

MDL's Newsmagazine for Communicating with Customers

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***MDL Global Consulting & Services***

Guiding business performance to new heights

***Chemical registration systems***

Out-of-the-box and custom-built approaches

***Managing in vivo data***

The new MDL® Assay Explorer 2.2







*John Galbraith is MDL's senior vice president of worldwide Consulting and Services. Working from the Allschwil office near Basel, Switzerland, John and his team have recently completed a reorganization into customer-focused domain areas. With a new management team in place, John is confident that MDL Consulting & Services is well positioned to assist customers with pragmatic, yet innovative, informatics solutions supported by world-class technical and educational services.*

## John Galbraith: On MDL's new **Consulting and Services** organization

### **1. How can MDL Consulting support the improvement of business performance in research?**

The business environment in pharmaceuticals and other research-based industries is increasingly volatile. Mergers, acquisitions, and partnerships are some of the answers to increasing cost pressure and the need to bring more and innovative molecules to market. Whatever the strategy pursued, the unavoidable challenge companies must face is the effective management and integration of information. Unfortunately, many companies are spending up to 90% of their research IT budget just to maintain the *status quo* in hardware, software, and staffing. With the remaining 10%, managers are expected to make critical decisions on technology investments to support the needs of their scientist clients. Most large pharma companies have talented internal IT organizations excited about pushing the frontiers of informatics, but they are confronted with the reality of maintaining the existing environment on increasingly tight budgets.

MDL's consulting approach and solutions are very pragmatic, combining insights gained through our experiences with over 1,000 clients in the biopharma industry. Quite simply, we focus on helping the scientist do science. For instance, in chemistry scientists will typically spend up to a third of their time searching supplier catalogues and in-house inventories, conducting on- and off-line literature searches, requesting and retrieving test results, and handling similar administrative tasks. MDL Consulting has undertaken numerous projects to improve scientific methods and processes including automated compound registration, sample room inventory, global database searching, and electronic lab notebook systems. We have also built a strong track record in biology with the implementation of MDL<sup>®</sup> Assay Explorer. The true value of MDL Assay Explorer is realized through process redesign to drive some level of standardization in a notoriously non-standard environment. Standardization and common information definitions enable the rapid development of assays and make information

more accessible resulting in significant, quantifiable productivity gains.

MDL Consulting is also in the forefront of discovery logistics, an area that presents significant opportunities for very high and immediate returns on investment. Time spent ordering chemicals and reagents and waiting for supplies is scientific downtime. Additionally, reagent acquisition and disposal are increasingly concerns, both from a cost and regulatory point of view. We have redesigned and automated many of these processes, releasing scientists for more critical activities.

Information management is particularly challenging when discovery organizations comprise geographically dispersed, federated units. While smaller research organizations may harbor the potential for improved rates of discovery, they require greatly improved abilities to integrate and share information. MDL Consulting has developed information integration solutions for many research organizations, bringing together chemistry and biology data to support rapid and effective decision-making. The introduction of MDL<sup>®</sup> Core Interface in December of 2002 has greatly enhanced our ability to bring cost effective solutions to the scientist.

### **2. Why should clients use the services of the MDL Consulting team?**

I am continually impressed with the depth of knowledge and experience in our consulting team. Difficult process, programming, or infrastructure challenges appear almost daily in our email system. Invariably within a few minutes there are solutions suggested from MDL colleagues around the world. The fact that suggestions do not only come from Consulting points to a particular strength of our integrated organization.

MDL Consulting is organized into four Practice Areas: Biology, Chemistry, Information Integration, and Discovery Logistics, which correspond to similar areas of expertise in

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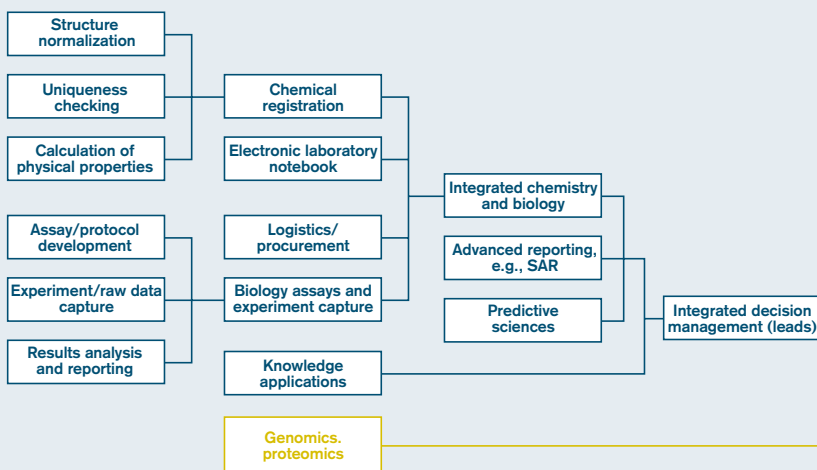
Customer Services and Marketing. This gives us a greatly expanded pool of proficiency to draw upon. Of course, Seth Pinsky's R&D team is also critical to the Consulting organization, providing extraordinary technology expertise and deep thinking on issues such as chemistry representation, integrating data sources, and taxonomy development for information management.

MDL consultants themselves offer an impressive background in science and informatics, with over 40% having worked at the bench in biology or chemistry. Most of my colleagues have PhDs in science and graduate degrees in informatics. This educational background, combined with strong consulting experience with a broad range of companies, helps us define and implement cost-effective solutions for our clients. Our strategic consultants, workflow analysts, project managers, application scientists, programmers, and trainers make it their business to understand our clients' informatics and business processes, so that they can ask the right questions, be they strategic or operational. As shown in the accompanying figure, Consulting considers a range of performance issues in discovery research, designs and implements solutions that streamline processes, and integrates the flow of information to enhance decision-making on an enterprise-wide basis.

### 3. What are the priorities for Customer Services?

A recent survey has shown that customer support is the second most important reason, not far behind performance, for the selection of IT solutions in the life science industry. MDL Customer Services must be a deciding factor in our customers' decisions to buy products or services from MDL. It is critical that we listen to our customers and ensure that they can perform their science using MDL applications and databases with minimal interruption and as little effort as possible.

Each client's informatics environment is different, and researchers and IT developers are highly varied in their expertise and understanding. The Customer Services team must deal with a huge variety of issues in a rapid and comprehensive manner and in more than six languages. To help us address the growing complexity of technology and our clients' demands, we recently organized into global response teams supporting Discovery



*Illustrative high-level diagnostic for the development of an information integration strategy*

Framework, Chemistry, Biology, and Predictive Science. This reflects our customers' view of MDL products and their associated skill sets. We have also established clear responsibility and accountability for customer support throughout the organization, from the primary support specialists who field customer calls through to the product specialists who deal with more complex technical issues and represent the customer in the product development teams. The goal is to simplify the support process and ensure that customers get rapid access to appropriately skilled individuals. Here again, our integrated organization is critical to MDL's success. Customer Services can call on individuals from R&D and from Lars Barfod's team in Marketing and Sales to supply our customers with technical and business-oriented solutions to their requests.

