharma budgets are flat, but small pharmas can be converted from tap water to pure, and new labs are being built. If we aren't selling a system, there are consumables, and there is always growth in service." Pharma accounts for about 40% of Millipore's water purification sales.

Asked about pricing, an official said, "We are not inexpensive. People buy quality and reliability. Pall is not impacting our pricing."

Millipore is divided into two divisions – bioscience and bioprocess – but only bioscience was represented at PITTCON. The bioscience (but not bioprocess) division also will display at the American Association for Cancer Research (AACR) meeting in Los Angeles, April 14-18, 2007. An official said, "Even the pharma attendees (e.g., Merck) are in analytical chemistry departments. Serologicals' products will be at the Neuroscience meeting." Key competitors, from Millipore's perspective are Invitrogen and Kiagen in bioscience and Celliance in bioprocess.

Sources all insisted that all recent acquisitions – Serologicals, Upstate, Linco, and Chemicon – have been fully integrated. An official said key chemists from those companies relocated with Millipore, but most of the marketing and corporate staff did not.

In terms of customer service, the same software is being used for all the tracking service of all the products, but there are still separate 800 numbers, and separate specialist techs handle queries, but a common 800 number is coming. A source commented, "Customers are application-oriented, not name-oriented." Another said, "We are fully integrated now. Sales people sell all the products, and they absolutely are able to bundle them."

PALL CORP.

Pall officials PITTCON booth traffic was mostly customers and some consultants. One source said that most people visiting the booth were coming to see:

1. **Syringe filters,** which a source said Pall invented. A source said virtually all blood transfusions in the U.S. go through Pall filters. Pall is the exclusive supplier to the American Red Cross and to ~98% of all independent blood banks. The key advantage cited for the Pall filters is that Pall makes its own membrane and doesn't outsource it as competitors (e.g., Millipore) do. Pall also claims to be the only company with 24-hour global tech support, a service that was launched at PITTCON this year.

   Asked how Pall filters compare to Millipore filters, a Pall source said, they are equivalent in quality and price. However, Pall also was showcasing its water filtration system that competes with Millipore.

2. **Filter plates,** which allows samples up to 96 or 380 at a time.

A Pall official also claimed the company supports its product line and analytical applications through the entire testing process, and competitors don't, "Thermo/Barnstead makes water systems, and they can support them, but they don't support the applications using the water, and we do."

However, Pall also has entered the water purification market and was showcasing its Cascada system at the booth, with an attractive water display to draw visitors. An official said this business started as a new product at PITTCON 2005, and customers now include pharmas, lab research, R&D, universities, forensics, etc. A Pall source said lab water pricing is competitive and coming down.

How does Pall compare to Millipore? A Pall official said, "We are No. 1 in quality and No. 2 in support. Millipore has experience, but we can make all of it because we are a filtration company."

Pall didn't introduce any new products at PITTCON, but new pre-packed columns will be launched in the spring.

THERMOFISHER SCIENTIFIC

Marijn Dekkers, president/CEO of Thermo, said that after the merger with Fisher, the company is 28% instrumentation, 56% consumables, and 16% software/service, with 30,000 employees in 38 countries and 350,000 customers in 150 countries. He said, "We think our size and breadth is a unique competitive advantage."

Dekkers said the company is investing $200 million in R&D in 2007, with new products "incredibly important to us, accounting for 29% of revenue in 2006 and 23% in 2005." Acquisitions in the past year – BioImage, Cohesive, and Flux – were all reported to be doing well.

However, some customers are worried about Thermo's ability to integrate and manage the merged company. A knowledgeable customer said, "Everyone is afraid of Thermo's growth pattern. We're worried to death about the integration. Everything they touch gets bureaucratically clunky and difficult to manage. We've seen slowing deliveries and parts and accessories are not coming." Another said, "I'm concerned with Thermo buying company after company. We have a Finnegan MS, and we needed a part, and they said they can't sell it to us because it is not on the inventory list yet. We

got that same answer for a year until our sales rep finally figured out the part number and solved it…Getting incompatible computer systems to integrate is ***very*** difficult." A pharma source said, "We haven't had any problems ourselves, but the integration is worrisome."

