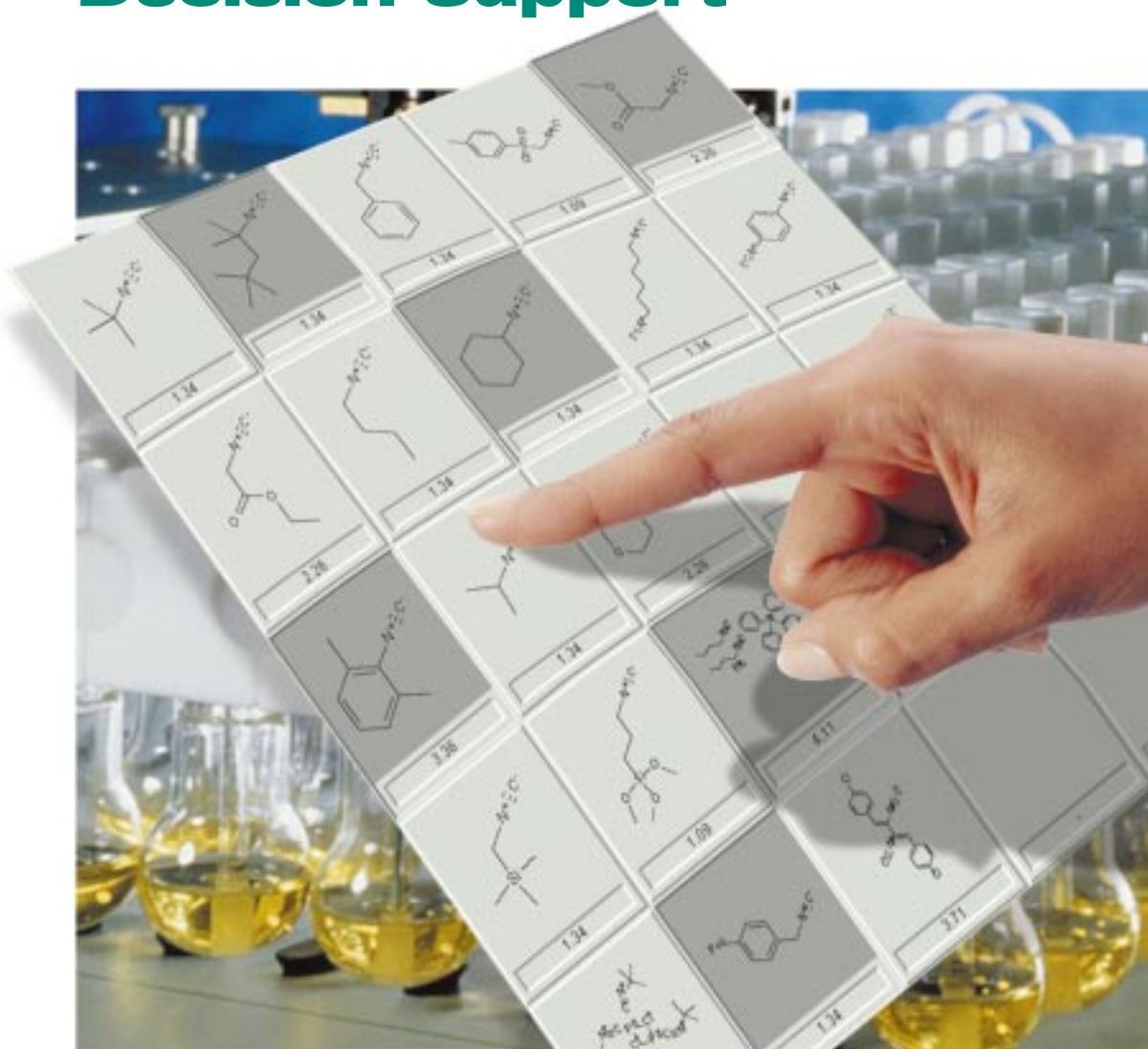



Uniting Science, Logistics, Decision Support



MDL's Reagent SelectorTM



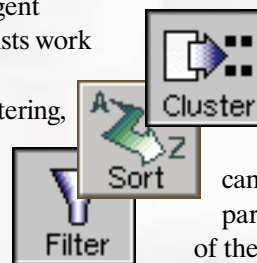
Reagent Selector integrates the scientific and logistical aspects of choosing, collecting, and purchasing reagents, while providing the tools necessary to make critical choices about the diversity, scope, and cost of chemical libraries.