Another clear priority for us is innovation. The Educational Services team has been developing and testing Web-based training approaches to supplement instructor-led training. These are highly cost effective and minimize time away from work. Short, web-based courses can be very effective in bringing people quickly up to speed with MDL software, or even as a quick introduction to a topic prior to embarking on a classroom course. We are also investigating the use of self-paced training modules available over the Web.

### 4. What is the significance of the new MDL® Discovery Framework for enterprise-wide information integration?

The MDL Discovery Framework architecture is open, scalable, flexible, and highly customizable. Openness is very important to developers, because it allows in-house and consultant access to the same environment without the

impediments of proprietary programming languages. We believe this will greatly increase the effectiveness of joint Client-MDL consulting teams in developing and delivering cost-effective solutions.

MDL Consulting has been closely involved in the planning and creation of developer interfaces for Discovery Framework. Our team is highly trained, experienced, and ready to help our clients migrate to the new Framework and develop solutions in the new environment.

### 5. What is your personal view for guiding MDL's global Consulting and Services organization?

MDL's executive team, lead by Pat Rougeau, has a clear view of where MDL needs to go to help our customers improve their business performance. MDL does not develop new drugs, but we believe our solutions help improve researchers' ability to do so. It is our mission to "power the process of invention," and it takes a truly integrated organization such as MDL to achieve this. The Consulting and Services team works with its MDL colleagues to ensure that the needs of our customers are not only met but also anticipated.

Advising a client requires understanding, and working within, the immense complexity at the heart of their R&D operation. MDL consultants need to immerse themselves in each customer's specific strategy, in their processes, their organization, and their people. Only after comprehending the total picture can we give our best, most considered opinion on the informatics piece of the puzzle—and help transform this critical research function into a major driver of business performance. ■

# MDL Consulting launches new practice areas

*“Our customers are under incredible pressure to justify ROI for products and services and their own projects, and we need to help them do this.”*

*Pat Rougeau, MDL CEO*

In her opening remarks at MDL's Global Consulting Meeting held this March in Orlando, Florida, MDL CEO Pat Rougeau stated: “On MDL's 25th anniversary, consulting has an important role at MDL—writing custom applications, making MDL products work in customers' environments, training customers, providing benchmark studies and analyses. I see consulting having an even more important role in the future, as integrated solutions become increasingly important and as our products become workflow oriented, where installation, data conversion, and customization are critical to solution success.”

To advance MDL's goal of becoming a strategic partner with customers, MDL Consulting is focusing on four practice areas, which customers themselves have identified as their most challenging discovery domains—Chemistry, Biology, Logistics, and Information Integration. *Molecular Connection* spoke with the practice area leads to understand MDL's offerings in each of these fields.

## **Chemistry—Maximizing the chemist's productivity**

With research chemists producing and optimizing more compounds faster than ever, discovery organizations must provide efficient chemical registration, data management, workflow, reporting, and decision support systems that are fully embedded with cross-functional research processes. MDL's core competency in cheminformatics provides a baseline capability and proven track record in all of these critical areas.



*Aleksandar Ruzicic, Chemistry*

Working with some of the largest companies in the pharmaceutical and chemical industries, MDL's global solution experts have put their strong chemistry expertise to work designing and implementing centralized and distributed data management systems for handling compound registration and electronic laboratory notebooks. For example, the Aventis Registration Process (ARP) was developed with professional guidance and tools from MDL (refer to *Molecular Connection*, Volume 20, Number 2). MDL consultants have also developed custom applications supporting chemical database searching, compound activity profiling, and chemical/biological data integration and analysis.

Aleksandar Ruzicic says the goal of MDL's chemistry consulting group is to “power the cross-functional research process by maximizing the chemist's productivity.” Chemistry consultants can help customers gain maximum advantage from tailored solutions based on applications like MDL® Relational Chemistry Server, MDL® Chemistry Rules Interface, MDL® Draw, MDL® ChemBio AE and MDL® Elan—helping chemists manage the discovery process better and identify successful candidates faster. Consultants can also help customers take full advantage of third-party software such as SciTegic's Pipeline Pilot™, which streamlines the flow and analysis of large datasets from diverse sources. To lay the groundwork, MDL's chemistry solution experts will work closely with chemists at customer sites to gather requirements and validate designs. To ensure successful project implementations, they can then consult with IT departments on strategies for securing the early acceptance of new technologies by researchers.

“MDL Chemistry consultants can tailor current informatics technology to address a client's unique business challenges. The systems need to streamline work processes and be easy to modify as those processes evolve,” says Ruzicic. “With a view to emerging technologies, MDL consultants can also help clients migrate to MDL's new Discovery Framework, thereby leveraging the power of a modern n-tier architecture.”

## **Biology—Transforming biological information into knowledge**

Biology is a major cornerstone of the discovery process. The complex challenges faced by MDL's clients in the biology area range from creating and managing plate libraries to capturing biological data, designing and running assays, analyzing assay results alongside associated chemical data, registering biological and chemical data, and producing detailed SAR reports to share with colleagues.

John McCarthy believes it is essential to address these data management challenges through detailed workflow analysis, system design, and solution implementation based on a thorough understanding of each client's unique development goals and discovery processes. McCarthy says: “Integrated technologies, scientific software applications, and content databases, correctly tailored to each client's needs, are key to transforming biological information into knowledge and improving the candidate selection process.”

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Besides MDL® Discovery Framework, which supports integrated chemical and biological research, MDL offers a breadth of workflow solutions from plate inventory management (MDL® Plate Manager) through assay data management (MDL® Assay Explorer) to report generation (MDL® Report Manager), as well as integration with complementary screening tools like SciTegic's Pipeline Pilot®.

MDL Biology consultants are well versed in all phases of the discovery workflow and are fully conversant with the needs of developers, technicians, research scientists, and IT management at pharmaceutical and biotechnology companies of all sizes. The Biology practice area also offers the proven ability to manage small projects lasting a week to large projects spanning years and continents.

### **Logistics—Reducing costs, saving time, facilitating compliance**

Research organizations in the pharmaceutical, biotechnology, and chemical industries require efficient systems to manage procurement and inventory of chemical reagents and research samples. Besides the need to control costs and minimize the time spent searching for and ordering materials, inventory systems must meet increasingly stringent regulatory requirements, from special controls on the ordering, use, and storage of certain compounds to regulations governing the transportation of hazardous materials. As reagent and sample stockrooms are increasingly automated, logistics systems must also integrate effectively with robotics, plate management, liquid handling, bar coding, purchasing, and other systems.



*Roger Abraham, Logistics*

MDL has over 20 years of experience providing workflow logistics solutions like these to over 4,000 researchers at over 40 companies around the world, including Boehringer Ingelheim and Aventis. According to Roger Abraham, "MDL's goal is to help customers optimize their logistics processes by leveraging MDL's knowledge of industry best practice to deliver solutions that reduce costs, save time, and facilitate safety and regulatory compliance."