But not all Thermo customers reported problems. A customer said, "We use Thermo, and we haven't had any problems at all." A university source said, "We haven't had any Thermo problems, but we haven't ordered anything recently."

A Thermo official offered interesting comments:

- Invitrogen is big in cell cultures and mediums; Thermo is big in serum.
- In RNA, Thermo is No. 1, but Kiagen is a major competitor, and Invitrogen also competes.
- In QPCR, Invitrogen does reagents but not instruments, and Thermo doesn't do either.

Thermo introduced FTMS four years ago, and it did "fantastically well," according to one official, and more than 100 have been sold at $800,000, but sales have "plummeted." The official explained, "There are a finite number of labs who could spend that much, but we sold more than we expected. We anticipated the market (for FTMS) would slow, so we preempted it with the Orbitrap, which doesn't need a superconducting magnet. At $600,000, we've sold more than 300 of those. The LTQ-Orbitrap market can still grow another year or two. Over the next five years, we will take the Orbitrap technology and bring it down to a lower price point to expand the technology."

How products highlighted at PITTCON 2006 are doing:

- **LTQ Orbitrap MS.** An official said this has become a "workhorse." Another official said, "Orbitrap is the way to do serum biomarkers for cancer." However, a customer said, "Thermo's Orbitrap technology is not perfect yet. It has an opportunity in technical and environmental areas, but it is too expensive."
- **iCAP instrument** for elementary analysis. An official said this also has "taken hold as routine." For example, Midwest Labs in Omaha is using it to test soil nutrition and plans to expand its use in 2007 for EPA drinking water and waste water analysis.
- **Life science reagents.** An official said these have been well received in the marketplace. Merck was reported to be using the company's latest generation reagents.
- **Mercury Freedom System.** New regulations go into effect on January 1, 2009, on mercury emissions, and most coal-fired power plants are now using this system, including Duke Energy, Southern Companies, and Xcel Energy.

A Thermo official insisted that the company has not pulled back from triple quad, "The pieces we've added to workflow are very aggressive. We acquired LIMS and implemented FAIMS. And we have Accela. We acquired Cohesive specifically for triple quad…We have patent issues with ABI in court, but that hasn't changed our outlook. We are pretty confident we are okay."

Four new products were launched at PITTCON 2007 – UV vis system, K-Alpha, Noran 6, and 2 variants on handheld XRT, but Thermo was featuring a number of new items at the show.

➢ **Sample prep:**

- **Finnpipette Novus.**
- **Sorvall Legend T and RT Plus.**
- **Pierce reagents.**
- **RED device.**
- **DyLight conjugates.**
- **Krypton stains.**

➢ **Sample analysis:**

- **K-Alpha,** higher performance x-ray photoelectron spectroscopy. An official said, "We have taken very expensive and complicated technology and reduced it at about two-thirds the cost of previous systems. It has unparalleled ease of use – automatic tuning and calibration, point and shoot sample navigation system, and auto-analysis for optimized workflow. There are widespread applications for this. I think this will move into the area of routine."
- **DSQ II GC MS.** An official said this is "revolutionizing GC MS," handling a wide range of sample concentrations and requiring less sample preparation time.

Thermo View of Competitor Offerings

Company	Lab equipment	Lab reagents	Lab consumables	Instruments	Lab informatics	Lab services	Process instruments
Thermo	●●	●●	●●	●●	●●	●●	●●
Agilent			●	●●	●	●	
Waters			●	●●	●		
GE Healthcare	●		●	●			
Invitrogen		●●	●				
PerkinElmer	●	●		●●	●	●	
Sigma Aldrich		●●					