The complex, often cumbersome process of selecting and procuring reagents for medium- and high-throughput synthesis can delay and disrupt the discovery workflow. Reagent selection requires that chemists work through a daunting series of steps—structure searching, filtering, structural classification, etc.—and each step often involves repetitive tasks, independent searches, and combining hit lists to see iterative effects. Once selected, the compounds must be acquired either from in-house inventories or outside suppliers, a sometimes frustrating procedure that can require considerable time and effort. Now MDL Information Systems, Inc. offers Reagent Selector to address these issues, a new system that derives its unique power from the ability to unify and streamline the otherwise laborious and fragmented process.

At the most general level, Reagent Selector integrates the scientific and logistical aspects of choosing, collecting, and purchasing reagents, while providing the tools necessary to make critical choices about the diversity, scope, and cost of chemical libraries. More specifically, the system

- **Unifies the steps of the selection process:** In a single package, the

software provides scientists with an array of integrated tools for creating, filtering, clustering, and manipulating lists of reagents; locating and obtaining reagents from corporate inventories; and “shopping” for compounds from databases of commercial suppliers. Organizations can also add in-house or third-party tools to enhance many of these functions.



- **Consolidates compound sources:** Reagent Selector allows scientists to create a single virtual datamart that combines commercial reagent sources with in-house inventories. The datamart provides an up-to-date, customizable, and consolidated view of available compounds, where they are located on-site, or where they can be purchased.
- **Simplifies the sharing of scientific information:** Reagent Selector makes it easy to share reagent lists and list histories at any stage in the selection process, minimizing the need to transfer information and reducing duplication of effort.
- **Integrates systems throughout an organization:** Since all of the data in Reagent Selector is readable in Oracle, the system easily integrates with inventory-management, purchasing, and other systems.

Scientists operate Reagent Selector in three modes—Selection, Collection, and Shopping—which capture the workflow from beginning to end. Each of these areas complements the others, and users can move back and forth with the click of a mouse. Each has its own browsing window with a display area, buttons, and commands appropriate to the activity at hand. The combined functionality allows researchers to simplify and collapse steps, automate repetitive tasks, and eliminate barriers enterprise wide.

Filtering, Clustering, Selecting from Unified Compound Sources

The reagent selection process is a crucial part of medium- and high-throughput chemistry, ultimately determining the structural diversity and focus of a library, the cost, and the properties of the products produced. The steps often require a series of sophisticated database searching and refining techniques to generate lists of reagents possessing the needed diversity, chemical functionality, and synthetic compatibility. In the selection mode, Reagent Selector offers a variety of features that merge and expedite these tasks, including

- A single, up-to-date view of multiple databases
- A variety of filters for refining lists
- Clustering tools for assessing diversity
- The ability to configure data display and filtering and clustering functions

Data Display and the Reagent Datamart

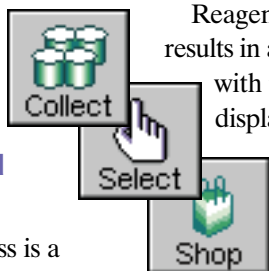
Reagent Selector incorporates the concept of a Concordance database or “reagent datamart”—i.e. a virtual datamart in Oracle tables that combines commercial reagent sources, such as ACD and the Chemical Products Information (CPI) file, with data from in-house inventories. The Concordance

database eliminates the need for separate searches of multiple databases and also consolidates structurally identical hits, displaying a single structure and pointing to the multiple databases where the structure is located. A scientist can draw a substructure in ISIS/Draw, import it into Reagent Selector, and retrieve the relevant structures from all of the databases at once. A server-side daemon regularly updates source information by monitoring the addition or deletion of compounds from in-house inventories.

Reagent Selector presents search results in a large grid for easy inspection, with the search-query substructure displayed on top. Panes on the right side of the selection browser display private and public folders for saving lists and a graphical tree of temporary lists that

corresponds to the history of lists generated during filtering or clustering. Researchers can refine a current list—or any list in the list history—by applying a variety of filters and clustering options and by sorting by data. In Reagent Selector data can also be displayed in conjunction with structures to aid the selection process. Scientists can select reagents simply by clicking on compounds in the grid. Reagent Selector highlights the structures, adds them to the list, and displays the number of reagents selected. Scientists can also share their work by saving lists in the public folders. This eliminates the time and hassle of transferring lists within a team and reduces duplication of effort by scientists working on similar projects.

A program interface provides tools for the administration of the reagent datamart, allowing administrators to easily add or drop source databases, and add new properties and different clustering algorithms.



**A scientist can
draw a substructure
in ISIS/Draw,
import it into
Reagent Selector,
and retrieve the
relevant structures
from all of the
databases at once.**



At Work

Reagent Selector streamlines the task of filtering reagent lists by means of a fluid dialog box interface. Figures 2-6 show some of the filters that allow scientists to select compounds based on functional groups, elements, properties, suppliers, and other information. Here, chemists have opted to exclude isotopes and salts, heavy metals and other elements, and reagents with incompatible groups. The selection includes compounds with a molecular weight between 100 and 300 that are available

from four suppliers at less than \$10 per gram and in packages of 10 grams or less. Figure 8 shows a custom filter dialog box where researchers can use ISIS/Draw to create a filter for functional groups not included in Reagent Selector's standard list.