Solution experts in the Logistics practice area are currently focusing on the creation of MDL® Discovery Logistics. This integrated software and services initiative will provide a complete inventory/

procurement solution for reagents and samples. Developed as a consortium collaboration with two large pharmaceutical companies, this new offering will leverage MDL® Core Interface, MDL® Relational Chemistry Server, MDL® Draw, and MDL® Report Manager to create the next-generation core for effective logistics solutions in life science R&D.

### **Information Integration—Integrating the discovery process**

With high throughput research techniques increasing the quantity and complexity of data in the pipeline, information integration represents a great opportunity for MDL to streamline the discovery process and generate lasting value for clients.



*Francis Benett, Information Integration*

Francis Benett considers MDL's new three-tier Discovery Framework to be "the ideal platform for data and application integration, because it is an open, standards-based, flexible, scalable, and extensible architecture." The underlying database tier provides the searching and registration engines for domain-specific and general-purpose database access. MDL is using the experience gained in building DiscoveryGate<sup>SM</sup> to offer integration in the database tier. System integration occurs in the middle tier where MDL® Core Interface provides query/database services that can be shared by multiple applications, and a standard interface for custom development. The user interface tier provides an integrated front end for scientists using the system. Depending on the application's needs, this can range from a thin web client to a thick conventional application.

"Using the new Discovery Framework, MDL solution experts can integrate data from diverse sources and make data accessible to diverse groups," says Benett. "It is also much easier to build applications with different workflows and appearances, but with consistent user interfaces and functionality."

MDL's overall goal for the new Discovery Framework is integration of the discovery process. MDL consultants working in the Information Integration practice area will implement this vision at individual customer sites within the context of an enterprise-wide business performance solution. ■

## SciTegic® alliance in full swing

### MDL and SciTegic co-marketing Pipeline Pilot™, exploring product integration

**MDL** and SciTegic's strategic marketing alliance centered on SciTegic's innovative data analysis and mining tool, Pipeline Pilot™, is generating exciting data integration and analysis opportunities for life sciences researchers in the cheminformatics, screening, and ADME-Tox areas.

Pipeline Pilot is a high-throughput data analysis and mining tool for drug discovery informatics that can be used to define and automate complex operations on extremely large data sets. "Pipeline Pilot complements the informatics infrastructures that MDL customers have in place and provides for tremendous flexibility in analysis of diverse collections of data," said Mathew Hahn, Ph.D., President and CEO of SciTegic ([www.scitegic.com](http://www.scitegic.com)).

Under the agreement, MDL is co-marketing Pipeline Pilot in the life science informatics field, offering consulting services related to the product, and using Pipeline Pilot internally, in part to explore areas of further integration between MDL and SciTegic's respective products. The first integration components—for accessing MDL® ISIS for Excel and MDL® Relational Chemistry Server—are available in the current release of Pipeline Pilot.

MDL President and CEO Pat Rougeau views the collaboration's prospects for researchers with enthusiasm. "When used together, MDL Discovery Framework and Pipeline Pilot offer powerful management and analysis capabilities that can help our customers master the unprecedented volumes of data created in discovery research today," she said.

Pipeline Pilot solves common interdisciplinary and inter-organizational research problems by collectively processing whole data sets of disparate types. For example, Pipeline Pilot can be used to evaluate a vendor's compound library against a company's internal collection, or mine different chemical databases for candidate leads, while simultaneously applying outside criteria from text collections and other scientific domains.

Check the next issue of *Molecular Connection* for workflow illustrations of Pipeline Pilot in conjunction with MDL applications. For a demonstration of how Pipeline Pilot and MDL solutions can accelerate your research, contact your MDL sales representative. ■

## Scientific Advisory Board in cliffhanger!

**MDL**'s Scientific Advisory Board met for the first time on an ocean-side bluff surrounded by best boys, gaffers, focus pullers, dolly grips, and clapper loaders—and despite the distractions, the Board and its MDL hosts enjoyed a successful casting call, accomplishing everything they set out to do.

The group's inaugural meeting was held February 26-28 at the Ritz-Carlton Resort in Half Moon Bay, California, just south of San Francisco. As luck would have it, the meeting coincided with on-location filming of Universal Studio's "American Pie 3," which afforded an interesting crosscut to high concept conversations on discovery research and informatics.

With nine of the Board's 11 members attending, there was undeniably a quorum for discussions on a wide range of topics including high throughput chemistry, biology, and screening; bioinformatics, genomics, and proteomics; quantitative structure activity relationships; molecular modeling; computer-aided drug design; advanced cheminformatics research; and industrial discovery technology management.

The meeting commenced with MDL CEO Pat Rougeau, CBO Lars Barfod, and CTO Seth Pinsky providing overviews of the company's business and technical strategies and product offerings. According to Dr. Phil McHale, MDL's vice president of corporate communications and scientific affairs, "the Scientific Advisory Board members responded with open, frank, and informative feedback on MDL's strategic direction. They helped to identify and prioritize new discovery technologies of relevance to MDL



*Inaugural meeting of MDL's Scientific Advisory Board, Ritz-Carlton Resort, Half Moon Bay, CA (front row, left to right) – Dr. Sangtae Kim, Dr. Berta Strulovici, Dr. Helen M. Berman, Pat Rougeau (MDL), Doug Hounshell (MDL), and Lars Barfod (MDL) (back row, left to right) – Dr. Irwin D. Kuntz, Dr. Joseph Guiles, Seth Pinsky (MDL), Dr. Alexander Tropsha, Kevin Cannon (MDL), Dr. James Summers, Dr. Johann Gasteiger, Dr. Hugo Kubinyi, Phil McHale (MDL), and Guenter Grethe (MDL)*

and its customers and identified other companies with whom MDL might consider working. The atmosphere was cordial, collegial, and constructive."

With the consensus being that this inaugural meeting was Oscar®-caliber, a sequel is being planned for September or October—at an as-yet-undisclosed location. ■

# First combined UK-European User Group Meeting a success

*“The goal of integration within MDL Discovery Framework is not to make MDL the center of the universe, but to integrate MDL solutions effectively into the customer environment...”*

*Tom Blackadar, director,  
MDL Discovery Framework*

The first European Users' Group Meeting to be held in the UK took place at the Royal Lancaster Hotel, London, from March 12-14 with about 120 MDL customers in attendance. This joint gathering, combining the 20th European meeting with the 12th UK meeting, was very well received, and the organizing committees are considering combining the meetings every three years.

A major theme of this year's session focused on the practicalities of creating and implementing integrated informatics solutions. Dr. Thomas Lorenz of BASF set the tone in his keynote address on the first morning, as he spoke on “The Impacts of Changing Technology on Service Provision at BASF” with special emphasis on the importance of integrating internal and external data. Tom Blackadar, director of MDL® Discovery Framework, followed up with a progress report on integrating workflow and data management solutions using MDL's Framework products. Tom stressed that the goal of integration within MDL Discovery Framework is not to make MDL the center of the universe, but to

integrate MDL solutions effectively into the customer environment, thereby contributing to a superior discovery research solution.