- **Noran System 6.**
- **New Orion Electrodes.**
- **Niton XLt Series.** An official said helium pulse for light elements was added, which he described as a "major advance for applications, especially in aerospace manufacturing and alloys that were not analyzable before. It is a significant extension of applications. It has a 20x smaller spot than other portable XRF analyzers."
- **Evolution 600 spectrophotometer.**
- **Accela UHPLC.** This is designed to run at conventional ***and*** very high pressures, integrating seamlessly with MS/MS. It was described as "2 HPLC systems in one, conventional and ultra high pressure." It is a single pump, with no dual mode; the single pump handles very high pressures up to 15,000 psi or can work conventionally at lower pressures, using Flux technology, which is a key reason why, an official said, Thermo bought Flux.
- **LTQ XL with ETD, a linear ion trap MS.** The University of Virginia licensed the ETD (linear ion trap) technology exclusively to Thermo, but other companies are offering a version of it, and Thermo has not filed any patent infringement lawsuits yet. An official said, "We haven't decided what to do. One could argue there is too much litigation going on. If it is implemented on 3-D trap, it is not competitive, so at the moment we may not be worried…ABI has a linear ion trap but not a segmented one."

  A Thermo official said, "Everyone is moving pretty quickly to quantification. A linear ion trap is quite quantitative…For large peptides, you have to do LTQ-ETD, which is very good as a first pass."

  LTQ costs $350,000. With ETD it is $425,000. Or customers can upgrade an existing LTQ for $100,000. An official said more than 1,000 LTQs are installed, with 200-250 sold annually.

  What new technology will impact MS, HPLC, and sequencing? A Thermo official said, "In sequencing and proteomics, ETD is pretty major."

➢ **Data Interpretation and storage:**

- **Darwin LIMS v 2.0**
- **Nautilus LIMS v 8.0**
- **QUANTLab v 2.0**
- **ToxLab v 2.0**
- **SIEVE**
- **PEAKS**

➢ **Services.** Lifecycle Enterprise solutions portfolio.

VARIAN MEDICAL SYSTEMS

At its PITTCON booth, Varian was showcasing:

➢ **400 NMR (nuclear magnetic resonance) system.** NMR, which was described as designed for routine organic chemistry and is complementary to the 500 MS, was launched in June 2006. What's new is FTMS, which was acquired from Ionspec, and Varian has launched its first generation FTMS with its own magnet and vacuum component. Officials declined to say how many NMRs have been sold, but they insisted it is "doing well worldwide." The key competitor is Brooker. Since sales are to pharma and academic centers, the health of pharma spending might be a concern, but an official noted, "Pharma is only flat in the U.S."

➢ **500 LC-MS.** This is the second PITTCON where this has been shown. Data-dependent scanning was added this year. An official said, "We are strengthening our core strength in the industrial market and adding capability for pharma…LC can hook to separate GCs or LCs. It is primarily used in a mid-level research environment (especially academic and industrial research)…People new to LC-MS like the ability (of this device) to change (from GC to LC)." But it only changes to Varian GC or LC; it is not open architecture.

The triple quadrupole was described as comparable to Applied Biosystem's API 3200 or API 4000 quadrupoles in sensitivity, with a cost of ~$135,000 for LC-MS, and the triple quad starting at ~$180,000.

➢ **Chromatography data systems – Galaxie.** This networks, controls, and streamlines HPLC and GC modules, including competitors' (except Waters) instruments with a single solution in lab data. It reduces manual tasks in a high throughput lab. Galaxie has been around a few years, with a "large" worldwide installed base. An official commented, "Productivity gain products tend to do well in tight pharma spending time, and there is a lot of thrust in that area."

- The **Scheduler** feature was launched about three months ago. It was designed for petrochemical labs, not pharma.
- For pharmas, there is **Fusion for Galaxie**, which allows a pharma's R&D department to develop methods, optimize them, and then validate them. Fusion for Galaxie was launched a year ago and reportedly is installed in several sites in Europe and North America, with GlaxoSmith-Kline one customer. An official said, "Some customers put Fusion on top of Galaxie (as an add-on), and others bought the full package…Fusion improves efficiency, especially in validation, saving up to 65% of time."