Figure 1 displays a filtered list of primary amines. The list history box on the lower right tracks the sequential application of each filter. Scientists can click on the numbers to return to an earlier list, making it easy to modify and compare lists. The reagent list pane (upper right) archives

private and public lists for future reference and list sharing. The Compare Lists button at the bottom of the list history box allows users to compare consecutive nodes of reagent lists by activating a Compare Lists dialog (Figure 7). For example, a scientist might first apply a molecular weight filter and then decide to inspect the excluded reagents and return the more interesting compounds to the main list.

F I L T E R I N G

Figure 1

Figure 8

Figure 7

Figure 3

Figure 4

Figure 6

with Reagent

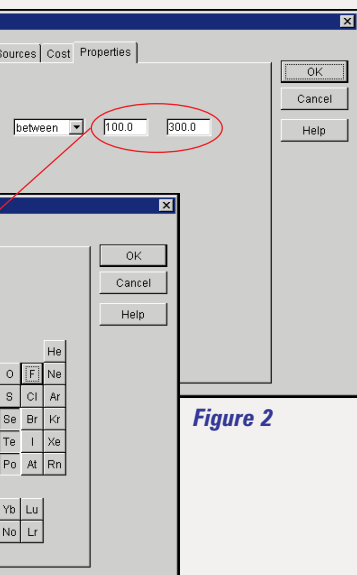


Figure 2

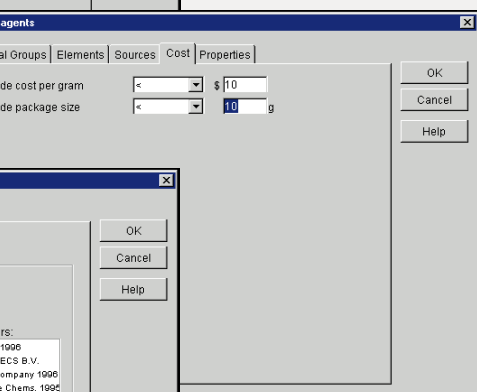
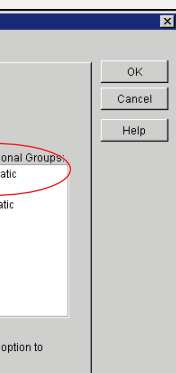