Other keynote speakers included Professor Robert Glen, director of the Unilever Cambridge Centre for Molecular Informatics, who spoke on “New Horizons for Molecular Informatics” and Dr. Jayne Cartmell of Abbott Laboratories, who spoke on “The Global Rollout of Abbott's Discovery Database.” Dr. Cartmell discussed the successful integration and global rollout of MDL® Assay Explorer into Abbott's biological data management infrastructure, pointing out a number of key steps needed for such success. She also noted that Abbott scientists had responded favorably to migrating to Assay Explorer, as a result of a careful partnership between IT and the scientists. There were also sessions on integrating MDL® Chemistry Rules Interface and MDL® Draw at customer sites and lively discussions of Electronic Laboratory Notebook initiatives currently underway at MDL and within various customer organizations.

A one-day hands-on workshop on programming with MDL Discovery Framework addressed application development in the new technology environment and administrative strategies for integrating new applications into existing production systems. By all accounts, attendees found this two-track workshop, with its breakout sessions on development and administration issues, to be very helpful.

The Welcome Dinner at this year's event was held at the Science Museum in South Kensington. The evening featured a private tour of the overwhelmingly popular “Bond, James Bond” exhibit celebrating 40 years of Bond films, followed by dinner beneath a number of famous aircraft in the Aviation Hall. For those who had not had their fill of chemistry during the day's sessions, the museum offered an added bonus—an exhibit of mid-19th to mid-20th century analytical chemistry apparatus. ■



*(Left to right): Markus Fassbender (Roche Diagnostics GmbH, Vienna), Jean-François Leclere (MDL-Southern Europe), and Simon Valentine (SciTegic, Inc.) at the Welcome Dinner.*



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typically differentiated by five key factors: acceptance, time, flexibility, cost, and support.

- **User acceptance:** Are the scientists convinced by the functionality? Do they see a benefit for themselves in the workflow? Does the system bring workflow improvements?
- **Time to deployment:** How long will it take to become productive with the system?
- **Flexibility:** Can the system accommodate changing needs? Does it integrate with existing systems?
- **Costs:** What is the return on investment? Does it lower the total cost of ownership?
- **Maintenance/support:** Is support available for training, user advice, and enhancement?

Table 1 evaluates the three basic approaches using the above factors, based on tendencies observed by MDL consultants and account representatives during projects and in discussions with customers. Each system entails inherent trade-offs; an informed decision on a registration system involves both R&D and IT management in a frank analysis of strategic priorities and corporate resources.

#### Out-of-the-box case study: Allergan

Allergan Inc. (NYSE: AGN), with headquarters in Irvine, California, is a specialty pharmaceutical company that develops innovative products for the eye care, neuromodulator, skin care, and other markets.

Though known for Botox (botulinum toxin is being tested with encouraging results as a treatment for ailments ranging from stroke paralysis to migraine headaches and carpal tunnel syndrome, according to the *New York Times*), Allergan also produces small molecule pharmaceuticals. The company recently decided it was time to update the registration system used by its small molecule research division.

"We weren't catching much batch level information," said Robert Cain, senior scientist, Spectroscopy, for Allergan. "And our data model wasn't extensible."

According to Cain, the company considered pursuing a better data model and incorporating additional features, but realized that it was going to be difficult to make the existing in-house system into a professional level system.

"We didn't have the resources in house," Cain recalled. "We aren't big-pharma. We are a mid-sized, specialty pharmaceutical company and thus we don't have a big-pharma

Factor	Out-of-the-box	Custom Internal IT	Custom MDL Consulting
User acceptance	++	+++	++++
Time	++++	+	+++
Flexibility	+	++++	++++
Costs	++++	++	++
Maintenance/support	++++	++	+++

*Table 1 assigns rankings of one through four (with four representing the most favorable ranking) to key factors that differentiate between the basic approaches to chemical registration systems.*

#### Notes:

**User acceptance**—In-house builds can suffer from poor communication between science and informatics. Since consultants speak the language of the scientist, MDL-supported projects generally meet with high acceptance. Out-of-the-box solutions are occasionally accepted only with the caveat that modifications will be made—though in cases where an organization has a well-defined research focus or the system represents a significant improvement over an existing registration process, acceptance can be high.

**Time**—Provided no customization is undertaken, an out-of-the-box solution can rapidly be made operational. In-house builds do not necessarily take longer than 3rd-party consultant projects to become productive, but factors such as lack of specialized experience, lack of training support, and changing informatics priorities can impede rapid productivity.

**Flexibility**—Custom systems are inherently more flexible. However, inexperience in building systems

can hamper the flexibility through errors in architecture and build. Experience and broad understanding of the technology are critical to ensuring a cost effective and flexible system.

**Cost**—Out-of-the-box systems with no customization are by far the most inexpensive solutions. However, cost benefit analysis for a custom solution will frequently reveal a higher return even though the initial outlay is higher. Improvements in process through custom process design can drive significant productivity improvements.

**Maintenance/support**—Maintenance and support are critical to moving scientists rapidly up the learning curve and maintaining their proficiency with a system. In-house builds often rely on a cadre of power users to spread the word, a process that can require scientists to dedicate time to training tasks. Professional external organizations offer training and management support to facilitate process and organizational changes.

research IT staff to support us. We try not to develop things that are already developed, so if an out-of-the box solution meets our needs we will use it."

Allergan had several requirements for an off-the-shelf registration system in addition to a better data model. The system had to be extensible. It had to integrate well with other applications, including a 3rd party system for biological information. And to replace the quality control function of registrars in the existing centralized system, it had to offer built-in validation tools for incorporating business rules.

In the end, Allergan selected MDL® ChemBio AE as the best fit between its needs and resources (see Figures 1 and 2).

"We went with ChemBio because it was an MDL application and we knew that they were a reliable software partner," said Cain. "MDL helped us design small, easy-to-maintain customizations that we needed. These will allow us to maintain support and lower the amount of in-house development we need to do."

MDL ChemBio AE (<http://www.mdl.com/products/chembio.html>) is an out-of-the-box registration and storage system for chemical

data that lets scientists retrieve and view chemical and biological data side by side. Scientists can register single compounds or entire libraries while ChemBio AE automatically checks for duplicates, strips salts and solvents, assigns ID numbers, and calculates chemical properties.

MDL ChemBio AE combines easily with MDL® Assay Explorer and MDL® Report Manager to offer a complete solution for managing and reporting chemical and biological information.

"On the West Coast I see a lot of small or mid-sized companies, particularly biotechs, that need a flexible, extensible registration system that can be implemented with a minimum of internal resources," said Bob Olszewski, the western regional sales manager for MDL in North America. "Because ChemBio AE integrates with other applications and has the potential to grow with companies, it's the right solution for many discovery research organizations."

In Allergan's case, the flexibility of ChemBio AE was an important factor since it had to integrate with their existing, 3rd-party system for biological information—something it has done well.