➢ **FT-IR (infrared chemical imaging).** In Canada, a site is using it to identify antibiotic-resistant bacteria. Another site is using it to look at artwork and see pitting on masterpieces. Industry is using it for sample analysis – for example to determine the physical properties of copolymers – and for failure analysis. Quality control labs are also using it. Right now it is designed for the lab environment. Interestingly, it uses technology that came from heat-seeking missiles. There is no automated interface yet.

➢ **Molecular spectroscopy.** This was described as a long-term core competency for Varian.

➢ **Consumables for sample preparation (HPLC and GC).** An official said the company is building the consumables and column business, "Consumables are an important strategic area for us…We have the broadest range, from nano LC columns though the full systems and everything in between, from capillary to big process columns…We can provide everything from lab discovery to process scale, which is an advantage since scale-up is a big issue for pharma." Most of the customers for these products are pharmas and biotech firms. The columns fit on competitors' as well as Varian instruments.

➢ **Polymer Laboratories.** This is a recent acquisition, offering:

- **Solutions in polymer characterization,** which was described as a niche market but complementary to Varian's small molecule business since it helps in large molecule research. Dow, ExxonMobil, and Dupont are customers.
- **Particle size analyzers.**
- **HPLC and solid phase synthesis.**
- **Refractive index detector.**

➢ **Vacuum solutions (dry vacuum pumps).** The claimed advantage to the Varian pumps are low maintenance (>2 years before it is needed), and no fluid (so no fluid disposal cost). An official said sales are "doing extremely well." Semiconductor companies are the biggest customers, but the pumps are also sold to medical and analytical customers.

WATERS

Rohit Khanna, VP of worldwide marketing, commented, "It can be challenging to change people's minds," but he noted that Waters introduced disruptive technology with Acquity UPLC and now is "redefining the world of high definition mass spec (HDMS)" with Synapt. He also emphasized Waters services business, saying, "Waters is no longer just a provider of products and services. Today we are an essential strategic business partner."

Another Waters official said, "More than half our tandem quadrupole business is environmental, and pharma share shrank a little – from 60% of business in 2005 to 58% in 2006. Seventy-five percent of our business is life science…We've engineered MS as an accessory to Acquity. We want to blur the line between UPLC and MS and sell a solution. Our target customer is the liquid chromatographer. Our system does better than what Agilent can cobble together." Another Waters official said, "We are heavily focused on pharma."

Asked about Agilent pricing its triple quad 20% below Waters' price, a Waters official said they did a number of head-to-head comparisons with Agilent's 1200, claiming, "The (Agilent) 1200 is fast chromatography, but it doesn't have enhanced resolution, enhanced sensitivity – just speed… We are never the cheapest." Another Waters official said, "Agilent doesn't have the support we do. A 20% discount says they need a compelling reason for people to buy (their product), and it isn't compelling if you can't support it." A third Waters official said, "Agilent is a formidable competitor. We will never play the price game. We differentiate on technology."

What's new at PITTCON 2007 for Waters:

Mass spec

➢ **Synapt HDMS.** A Waters official said, "Synapt is the first of its kind to employ high efficiency and specialized software to enable analysis of sample ions by size and shape as well as mass." Another official said Acquity changed how people thought about LC, adding, "We are seeing the same response to Synapt HDMS. Synapt enables new structural biological investigations not achievable with any other methods…While other vendors work to perfect older technology, we moved ahead…The difference that Synapt brings to the market…is that not only can it distinguish molecules on the basis of mass and charge but also on the basis of shape… Proteins have different functions as they assume different shapes…and some diseases, like Huntington's are based on protein mis-folding. This (shape identification) is a breakthrough. The really unique applications for this instrument are quite remarkable…HDMS will be to mass spec what UPLC is to liquid chromatography."

Another official said, "Synapt is really a remarkable instrument…and the work customers are getting out of it is groundbreaking. You will see a lot of work focused on how to use Synapt HDMS to distinguish between biotherapeutic products that are active and ones that aren't, between good and bad batches of proteins…This is the first tool to tell in a short time the differences in various batches of proteins."

Asked if Synapt and Acquity are being combined, an official said, "Many customers are already doing that."