Figure 5

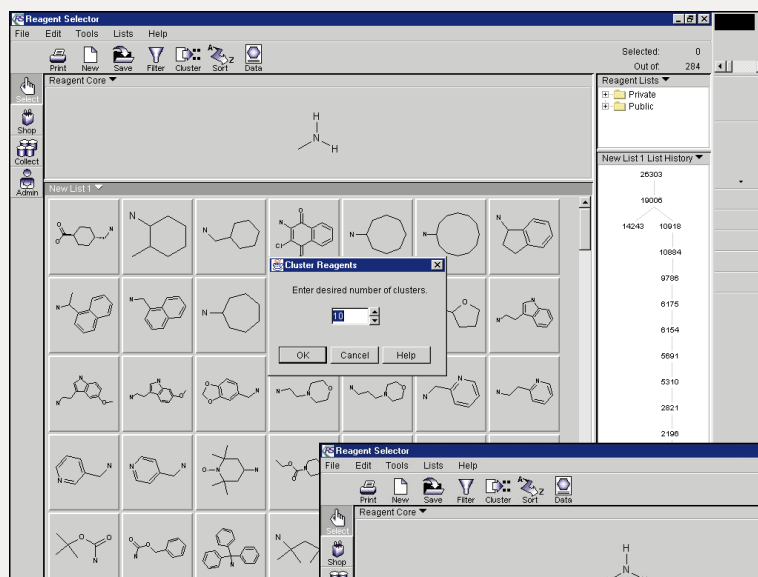


Figure 1

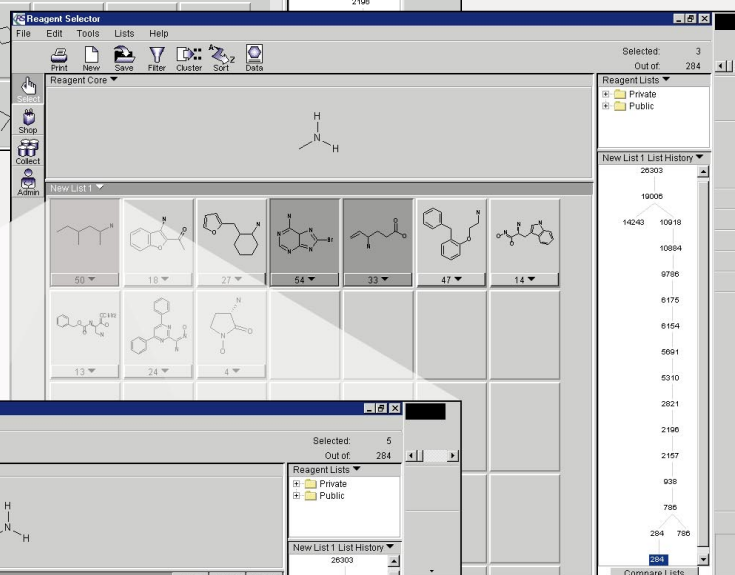


Figure 2

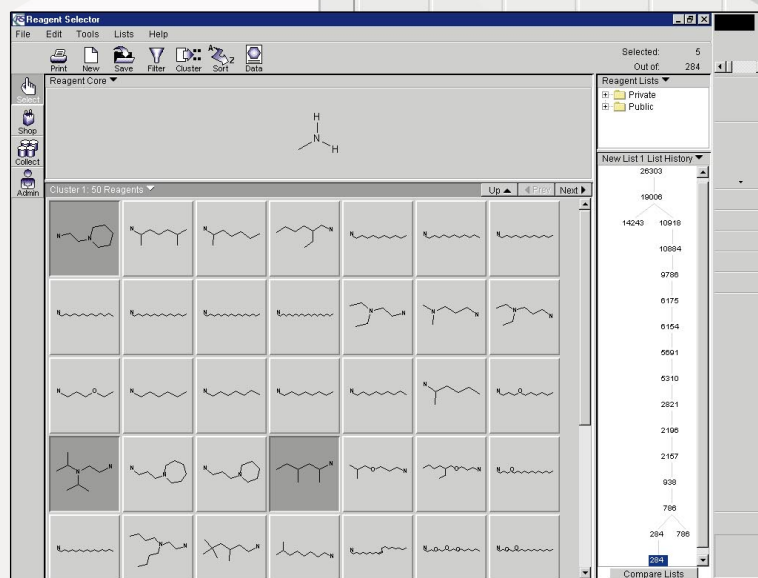


Figure 3

CLUSTERING

Reagent Selector's clustering algorithm and cluster browsing display offer a simple, efficient way to select reagents that meet library criteria. K-MEANS—a non-hierarchical, distance-based clustering algorithm commonly used to process both small and large numbers of molecules—comes standard with Reagent

Selector. The system can also be customized to work with other commercial or proprietary clustering algorithms.

In Figure 1, Reagent Selector prompts researchers to enter the number of clusters desired for a list of 284 primary amines. The system uses ISIS substructure-search keys to group the compounds into 10 clusters

t S e l e c t o r

Once scientists have selected the list of reagents they require, the last step is to locate the samples available in-house and purchase others from commercial suppliers. Reagent Selector assists scientists by allowing them to add other data from the reagent datamart to the grid-based reagent display. Figure 1 shows how data such as price per gram and source (ACD or in-house) can be added to help with final selection.

Clicking the **SHOP** button opens the shopping view shown in Figure 2, which displays detailed supplier information from ACD for compounds in the list. The bottom pane does not contain any suppliers that scientists excluded during the selection process. When users highlight compounds in the top pane, Reagent Selector displays key availability information (supplier, purity, catalog number, package size, and price) below in a sortable table. Clicking **ADD** by any particular item adds that specific product

to the top pane. Once the shopping list table is filled, it can be exported to Microsoft Excel or other applications, such as an approval or purchasing system.

Clicking the **COLLECT** button opens the collection area. Figure 3 shows the location of samples available from in-house inventories. Reagent Selector helps scientists choose samples by displaying the location and real-time availability of reagents. Users can then print the table and use it to mark off reagents as they are obtained.