ChemBio AE was rolled out to approximately 40 scientists at Allergan's Irvine location.

Because it offers clear advantages over the previous system, scientists adopted the new technology and found it to be a considerable improvement.

"It's saving time for the synthetic chemists to register compounds and get a corporate number—and avoiding mistakes," Cain says. "And the support has been very good since we've moved to ChemBio AE."

According to Cain, Allergan is already looking to improve their workflow by tying spectroscopic data into the system. "When people register compounds they'll register identifiers for their spectral data," Cain said. "It's just in the planning stage at this point, but we think we know how it will be done."

### Custom solution case study: Aventis

In a global business climate where mergers and acquisitions are commonplace, research organizations often face the challenge of consolidating disparate information systems.

On the bright side, mergers and other large-scale transformations present opportunities to replace outdated or inefficient systems, and implement best practice business rules and standard operational procedures.

When Hoechst Marion Roussel and Rhône-Poulenc Rorer merged to form Aventis (NYSE, Paris, FRA: AVE), the resulting company had scientists at research labs in three countries, speaking different languages and running multiple systems.

"We realized very early that we had to deal with many sites, many chemical information systems, and many different processes for registering chemical data," said Dr. Ludwig Franzisket, global project manager for Aventis Pharma. "We saw the need to consolidate this—to define a common process for chemical registration at all sites."

With mergers, adopting one of the existing systems is not always practical or politically desirable. In Aventis' case, the range of chemistry techniques employed in various labs and the desire for additional functionality beyond chemical registration required management to start from scratch.

"How we started this project was not to think about an IT system, but to define the process we have in the labs," said Dr. Franzisket. "We looked at what are the similar steps and what is different."

Beyond registering chemical batches and linking 5,000 scientists and support staff at multiple locations on two continents, the system had

to provide a repository for structural data that was linked to test results, in order to support structure-activity relationship analysis. The long-term goal was to enable an electronic notebook capability to capture all chemically relevant experimental information.

To design and build the new Aventis Registration Process (ARP) system, Aventis turned to MDL Consulting.

Charles Buse was the project leader of the MDL consulting team. "The primary technical challenge we faced was finding a database structure flexible enough to handle classical synthetic experiments, parallel synthesis, and combiChem," said Buse.

To meet these challenges and connect with all of the Aventis labs on the wide area network, MDL designed a hybrid system with a distributed architecture that is between a client-server and a true multi-tier system. It consists of a thick client with some services running on NT servers, and Oracle® databases on UNIX platforms. The ARP system is built on a framework of MDL® ISIS (Integrated Scientific Information System) and incorporates MDL® Chemistry Rules Interface to automate chemical structural analysis and manipulations.

Now chemists at every Aventis lab can register synthesized, isolated, or acquired physical batches into a central repository, through manual entry of single batches or automated processing of multiple batches. Each batch is normalized in accordance with Aventis' global business rules and assigned a unique ID.

"We use the same business rules implemented at each site, so the data is of high quality and is comparable between the sites," said Dr. Franzisket.

Scientists have adopted the new system because it is specifically designed to do everything they need. "ARP really covers the whole range of different technologies of

chemical synthesis," said Dr. Franzisket. "That means traditional experiments and multi-step syntheses, as well as the parallel approach of chemical synthesis and the combiChem approach that generates hundreds of thousands of compounds at the same time."

The ARP system helps chemists plan and document their experiments, search and review others' work, analyze results, and generate reports to share with colleagues. To further simplify scientists' day-to-day tasks, the system interface integrates with Aventis' global logistics and analytical systems.

"MDL delivered on our primary requirement," said Pete Loupos, vice president Aventis Drug Innovation & Approval Information Solutions. "They built a system that conformed to the specifics of our scientific workflow, not the confines of software or technology."

### Making the right choice

Finding the right registration system requires an awareness of an organization's operational needs and available resources—and an understanding of the attributes of the various systematic approaches.

The unheralded workhorse of an informatics infrastructure, a well planned and executed registration system can improve efficiency and ensure consistency in even the most Byzantine organizations. But don't expect a celebration if you get it right.

"With a registration system, the baseline expectation is one of seamless infallibility," said Aleksander Ruzicic, chemistry practice lead for MDL Consulting. "People tend not to think or talk about it unless there's a problem. But its function is critical to successful discovery research."

For more information on chemical registration systems, or guidance on your unique situation, contact an MDL consultant or your MDL sales representative. ■

## The next generation in custom registration

The recent introduction of the n-tier MDL® Discovery Framework opens the door to a new generation of registration systems.

MDL® Core Interface—the middleware integration engine of MDL Discovery Framework that provides a standard interface for custom development—combined with MDL chemistry registration services enable consultants to build extremely flexible systems designed with a custom user interface and a maintained and supported middle layer registration service.

This next-generation solution offers the advantages of an earlier deliverable combined with customization. A European pharmaceutical company recently selected to implement this new Discovery Framework-based solution. The project, managed by Cap Gemini Ernst & Young in collaboration with MDL Consulting, features a custom interface and custom functionality, including a simple plate management and analytical requests interface.

# Managing *in vivo* data

## MDL<sup>®</sup> Assay Explorer

The *in vivo* research environment, with its frequent change in test variables and complex calculations, poses a unique set of data management challenges.

Biological researchers and developers have been looking for ways to simplify tasks such as moving Microsoft Excel data into a central database, storing images and documents with experimental results, and linking to third-party statistical applications. With the release of MDL<sup>®</sup> Assay Explorer 2.2 this summer, scientists have the infrastructure and flexible tools to capture and analyze *in vivo* data.

“Enhancements in MDL Assay Explorer 2.2 will be especially valuable to project teams carrying out *in vivo* research, including pharmacokinetic and ADME/Tox researchers,” noted Debra Toburen, group manager for biology products. “These improvements were developed through direct conversations with biologists about their critical *in vivo* research needs.”

This issue’s **At the Bench** looks at techniques for efficiently managing *in vivo* data, including using layouts, importing data from Excel, using variable groups, and integrating other applications and external calculations.

### Flexibility: Using layouts

When it comes to capturing data, *in vivo* experiments pose a far different challenge from high-throughput screening. Relatively few compounds are tested through many animal or test groups or tissue sources. The number of doses, the number of animals, the tissue types, and the types of tests can vary from day to day. Many calculations must be made on a few samples, rather than repeating a few calculations on thousands of samples.