Synapt users include: the Max Planck Institute which is studying Huntington's Disease with a Synapt, and Oxford University's Chemistry Department which is studying how cells process oxygen.

However, sources outside Waters were a bit dubious about the near-term outlook for Synapt. A competitor said, "It seems to be an instrument looking for an application. It is a technology that is not tried and tested. The problem it addresses either isn't there or there are easier ways to solve the issue." A CRO source said, "I'm concerned that this could be a bit like the Beta vs. VHS videotape format war. That is the feeling I have. Integration could be a burden." A customer said, "I don't know yet how people will use it. We are scratching our head over it. Its utility is ***many*** years out. Very basic research

may use it, but drug company use may be far away…If you buy Synapt, you become captive to Waters; you can't use other companies' columns with it, for example."

- **Empower 2 for MS.** She said Waters' customers asked that they open it to other vendors – Agilent, Hitachi, Shimadzu Scientific Instruments, etc. – and they did. She said Solvay Pharmaceuticals is in the process of phasing in a new scientific data management tool that was co-developed with Waters, linking data to SAP software.

Asked what it is about Empower that is putting it in demand even when customers are not using Waters instrumentation, a Waters official said, "It is fair to say that the regulatory support, the stringent care we took behind that, launched us very strongly, especially in the pharma industry…We did expand to support Agilent a number of years ago, and we are expanding that further this year. One of the key components of that is that, unlike some other products in the marketplace, we will work together with competitive instrumentation companies to make sure the solution the customer gets is rock solid."

Ultra Performance LC (UPLC) - Acquity

A Waters official declined to say what the Acquity installed base is but commented, "It is fair to say that when you have new technology, especially something that is disruptive, it is not the same ramp rate…and there is a strong HPLC installed base with a 7-10 year life…The real question is how many of the replacements are moving to UPLC, and we see that shift moving very quickly, especially in the discovery area, and then in development. QC (quality control) sometimes is having to wait for development to get it first."

There were some suggestions that Acquity sales have not been as strong as Waters expected, but the Waters official said, "There is nothing wrong with the growth of Acquity. It is meeting expectations. Our customers are very conservative and want to see 1-2 years before adoption. But HPLC has moved from research to routine. A change to new technology is not going to happen overnight. From research to development to QA/QC takes less than five years. Right now, we are between research and development on that timeline." A CRO source said, "The Waters sales rep said Acquity is becoming the new standard, but I sense that is not happening as quickly as Waters would like. I think it will head that direction, but slowly." However, another Waters customer said, "I want an Acquity. It would be good for measuring vitamin D in patients with chronic kidney disease (CKD), kidney transplant, or cystic fibrosis…I would buy a non-Waters device if a competitor had equal sensitivity at the same or a lower price, but I wouldn't accept lower sensitivity at the same or lower cost."

Asked what is driving HPLC + MS, the official said, "Customers want a higher degree of confidence. Most LCs have spectrophotometers for visualization, which is not as compound-specific as MS. LC doesn't give information directly correlated to structure and MS does." A CRO source said, "The convergence of HPLC and MS is real. There is more and more interfacing."

Asked what the follow-on to Acquity is, a Waters official said, "Chromatography on small particles. The key technology is packing material. Where we are going with packing material technology is what will drive this. The future is <1.7 microns. We think we can do that by changing the chemistry of surface coating on particles and with instruments that fuse chromatography and MS (HPLC plus MS), and we are starting to approach that."

- **Acquity FLD.**
- **Acquity TQD.**
- **Acquity UPLC HSS T3** which has new peptide separation technology, amino acid analysis, and oligonucleotide separation technology. She said it has "one of the fastest adoption rates of any new MS technology. It is robust and easy to use."
- **Acquity Fluorescence Detector**, which was described as sensitive and selective, with a high intensity light source. She cited the speed with which 52 pesticides in baby food can be detected and confirmed in 4 minutes using UPLC/MS/MS with a fluorescence detector. Rapid results with greater confidence are particularly important in Europe where pesticides in food are carefully regulated.

Column technology

VanGuard Pre-Columns for UPLC separations.

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