L O C A T I N G / P U R C H A S I N G

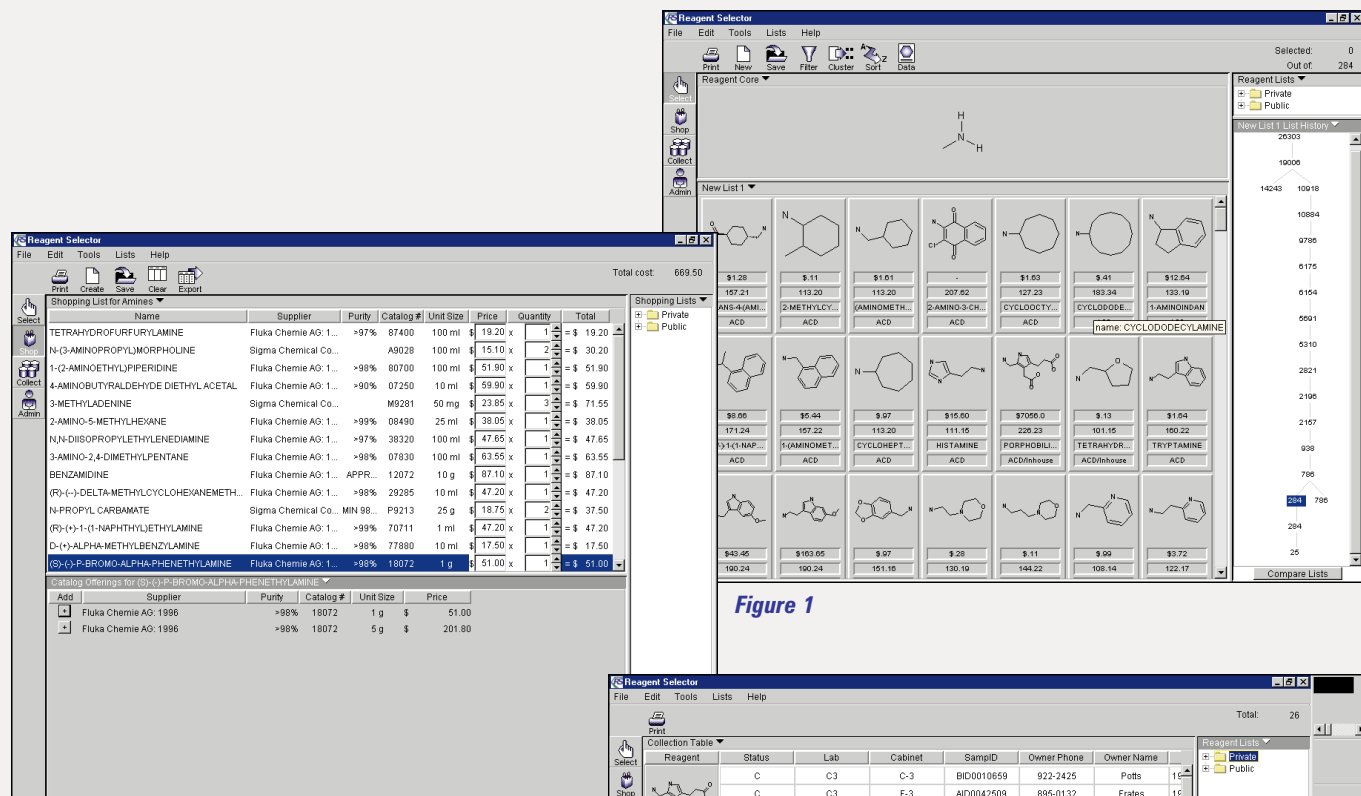


Figure 2

N G

and displays the results in Figure 2. Each bin displays one centroid, the most representative compound of each cluster. The buttons located at the bottom of bins indicate the number of compounds within the clusters. By clicking a button, users can drill down into a specific cluster. Figure 3 shows the compounds in cluster 1, which consists of 50 primary amines containing lipophilic, aliphatic chains.

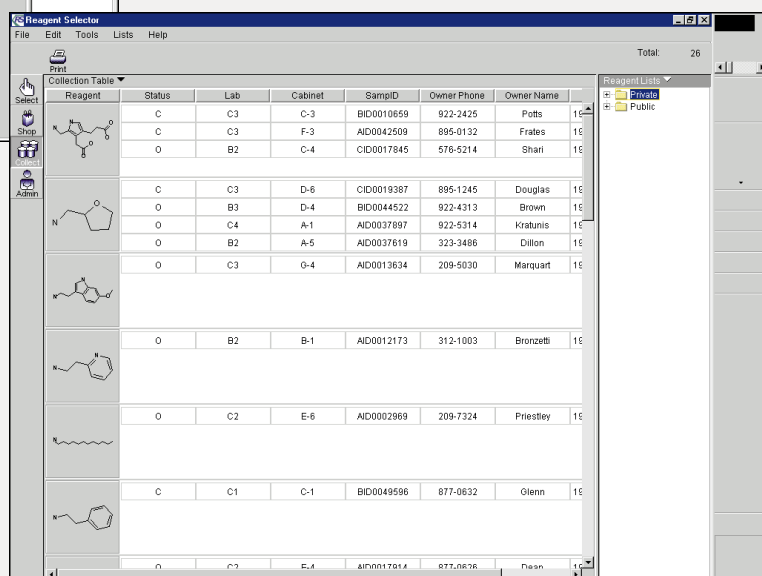


Figure 3

At Work with Reagent Selector

Reagent Selector includes a flexible application interface that helps program administrators create, customize, manage, or drop Concordance databases; modify and remove source databases; set registration filters; add clustering algorithms and property calculators; manage system security and the Reagent Selector Concordance Daemon—and more.