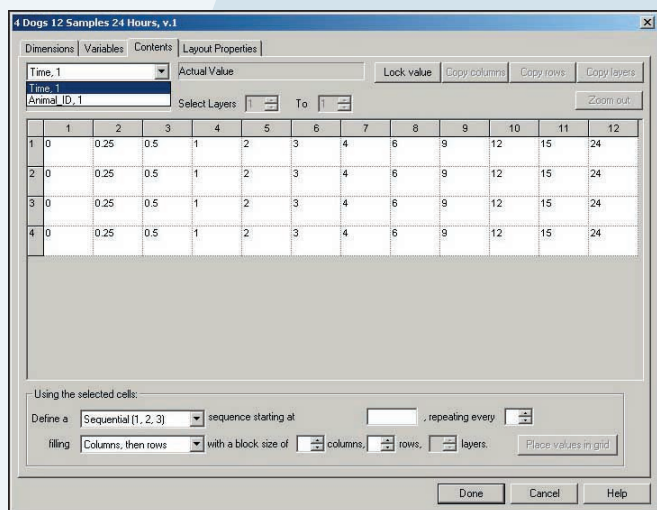


Figure 1: A layout can be used to define a group of animals, number of doses, or number of days, for example, and can be three dimensional in its description of the experiment parameters. A layout is selected for each group of animals in the experiment.

With *in vivo* research, change is constant. Scientists need the flexibility to make experimental changes without calling IT or support to adjust the data analysis template.

To provide this flexibility, Assay Explorer separates the layout of the assay from the calculations by removing the positional dependency. The layout (see Figure 1) describes the matrix of the assay: how many animals, how many time points, concentrations, plate size, location of controls, etc.

Calculations are based on variable names (high control, low control), not a position on a spreadsheet (see Figure 2). So if you move a control, there is no need to alter the calculation; it follows the name of the control. An experiment can be assembled from multiple layouts. As additional data is collected over time, additional layouts are added to the experiment.

### Importing from Microsoft Excel

Microsoft Excel spreadsheets are popular with scientists for capturing and analyzing low throughput and *in vivo* data. When multiple spreadsheets reside on individual computers, these islands of data can create a host of issues, including data loss, inaccessibility to team members and managers, and impaired reporting and decision making.

Storing important pharmacokinetic or toxicology data in a central database that can be quickly accessed by chemists, biologists, and other project team members offers significant advantages in timesaving, efficiency, and security.

Assay Explorer version 2.2 introduces a tool for importing data directly from Excel into the Assay Explorer database. Selecting from a menu, scientists simply map data from their Excel spreadsheet to the appropriate variable group in Assay Explorer (see Figures 3 and 4).

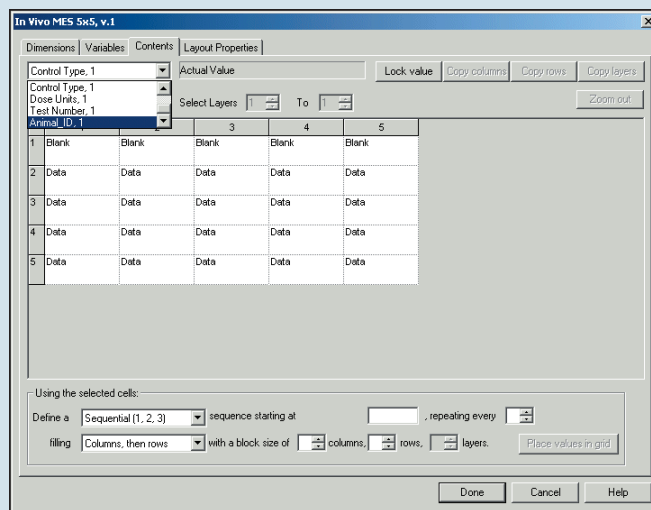


Figure 2: Controls and standard curves are designated by names rather than positions on a spreadsheet. Calculations are generated using these names, freeing scientists to move controls, add additional standards, or change density at experiment creation time.

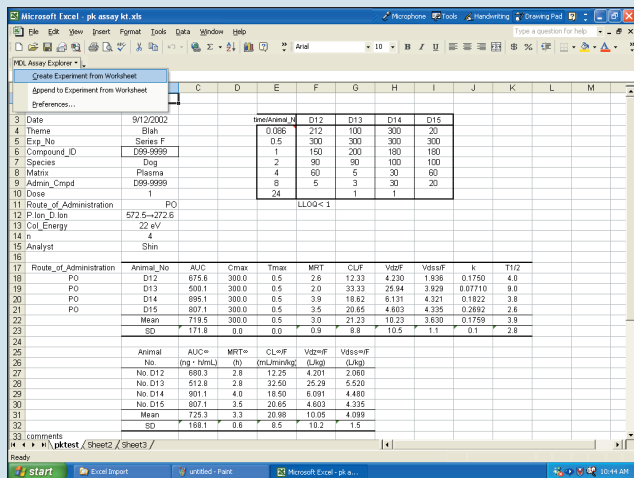


Figure 3: With Assay Explorer 2.2, scientists can access an Assay Explorer menu from within the Microsoft Excel environment.

This new functionality allows scientists to remain in the Excel environment, while capturing data in a central repository and eliminating islands of data. Teams can make decisions based on all available information so that more intelligent leads can progress.

**Using variable groups**

The design of Assay Explorer provides administrators and power users with the flexibility to capture and organize any type of information.

The variable group is a collection of variables or information that scientists wish to calculate or store in the database (see Figure 5). The variable can be any administrator-defined item, backed by administrator-created dictionaries or calculations. This offers the flexibility to use company terminology that is familiar to scientists.

The Assay Explorer user interface reflects the administrator-defined terminology, so the scientist is entering and viewing data in a recognized environment (see Figure 6).

**Integration**

A key component of an efficient work environment is the ability to integrate various applications into a workflow process. Scientists often have preferences for particular tools to use in specific situations, and want to have access to those applications in a seamless environment.

Assay Explorer has a Microsoft Visual Basic for Applications engine that gives IT staff the flexibility to develop add-ins to integrate in-house or third-party applications into the Assay Explorer environment. Add-ins can also be written for specific validation routines, custom data entry screens, or workflow processes that are specific to a work group or company.

Furthering its integration capabilities, the next version of Assay Explorer offers out-of-the-box integration with leading third-party statistical analysis packages. Assay Explorer 2.2 has been designed to leverage the expanded set of regression models and analytical tools available from these applications for handling the complex calculations and multiple steps associated with pharmacodynamic and pharmacokinetic studies. The next issue of *Molecular Connection* will provide an update on third-party statistical packages and the methods of integration.

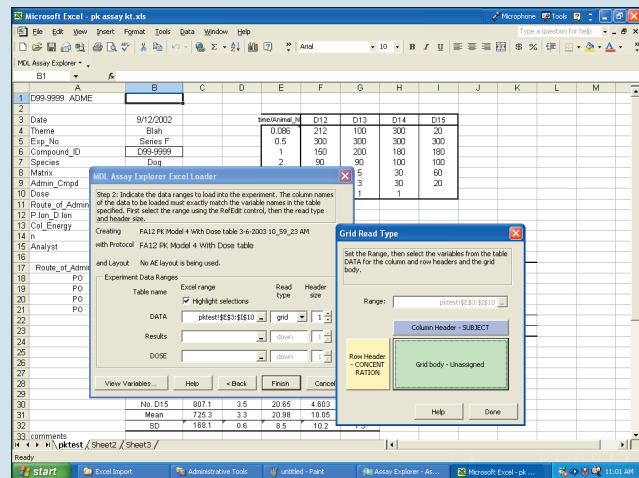


Figure 4: By selecting the Assay Explorer protocol and mapping the data to variables in the variable group, scientists can easily import tables and grids of data into the Assay Explorer database. This mapping can be reused for other experiments in the same Excel format.