Figure 1 shows the list administration area and contains the functional group filters that come standard with Reagent Selector. Users with list administrator privileges can click on an administration button and create new classes of functional group filters to be used by the entire research team. An administrator can construct a new filter in ISIS/Draw or customize an existing MDL filter by copying it into ISIS/Draw, modifying the filter, and then pasting it into a cell on the grid.

ADMINISTERING

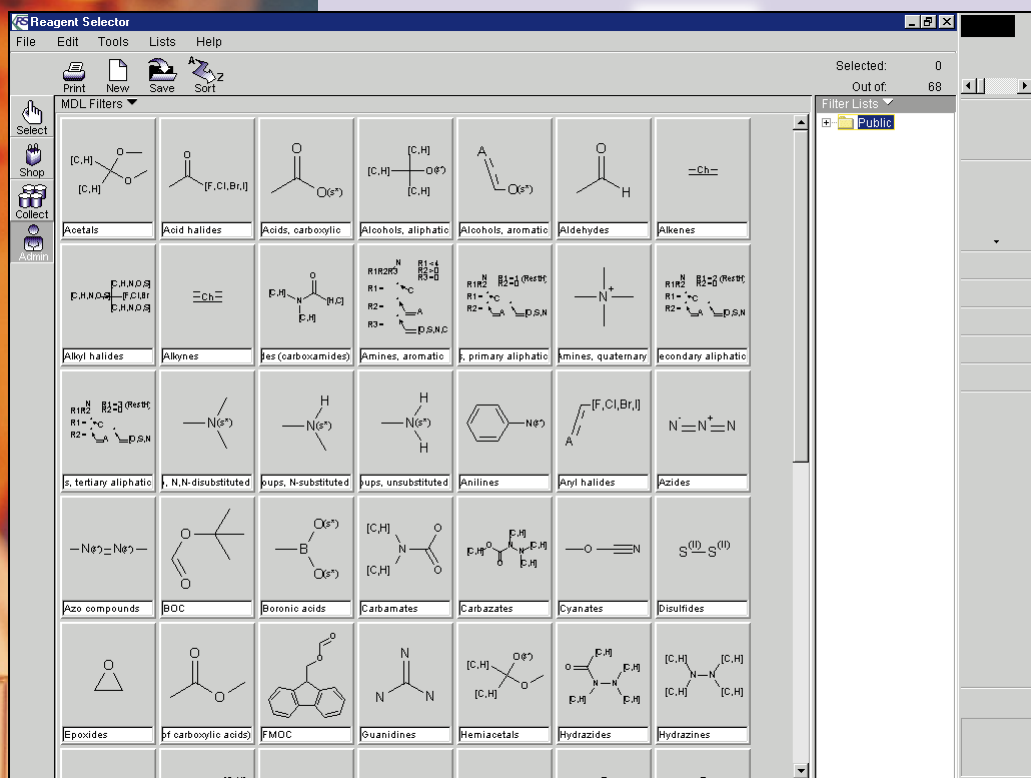


Figure 1

If scientists, for example, are interested in diversity and lead generation, they can choose structures from a variety of different bins.

If they are interested in similarity and lead optimization, they can collect structures by drilling into a single bin.

Standard and Customized Filters

Although Reagent Selector incorporates the structure searching capabilities of ISIS, it also adds powerful filtering functionality for winnowing inappropriate reagents from a list. Filtering lists formerly required many individual searches and expertise with queries and list logic operations. Reagent Selector streamlines this work with a variety of filters that can be applied within an intuitive dialog-box interface.

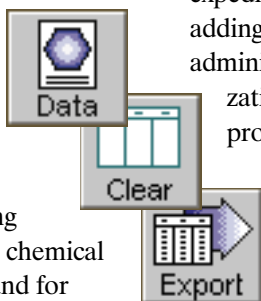
The system allows users to apply filters for eliminating functional groups, elements, chemical suppliers, salts, or isotopes and for refining lists by molecular weight, physico-chemical parameters such as LogP, or cost. Scientists can create their own functional group filters and property filters, in some cases on the fly, and apply them to lists one step at a time or simultaneously. For example, if scientists want to reduce an aldehyde list from thousands to several hundred quickly, they might use the

1. elements and salts filters to exclude heavy metal complexes and salts
2. molecular weight filter to exclude compounds with molecular weight greater than 300
3. supplier filter to remove unwanted suppliers
4. cost filter to exclude compounds that cost more than \$10 a gram

If scientists are dissatisfied with the filtering results—e.g. if the list includes too few reagents or too many of a certain kind—they can use the list history pane to return to any earlier list and modify the criteria. This capability allows researchers to track the filters they've applied and simplifies the intrinsically iterative process of filtering lists.

Companies can also enhance and expedite the process of filtering by adding new properties. The system's administration program allows organizations to install site-specific property calculators—proprietary software or calculators provided by third parties—and use the Concordance Daemon to perform calculations behind the scenes as compounds are registered into the reagent datamart. The daemon will attach the calculations to the structures that end-users access through the normal user interface. By this means, Reagent Selector makes property calculations immediately and transparently available.

Standard sorting techniques allow researchers to rearrange individual compounds within grids based on any compound property in the database. This provides a way to scan a specific list quickly for the most suitable reagents. For example, sorting on the compound source will show which compounds are available in internal inventories and do not have to be purchased.



Clustering with K-MEANS, In-house and Third-Party Algorithms

The clustering feature of Reagent Selector provides a powerful method for grouping similar compounds and maximizing similarity or dissimilarity within a library. The system comes standard with K-MEANS, a non-hierarchical, distance-based clustering algorithm that works with ISIS substructure-search keys. Unlike many clustering algorithms, K-MEANS' effectiveness does not decrease with an increase in the number of the molecules clustered, and provides fast, accurate results with populations as high as a million or more. Companies can substitute in-house or commercial clustering algorithms through an API. Organizations can use their own clustering methods in much the same way they use property calculators, i.e. drop in the results of clustering operations in advance, and make them available to end-users at the application level.

Working with lists of structures, researchers simply choose how many clusters to create, and Reagent Selector will use K-MEANS to collect similar

<chem>O=C1C=CC(=O)C=C1</chem>	<chem>N1CCCCC1</chem>	<chem>O=C1CCCCC1</chem>
\$1.63	\$1.41	\$1.41
127.23	127.23	127.23
AMINO ACID	CYCLOOCTYL	GLUCOSE
ACD	ACD	ACD/inhouse
<chem>N1CCCCC1</chem>	<chem>N1CCCCC1</chem>	<chem>N1CCCCC1</chem>
\$1.13	\$1.13	\$1.13
101.15	101.15	101.15
HISTAMINE	POPHOBILI...	TETRAHYDR...
ACD	ACD/inhouse	ACD/inhouse
<chem>N1CCCCC1</chem>	<chem>N1CCCCC1</chem>	<chem>N1CCCCC1</chem>
\$1.28	\$1.11	\$1.11
130.19	144.22	106.12

reagents into “bins” on the grid. Each bin displays one centroid, the structure most representative of the cluster. A button indicates the number of compounds within the bin. By clicking on the button, users can display all of a cluster’s structures. If scientists, for example, are interested in diversity and lead generation, they can choose structures from a variety of different bins. If they are interested in similarity and lead optimization, they can collect structures by drilling into a single bin. They can also sort the clusters by properties—e.g., cost, supplier, etc.—just as they do with any other list.

Obtaining Reagents from Internal or Commercial Sources

Obtaining compounds from in-house or outside sources can be almost as time-consuming as selecting reagents. Through the combined functionality of the Reagent Selector’s Concordance database—its Oracle-based datamart—and ISIS/HOST, the system integrates with existing inventory-management and purchasing systems.

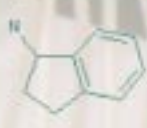

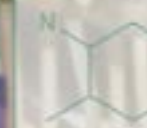

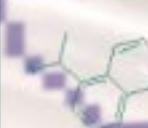




Up-to-date Access to In-house Inventories

When obtaining reagents, scientists must first determine the compounds’ real-time availability in internal inventories. This is often easier said than done with traditional tracking systems. Scientists might find reagents on an inventory list, go to the stockroom, and discover that the last of the samples have already been checked out. They then have to go back to their supplier databases, find and order their compounds.

The challenge for MDL was to create a unified view of all in-house and commercial databases in the reagent datamart and at the same time keep the datamart up-to-date. Reagent Selector achieves this by storing structures and IDs in Oracle tables that can be transparently accessed through ISIS/HOST. This architecture underlies the system’s ability to avoid the display of duplicate structures while pointing to structure sources in multiple databases. Hence, scientists can locate a compound in a particular database and update the database. Reagent Selector’s server-side daemon automatically checks internal inventory databases on a regular basis and updates the datamart accordingly.

Researchers can move from the selection mode to the collection or shopping areas with the click of a button. The Collect view displays the saved lists folders and a reagent table, which can be customized with columns that reflect the data fields of in-house databases. The table might indicate where reagents are located, their real-time availability, whether a reagent bottle has been opened, and other relevant information. If the same compounds are available in different inventories, the reagent table includes this information for each sample. Researchers can print the table and use it to collect samples from different stockrooms.

As scientists add compounds, Reagent Selector will calculate the total cost of the selected items. Researchers can then print the list or export it to an ASCII file that can be read by Microsoft Excel or other programs used to create purchasing orders.