Assay Explorer's ability to integrate in-house and third-party applications and its accommodation of important external modeling calculators give scientists access to a flexible array of specialized, familiar tools for managing the complexities of *in vivo* research.

**IT flexibility**

Assay Explorer has the capability to define and add custom tables or additional data fields to the default data model. In Assay Explorer 2.2, a set of tables for *in vivo* data is part of the default data model shipped with the product. This enables the storage of *in vivo* data in an intuitive manner, enabling efficient access for searching and reporting.

**A corporate solution**

Different companies—and research groups within a company—have their own workflows and terminology for their discovery process. By accommodating the constant change in assays, collecting information in a central database, integrating external calculations, and offering developmental flexibility, Assay Explorer and its new features offer biologists solutions to the key data management challenges of *in vivo* research.

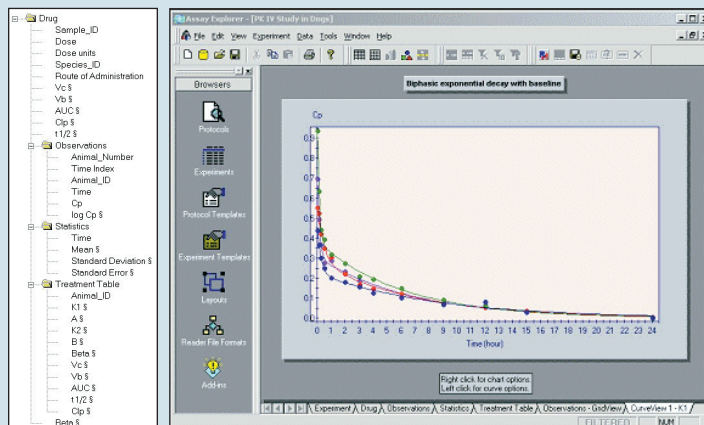


Figure 5 (left) A variable group used for an *in vivo* assay.

Figure 6 (right): This experiment in Assay Explorer reflects the variable group illustrated in Figure 5 with the column headers and tab names.

## Technology infrastructure upgrades tailored to customer needs

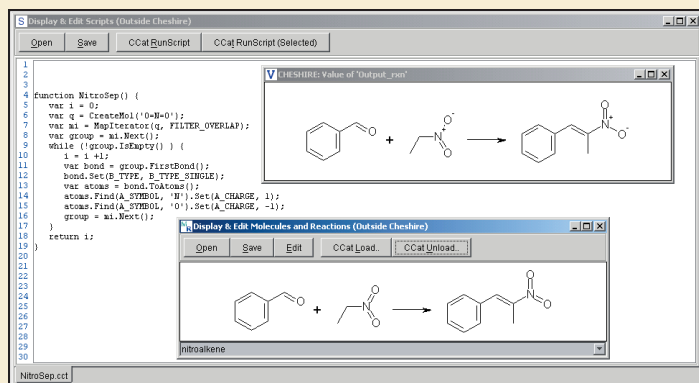
Building on 25 years of innovation in chemical structure representation, the MDL® Discovery Framework group is rolling out a series of exciting product upgrades this spring. Considered together, these product releases signify a new gold standard when it comes to managing chemical data in an open environment and handling the accurate representation of stereochemical information.

### Enhanced stereochemical representation

All of the product upgrades described below incorporate MDL's new, enhanced stereochemical representation. This new system is a major enhancement to chemical representation and meets a long-standing industry need for a relative stereochemical representation that is structure defining, searchable, and capable of differentiating between absolute and relative stereogenic centers within a single chemical structure. The new representation permits different configurations to be stored for each center or group of centers, enabling the chemist to specify more than one relative grouping of stereogenic centers. It does not set arbitrary limits on the number of groups of centers that can be defined, and it is fully searchable, substantially enhancing an organization's ability to manage stereochemical information in databases.

### Improved chemical structure manipulation service

The latest release of MDL® Chemistry Rules Interface, MDL's industry-leading chemical structure manipulation service, provides major extensions to chemical representation and is the first middle-tier domain



MDL Chemistry Rules Interface applies a chemical representation business rule to a reaction prior to registration.

service launched in MDL's next generation, n-tier discovery informatics architecture, MDL® Discovery Framework. MDL Chemistry Rules Interface is currently in use at over 125 sites supporting chemical structure representation and business rules implementation. The Version 3.0 upgrade provides the following high priority enhancements:

- Reaction manipulation, enabling the application of business rules to reactions for reaction registration systems and electronic laboratory notebooks (ELN)
- Improved management of scripts, providing full integration with Cheminformatics Business Rules Manager (CBRM), an Oracle® application for the storage and deployment of scripts
- Enumerators for generic structures and reactions
- Enhanced stereochemical representation

### Coordinated upgrades to server products

Concurrent releases of MDL® ISIS/Host 5.0, MDL® Relational Chemistry Server 5.0, and MDL® Central Library 5.0 will provide increased flexibility in searching and managing chemical structures, reactions, and combinatorial chemistry libraries. The Version 5.0 upgrade, a coordinated release across the MDL® ISIS product line, includes the following enhancements:

- Database size expansion, creating the only production quality systems for in-house use that are tested and certified on databases of up to 20 million structures
- Streamlined database maintenance, removing the need to take databases offline for index updates
- Replication support, allowing organizations to maintain databases at multiple sites using native Oracle® tools
- Oracle9™ support, including both 32-bit and 64-bit Unix versions
- Enhanced stereochemical representation

MDL ISIS/Host is MDL's primary server platform for registering, retrieving, displaying, and analyzing scientific information. MDL Relational Chemistry Server enables the design and deployment of sophisticated systems for managing reaction and molecule structure databases while also integrating other enterprise data in an Oracle environment. MDL Central Library is a server-based system for managing generic structure libraries and accessing reagent databases. ■

## EXPERIMENT MANAGEMENT

## Introducing MDL Assay Explorer 2.2

In response to biologists' requests for enhanced tools to manage *in vivo* research, MDL will release MDL® Assay Explorer, version 2.2 this summer. Featuring flexible layouts, data import from Microsoft Excel, and links to third-party applications for analysis of models, the new version supports the specific challenges researchers face in the *in vivo* research environment.

Assay Explorer 2.2 enables scientists to collect low throughput screening, secondary screening, ADME, PK/PD, toxicity, and *in vivo* data in a centralized data management system. It supports the ability to store histochemistry, histology, fluorescent, and other images, as well as graphs, Microsoft Word documents, and Microsoft Excel spreadsheets as experimental results. (For an overview of *in vivo* data management capabilities in Assay Explorer 2.2, see the **At the Bench** feature on page 12 of this issue.) ■

## A unique offering—CrossFire Beilstein plus MDL's bioactivity, metabolism, and toxicology databases

Comprehensive data available via DiscoveryGate<sup>SM</sup> facilitates lead generation

Lead generation projects in the pharmaceutical industry require interdisciplinary research teams to establish increasingly complex pharmacological activity profiles for hypothetical molecular targets. Researchers must query diverse databases to retrieve compounds that have a pharmacological profile that closely, but not necessarily exactly, fits the target profile, or compounds that have the potential to fit the target profile but need further testing.

DiscoveryGate<sup>SM</sup> from MDL is unique in offering comprehensive, integrated chemistry, pharmacology, metabolism, and toxicology information—all with one login, from a Web browser. The complementary content of these diverse databases can greatly assist today's cross-functional research teams in understanding the mechanisms of biological and pharmacological performance and how to alter chemical structures to achieve improved performance.

For example, researchers can access over eight million organic compounds and nine million preparations in CrossFire Beilstein, extracting key chemical/physical property and other pharmacological data, as well as knowledge reported in scientific journals. Using

MDL<sup>®</sup> Comprehensive Medicinal Chemistry, researchers can assess biochemical properties like drug class, logP, and pKa, while acquiring general knowledge about the medicinal applications of compounds. By pulling up the MDL<sup>®</sup> Drug Data Report, developed by Prous Science, researchers can review current bioactivity findings and the approval status of newly launched or developmental drugs. MDL<sup>®</sup> Metabolite Database and MDL<sup>®</sup> Toxicity Database can assist with targeting viable compounds early in the discovery process by providing critical metabolic and toxicological data. Finally, the National Cancer Institute's Cancer and AIDS databases are both available at no charge to MDL customers.

Crossfire Beilstein—complemented by MDL's focused bioactivity, metabolism, and toxicology databases—provides comprehensive, up-to-date information supporting interdisciplinary research on the physiological and biochemical mechanisms affecting drug actions. And through DiscoveryGate<sup>SM</sup>, researchers are just one login away from this wealth of Web-based discovery information. ■

## PARALLEL REACTIONS

# Mark your calendars!

You can find MDL at the following events over the next few months.

### MDL US USER CONFERENCE

Hilton San Diego Resort, San Diego, CA, May 4-8, 2003

### DATA INTEGRATION AND ANALYSIS WORKSHOPS

London, England, May 12-13

Paris, France, May 15-16

Cologne, Germany, May 19-20

Basel, Switzerland, May 22-23

For more information, contact Uli Heigl at +41-61-486-88-33 (u.heigl@mdl.com).

### TOXICOLOGY INFORMATION ROUNDTABLE

Wilmington, DE, May 7-9, 2003

### INTERNATIONAL BIO EXPO

Tokyo, Japan, May 14-16, 2003

### DRUG DISCOVERY TECHNOLOGY

Boston, MA, August 11-13, 2003, Booth 2204

### AMERICAN CHEMICAL SOCIETY

New York, NY, September 8-10, 2003, Booth 909

### JAPANESE USER GROUP MEETING

Tokyo, Japan, September 15-17, 2003

### SOCIETY FOR BIOMOLECULAR SCREENING

Portland, OR, September 22-24, 2003

For more details, go to [www.mdl.com](http://www.mdl.com).  
Click on **Company Info** and **Events**.

# MDL Web Workshops

**MDL** offers 2-hour, interactive Web Workshops for small groups of up to eight participants. These short, focused sessions will quickly bring you up to speed with the MDL products listed below.

For general information on the Web Workshops, or to register for a scheduled event, contact Veronica Zuniga at [edservices@mdl.com](mailto:edservices@mdl.com) or 1 (800) 955-0051, extension 1326.

To schedule special sessions of any of the workshops listed below (which can also be offered on alternate dates or "closed" to participants at your site alone), or to arrange custom workshops on topics of your own choosing, contact your MDL Sales Representative or Peg Renery at [p.renery@mdl.com](mailto:p.renery@mdl.com) or 1 (800) 955-0051, extension 1377.

For more information on MDL's training programs, click on Education at [www.mdl.com](http://www.mdl.com)

## Web Workshop Topics

### Using MDL® CrossFire Commander 6.0

This workshop introduces the functionality of MDL CrossFire Commander and the contents of the Beilstein and Gmelin databases through search examples. Participants will retrieve substances based on structure and factual input, physical and chemical properties, and reaction or reacting conditions.

### Exploring MDL® Metabolite and MDL® Toxicity Databases

Participants will conduct structure and data searches to find the toxicity and metabolic data of interest. Participants will explore the "hot-link" between the two databases and retrieve related literature references using the MDL® LitLink online service.

### MDL® ISIS for Excel for the Current ISIS User

Participants will retrieve structures and selected data fields into a Microsoft Excel worksheet, where they can format, manipulate, and analyze the data.

### Exploring DiscoveryGate<sup>SM</sup>

This workshop shows the integrated capabilities of MDL's DiscoveryGate, and explores the individual capabilities of its main components: MDL® Draw, MDL® Compound Locator, MDL® Database Browser, MDL® LitLink, and Integrated Major Reference Works<sup>TM</sup>.

### Drawing Structure Queries with MDL® Draw

This workshop addresses the skills required to draw molecule and reaction queries efficiently using MDL® Draw.

### Exploring Integrated Major Reference Works<sup>TM</sup>

Integrated Major Reference Works comprises four electronic reference collections: Elsevier's *Comprehensive Organic Functional Group Transformations*, Springer's *Comprehensive Asymmetric Catalysis*, John Wiley & Sons' *Encyclopedia of Reagents for Organic Synthesis*, and Thieme's *Science of Synthesis*. Participants will conduct text and reaction searches across all four references.

### Creating Reports with MDL® Report Manager

Participants will retrieve structures and data from a database and use it to create a simple PDF report. The instructor will discuss options for creating more complicated reports, as well as creating reports in Word, Excel, and HTML formats.

### Custom Workshop

On request, featuring a topic selected by the customer.

Date	AM SESSION (09:00-11:00 Eastern Time)	PM SESSION (13:00-15:00 Eastern Time)
June 17	Exploring DiscoveryGate <sup>SM</sup>	Exploring DiscoveryGate <sup>SM</sup>
July 8	Using MDL® CrossFire Commander 6.0	Exploring MDL® Metabolite and MDL® Toxicity Databases
Aug. 5	Exploring Integrated Major Reference Works <sup>TM</sup>	Drawing Structure Queries with MDL® Draw
Sept. 9	MDL® ISIS for Excel for the Current ISIS User	Creating Reports with MDL® Report Manager
Oct. 7	Exploring DiscoveryGate <sup>SM</sup>	Exploring DiscoveryGate <sup>SM</sup>
Nov. 4	Exploring MDL® Metabolite and MDL® Toxicity Databases	Using MDL® CrossFire Commander 6.0
Dec. 2	Drawing Structure Queries with MDL® Draw	Exploring Integrated Major Reference Works <sup>TM</sup>
Dec. 16	Creating Reports with MDL® Report Manager	MDL® ISIS for Excel for the Current ISIS User



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