 \$12.64 133.19 1-AMINOINDAN ACD	 \$1.00 133.20 TRANS-AMIN ACD	 \$1.11 133.20 3-METHYLCY ACD
 \$1.66 160.22 1-AMINOINDAN ACD	 \$0.66 171.24 TRANS-AMIN ACD	 \$0.44 177.22 3-METHYLCY ACD
 \$0.72 122.17 1-AMINOINDAN ACD	 \$0.66 100.24 TRANS-AMIN ACD	 \$0.44 100.24 3-METHYLCY ACD

Shopping and Ordering with ACD

When scientists are unable to obtain compounds in-house, they can click on the Shop button to display ACD's detailed supplier information for reagents on a given list. The shopping view contains two panes. The bottom pane lists suppliers, ordering information, and key data about purity, catalog number, package size, and cost. Users can sort the information by any of these categories.

Clicking on an entry will move the data to the top pane, which functions as a shopping cart. As scientists add compounds, Reagent Selector will calculate the total cost of the selected items. Researchers can then print the list or export it to an ASCII file that can be read by Microsoft Excel or other programs used to create purchasing orders. Since this information is stored in Oracle tables, Reagent Selector can also be easily integrated with inventory-management and purchasing systems.



Transforming the Process

Reagent selection is a key step in medium- and high-throughput chemistry and will be effective and efficient to the extent that it unites science, logistics, decision support, and communication within a research team. Reagent Selector addresses all of these aspects of the process, merging tasks and eliminating bottlenecks. At MDL, we believe that there is no solution on the market today with a comparable capacity to boost productivity and free chemists for creative science. If you'd like to see it in action, just give us a call.

System Requirements

Client

- Intel or Intel-compatible PC running at greater than 133 MHz (>166 MHz recommended) with Microsoft Windows 95, Windows NT 4.x, Japanese Microsoft Windows 95, or Japanese Windows NT 4.x
- Apple Power Macintosh
- ISIS/Desktop 2.1.4 or greater

Server

- Digital Alpha computer with OpenVMS 7.1
- SGI computer with IRIX 6.2, 6.3, 6.4
- IBM RISC System/6000 computer with AIX 4.2 or 4.3
- ISIS/Host 3.1
- MDL Available Chemicals Directory database
- MDL Chemical Products Information File database
- Oracle Database Management System

Please contact your local MDL sales representative for specific requirements.

About MDL

MDL Information Systems, Inc. is the recognized leader in discovery informatics for the life science and chemical industries. Our software, content, and services provide the enterprise framework for identifying successful new products. A wholly owned subsidiary of Elsevier Science, MDL has offices worldwide with headquarters in San Leandro, California.

MDL[®]
Information Systems, Inc.

U.S.A.

World Headquarters & Western Sales

14600 Catalina Street
San Leandro, CA 94577
TEL: (510) 895-1313
FAX: (510) 483-4738
<http://www.mdli.com>

Eastern Sales

14 Walsh Drive
Parsippany, NJ 07054
TEL: (973) 299-3991
(800) 401-4321
FAX: (973) 299-3994

Midwest Sales

3 Westbrook Corporate Center
Suite 520
Westchester, IL 60154
TEL: (708) 409-8300
FAX: (708) 409-8305

Europe

Headquarters

MDL Information Systems AG
Gewerbestrasse 12
CH-4123 Allschwil 2
Switzerland
TEL: +41 61-486-88-88
FAX: +41 61-486-88-89

Cologne Office

TEL: +49 221-16025-255
FAX: +49 221-16025-68

Authorized Agent Scandinavia

Oslo Office

TEL: +47-22-44575-6
FAX: +47-22-43416-6

Paris Office

TEL: +33 1-45 36 80 00
FAX: +33 1-45 36 80 01

United Kingdom

Headquarters

MDL Information Systems (UK) Limited
Ground Floor, Building 4
Archipelago
Lyon Way
Camberley
Surrey GU16 5ER
England
TEL: 44 (0)1276 701500
FAX: 44 (0)1276 701501

Japan

MDL Information Systems Japan K.K.
Kojimachi M Bldg., 3F
3-12-12 Kojimachi
Chiyoda-ku
Tokyo 102
Japan
TEL: +81-3-3230-2641
FAX: +81-3-3230-2761

MDL is a registered trademark and Available Chemicals Directory, ISIS, and Reagent Selector are trademarks of MDL Information Systems, Inc. Microsoft is a registered trademark of the Microsoft Corporation. Oracle is a registered trademark of the Oracle Corporation. All other product names are trademarks or registered trademarks of their respective holders.

Copyright © 1998 by MDL Information Systems, Inc. All rights reserved. RS/12-98/10K